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ABSTRACT BOOK

# ORAL PRESENTATIONS

# SYMPOSIUM 1

## Attenuating Disease Progression

Fr-OP 001  
THE CIRCADIAN REGULATION OF GLOMERULAR FUNCTION

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**Aims/Purpose:** Peripheral tissues demonstrate circadian rhythmicity and dysfunction of core clock components has been implicated in the pathogenesis of diseases that are characterized by abnormal extracellular matrix, such as fibrosis (too much disorganized matrix) and tissue breakdown (too little matrix). Recent experimental evidence has revealed that cell-matrix interactions and the biomechanical properties of extracellular matrix have key roles in regulating peripheral circadian clocks. Structural changes in the glomerular basement membrane, a specialised extracellular matrix which crucially controls glomerular filtration, is the hallmark of glomerular disease. Both glomerular filtration and protein excretion display robust circadian oscillation, although the role of the circadian clock in the regulation of glomerular function is not well understood. We aimed to elucidate the role of the circadian clock in the regulation of glomerular function.

**Methods:** Circadian rhythmicity of gene expression was examined using real-time bioluminescence recordings from circadian reporter mice. To confirm the presence of intra-glomerular clock machinery, we employed mouse models expressing knock-in fluorescent fusion of endogenous BMAL1 and PER2, core components of the molecular clock. Global patterns of glomerular and podocyte circadian gene expression were defined using transcriptional profiling of glomeruli isolated from wildtype mice, and primary podocytes in culture, over a circadian time-course.

**Results:** We identified autonomous circadian oscillation in both glomeruli and podocytes. Quantitative live imaging revealed the circadian expression of endogenous BMAL1 and PER2, confirming their high molecular abundance in glomeruli and podocytes. Transcriptional profiling identified 375 glomerular rhythmic genes under circadian control with genes and pathways implicated in the regulation of the extracellular matrix. Furthermore, cell autonomous rhythmic podocyte genes were identified which are crucial to the integrity of the glomerular basement membrane.

**Conclusion:** We provide evidence for intra-glomerular clock machinery and have identified the first glomerular circadian transcriptome, giving insight into the regulation of extracellular matrix. Establishing a temporally resolved kidney matrisome may provide a useful tool for studying the two-way interactions between the extracellular matrix and the intracellular time-keeping mechanisms in this critical niche tissue. These results provide a firm basis for future studies that aim to elucidate the functional implication and therapeutic potential of chronotherapy in glomerular health and disease.

Fr-OP 002

THE ROLE OF ANTIMICROBIAL POLYPEPTIDES FOR THE PREDICTING OF URINARY TRACT INFECTION: UTILISE STUDY

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**Aims/Purpose:** Cathelicidin, Defensin- $\alpha$ , Defensin- $\beta$ , Hecpudin, Lactoferrin, RNAase7, secretory leukocyte protease inhibitor (SLPI) are antimicrobial polypeptides (AMPs). As a part of “Urinary Tract Infection and Levels of heat shock protein 70 In children as a Sensitive marker for Excluding other infections” (UTILISE) study, we evaluated usefulness of these AMPs for predicting urinary tract infection (UTI) and differentiating from other infections, asymptomatic bacteriuria, and contamination.

**Methods:** Totally 520 children between ages 0–18 years old with UTI, asymptomatic bacteriuria, contamination, non-UTI infections and healthy controls were participated from 37 pediatric nephrology centers. In all groups, pre-treatment blood and urine samples were obtained before the initiation of antibiotics at the admission. In the UTI group, also post-treatment samples were collected after treatment. Serum and urine level of AMPs were measured by enzyme-linked immunosorbent assay (ELISA) technique.

**Results:** In comparison of urine and serum levels of AMPs between the groups, urine Cathelicidin (uCat) and urine Defensin- $\beta$  (uDef $\beta$ ) were significantly higher in the UTI group compared to all other groups (both  $p < 0.0001$ ). Post-treatment uCat and uDef $\beta$  levels in the UTI group were significantly lower than pre-treatment values (both  $p < 0.0001$ ). ROC analysis revealed an optimal cut-off value for uCat to predict UTI is 2 pg/ml. The sensitivity and specificity of uCat predict UTI were 79% and 66%; respectively (AUC = 0.807). The optimal cut-off value for uDef $\beta$  to predict UTI is 0.7 ng/ml. The sensitivity and specificity of uDef $\beta$  to predict UTI were 81% and 73%; respectively (AUC = 0.812). uCat level was significantly higher in pyelonephritis than in cystitis ( $p < 0.0001$ ). Using a cut-off 2.42 pg/mL to distinguish pyelonephritis from cystitis, the sensitivity and specificity of uCathelicidin were 72% and 66%; respectively (AUC = 0.746). uDef $\beta$  level was significantly higher in pyelonephritis than in cystitis ( $p < 0.0001$ ). Using a cut-off 1.26 ng/mL to distinguish pyelonephritis from cystitis, the sensitivity and specificity of uDefensin- $\beta$  were 73% and 53%; respectively (AUC = 0.742).

**Conclusion:** uCat and uDef $\beta$  are increased in patients with UTI. They might be promising biomarkers for predicting UTI and differentiating pyelonephritis from cystitis. They can be used conjunction with urinalysis and other biomarkers in diagnostic panel for UTI.

# SYMPOSIUM 2

# Nephrology in the NICU

FR-OP 003

FIRST POSTNATAL SCREENING STUDY TO DETECT PRIMARY HYPEROXALURIA TYPES 1 AND 3

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**Aims/Purpose:** The three primary hyperoxalurias (PH) are ultra-rare diseases of the glyoxylate metabolism, at which three specific enzyme defects induce severe endogenous overproduction of oxalate, and thus its massively elevated urinary excretion. Clinical hallmarks are recurrent urolithiasis, progressive nephrocalcinosis and eventually end stage kidney failure. Early diagnosis should be mandatory to achieve better outcome, which is even more important now, as a new treatment option is available for type 1 PH.

**Methods:** After parents have signed informed consents, we include all routine newborn screening cards send to our screening lab for testing the presence of the most common mutations of the AGXT (c.508G > A, PH 1) and the HOGA1 (c.700+5G > T, PH 3) genes in Europe, respectively. We expect to test > 150.000 samples. If patients are homozygous, treatment will be started promptly, and outcome will be compared to historical controls from the German PH registry. If heterozygous mutations are found, 5 spot urines are collected to exclude hyperoxaluria. In those newborns with hyperoxaluria, further genetic analysis is done and, if being positive, they start treatment promptly.

**Results:** As of March 9th 2023, a total of 62235 newborns have been screened. So far, 486 heterozygous cases have been found. Of these, 236 newborns had a heterozygous HOGA1 (PH 3) and 244 newborns had a heterozygous AGXT (PH 1) mutation. Two newborns were heterozygous for both HOGA1 and AGXT, one infant each had a cystinosis mutation and either an AGXT or HOGA1 mutation. In addition, we found a different mutation in four patients than the one primarily pursued. We diagnosed one patient with PH 3, with elevated oxalate, but also significantly elevated hydroxy- (HOG), as well as dihydroxy-oxo-glutarate (DHG) and 4 hydroxy-glutamate. The clinical examination showed stones in both kidneys. The diagnosis was genetically confirmed (c.700+5G > T (father), second Mutation c134C > G (Pro45Arg) (mother)). In addition, we diagnosed PH 1 in a father of a screened child (homozygous c.508G > A). Analyzing the urine samples of all heterozygous newborns we recognized that molar oxalate/creatinine ratios are normal in > 90 % of all analysis. We did not find elevated glycolate levels in urine. However, the heterozygous PH3 newborns excreted tiny amounts (1-15 µmol/d) of 4OH-ketoglutarate in most of the cases. Rarely DHG or HOG was found.

**Conclusion:** We can hence conclude that this huge newborn screening program is answering multiple questions. First we can better calculate the true prevalence of two PH types in Germany. Secondly, we can promptly treat patients and prevent disastrous outcome. Lastly, the batches of urine analyzed are providing best normative molar creatinine ratios not only for oxalate and related metabolites, but also for other lithogenic substances during the newborn period.

FR-OP 004

## QTc PROLONGATION IS DIRECTLY CORRELATED TO (CREATININE BASED) ESTIMATED GLOMERULAR FILTRATION RATE

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**Background:** QTc prolongation, prematurity, and chronic kidney disease (CKD) are independent risk factors for cardiovascular disease in adulthood. The correlation between heart conduction and kidney function is poorly investigated and understood. Moreover, there are no pediatric studies investigating these two risk factors in relation to each other.

**Methods:** Twelve lead electrocardiograms (ECG) at rest, collected in the PREMATurity as predictor of children's Cardiovascular and renal Health (PREMATCH) (1) study in former ELBW cases and term controls during pre-adolescence (8-14 years) were analyzed on estimated glomerular filtration rate (eGFR, creatinine) and corrected QT time (QTc, Bazett) (2). Other data included anthropometrics, blood pressure (BP) and biochemistry (electrolytes in serum and urine). ECG findings were compared between groups (Mann-Whitney), and associations with clinical and biochemical findings were explored (Spearman, Wald). Associations between QTc and eGFR were explored (Pearson). Standardized residual variances were calculated based on linear regression analyses of eGFR and QTc based on risk factors and confounders.

**Results:** QTc was similar between 93 ELBW cases and 87 controls [409 (range 360-465) versus 409 (337-460) ms]. Uncorrected eGFR and QTc were only correlating for controls, not for cases ( $r = 0.440$ ,  $p < 0.001$  vs.  $r = 0.174$ ,  $p = 0.19$ , respectively). Regression coefficients ( $\alpha = 0.10$ ) showed that eGFR was associated with systolic BP and BMI for cases, and with female sex and urinary sodium excretion for controls. Moreover, QTc was associated with potassium for cases and with potassium and phosphate for controls. After correction for these factors, a strong correlation between eGFR and QTc remains with a  $r = 0.818$  and  $r = 0.794$  for cases and controls respectively (both  $p < 0.001$ ).

**Conclusions:** There was a strong and direct correlation between higher eGFR and prolonged QTc in children both born preterm as well as controls. How to integrate these findings in risk factor assessment and screening practices needs to be further explored.



# SYMPOSIUM 3

## Dialysis

Fr-OP 005

CHILDREN ON PERITONEAL DIALYSIS WITH DIFFUSE PODOPLANIN EXPRESSION SUFFER FROM SEVERE PERITONEAL MEMBRANE AND VESSEL TRANSFORMATION

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**Aims/Purpose:** Encapsulating peritoneal sclerosis (EPS) in adult peritoneal dialysis (PD) patients is associated with diffuse podoplanin staining (DPS), its prevalence and prognostic value in children on PD is unknown.

**Methods:** Digital histomorphometry and image analyses were applied to peritoneal tissues followed by hierarchical clustering of histological markers related to peritoneal and vascular transformation. High-content multiplex imaging was established by imaging mass cytometry (IMC; Hyperion Imaging System<sup>®</sup>). Deep learning-based segmentation and single-cell analysis was conducted to characterize different peritoneal cell types with positive podoplanin signals.

**Results:** In healthy peritoneum, podoplanin expression was confined to mesothelial cells and lymphatic endothelium. Podoplanin positivity beyond these structures was present in 15/71 children on PD with low glucose degradation product (GDP) containing fluids (21%) and 14/30 children on high GDP PD (46%;  $p = 0.006$  vs low GDP PD). All DPS positive children were devoid of any clinical, radiological or histological feature of EPS. In children on low-GDP PD, DPS positive patients were younger, had higher dialytic glucose exposure and exhibited more arteriolar lumen narrowing. PD duration [median 20 (14.5, 48) months] and peritonitis incidence were similar to non-DPS patients. Dialytic glucose exposure, PD duration, peritoneal epithelial-to-mesenchymal (EMT) transformed cell counts, and lower body surface area (BSA) were independently associated with DPS. DPS and lower mesothelial surface coverage were independently associated with arteriolar lumen narrowing. In subgroups matched for age [median 3 (IQR 2, 12) yr], BSA, PD duration and dialytic glucose exposure, DPS children had higher leucocytes (CD45+) and macrophages (CD68+) counts and higher abundance of bacterial fragments (LPS) and cell adhesion molecule CD44. DPS intensity grade was higher with history of bacterial or fungal peritonitis (50%). Hierarchical clustering demonstrated highest similarity of DPS positive areas with CD68 positive areas. In IMC analysis, highest podoplanin signals were derived from M2 classified macrophages (CD68+CD163+) and fibroblastic cells ( $\alpha$ SMA positive/non-endothelial/non-macrophage ( $\alpha$ SMA+PROX1-CD31-CD68-CD163-)). Signals derived from M1 classified macrophages (CD68+CD163-) were lowest.

**Conclusion:** DPS is prevalent in children on PD, but not associated with any clinical or histological signs of EPS. Independent DPS risk factors are low BSA, high dialytic glucose exposure, history of peritonitis, peritoneal inflammatory and EMT cell invasion. DPS is associated with obliterating peritoneal vasculopathy. Our findings suggest a key role of M2 macrophages for peritoneal podoplanin accumulation in children with DPS and thus in severe peritoneal transformation including obliterating vasculopathy.

Fr-OP 006

A BIOENGINEERING APPROACH TO STUDY AND OPTIMISE THE FLUID DYNAMICS IN CATHETERS FOR PAEDIATRIC DIALYSIS

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**Aims/Purpose:** Central venous lines (CVLs) for haemodialysis (HD) have frequent complications including poor blood flow, thrombosis and infections, necessitating replacement in nearly 45% of children on HD. This high complication rate may be due to poor CVL design. Using a bioengineering approach, we aim to provide a fluid dynamics characterization of different CVL models commonly used in children to establish an association between CVL design and clinical complications, and to improve CVL performance by optimizing their design.

**Methods:** Computational fluid dynamics (CFD) using modelling and simulations is a powerful engineering tool that use computers to study complex systems, applying mathematics, physics and computer science. Four models of CVLs of varying designs and sizes (6.5Fr, 8Fr, 10Fr and 14Fr) were scanned by microCT to reconstruct computational models. CFD analyses were set up to simulate the CVLs' performance under both ideal and realistic models of superior vena cava. A variety of flow rates, routinely used in clinical practice, were applied to study the whole range of working conditions. Haemodynamic features such as high shear stresses and large areas of stagnation, were analysed. CFD findings were compared to clinical outcomes (n = 26 patients with 57 lines) and to the blood clots distribution of CVLs removed from patients (n = 8). Fluid dynamics characteristics of the CVLs studied were used to set up a preliminary design optimisation process.

**Results:** In all the simulated CVLs, the arterial lumens showed the highest stagnation and recirculation areas. The role of arterial tip configuration was negligible for the blood flows and the proximal side holes played a major role for blood aspiration being also subject to the highest levels of shear stress, regardless of the design. In all the anatomical models, blood velocity increased after catheter insertion (Figure 1a) together with wall shear stresses. CFD results were in accordance with the clinical data which showed a higher recurrence rate of thrombosis for the 8Fr and 10Fr CVLs. Also, microCT of the CVLs removed due to complications confirmed presence of thrombosis at the catheter tips. Results suggest that shear stress is the parameter most strongly related to clinical complications. Preliminarily optimised designs showed a better haemodynamic performance, reducing stagnation areas (Figure 1b).

**Conclusion:** In this project, we carried out the fluid dynamics characterisation of commercially available CVLs to explain the associated clinical outcomes. Identification of potential design-related complications in CVLs has allowed to set up the optimisation process which will lead to new CVL designs with improved blood flow distribution and minimal damage to blood cells.

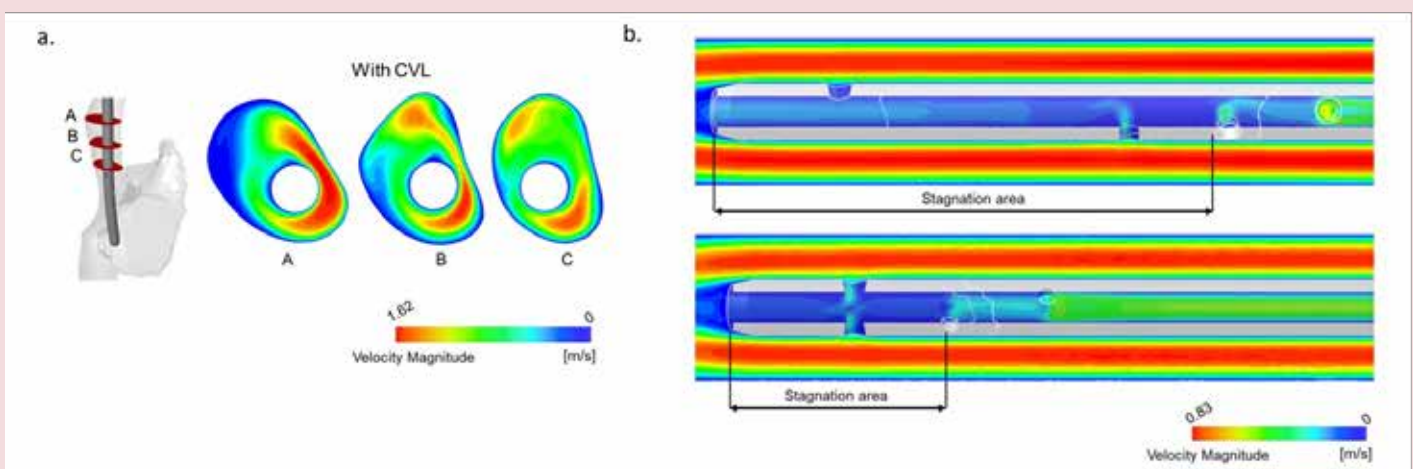


Figure 1: Velocity magnitude contours: a) inside the vein after CVL insertion; b) inside a 6.5Fr model before and after optimisation to reduce stagnation areas.

# PLENARY LECTURE 3 AND BEST ABSTRACT PRESENTATIONS

Fr-OP 007

ADULT OUTCOMES OF CHILDHOOD-ONSET IDIOPATHIC NEPHROTIC SYNDROME (INS)

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**Aims/Purpose:** While childhood-onset INS is generally believed to largely resolve upon reaching adult age, some patients have persistent disease activity and are transferred to adult nephrology centers for further care. We were interested in studying the disease activity, potential comorbidities and long-term kidney outcomes in these patients.

**Methods:** In a collaboration of the ERKNet consortium and the ESPN-Glomerular disease-group, 14 European centres participated in a survey on adult patients (= 18 y) with childhood-onset INS.

**Results:** Data from 227 adult patients with childhood-onset INS were collected. Disease onset was within the first 5 years of life in 53%, at 5–9 years in 22%, and at 10–17 years in 25% of patients. Median (interquartile) observation time was 16 (11 – 20) years and median age at last observation was 21 (19 – 24) years. SSNS was diagnosed in 61% and SRNS in 39% of patients. Among the SRNS patients, 24% showed sensitivity to second-line immunosuppression. Genetic forms of SRNS were excluded from the study. A histopathological diagnosis was established in 57% of patients during childhood (50% MCD, 36% FSGS, 14% other). 3% received a first biopsy and 11% a second biopsy at adult age. In 95% of these the diagnosis made at disease onset was confirmed in adulthood. During childhood, 77% of patients were treated with a steroid-sparing agent (CNI 71%, MMF 72%, rituximab 24%). In adulthood, 11% of patients were treated with steroids, 34% with steroid-sparing agents (CNI 12%, MMF 22%, rituximab 9%), and the remaining 55% received no treatment. 23% of the patients showed a relapse of NS during the last year of observation. At last visit, 96% of patients were managed conservatively (85% CKD1, 11% CKD 2, 4% CKD 3–4) while 6 patients (2 SSNS, 4 SRNS) had attained ESKD. 86% were normotensive without treatment, 14% had controlled and 4% uncontrolled hypertension. RAAS therapy was applied in 18% of patients. Overweight and obesity were present in 22% and 9% of the population, respectively. Osteopenia was reported in 21% and cataracts in 6% of patients. Depression was reported in 14 patients (6%; thereof 9 were treated with antidepressants) and another 9 patients suffered from other mental conditions. Major cardiovascular events, diabetes, severe bacterial infections, and malignancies were reported in 1–2% each. 90% of the patients (> 20 years) had completed their education and 39% had at least one academic degree. 4% had at least one child.

**Conclusion:** While 45% of young adults with childhood-onset INS under continued medical care require extended immunosuppressive medication, long-term kidney survival appears to be excellent with less than 3% progressing to ESKD. While persistent obesity is not a major health issue (BMI distribution does not differ to the normal population), osteopenia, cataract and neuropsychological disorders appear to be frequent late outcomes of childhood-onset INS.

Fr-30P 008

PHASE 3 TRIAL OF TOLVAPTAN IN PEDIATRIC AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD): TWO YEARS OF DATA FROM AN OPEN-LABEL EXTENSION

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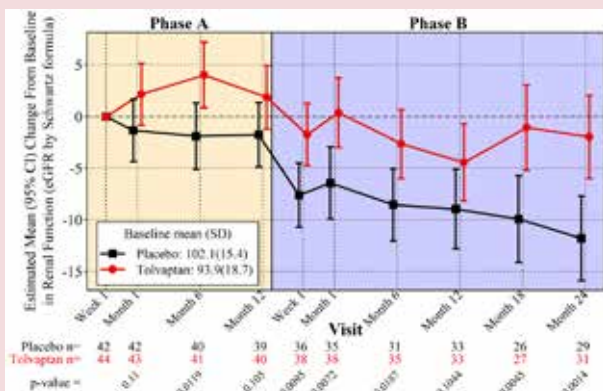
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**Aims/Purpose:** The 1-year, randomized, placebo-controlled phase (Phase A) of a 2-part trial of tolvaptan in children/adolescents with ADPKD (NCT02964273) demonstrated acceptable safety/tolerability and evidence of vasopressin V2 receptor antagonism. A 2-year, open-label extension (Phase B) evaluated longer-term outcomes.

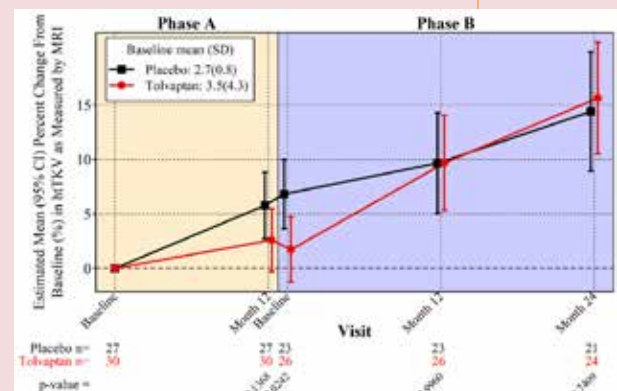
**Methods:** Phase A entry criteria were age 4-17 years, ADPKD, eGFR  $\geq$  60 mL/min/1.73m<sup>2</sup>, weight  $\geq$  20 kg. Participants who received tolvaptan or placebo in Phase A could enter Phase B to receive tolvaptan for 24 months. Dosing was by body weight and tolerability. eGFR and height-adjusted total kidney volume (htTKV) were calculated using the mixed model repeated measures method with model terms treatment, visit, treatment by visit, and baseline by visit interaction. To exclude the acute hemodynamic effect of tolvaptan, change in eGFR after week 1 of treatment is shown.

**Results:** Of 83 Phase A completers, 81 enrolled in Phase B; 33/42 (78.6%) prior tolvaptan and 30/39 (76.9%) prior placebo participants completed Phase B on tolvaptan. Average daily tolvaptan dose was 41.1 mg in the prior tolvaptan group (mean [SD] age 14.3 [3.2] years) and 38.0 mg in the prior placebo group (13.9 [2.9] years). In Phase A, eGFR increased in the tolvaptan group and decreased in the placebo group (significant difference at Month 6), with significant benefit maintained at most assessment visits in Phase B for prior tolvaptan versus prior placebo (Figure 1A). Growth in htTKV on MRI (participants ages 12-17) was slowest during the first year of tolvaptan treatment, i.e., during Phase A for those randomized to tolvaptan and Phase B year 1 for the prior placebo group (Figure 1B), with growth rates higher thereafter, although sample sizes did not permit meaningful statistical comparison of the changes. Common adverse events in Phase B ( $>$  15% participants overall; prior tolvaptan and prior placebo, respectively) were headache (36%, 44%), nasopharyngitis (26%, 33%), rhinitis (26%, 10%), oropharyngeal pain (21%, 18%), pyrexia (19%, 18%), cough (17%, 21%), abdominal pain (12%, 31%), polyuria (5%, 33%). Eleven Phase B participants overall experienced elevated liver enzymes by investigator report (no prespecified enzyme levels were required to report an event): 6 recovered without intervention, treatment was interrupted in 4, and in 1 tolvaptan was withdrawn for a reason other than the hepatic event. No participant met predefined laboratory criteria for serious drug-induced liver injury in either phase.

**Conclusion:** Pediatric patients who received tolvaptan during a randomized trial exhibited eGFR benefit relative to those who received placebo, a difference that was preserved during a 2-year, open-label extension. As in adults, kidney volume growth was higher after 1 year of treatment. Tolvaptan exhibited acceptable safety and tolerability with few discontinuations.



A) eGFR over time



B) htTKV over time

Fr-OP 009

BELATACEPT OUTCOMES IN PEDIATRIC KIDNEY TRANSPLANTATION: AN INTERNATIONAL MULTICENTER STUDY

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**Aims/Purpose:** Belatacept is a co-stimulation blocker associated with improved long-term outcomes in adult kidney transplant (KT) recipients compared to CNI based regimens. Data on its use in older children and young adults are lacking. We report outcomes for 45 pediatric KT patients converted to belatacept and compared their outcomes to a matched cohort of CNI treated patients.

**Methods:** 45 patients were included from 4 centers (USA and France) between 05/2018 and 12/2021. The first 5 belatacept injections were administered at 5mg/kg/dose (10mg/kg/dose if early conversion) every 2 weeks, then monthly. CNI were progressively reduced and stopped and MMF increased at CNI withdrawal. Patients' viral status (EBV, CMV, BKv) were monitored monthly and allograft biopsies performed before and 6 months post belatacept initiation. Belatacept patients were matched 1:1 to patients remaining on CNI based on a propensity score including: country, age at and time since KT, donor type, history of rejection and eGFR. Cumulative incidence of rejection was compared using the Kaplan-meier method.

**Results:** Median age at conversion was 17.7 y (range 10.3–20.6). 7/45 patients received an early conversion (= 3 months post KT): 6 because of peri-operative ischemic injury and 1 to minimize CNI toxicity (diabetes). 38/45 patients were converted after a median of 4.1 years post KT. Conversion indication was based on the need for long term CNI avoidance: either because of toxicity (histology, post-transplant diabetes, tremors; n = 13) or sub-optimal creatinine (n = 12) or to improve adherence (e.g. monthly IV-treatment, n = 13). CNI was withdrawn in 42/45 patients by a median of 2.4 months. All patients were EBV+ at conversion (4 were EBV- at the time of KT). No EBV replication was observed. However, 1 severe BKv nephropathy required the discontinuation of belatacept. eGFR was stable or improved over a median follow-up time of 1.6 years, Figure 1. Rejection episodes were observed in 11/45 patients (24.4%) after a median of 10.2 months and included 7 TCMR, 3 ABMR and 1 mixed rejection. Similar rejection rates and no significant improvement in eGFR were observed in the belatacept group compared to the CNI group (Figure 2).

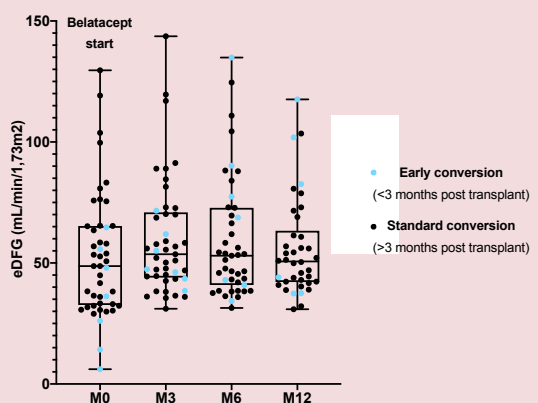


Figure 1: Evolution of eGFR after initiation of belatacept.

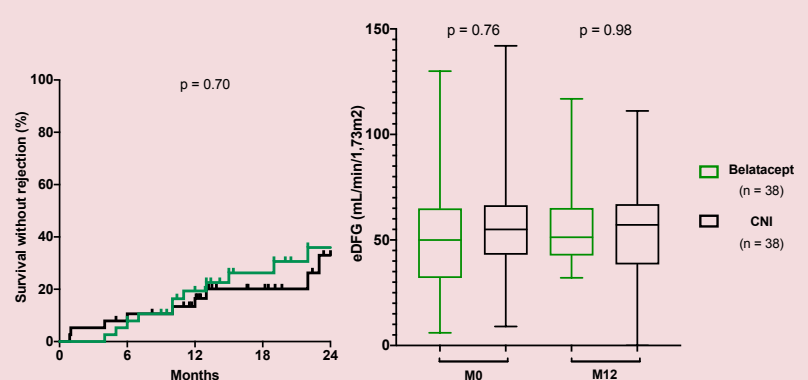


Figure 2: Propensity score matching to compare rejection rates and eGFR in belatacept- and CNI-treated pediatric KN recipients.

**Conclusion:** This study demonstrates the safety of belatacept among pediatric patients with no increase in the risk of infection or rejection compared to patients remaining on CNI. Further studies are needed to determine pediatric kTx recipients likely to benefit the most from belatacept.

Fr-OP 010

STUDY OF THE GUT MICROBIOTA AND PERMEABILITY IN LUPUS NEPHRITIS

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**Aims/Purpose:** To assess if there are differences in diet, physical activity, body composition, gut microbiota, gut permeability, and endotoxemia between systemic lupus erythematosus (SLE) patients with and without lupus nephritis (LN) and healthy controls (HC).

**Methods:** Children and adult SLE patients who fulfilled the 2019 EULAR/ACR SLE classification criteria were included, as well as HC. Individuals with inflammatory bowel disease, celiac disease, irritable bowel syndrome, diabetes, malignancy, or other immune-mediated diseases were excluded. Diet was assessed by three 24h-dietary recalls. Adherence to Mediterranean Diet (MD) was evaluated by PREDIMED/KIDMED questionnaires. Physical activity was assessed by the IPAQ questionnaire. Body composition was analyzed by whole-body air-displacement plethysmography. Gut microbiota was studied by next-generation sequencing, with amplicon sequencing-based 16S rRNA analysis. Gut permeability was evaluated by the lactulose/mannitol test, quantified by mass spectrometry (LC-MS/MS). Zonulin and sCD14 were measured by ELISA. The biological activity of LPS was assessed through serum-induced toll-like receptor 4 stimulation in a reporter cell line exposed to polymyxin b.

**Results:** We studied 16 HC (median age 35.5Y [14–50Y], 88% females), and 45 SLE patients (median age 32Y [11–57Y], 87% females, 64% with LN). SLE patients were less active, had lower adherence to the MD and higher fat mass than HC ( $p < 0.05$ , in all). In SLE, the gut microbiota had lower  $\alpha$ -diversity compared to HC ( $p < 0.05$ ). In addition, Rikenellaceae were increased in SLE, particularly in LN ( $p < 0.05$ ). SLE patients had a higher lactulose/mannitol ratio (0.0180) than HC (0.0140;  $p < 0.05$ ), which was higher in LN patients than SLE patients without LN ( $p < 0.05$ ), meaning that LN patients had increased paracellular gut permeability than patients without LN. In SLE, there was also an overexpression of zonulin ( $p < 0.01$ ), a gut permeability modulator that disassembles tight junctions between cells of the gut wall. Moreover, SLE patients displayed increased levels of sCD14 ( $p < 0.05$ ) and endotoxemia.

**Conclusion:** In this cohort, SLE patients had dysbiosis of the gut microbiota and an increased gut permeability when compared to HC, particularly if there was renal involvement. Our results suggest that gut microbiota, the gut barrier, and endotoxemia may have a role in LN pathogenesis and these might be new potential therapeutic targets.

Keywords: systemic lupus erythematosus, lupus nephritis, microbiota, gut permeability, endotoxemia



Fr-OP 011

LEFT VENTRICULAR HYPERTROPHY IN PEDIATRIC MAINTENANCE HEMODIALYSIS PATIENTS – FINDINGS FROM THE INTERNATIONAL PEDIATRIC HEMODIALYSIS NETWORK (IPHN)

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**Aims:** To assess prevalence and modifiable factors of left ventricular hypertrophy (LVH) in pediatric hemodialysis (HD).

**Methods:** Analysis of 1135 echocardiography findings and LVH risk factors in 552 patients prospectively followed in the IPHN.

**Results:** 51% of the echocardiography studies demonstrated LVH. In multivariable analysis, presence of LVH was independently predicted by higher systolic BP-SDS (OR 1.06, 95%CI 1.04-1.09), lower hemoglobin level (OR 0.97, 95%CI 0.95-0.99,  $p = 0.004$ ), older age (OR 1.02, 95%CI 1.01-1.04), HD vs. HDF modality (OR 1.09, 95%CI 1.02-1.18,  $p = 0.01$ ), UF/h/m<sup>2</sup> BSA (OR 1.29 CI 1.01-1.65,  $p = 0.03$ ) and higher interdialytic weight gain (IDWG; OR 1.02, 95%CI 1.02-1.18,  $p = 0.04$ ), without significant regional variation. IDWG was in turn predicted by low urine output (OR 0.27, 95%CI 0.23-0.32,  $p < 0.0001$ ) and high dialysate sodium concentrations (OR 1.06, 95% 1.01-1.10), with the latter not being associated with intradialytic hypotension. 202 patients not switching dialysis modality during 6-36 months of follow-up were analyzed longitudinally for LVM change. Factors independently associated with de novo or persistent LVH (time-averaged measures) were HD vs HDF (OR 1.26, 95%CI 1.06-1.51,  $p = 0.008$ ), older age (OR 1.03 95%CI 1.01-1.04,  $p = 0.001$ ), and higher pre-dialysis systolic BP-SDS (OR 1.01, 95%CI 1.02-1.19). In a subgroup of patients with both echocardiographic and ABPM evaluation ( $n = 304$ ), presence of LVH (53%) was associated with elevated 24-hour mean arterial pressure (MAP)-SDS (3.21 vs. 1.42), and with daytime (2.5 vs. 1.00) and nighttime MAP-SDS (3.01 vs 1.61; all  $p < 0.0001$ ). In multivariable analysis of the 304 patients, LVH was exclusively predicted by 24h MAP-SDS (OR 1.4, 95% CI 1.19-1.64), but not by pre-dialysis BP-SDS, hemoglobin, UF rate or dialysis modality.

**Conclusions:** LVH is still highly prevalent in pediatric HD. This could be improved by strict blood pressure control (using ABPM), use of HDF instead of HD, anemia control and lowering IDWG by reduction of dialysate sodium concentrations.

# SYMPOSIUM 4

# Hypertension

Sa-OP 012

EARLY VASCULAR CALCIFICATION RELATED MOLECULAR PATHWAYS IN CHILDREN WITH CHRONIC KIDNEY DISEASE

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**Background and Aims:** Children with advanced stages of chronic kidney disease (CKD) suffer from an exceedingly high risk of cardiovascular disease (CVD). Vascular calcifications (VC) may already develop in childhood, but underlying molecular pathomechanisms of early processes are only partly understood.

**Method:** Arterioles from children with normal renal function and children with CKD5 (median age 8.9 and 8.8 years respectively) were analysed for calcium deposits by Von Kossa staining and 18F-sodium autoradiography (18F-NaF), and by digital quantitative histomorphometry. Arteriolar transcriptome and proteome analyses (n = 7/group; age 7.3 ± 3/6.8 ± 3 years) underwent Gene set enrichment (GSEA) and Ingenuity pathway analysis. A literature-mining based VC pathway library comprising 442 biological processes/molecular functions was established and associated genes were extracted from Gene Ontology database. Identified molecular key mechanisms were validated in independent pediatric CKD cohorts (n = 32) and healthy controls (n = 20) by quantitative immunostaining.

**Results:** While von Kossa staining was negative, autoradiography using 18F-NaF revealed microcalcifications in arterioles from children with CKD5. Calcium deposit abundance was associated with serum inorganic phosphorus (R<sup>2</sup> = 0.82; p = 0.03). Arteriolar lumen narrowing was present in CKD5 children (p = 0.001), intima and media thickness were increased (p < 0.0001 and p = 0.02). CD68+ macrophages infiltrated subendothelial space in CKD5 arterioles, but not in controls. Arteriolar macrophage counts correlated with serum inorganic phosphorus (R<sup>2</sup> = 0.18; p = 0.04). Multi-omics VC pathway analysis identified 30 pathways, mainly related to actin cytoskeleton, Wnt signaling, extracellular matrix (ECM) organization, complement activation, apoptosis, endoplasmic reticulum stress and ossification regulation. In independent age-matched cohorts, vascular endothelial growth factor and endothelial cell number/ $\mu$ m endoluminal circumference were reduced in children with CKD versus controls. Arteriolar DKK3 and Wnt2b, two components of the Wnt pathway, were significantly decreased (p = 0.0004 and p = 0.009, respectively). Arteriolar fibronectin-1 (FN1), a major regulator of ECM was identified as Hubgene of VC, and was less abundant in children with CKD5 (p = 0.001). Arteriolar osteoglycin, inducing ectopic bone formation, was increased in CKD5 (p < 0.001) and correlated with serum PTH (R<sup>2</sup> = 0.61; p = 0.01).

**Conclusion:** Arteriolar microcalcifications are present in young children with CKD5. We comprehensively describe associated molecular pathways activated in early stages of VC development. In-depth understanding the processes involved in vascular remodelling propel our mechanistic understanding and open novel avenues for therapeutic targets.

Sa-OP 013

AGE-RELATED PEDIATRIC REFERENCE VALUES FOR PARAMETERS OF PHOSPHATE HOMEOSTASIS, INTACT FIBROBLAST GROWTH FACTOR 23 AND SOLUBLE KLOTHO

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**Aims/Purpose:** The diagnosis and treatment of disorders of phosphate (Pi) homeostasis in children is hampered by the lack of reference values for the phosphaturic hormone fibroblast growth factor 23 (FGF23) and the soluble form of its co-factor Klotho (sKlotho). Currently available reference values for the maximum tubular Pi reabsorption (TmP/GFR) do not cover the whole pediatric age range (0–18 years) or are based on outdated laboratory methods. The aim of this study was to establish pediatric reference values for intact FGF23 (iFGF23), sKlotho, Pi, calcium (Ca), TmP/GFR and urinary Ca and Pi to creatinine ratios (UCa/Crea/UPi/Crea) using state of the art laboratory assessments.

**Methods:** 456 children (255 boys) aged 0–18 years were included in this study. Relevant renal/bone diseases and infections were excluded clinically and by laboratory tests. iFGF23 and sKlotho in plasma by ELISA. Pi, Ca, and Crea in serum and urine were measured by automated methods, Percentile curves and LMS values were generated according to the method of Cole and Green and used to calculate z-scores.

**Results:** Concentrations of all parameters studied were found to be age-dependent. Klotho, serum Pi, and TmP/GFR also correlated with sex. iFGF23 concentrations are highest in the first two years of life, then decrease steadily achieving a steady level from age 5 onwards. sKlotho concentrations peaked between 9 to 13 years of age followed by a marked decline until adult age. Pi and TmP/GFR values are highest in infancy, rapidly decline within the first 2–3 years of life, followed by a slow further decline until the end of the growth period, after which they markedly drop to adult values. The latter was delayed in male compared to female adolescents, probably reflecting physiological maturation. iFGF23 and sKlotho concentrations were significantly associated with serum Pi and Ca concentrations. UCa/Crea and UPi/Crea values were highest in infancy and constantly declined until adult age. Our normal values for serum Pi and Ca are almost congruent with the 2012 Canadian Caliper study data, whereas the reference values for TmP/GFR are significantly higher compared to those published in the 1980s.

**Conclusion:** The observed age- and partly also sex-dependence of the presented reference values explain the partly contradictory findings concerning parameters of Pi homeostasis and circulating levels of iFGF23 and sKlotho in pediatric studies. These normal values will improve the diagnosis and treatment of FGF23 associated disorders of Pi homeostasis in infants, children and adolescents.

# SYMPOSIUM 5

# DIAGNOSTICS

Sa-OP 014

IMPAIRED METABOLISM AND INCREASED MITOCHONDRIAL OXIDATIVE STRESS CAUSE PODOCYTES DYSFUNCTION IN CYSTINOSIS

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**Aims/Purpose:** Cystinosis is a rare, incurable, autosomal recessive storage disease caused by mutations in the CTNS<sup>-/-</sup> gene and leading to lysosomal cystine accumulation in all cells of the body. While cystinosis is considered as a prototype of proximal tubular dysfunction, the disease also affects glomerular podocytes and presents with increased podocyte losses into urine and glomerular proteinuria at early disease stages. Cysteamine, the current standard of care treatment, decreases lysosomal cystine accumulation but does not reverse podocyte injury. Thus, other pathogenic mechanisms than mere cystine accumulation are involved in glomerular dysfunction in cystinosis.

**Methods:** Immortalized cystinosis patient-derived (n = 2), healthy control (n = 1) and CTNS<sup>-/-</sup> knockdown (n = 2) podocytes were used in this study. The results were validated in a new in-house developed fluorescent ctns<sup>-/-</sup> zebrafish larvae model (l-fabp:DBP-eGFP;CTNS).

**Results:** Patients-derived and knockdown cystinosis podocytes present decreased adhesion and increased static and dynamic permeability caused by accumulation of mitochondrial reactive oxygen species (ROS). Moreover, they show fragmented mitochondrial network with impaired energy and TCA cycle metabolism, and decreased expression of superoxide scavenging enzyme superoxide dismutase 2 (SOD2). Interestingly, treatment with the mitochondrial superoxide scavenger MitoTEMPO in combination with cysteamine can rescue the impaired adhesion and permeability in vitro and in vivo while treatment with cysteamine alone had no effect.

**Conclusion:** Impaired mitochondrial function and increased oxidative stress are critical features in cystinosis podocytes. The combinatory treatment of cysteamine with targeted mitochondrial antioxidant improves podocytes adhesion and permeability.

Sa-OP 015

LONG-TERM CLINICAL OUTCOMES IN PATIENTS WITH DISTAL RENAL TUBULAR ACIDOSIS AFTER 6 YEARS TREATMENT WITH SIBNAVAL

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**Aim:** Distal renal tubular acidosis (dRTA) is a rare disease characterized as a hyperchloremic metabolic acidosis affecting growth, bone and kidney health. The aim of the study was to demonstrate the long-term safety and efficacy of Sibnaval<sup>®</sup>, a prolonged-release alkalinizing formulation with twice daily dosing, in pediatric and adult dRTA patients.

**Methods:** Thirty patients with inherited dRTA, were followed up to 6 years on average in a multicenter open-label extension trial (B22CS) to evaluate the long-term effect of Sibnaval on metabolic acidosis, height, weight, body mass index (BMI), bone mineral density (BMD) Z-score spine, estimated glomerular filtration rate (eGFR), nephrolithiasis and safety. Paired t-tests were performed between Baseline and End of Study (EoS) when appropriate. Covariance ANCOVA tests were performed to analyze spine BMD Z-score. Data are presented as mean  $\pm$  standard error of mean).

**Results:** After an average of 6 years of treatment with Sibnaval<sup>®</sup>, data from the 24 children and 6 adults (mean age 11.2), demonstrated sustained control of metabolic acidosis (plasma bicarbonate 22.0  $\pm$  0.6 mmol/L Baseline to 22.8  $\pm$  0.56 mmol/L EoS). From Baseline to EoS, standard deviation score (SDS) for height and weight increased significantly (-0.6  $\pm$  1.0 to -0.3  $\pm$  0.9 p = 0.04 and 0.2  $\pm$  1.5 to 0.7  $\pm$  1.4 p = 0.03, respectively), without significant difference in BMI. Spine BMD Z-score underwent a continuous and significant increase from Baseline over 6 years of treatment (difference [95% CI] = 0.404 [0.170; 0.639]). At EoS, spine BMD Z-score was improved in pre- (mean age 10.8) and post- (mean age 24.1) pubertal patients (mean 0.76  $\pm$  0.54 and 0.56  $\pm$  0.22 respectively), while it was stabilized in pubertal (mean age 15.5) patients (mean -0.01  $\pm$  0.39). There were no significant changes in eGFR from Baseline to EoS (respectively 108.4 and 105.2 mL/min/1.73/m<sup>2</sup>). Nephrolithiasis increased slightly according to the increased age of the patient, with a single surgical intervention for stone removal concomitant to reduced treatment adherence. Sibnaval<sup>®</sup> showed a good safety profile over 6 years.

**Conclusion:** These long-term data support the safety and efficacy of Sibnaval<sup>®</sup> in the treatment of dRTA and are the first to report significant positive long-term outcomes impacting growth, spine bone density, and stabilization of kidney function in patients with dRTA treated over 6 years. All but one patient remained on therapy.

# SYMPOSIUM 6

# MANAGEMENT DILEMMAS



Sa-OP 016

DEVELOPMENT OF A HNF1B PREDICTION MODEL IN CHILDREN WITH CONGENITAL ANOMALIES OF THE KIDNEYS AND URINARY TRACT – AN INTERNATIONAL, MULTICENTER STUDY

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A mutation in the HNF1B gene is the leading monogenic cause of congenital anomalies of the kidneys and urinary tract (CAKUT) and kidney failure. Multiorgan expression of the gene is also responsible for other complications, which may occur later in life. Thus, early diagnosis of HNF1B disease is crucial for personalized care. Until now there was no accurate tool, which could assist clinicians in the selection of patients for genetic testing.

**Aims/Purpose:** To develop a model based on clinical and laboratory data, which could predict HNF1B mutation in children with CAKUT.

**Methods:** A total of 234 children and young adults suspected of HNF1B mutation were recruited internationally from pediatric nephrology centers. The clinical and laboratory data were collected and analyzed retrospectively. All subjects were randomly divided into a training (70%) and a validation set (30%). A random forest prediction model was constructed to predict the occurrence probability of HNF1B mutation. Recursive feature elimination algorithm was used for feature selection into the model, and the receiver operating characteristic curve to verify its prediction effect.

**Results:** 213 patients were analyzed, including HNF1B positive (mut+, n = 109) and HNF1B negative (mut-, n = 104) subjects. The majority of patients had chronic kidney disease stage 1 or 2 (91% and 84% of mut- and mut+ cohorts, respectively). Cystic kidney disease and multicystic dysplastic kidney were the most common renal phenotypes in both groups, but their frequencies between the groups were similar. Only bilateral defects were observed more frequently in the mut+ group (OR 4.85). Hypomagnesemia and hypermagnesuria (FEMg > 5%) were the most frequent abnormalities in mut+ patients, and were noted in 59% and 65% respectively. Hypomagnesemia based on age appropriate norms had better discriminatory value than the age independent cut-off of 0.7 mmol/l (OR 23.6 vs 10.05 respectively). Pancreatic anomalies were almost exclusively found in mut+ patients (OR 13.95). None of the subjects presented with hypokalemia, however, the mean serum potassium level was significantly lower in the HNF1B cohort. Hypermagnesuria, hypomagnesemia, the presence of bilateral kidney anomalies, pancreatic anomalies, and serum potassium were selected as the most important variables, and were included in the model. The final model had accuracy of 82.66% (95%CI: 81.68–84.52%), a sensitivity of 93.67% and specificity of 73.57%.

**Conclusion:** This study developed a prediction model of HNF1B mutation in children, which could be helpful in the selection of patients with CAKUT for genetic testing. Utilization of age appropriate lower limits for serum magnesium is highly recommended to achieve a good model performance.

Sa-OP 017

EFFECT ON IMMUNOSUPPRESSIVE TREATMENT ON MEDIUM-TERM KIDNEY OUTCOMES IN A LARGE COHORT OF CHILDREN WITH HISTOLOGICALLY CONFIRMED IGA VASCULITIS NEPHRITIS

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**Aims/Purpose:** The aim of this study was to compare kidney outcomes in children with biopsy proven IgA vasculitis with nephritis (IgAVN) after treatment with different immunosuppressive drugs.

**Methods:** Retrospective data were collected on children with biopsy proven IgAVN from 41 international paediatric nephrology centres across 27 countries and 6 continents. The outcomes studied were reduced kidney function, estimated glomerular filtration rate (eGFR) and level of proteinuria at last follow up.

**Results:** 1174 children were included in this study with a median follow up of 3.7 years (IQR 4.2). 80% were treated with ACE-inhibitors. Intravenous steroids followed by oral steroid treatment was given to 42.2% and 38.8% received oral steroid treatment alone. Additional drugs used included mycophenolate mofetil (13%), azathioprine (11.9%), cyclophosphamide (17%), calcineurin inhibitor (10%), rituximab (1%), intravenous immunoglobulins (0.6%) and anticoagulants (10.2%). At last follow up 31% had an eGFR below 90 ml/min/1.73m<sup>2</sup> and proteinuria was persistent (UPUC > 20mg/mmol) in 36%. Older age, male gender and lower eGFR at onset were predictors for a lower eGFR at last follow up. Endocapillary proliferation (E1) segmental sclerosis (S1), tubular atrophy/interstitial fibrosis = 25% (T1 and 2) and crescents (C1 and 2) in the Oxford classification and ISKDC stages IV and V were also associated with a worse eGFR. There was no evidence of improvement in the primary outcome with any of the immunosuppressive treatments, compared to other treatments or no treatment. Further subgroup analyses of children with eGFR below 60, respectively 90 ml/min/1.73m<sup>2</sup>, nephrotic syndrome at onset and hypoalbuminemia could also not reveal any impact of treatment. Neither could subgroup analyses comparing no immunosuppressive treatment (n = 156), steroids only (n = 399), mycophenolate (n = 64), azathioprine (n = 71), cyclophosphamide (n = 83), calcineurin inhibitor (n = 56) or a combination of those with each other (n = 102), see Figure.

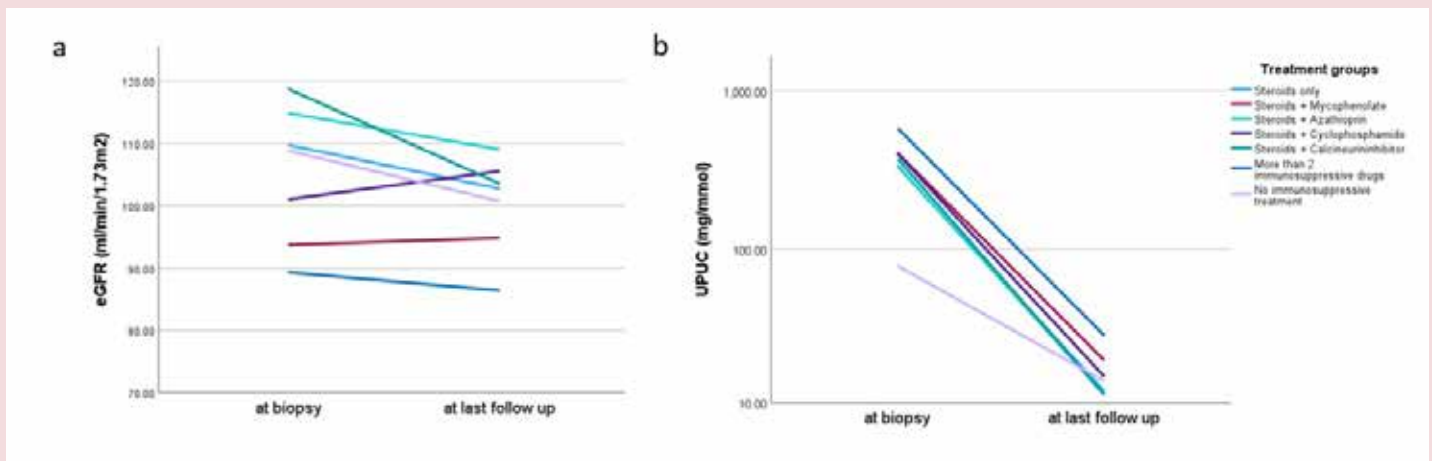


Figure: Line blots: a) Median estimated glomerular filtration rate (eGFR) and b) median urinary protein/creatinine ratio (UPUC) at onset and at last follow up for different treatment groups.

**Conclusions:** There was no evidence that any particular immunosuppressive treatment was superior to others in this large retrospective cohort of children with biopsy proven IgAVN. This is of interest as modern guidelines and treatment recommendations, are based on expert opinion only.

# SYMPOSIUM 7

## Complement Mediated Disorders

Su-OP 018

CROSS-OMICS PROFILING OF PROTEOME, METABOLOME, AND TRANSCRIPTOME REVEALS MOLECULE AND CLEARANCE DYNAMICS AND ORIGIN IN PERITONEAL DIALYSIS

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**Aims/Purpose:** Peritoneal dialysis (PD) effluent is not only a rich source of markers for therapy monitoring and investigation of deregulated processes during PD it is also surprisingly underexplored and therefore poorly defined. Modern high performance mass spectrometry (MS) and sequencing methods allow monitoring of hundreds of analytes in parallel. For understanding PD transport dynamic and pathomechanisms and on a systems biology level, a multi-level omics approach is particularly attractive.

**Methods:** Samples were obtained from stable patients chronically treated with PD at different time-points of standard 4h peritoneal equilibration tests (PETs). Effluent was collected after the pre-PET (overnight) dwell and at 0h, 1h and 4h dwells. Plasma samples were taken at the 2h PET time point. Effluent was separated into a cellular and cell-free component. Soluble proteins and metabolites in the cell-free compartment were processed using material-specific protocols and standardized LC-MS workflows. The cellular material was subjected to RNA sequencing. The Plasma-Proteome database was used for referencing plasma proteins and estimating plasma concentration. A bioinformatic workflow conjoined information from the datasets to reveal novel insights into the “PD-effluentome”, especially unravelling the origin of proteins and metabolites in PD effluent.

**Results:** Metabolomics enabled detecting of 207 unique metabolites in cell-free PD effluent. A mixed-effect ANOVA of all metabolites demonstrated dwell time-dependent concentration changes in 173 metabolites. Post-hoc testing revealed most metabolites to be changed between 1h and overnight time points, followed by 114 and 46 differently concentrated metabolites between 4h and overnight and 1h and 4h, respectively. We quantified 9,797 transcripts in PD-effluent cells and 2,729 proteins in PD effluent. 342 proteins were filtered from plasma, while 800 proteins were attributable to local origin or production. A quantitative analysis of the interaction proteome and cellular transcripts of ~1700 protein-transcript pairs showed clusters of proteins explained by over-expression in peritoneal cells compared to plasma concentrations.

**Conclusion:** Cross-omic profiling of PD effluent can be a valuable approach for revealing small molecule related changes during PD. The exploitation of PD effluent on multiple levels could improve the understanding of pathophysiological molecular processes and transport dynamics in the peritoneal cavity and their role in development of PD complications.

Su-OP 019

DEEP INTRONIC VARIANTS IN X-LINKED ALPORT SYNDROME: FROM DETECTION TO THERAPEUTIC HOPES

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**Aims/Purpose:** X-linked Alport syndrome (XLAS) is a monogenic inherited nephropathy caused by pathogenic variants in the COL4A5 gene which encodes collagen IV  $\alpha 5$  chain. In up to 20% of cases, no molecular cause is identified in COL4A5 exons or flanking regions [1]. This suggests that deep intronic variants affecting splicing may be involved. Furthermore, these variants are eligible for antisense oligonucleotide (ASO) therapy, with data showing that ASO can restore normal splicing [2-3]. Our study thus aimed to [1] identify these variants and [2] restore physiological splicing with ASO.

**Methods:** We used a transcriptomic approach in 19 patients in whom XLAS was highly suspected (compatible clinical features, positive family history, abnormal collagen IV  $\alpha 5$  chain staining on skin biopsy) but with no identified variant by Alport gene panel sequencing. We used targeted RNA sequencing in patient-derived fibroblasts to detect alternative splicing events caused by deep intronic variants in the COL4A5 gene. With a bioinformatic score, we excluded false events. We then developed an ASO therapy to correct missplicing.

**Results:** We identified a pathogenic splicing event in 17/19 patients, causing pseudo-exon retention in 14 patients and exon skipping in 3 patients. A rare deep intronic variant involved in splicing was found in each patient. In male patients, we identified a correlation between the use of cryptic splice site and the severity of the disease. We then successfully restored physiological splicing by using specific ASO in 8/10 patients, leading to rescue of wild type protein localization in fibroblasts.

**Conclusion:** The therapeutic potential of ASO compels us to develop a bioinformatics tool for accurate diagnosis of splicing variants. We developed a reliable method identifying aberrant transcripts in patients with no variants in coding region. These findings illustrate the importance of discovering deep intronic variants and the applicability of ASO therapy in patients with XLAS.

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# SYMPOSIUM 8

# Critical Care Nephrology

Su-OP 020

USE OF TOCILIZUMAB IN THE TREATMENT OF CHRONIC ACTIVE ANTIBODY-MEDIATED REJECTION IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS

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**Aims/Purpose:** Chronic active antibody-mediated rejection (caAMR) has a deleterious impact on allograft survival. Current evidence for treatment of caAMR is limited, especially in children. Tocilizumab (TCZ) is a potential therapeutic option thanks to its action against IL-6-mediated inflammation and humoral immunity. We describe the effects of TCZ therapy in pediatric kidney transplant (pKT) recipients with caAMR.

**Methods:** We retrospectively analyzed the outcomes (in terms of renal function and histological lesions) of a 6-months TCZ therapy in 6 pKT recipients treated between November 2021 and December 2022. All patients had caAMR according to the Banff classification 2018 (category 2) and all received intravenous TCZ (8mg/kg/month for 6 months). Collected data included creatinine, eGFR, proteinuria, HLA and non-HLA antibodies at baseline, month +3 (M3) and month +6 (M6) after TCZ initiation. For each patient, a follow-up biopsy was scheduled at the end of the treatment.

**Results:** Six patients (average age  $15 \pm 16$  years, 4 male) were included. Immunosuppression at the time of caAMR included tacrolimus with MMF (4 patients, 66.6%) or mTOR inhibitor (2 patients, 33.3%), and daily prednisone. AntiHLA antibodies (DSA) were detected in 3 patients and nonHLA antibodies (AT1R and ETAR) in 2. caAMR diagnostic was based on peculiar histological findings in the 3 patients without detectable HLA-DSA. Mean time to caAMR was 4 years after transplantation. At the time of caAMR diagnosis, mean eGFR was  $40.6 \pm 12.8$  mL/min/1.73m<sup>2</sup>. In one patient, TCZ treatment was discontinued after 3 doses due to graft failure. Another patient performed follow up biopsy, which showed persistent caAMR with worsened histological lesions, and subsequently lost his graft. Two patients showed a stable renal function, but histological lesions had worsened (ct1, ci3, IFTA2). In one patient, with worsened renal function, follow up biopsy was not performed due to intrarenal arteriovenous fistula. In the last patient, the biopsy is yet to be performed. Globally, mean eGFR worsened to  $31.4 \pm 15.3$  mL/min/1.73m<sup>2</sup> at M3 and remained stable at M6. Proteinuria and antiHLA and nonHLA antibodies remained stable.

**Conclusion:** In our experience, TCZ therapy did not appear to be significantly effective in modifying the natural history of caAMR. However, more studies are needed to clarify the role of TCZ in caABMR.

Su-OP 021

THE IMPACT OF THE MOLECULAR HLA-EPIOTOPE MISMATCH LOAD ON ALLOSENSITIZATION AFTER KIDNEY TRANSPLANTATION IS MOST PRONOUNCED IN CHILDHOOD, ADOLESCENCE, AND EARLY ADULTHOOD

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**Background:** Patients who undergo kidney transplantation during childhood (0-9), adolescence (10-19), and early adulthood (20-25) face specific threats for poor long-term survival. Due to differences in alloimmune responsiveness and a higher likelihood of nonadherence, they are at increased risk for developing donor-specific antibodies (DSA) and subsequent antibody-mediated rejection (ABMR).

**Methods:** We analyzed 153 kidney transplant recipients (KTRs) who underwent kidney transplantation in childhood (n = 25), adolescence (n = 76), and early adulthood (n = 52) at the University Hospital or University Children's Hospital Zurich from 1990 to 2018. 862 KTRs who underwent kidney transplantation in later adulthood were used for comparison. KTRs were compared concerning the development of DSA and ABMR. The HLA-derived epitope-mismatches were calculated per HLA-locus and in total using the Predicted Indirectly Recognizable HLA-Epitopes (PIRCHE-II) algorithm. High-resolution re-typing was performed from kidney allograft biopsies if necessary.

**Results:** 75 of 153 KTRs (49%) developed de novo DSA, and 30 of 153 KTRs (20%) developed subsequent ABMR. The PIRCHE-II score for HLA-loci DRB plus DQB independently increased the risk for the development of DSA (HR 1.019, CI 95% 1.010-1.027, p < 0.001), but not the total PIRCHE-II score (p = 0.763) or the individual PIRCHE-II scores per HLA-locus (p = 0.05). Similarly, the PIRCHE-II score for HLA-loci DRB plus DQB independently increased the risk for the development of ABMR (HR 1.021, CI 95% 1.011-1.036, p < 0.001). The impact of the PIRCHE-II score for HLA-loci DRB plus DQB on the development of DSA was most pronounced among KTRs who underwent kidney transplantation in childhood (HR 1.045, CI 95% 1.007-1.084, p = 0.019) compared to adolescence and early adulthood (HR 1.018, CI 95% 1.008-1.027, p < 0.01), and adulthood (HR 1.005, CI 95% 1.002-1.008, p < 0.001).

**Conclusions:** An increase of the molecular HLA-epitope mismatch load for HLA-loci DRB plus DQB by 20 epitopes has 2.41 times the risk for developing DSA in childhood, 1.43 times the risk in adolescence and early adulthood, but only 1.10 times the risk in later adulthood. Factors explaining these differences are likely primarily nonadherence and higher alloimmune responsiveness. This result is of particular importance for allocation policies and immunosuppressive strategies.



# SYMPOSIUM 9

## ESPN/ERA and ERKNet Registries

Su-OP 022

**CALORIC RESTRICTION DURING PREGNANCY IMPAIRS NEPHROGENESIS BY MODIFYING EPIGENETIC REGULATION IN NEPHRON PROGENITOR CELLS**

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**Aims/Purpose:** Poor intrauterine environment, such as maternal malnutrition, impairs offspring nephron endowment and increases the risk of chronic kidney disease. We have previously demonstrated that methionine metabolism has an important role in mediating the negative effects of caloric restriction during pregnancy on nephron endowment. Furthermore, methionine is pivotal in many epigenetic gene expression regulation processes as a methyl donor. Here we examine the effects of malnutrition on DNA methylation in nephron progenitor cells.

**Methods:** The caloric intake of pregnant mice was limited to 70% of daily intake. Nephron progenitor cells were FACS-based cell-sorted using transgenic mice, and DNA was extracted. Methylation patterns were characterized using reduced representation bisulfite sequencing. Results were cross-referenced with chromatin accessibility and histone modification available data. The effects of methylation changes in regulatory regions on the expression of identified genes were validated using RT-qPCR. In addition, the effects of methionine supplementation on methylation patterns were evaluated using Bisulfite Amplicon Sequencing.

**Results:** Caloric restriction during pregnancy leads to a global decrease in DNA methylation in nephron progenitor cells. Most changes in DNA methylation were localized to gene regulatory regions, including genes involved in nephrogenesis and pivotal intracellular signaling pathways. The perturbations in regulatory DNA methylation patterns of these genes were correlated with expression profile changes. Methionine supplementation alleviated the changes in methylation patterns caused by maternal malnutrition

**Conclusion:** These findings are the first evidence that maternal malnutrition during pregnancy impairs nephrogenesis by modifying DNA methylation patterns in nephron progenitor cells, an effect significantly attenuated by methionine supplementation.

Su-OP 023

A PROSPECTIVE SURVEILLANCE STUDY OF CONSERVATIVE CARE IN CHILDHOOD KIDNEY FAILURE IN THE UNITED KINGDOM AND REPUBLIC OF IRELAND

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**Background:** For children with chronic kidney disease (CKD), progression to kidney failure is a life-limiting condition which requires kidney replacement therapy (KRT) for survival. While KRT offers a chance for survival, it isn't a cure and can fail. As technology advances, KRT is increasingly acceptable for most children; in some cases, however, it is deemed in the best interests of the child not to pursue KRT and to instead opt for conservative care. Few studies have described the epidemiology and outcomes of this cohort. Our aim was to determine the national incidence of children reaching kidney failure for whom a decision was made to conservatively manage their kidney disease.

**Methods:** We conducted a national (UK and Republic of Ireland) prospective study over 25 months (September 2020–October 2022) through the British Paediatric Surveillance Unit, an established research platform for the surveillance of rare disease. Each month, paediatricians received a monthly email asking them to notify the study of any child under 16 years who had reached kidney failure (defined as an estimated glomerular filtration rate  $< 15\text{ml}/\text{min}/1.73\text{m}^2$ ) for whom a decision had been made to conservatively manage their kidney disease. Notifying clinicians completed a questionnaire to describe the clinical and patient characteristics of this cohort. Clinicians were contacted 12 months after notification to determine the outcomes of cases.

**Results:** Over the surveillance period, we received 74 notifications to the study. Of these, 33 were ineligible cases; 8 were duplicate reports and 2 cases were unable to be followed-up. This resulted in 27 confirmed cases, with 4 notifications pending. The median age at notification was 2.6 (IQR 0.3–8.7) years; 56% were male; 52% were White, 41% Asian, and 7% of Black/Other ethnicity. The highest number of reported cases was from England, with an incidence of 0.9 per million of the age-related population (pmarp); notably higher incidence rates were seen for Scotland and Northern Ireland (2.2 and 2.6 pmarp, respectively). The most common underlying kidney diagnosis was a congenital kidney anomaly ( $n = 10$ , 37%), followed by suspected cystic kidney disease ( $n = 6$ ). Reasons for opting for conservative care are captured in our baseline collection. Data collection on 12-month outcomes is still ongoing.

**Conclusion:** This is the first prospective, nationally representative study to determine the incidence of conservatively managed kidney failure in children. Compared to the incidence of KRT-treated kidney failure of 8.3 pmarp, the incidence of conservatively managed kidney failure in UK children is 1.0 pmarp. These children account for approximately 11% of the UK paediatric kidney failure cohort. We expect this cohort will advance our knowledge of the epidemiology of childhood kidney failure and provide prognostic information to patients and families.

# 3-MINUTES PITCH

# SYMPOSIUM 1

## Attenuating Disease Progression

Fr-3MP 001  
PHENOTYPIC VARIABILITY OF INDIVIDUALS WITH CAKUT

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**Aims/Purpose:** Congenital malformations of the kidney and urinary tract (CAKUT) are a major cause for the development of chronic kidney disease in children and adolescents. CAKUT is characterized by significant phenotypic variability and includes defects in the kidneys and/or the urinary tract. In some cases, extrarenal manifestations can be found. Early detection and diagnosis of CAKUT play an important role in preventing progression to end-stage kidney disease. The aim of this study was to describe the phenotypic variability of a large cohort of individuals with CAKUT.

**Methods:** The study was approved by the ethics committee of the Technical University of Munich, Munich, Germany. The clinical phenotype of the individuals was collected using a standardised questionnaire.

**Results:** 432 individuals with CAKUT were included in the study. 48% suffered from an isolated urinary tract phenotype (e.g., obstructive uropathy, obstructive nephropathy, vesicoureteral reflux or duplication of the ureter and pelvis). Renal malformations were detected in 52% of the study population which included renal dysplasia (43%), renal hypoplasia (31%), and renal agenesis (26%). Extrarenal manifestations were seen in 42% of individuals with renal malformations. Skeletal anomalies were reported in 37%, heart defects and growth retardation in 22% each, intellectual disability in 19%, hearing impairment in 11%, and ocular malformations in 7% of these individuals. Individuals with an isolated urinary tract phenotype showed extrarenal manifestations in only 14% of cases.

**Conclusion:** This study demonstrates the phenotypic variability of individuals with CAKUT with isolated urinary tract, renal, and extrarenal manifestations. Our study could show that renal dysplasia was the most common form of renal anomaly. Of note, a significant number of individuals with renal anomalies had extrarenal manifestations (42%). Therefore, it is important to assess for extrarenal manifestations in these individuals.

FR-3MP 002

RELATIONSHIP BETWEEN ULTRASOUND DATA AND THE UNDERLYING PATHOLOGY IN PEDIATRIC URINARY TRACT DILATIONS: PROPOSAL FOR A PREDICTIVE MODEL

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**Aims:** Urinary tract dilations (UTDs) are one of the most frequently detected anomalies at pediatric ultrasound (US). Although transient and benign in most cases, UTD can represent the first finding in cases of obstructive uropathies or vesicoureteral reflux (VUR). The challenge is to find the dilations needing further investigation, thus avoiding unnecessary testing. This study aims to identify the value of US for the diagnosis of VUR or obstructive pathologies.

**Methods:** This is a multicenter retrospective study involving a cohort of 1784 children treated for UTD at the Pediatric Nephrology Units in Bologna, Milan, Modena, and Naples between 2000 and 2019. Patients that underwent second-level imaging (scintigraphy and/or voiding cystourethrography (VCUG)) were selected to evaluate the presence of obstructive uropathy or VUR; subjects that underwent second-level imaging after surgery were excluded. We considered as possible predictors of UTD evolution: the time of diagnosis – prenatal, postnatal post urinary tract infection (UTI), postnatal due to incidental findings – and first postnatal diagnostic US data, in particular the maximum dilation of the pelvis and ureter, calyceal dilation, bilaterality of the dilations.

**Results:** Of the whole cohort, 1150 children (65%) underwent at least one second-level exam. Both VCUG and scintigraphy were performed in 736 children (41.3%), VCUG in 256 (14.3%), scintigraphy in 158 (8.9%). Following second-level examinations, only 28 children (3.8% of those with two exams) had both VUR and an obstructive pathology, 324 (36.2% of those who had scintigraphy) had an obstruction, 317 (32% of those who had VCUG) had VUR  $\geq$  III grade. Using multiple logistic regression and placing obstruction as an outcome, we obtained a predictive model according to which this is more probable in prenatal diagnosis, in significant pelvic dilation ( $\geq 13$  mm identified by Youden index), in the presence of calyceal dilation and of unilateral dilation of the pelvis or calyx. This model has an accuracy of 69.7% (95%CI: 66.6%–72.7%), sensitivity of 75.3%, specificity of 66.5%, negative predictive value (NPV) of 82.5%. Using multiple logistic regression and setting VUR  $\geq$  III grade as an outcome, we obtained a predictive model according to which this is more probable in postnatal diagnosis post UTI, with bilateral ureteral dilation, without quantitatively important pelvic dilation ( $\leq 10.5$  mm identified by Youden index). This model has an accuracy of 63.9% (95%CI: 60.8%–66.9%), sensitivity of 68.4%, specificity of 61.8%, NPV of 80.7%.

**Conclusion:** The predictive models could be useful for identifying the conditions that need further investigation and type of second-level examination to be performed. With these models, we would identify 75% of obstructive uropathies and 68% of VUR after the first postnatal US, with a halving of the second-level exams performed after the first postnatal US.

FR-3MP 003

ACUTE KIDNEY INJURY IN CHILDREN HOSPITALIZED FOR FEBRILE URINARY TRACT INFECTION

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**Aims/Purpose:** Acute kidney injury (AKI) is associated with poor health outcomes. As AKI is favored by a reduced nephron mass, its occurrence could represent a predictor of the presence of congenital anomalies of the kidney and urinary tract (CAKUT). We aimed to determine the prevalence of and the risk factors for AKI in children hospitalized for fUTI and its role as a predictor of an underlying CAKUT and of vesico-ureteral reflux (VUR).

**Methods:** This is a retrospective study involving university and urban hospitals from all Italy. Children aged  $\leq 18$  years with fUTI were enrolled. AKI was defined by KDIGO serum creatinine criteria. In 194 patients a measured basal serum creatinine was available. For the others ( $n = 655$ ), we estimated the basal serum creatinine value by back-calculating it by Hoste(age) equation. Univariate and multivariate logistic regression models were used to explore associations.

**Results:** Of 849 children hospitalized for fUTI (44.2% females, median age 0.5 years; IQR = 1.8) and enrolled in the study, 124 (14.6%) developed AKI. The prevalence raised to 30% in presence of an underlying CAKUT. The Kaplan-Meier analysis showed longer time to discharge for patients with AKI compared with those without AKI. At the multivariate logistic regression analysis both presence of CAKUT (odds ratio [OR] = 13.1; 95%CI:4.4-39.4;  $p < 0.001$ ) and procalcitonin levels (OR = 1.4; 95%CI:1.1-1.7;  $p = 0.001$ ) were independently associated to AKI. Kidney hypoplasia (OR = 10.2; 95%CI:4.4-23.7;  $p < 0.001$ ), pelvi-caliceal dilation (OR = 6.7; 95%CI:3.4-13.3;  $p < 0.001$ ), ureteral dilation (OR = 32.1; 95%CI:10.5-97.5;  $p < 0.001$ ), uroepithelial thickening of the renal pelvis (OR = 2.2; 95%CI:1.2-4.0;  $p < 0.001$ ), and the occurrence of AKI during the fUTI episode (OR = 3.6; 95%CI:1.8-7.2;  $p < 0.001$ ) showed to be significant predictors of CAKUT at the multivariate analysis. Only the occurrence of AKI (OR = 3.1; 95%CI:1.7-5.8;  $p < 0.001$ ) persisted significant when evaluating predictors for VUR.

**Conclusion:** AKI occurs in 14.6% of children hospitalized for fUTI and is a significant predictor of CAKUT. This could mean that a reduced nephron mass, present in hypodysplastic kidneys and CAKUT, favors the occurrence of AKI during stress. AKI could be an important factor to suspect an underlying CAKUT and to guide the post-fUTI diagnostic follow-up.



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Fr-3MP 004  
RISK FACTORS FOR CHRONIC KIDNEY DISEASE IN CHILDREN WITH POSTERIOR URETHRAL VALVE

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**Aims/Purpose:** Posterior urethral valve is an obstructive uropathy and occurs in 1/3000–8000 babies born alive. Chronic kidney disease develops in approximately 20% of these patients. Our aim is to determine the frequency of chronic kidney disease (CKD) in children with PUV and to investigate the risk factors for progression to CKD.

**Methods:** A total of 52 boys who were followed up with the diagnosis of posterior urethral valve have been evaluated retrospectively. Serum creatinine level and glomerular filtration rate, ultrasonographic findings, urodynamic findings, DMSA findings, voiding cystourethrography findings, lower urinary system symptoms and urinary tract infection frequency have been recorded.

**Results:** Average age of diagnosis was  $6.5 \pm 28$  months. While 32 (64%) patients were antenatally diagnosed, 20 (36%) were postnatally diagnosed. Ten (%19,2) patients were diagnosed chronic kidney disease secondary to posterior urethral valve. No significant difference was observed in terms of the presence of antenatal diagnosis between the groups with and without CKD ( $p = 0.182$ ). Although the hydronephrosis grades of non-CKD patients decreased significantly at the last follow-up compared to the admission evaluation ( $p = 0.0001$ ), no significant change was observed in the CKD group, and more and higher degrees of hydronephrosis were observed in the CKD patients in the final control evaluation ( $p = 1$ ). In the CKD group, increased bladder wall thickness at the initial evaluation and ureteral dilatation at the final evaluation were significantly higher ( $p = 0.016$  and  $0.034$  resp.). Vesicostomy was performed for 10 patients with the situations where the baby is too small to undergo valve ablation, when a severe obstruction is noted or persistent urinary tract infection ( $n=2$ ). Three children with CKD and 7 children with non-CKD had undergone vesicostomy ( $p = 0.382$ ). Proteinuria was observed significantly higher in the group with CKD ( $p = 0.001$ ). There was no significant difference between the two groups in terms of severe bladder dysfunction, scar presence in DMSA, VUR grades, recurrent urinary tract infection and incontinence ( $p > 0.05$ ).

**Conclusion:** Renal damage of children with PUV had been developed at the antenatal period, and the possible negative effects of bladder dysfunction, VUR grade and recurrent urinary tract infections in the postnatal period have not been demonstrated in our study. Patients with persistent hydronephrosis and high creatinine value at the initial admission has high risk of CKD and these children must be followed up closely by clinicians.

# SYMPOSIUM 2

# Nephrology in the NICU

Fr-3MP 006

## THE ASSOCIATION BETWEEN BIRTH WEIGHT AND BLOOD PRESSURE IN YOUNG ADULTS

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**Aims/Purpose:** Low birth weight has been associated with increased risk of hypertension later in life. The purpose of this study was to examine the association between birth weight and blood pressure (BP) indices in healthy young adults.

**Methods:** Subjects were recruited from a cohort of 970 adults aged 20–22-years who participated in a population-based study of BP in 9–10-year-old Icelandic children. All participants underwent 8 resting clinic BP measurements during two separate visits and an ambulatory BP (ABP) measurement. Information on birth weight and gestational age were recorded from birth records. Absolute birth weight and birth weight Z-scores adjusted for gestational age were used in the analyses. Pearson correlation was used for correlation analysis, p-value = 0.05 was considered significant.

**Results:** Of 170 young adults who completed the follow-up study, 102 were women (60%). The mean clinic BP was 120/65 mm Hg in men and 112/66 mm Hg in women. The mean birth weight for men was 3625 ± 736 g and 3646 ± 592 g for women. A negative correlation was observed between birth weight and systolic ABP ( $r = -0.18$ ,  $p = 0.016$ ) and between birth weight Z-score and systolic and diastolic ABP ( $r = -0.14$ ,  $p = 0.026$  and  $-0.10$ ,  $p = 0.20$ , respectively). When the sexes were analyzed separately the correlation with systolic ABP was statistically significant only in women, for whom it was  $r = -0.30$ ,  $p = 0.002$  for absolute birth weight and  $r = -0.24$ ,  $p = 0.014$  for birth weight Z-score. A statistically significant correlation was observed in women between absolute birth weight and both diurnal and nocturnal ABP ( $r = -0.31$ ,  $p = 0.0015$ ,  $r = -0.20$ ,  $p = 0.044$ , respectively). The association between birth weight Z-score and diurnal systolic ABP was significant ( $r = -0.26$ ,  $p = 0.013$ ) while the correlation with nocturnal systolic ABP was not ( $r = -0.16$ ,  $p = 0.097$ ). No correlation was found between birth weight ( $0.09$ ,  $p = 0.24$ ) or birth weight Z-score ( $-0.070$ ,  $p = 0.37$ ) and clinic BP at follow-up.

**Conclusion:** Low birth weight has as strong association with systolic ABP in young women and this relationship is stronger for diurnal systolic blood pressure.

FR-3MP 006

## ACUTE KIDNEY INJURY IN INFANTS HOSPITALIZED FOR VIRAL BRONCHIOLITIS: PREVALENCE AND RISK FACTORS

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**Aims/Purpose:** We aimed investigating prevalence of and risk factors for acute kidney injury (AKI) in a group of patients hospitalized with viral bronchiolitis.

**Methods:** We retrospectively enrolled 139 children (mean age =  $3.2 \pm 2.1$  months; males = 58.9%) hospitalized for viral bronchiolitis in a non-pediatric intensive care unit (PICU) setting. The Kidney Disease/Improving Global Outcomes creatinine criterium was used to diagnose AKI. We estimated basal serum creatinine by back-calculating it by Hoste (age) equation assuming that basal eGFR were the median age-based eGFR normative values. Univariate and multivariate logistic regression models were used to explore associations with AKI.

**Results:** Out of 139 patients, AKI was found in 15 (10.8%). AKI was found in 13 out of 74 (17.6%) patients with and in 2 out of 65 (3.1%) without RSV infection ( $p = 0.006$ ). No patient required haemodialysis, 1 out of 15 (6.7%) developed AKI stage 3, 1 (6.7%) developed AKI stage 2, and 13 (86.6%) developed AKI stage 1. Among the 15 patients with AKI, 13 (86.6%) reached the maximum AKI stage at admission, 1 (6.7%) at 48 hours and 1 (6.7%) at 96 hours. At multivariate analysis, birth weight < 10th percentile (Odds Ratio, OR = 34.1; 95% confidence interval, CI = 3.6–329.4;  $p = 0.002$ ), preterm birth (OR = 20.3; 95%CI = 3.1–129.5;  $p = 0.002$ ), respiratory syncytial virus (RSV) infection (OR = 27.0; 95%CI = 2.6–279.9;  $p = 0.006$ ), and hematocrit levels > 2 standard deviation score (SDS) (OR = 22.4; 95%CI = 2.8–183.6;  $p = 0.001$ ) were significantly associated with AKI.

**Conclusion:** About 11% of patients hospitalized with viral bronchiolitis in a non-PICU setting develop an AKI (frequently mild in degree). The risk is significant in case of preterm birth, birth weight < 10th percentile, hematocrit levels > 2SDS, and RSV infection.

FR-3MO 007

**DOES A NON REASSURING FETAL HEART RATE PATTERN IMPAIR RENAL FUNCTION IN NEONATES PRENATALLY DIAGNOSED WITH CONGENITAL ANOMALIES OF KIDNEY AND URINARY TRACT?**

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**Aims/Purpose:** To determine the effect of non-reassuring fetal heart rate (NRFHR) patterns in labor on the postnatal renal function of neonates with a prenatal diagnosis of Congenital Anomalies of the Kidney and Urinary Tract (CAKUT).

**Methods:** A retrospective cohort study was conducted in a single tertiary referral center between 2012 and 2020. All cases with a prenatal diagnosis of CAKUT were extracted, and their fetal, maternal, obstetrical, and neonatal characteristics were analyzed. Cases of multiple gestations, preterm delivery, small for gestational age, associated major malformations or genetic aberrations, and pre-labor acute obstetrical events were excluded from the analysis. The study group was comprised of patients who experienced NRFHR during labor. The control groups included (1) patients who had a trial of labor with a normal fetal heart rate pattern and (2) patients who delivered by elective cesarean section (CS). The primary outcome was abnormal serum creatinine levels in the perinatal period. For statistical purposes, the CAKUT cases were classified into a low and high estimated risk for an abnormal post-natal renal outcome. A subgroup analysis of the results was performed accordingly.

**Results:** During the study period, 256 fetuses were diagnosed prenatally with CAKUT. Of them, 214 (83%) women underwent a trial of labor, and forty-two patients (17%) underwent an elective Cesarean Section. Of the patients who underwent a trial of labor, 21/214 (9.8%) experienced NRFHR during labor. No statistically significant between-group differences were found in maternal and fetal characteristics. NRFHR patterns were not associated with a deterioration in neonatal serum creatinine compared to those with normal fetal monitoring or those born by an elective CS.

**Conclusion:** NRFHR patterns during labor and delivery did not impair neonatal renal function status in fetuses diagnosed prenatally with both low and high-risk CAKUT. Delivery can be managed according to standard obstetrical guidelines.

Table 1: Comparison in perinatal creatinine in the study and control groups

Compared groups		First creatinine		
Group 1	Group 2	p	Mean group 1	Mean group 2
Total trial of labor (n = 214)	CS (n = 42)	0.58	0.67 ± 0.26	0.67 ± 0.28
NRFHR (n = 21)	CS (n = 42)	0.78	0.66 ± 0.23	0.67 ± 0.28
NRFHR (n = 21)	Normal fetal monitor (n = 193)	0.80	0.66 ± 0.23	0.67 ± 0.27

Fr-3MP 008

TO GIVE ALBUMIN OR NOT? IS IT SAFE TO MANAGE CONGENITAL NEPHROTIC SYNDROME WITHOUT REGULAR ALBUMIN INFUSIONS?

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**Aims/Purpose:** Recent guidelines on managing congenital nephrotic syndrome (CNS) advise a conservative approach in contrast to Finnish recommendations for early bilateral nephrectomies. Our unit's conservative management has evolved with most children not routinely receiving 20% albumin infusions. The aim of this study was to compare clinical outcomes in patients managed with regular 20% albumin infusions (at least once per week, excluding initial 3-month management) compared to those managed without.

**Methods:** This retrospective study was conducted at a large regional paediatric nephrology centre and included all children diagnosed with CNS between 01 January 2005 and 31 December 2021. Inclusion criteria were nephrotic syndrome presenting in the first 3 months of life, including not only those with known NPHS1/ NPHS2 mutations but also those where an underlying genetic mutation has not yet been found. All other genetic mutations and those who had an underlying infective cause for CNS were excluded. The primary outcome was survival with secondary outcomes including length of hospital admission, number of central lines and infections.

**Results:** 24 patients met the inclusion criteria. Of these 18 (75%) had a mutation in NPHS1 gene, in 4 (17%) no genetic defect was identified and 2 (8%) had a mutation in NPHS2 gene. 8 (33%) patients were managed as per the Finnish recommendations with 14 (56%) managed conservatively. 1 patient had a unilateral nephrectomy, a further patient declined bilateral nephrectomies opting for palliative care. From 2011 onwards all patients were managed as per the conservative approach. Of the 24 patients, 6 (25%) patients died with 1-year survival 79%. Within the Finnish cohort there were 3 (38%) deaths and 2 (14%) deaths within the conservative cohort. Of the 14 patients managed conservatively, 11 (79%) did not receive regular 20% albumin infusions. Those managed without albumin infusions had a significantly shorter number of days in hospital in the first year of life (42 days) compared to the group managed with regular albumin infusions (183 days)  $p = 0.0089$ . Those managed without albumin had an average of 1 central line insertion prior to renal replacement therapy compared to 2.3 central lines in regular albumin group ( $p = 0.0026$ ). Those managed without albumin had an average of 1.3 infective episodes compared to 2 infective episodes in those managed with regular albumin infusions ( $p = 0.045$ ).

**Conclusion:** In a retrospective cohort of children with CNS there was no evidence of a significant difference in clinical outcomes between those managed with regular 20% albumin infusions, compared to those managed without regular 20% albumin infusions. Median hospital stay in the first year of life was significantly lower in those managed without regular 20% albumin infusions. International collaboration will be required to confirm these findings in a larger multi-centre cohort.

# SYMPOSIUM 3

## Dialysis

FR-3MP 009

FLUID STATUS EVALUATION BY SONOGRAPHY AND BIOIMPEDANCE SPECTROSCOPY IN CHILDREN ON PERITONEAL DIALYSIS

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**Aims/Purpose:** Fluid overload is one of the common complications in chronic kidney disease and increases mortality in pediatric patients on peritoneal dialysis. Reported studies on the assessment of fluid overload in children on peritoneal dialysis have increased, but the lack of an optimal assessment method is still a clinical problem. In this study, it was aimed to evaluate the volume status of children on peritoneal dialysis using ultrasonography and bioimpedance spectroscopy.

**Methods:** Thirteen children on peritoneal dialysis were included in the study. The hydration status of the patients was clinically evaluated. Furthermore, 28 predialysis and 28 postdialysis lung ultrasound, the inferior vena cava collapsibility index (cIVC), and bioimpedance spectroscopy (BIS) measurements were performed.

**Results:** The mean age of the patients was  $8.61 \pm 4.07$  years, and eight (61.5%) were male. The mean period of peritoneal dialysis of the patients was  $20.53 \pm 18.32$  months. The cIVC increased ( $26.3 \pm 10.01\%$  vs  $44.42 \pm 9.4\%$ ) and the total number of B-lines decreased (22 vs 11.5) after a single dialysis exchange in patients ( $p = 0.001$ ). There was a positive correlation between the predialysis total number of B-lines and predialysis fluid overload ( $r = 0.504$ ,  $p = 0.006$ ) (Figure 1). Also, a positive correlation was determined between the postdialysis fluid overload and total number of B-lines ( $r = 0.528$ ,  $p = 0.004$ ). However, there was no significant correlation between both pre- and post-dialysis fluid overload, total number of B-lines and cIVC.

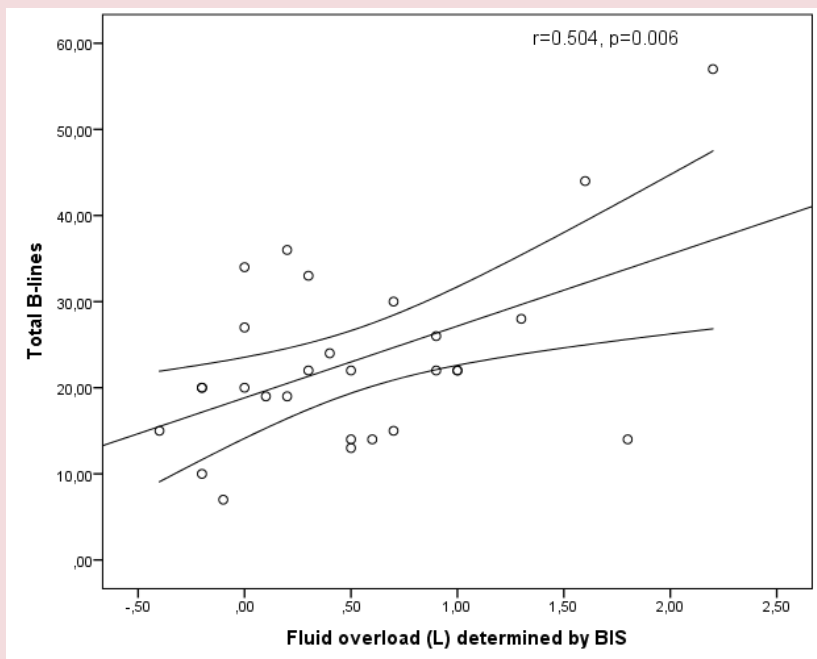


Figure 1: Correlation of total number of B-lines and fluid overload (L) determined by BIS.

**Conclusion:** The lung ultrasonography is a fast and reliable method to evaluate fluid overload in children on peritoneal dialysis, however further studies are needed for correlation with cIVC.



Fr-3MP 010

A RANDOMIZED CROSS-OVER TRIAL OF PRE- VS POST-DILUTION HAEMODIAFILTRATION IN CHILDREN ON MAINTENANCE DIALYSIS: EFFECT ON BLOOD PRESSURE

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**Aims/Purpose:** Children on post-dilution haemodiafiltration (post-HDF) have reduced cardiovascular damage and show improved growth compared to those on conventional haemodialysis. High convective volumes in post-HDF are associated with improved clearances across a wide molecular weight range. Even higher convective volumes can be reached with pre-dilution haemodiafiltration (pre-HDF), however data are limited. We compared the effect of pre- vs post-HDF on fluid management and blood pressure (BP) in a randomized cross-over trial.

**Methods:** Twenty-one prevalent dialysis patients were included. After a 4-week wash-out period (post-HDF), patients were randomized either to 4 weeks pre- then 4 weeks post-HDF, or vice-versa, keeping all other dialysis related parameters constant. Office BP (at the start of and during dialysis) and ambulatory BP monitoring (up to 48 hours after dialysis) were measured.

**Results:** The median age was 14.3 years, with 15 (71%) girls. The median convective volume was 49 vs 13.8 L/m<sup>2</sup> body surface area/session on pre-HDF and post-HDF respectively. The median pre-dialysis systolic and diastolic BP were significantly higher in pre-HDF than post-HDF [systolic 127 mmHg (IQR:117;135) vs 119 mmHg (114;123) respectively,  $p = 0.05$  and diastolic 80 mmHg (73;87) vs 65 mmHg (62;79) respectively,  $p = 0.004$ ]. The median systolic BP was 9.3% (-3.5;18) and diastolic BP was 21% (-2.4;36) higher in pre-HDF compared to post-HDF. However, ambulatory BP measurements ( $n = 11$  pairs) and nocturnal dipping (MAP) did not differ between two modalities [9.1% (6.1;22.8) in pre-HDF vs 16% (-6.2;22) in post-HDF,  $p = 0.95$ ]. The interdialytic weight gain and body composition monitor derived percentage over hydration were also comparable between modalities (0.4% (-6.6;6.2) vs 1.3 % (-4.2;5.0),  $p = 0.72$ ). Dialysate sodium was 137 mmol/L (135;140) in pre-HDF vs 137 mmol/L (135;138) in post-HDF,  $p = 0.32$ . Pre-dialysis plasma sodium [138 mmol/L (136;140) in pre-HDF vs 137 mmol/L (135;139) in post-HDF,  $p = 0.18$ ] and post-dialysis plasma sodium [136 mmol/L (135;136) in pre-HDF vs 135 mmol/L (135;137) in post-HDF,  $p = 0.26$ ] were also did not differ between modalities. Intradialytic symptoms (nausea-vomiting, muscle cramps, abdominal pain, hypotensive episodes, loss of circuit) and post-dialysis recovery time did not differ between modalities.

**Conclusion:** Pre-HDF was associated with higher pre-dialysis systolic and diastolic BP compared to post-HDF with similar dialysate sodium concentrations. Although this cannot be explained by dialysate sodium concentrations alone, it should be kept in mind that sodium exposure is higher in pre-HDF with higher convective volumes and total body sodium may have increased despite constant plasma sodium concentrations. Further studies on sodium mass transfer during dialysis are required to determine the optimal dialysate Na concentration in different HDF modalities.

Fr-3MP 011

HIGH PLASMA LEVELS OF FIBROBLAST GROWTH FACTOR 23 AND LEFT VENTRICULAR HYPERTROPHY ON CHILDREN ON HEMODIALYSIS

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**Background:** Fibroblast growth factor (FGF-23) is a recently identified circulating factor which causes renal phosphate wasting disorders. Mechanism of regulation of FGF-23 secretion is unclear but plasma FGF-23 level may be regulated or affected by serum phosphate levels because of its hypophosphatemic effect. In adults with chronic kidney disease, high plasma level of FGF23 is very variable among hemodialysis patients and has been described as an independent risk factor of left ventricular hypertrophy (LVH). We aimed to describe the pediatric population with high FGF23 levels and its correlation with cardiac function.

**Methods:** We tested the hypothesis that plasma FGF-23 levels may also be increased in hyperphosphatemia in pediatric patients with end-stage renal disease (ESRD) on maintenance hemodialysis. We measured monthly plasma FGF-23 levels in all patients from the pediatric hemodialysis unit of Robert Debré Hospital, Paris France from 2017 to 2022. Echocardiography was performed every 6 months.

**Results:** We included 55 patients with a median age of 12.5 years [6.3 – 15.7]. At initiation of hemodialysis FGF was 923 RU/mL [394 – 1662]. Median follow up was 18 months in hemodialysis [12.7 – 25.5]. Median FGF23 plasma concentration of all patients was 1187 RU/mL [644 – 4024]. Plasma FGF-23 level exhibited significant and positive correlations with phosphate level: 20/55 patients (36%) had high plasma levels of FGF23 ( $\geq 2000$  RU/mL) and a significant association with higher serum phosphate levels (2,18 mmol/L [2 – 2.34] versus 1.60 mmol/L [1.41 – 1.83]) ( $p < 0.001$ ). Furthermore, 6/35 patients (17%) had LVH one year after the initiation of hemodialysis and had a higher FGF23 median concentration (666 RU/mL [246 – 2014] versus 19220 RU/mL [12888 – 44555]) ( $p = 0.03$ )

**Conclusions:** Plasma levels of FGF23  $\geq 2000$  RU/ml was associated with a higher serum phosphate concentration. LVH after one year of hemodialysis was associated with higher plasma concentration of FGF23. FGF-23 levels is also linked to cardiovascular outcomes in pediatric patients. Further studies are required to evaluate whether decreasing FGF-23 levels improves cardiovascular outcomes.

Fr-3MP 012

THE ROLE OF PARK7 IN PERITONEAL DIALYSIS INDUCED PERITONEAL MEMBRANE- AND VASCULAR TRANSFORMATION

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**Aims/Purpose:** Oxidative and carbonyl stress is prevalent in chronic kidney disease (CKD) and is further aggravated in peritoneal dialysis (PD) patients. PD fluids induce major membrane alterations, as hypervascularization, fibrosis, inflammation and vasculopathy. We describe the role of the multifunctional (antioxidant, antiapoptotic and angiogenic) Parkinson Disease Protein 7 (PARK7/DJ-1) in the setting of PD.

**Methods:** Omental arteriolar multiomics datasets from age-matched children (non-CKD, CKD5, low- and high GDP PD, n = 6/group) underwent PARK7-related gene set enrichment analysis (FDR = 0.05). PARK7 was quantified by Western Blot in effluents (n = 8) and by immunohistochemistry in parietal peritoneal tissues of humans (n = 60, 6.4 ± 5.3y) and C57BL/6 mice, treated 7 days with chlorhexidine-digluconate (CG) and PARK7-activator compound-23 (n = 6-8/group). PARK7 activity-dependent cell viability (MTT assay) of endothelial cells (HUVEC), and secreted PARK7 levels of PD fluid treated mesothelial cells (HPMC) was measured in vitro.

**Results:** Arteriolar transcriptome and proteome PARK7-related GO term analysis demonstrated oxidant detoxification-, mitochondria- and apoptosis-related process enrichment in low- and high GDP PD vs. CKD5. Peritoneal arteriolar PARK7 levels were reduced in CKD5 compared to controls, arteriolar and mesothelial PARK7 was twofold increased in children on low GDP PD compared to CKD5, submesothelial abundance twofold with high GDP PD. In low GDP PD submesothelial PARK7 correlated with microvessel density (r = 0.55, p = 0.05), HIF1a and Angpt1 and -2 (ρ = 0.63 p = 0.02, r = 0.91 p < 0.0001, r = 0.60 p = 0.03), but not with VEGF. Endothelial PARK7 abundance correlated inversely with vessel lumen obliteration (r = 0.53, p = 0.06). In CG treated mice doubling of submesothelial thickness was prevented by compound-23 co-treatment. Microvessel density increased in half of the animals treated with compound-23 and in the ones treated with CG, but not further by the combined treatment. In vitro, GDP (methylglyoxal, 3,4-DGE) dose-dependently reduced HUVEC viability, co-incubation with compound-23 partially preserved viability. Low- and high GDP PD fluids dose-dependently increased secreted PARK7 levels of HPMC, while glucose alone did not.

**Conclusion:** Our findings suggest a vascular regulatory function of PARK7, related to oxidant detoxification, mitochondrial function-, and apoptosis-related processes. In parietal peritoneum PARK7 is ubiquitously expressed and regulated by the GDP content of PD fluids. In patients on low GDP PD, PARK7 abundance correlates with VEGF independent, HIF-1a and Angpt1/2 driven angiogenesis and arteriolar lumen narrowing. In vitro, activation of PARK7 preserves endothelial cell viability and in mice prevents CG induced peritoneal fibrosis. PARK7 represents a novel, targetable element of PD membrane- and vascular transformation.

# GUIDELINES SESSION

## Inherited Kidney Disorders WG

Fr-3MO 013

## A PREDICTION MODEL OF KIDNEY SURVIVAL IN PATIENTS WITH AUTOSOMAL RECESSIVE POLYCYSTIC KIDNEY DISEASE (ARPKD) AT THE AGE OF 2 MONTHS

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**Aims/Purpose:** Autosomal recessive polycystic kidney disease (ARPKD) is a rare hepatorenal disease with pronounced phenotypic variability. A subcohort of severely affected neonates and infants likely progresses to end stage kidney disease within early childhood. The aim of this study is to develop and validate a multivariable prediction model for the relative risk of kidney survival in ARPKD patients at the age of two months.

**Methods:** Clinical datasets of 550 ARPKD patients deriving from the international registry study ARegPKD with kidney survival > 2 months were divided into a development and validation set in a ratio of 75:25. Missing values of potential predictors were handled by multiple imputation. Cox regression and random survival forests were used to fit the models. Harrel's c and other concordance measures were used to quantify the performance of the models. Subtypes of genetic variants, radiological findings, patterns of clinical symptoms and markers of kidney function were considered as predictor variables. The selection of the 5 predictors in the final model was based on their performance and clinical considerations. The validation data set was unblinded only after the two final models were chosen and the study protocol was finalized.

**Results:** For both methods the final predictor set encompassed 5 readily-available datapoints. Both models showed very good performance in the validation set (Harrel's c 0.74 for the Cox resp. 0.72 for the RSF model) and were able to divide patients into a group with good and a group with bad kidney survival. Stratification to the low risk cohort nearly excluded events of kidney failure within the first year of life.

**Conclusion:** We developed a predictive model for risk classes of kidney survival for patients with ARPKD that is based on 5 readily-available datapoints and can be applied at the age of 2 months. The model can serve as a basis for the counselling of affected families, for identification of patients that can particularly benefit from new therapeutic options and for stratification of patients by risk profiles within future clinical trials.

FR-3MP 014

MUTATIONS IN SLC34A1/NPT2A AND SLC34A3/NPT2C ARE ASSOCIATED WITH DISTINCT PHENOTYPES

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**Aims/Purpose:** Mutations in the SLC34A1 or SLC34A3 genes encoding the sodium-dependent phosphate cotransporter NPT2a and NPT2c are rare causes of phosphate wasting. Data on clinical phenotypes of mutation carriers are scarce.

**Methods:** We invited ESPN/ERKNet members to provide clinical, biochemical and genetical data of individuals with mutations in SLC34A1 or SLC34A3 via an online questionnaire.

**Results:** Adequate data were available of 141 patients from 17 countries carrying either compound heterozygous/homozygous (comp het/hom) or heterozygous (het) mutations in SLC34A1 (n = 59) or SLC34A3 (n = 82). The median (range) presentation age was 5.6 years (0-68), and age at last visit was 13 years (0.3-70). Leading symptoms at presentation were signs of kidney stones (flank/abdominal pain, vomiting, hematuria) followed by growth failure, rickets and polyuria, predominantly reported in comp het/hom individuals. Polyuria was seen more often in SLC34A1 and rickets in SLC34A3 mutation carriers. Nephrocalcinosis was most frequent in SLC34A1 mutation carriers (comp het/hom: SLC34A1 96%, SLC34A3 72%; het: SLC34A1 61%, SLC34A3 49%, ANOVA p < 0.01), kidney stones were mainly observed in heterozygous SLC34A1 mutation carriers (comp het/hom: SLC34A1 9%, SLC34A3 26%; het: SLC34A1 53%, SLC34A3 28%, ANOVA p < 0.01). Individuals with comp het/hom SLC34A3 mutations showed hypophosphatemia due to renal phosphate wasting associated with elevated alkaline phosphatase (ALP) z-scores and 1,25(OH)2 vitamin D levels, hypercalciuria, and suppressed parathyroid hormone (PTH) levels (p < 0.01 each). Comp het/hom SLC34A1 carriers presented with elevated calcium z-scores which improved during follow-up, in conjunction with elevated 1,25(OH)2 vitamin D levels and calciuria but no renal phosphate wasting. Het SLC34A1/A3 carriers showed similar but less pronounced changes. CKD stages 2-4 were detected in about half of the patients. GFR at last visit was negatively associated with age in SLC34A3 mutation carriers. Phosphate supplementation was given in 50% of individuals (median dosage 21 mg/kg/day, median duration 3 years) leading to non-significant reductions in ALP, 1,25(OH)2 vitamin D and calciuria, and a significant rise in PTH levels, irrespectively of the underlying transporter defect.

**Conclusions:** Biallelic mutations in SLC34A1 and SLC34A3 are associated with nephrocalcinosis, kidney stones, growth failure, rickets and CKD. Biallelic SLC34A1 mutation carriers are more prone to nephrocalcinosis and hypercalcemia, while SLC34A3 mutation carriers present with hypophosphatemic rickets. Phosphate substitution led only to a partial improvement of the laboratory changes in these patients, which can be explained at least in part by the consecutive increase in PTH.

Fr-3MP 015

## RENAL PARAMETERS UNDER BUROSUMAB TREATMENT FOR X- LINKED HYPOPHOSPHATEMIC RICKETS

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**Aims/Purpose:** X-linked hypophosphatemic rickets (XLH), the most common type of hereditary rickets, is caused by uninhibited FGF23 activity, leading to phosphaturia and depressed 1,25 (OH)<sub>2</sub> Vitamin D levels. Conventional treatment with phosphate supplements and active vitamin D has led in the past to hypercalciuria (HC), nephrocalcinosis (NC) and hyperparathyroidism. Burosumab, an anti FGF23 monoclonal antibody is a novel therapy for XLH. The increase in 1,25 (OH)<sub>2</sub> Vitamin D levels with this treatment may result in higher serum calcium, potentially worsening HC and NC. The aim of this study is to evaluate the efficacy of burosumab treatment, while concentrating on potential adverse renal effects, including HC and NC/ nephrolithiasis.

**Methods:** We retrospectively evaluated a cohort of pediatric patients with XLH treated with burosumab (dose adjusted according mainly to serum phosphorus levels) for at least a year, in 3 referral centers. Clinical and biochemical treatment outcomes were regularly followed, including urine calcium excretion and NC severity, the latter assessed using a standardized sonographic scoring (0: no NC, 3: worst NC) (Dick et al, *Pediatr Radiol* 1999).

**Results:** 26 (13 male) children were included at a mean age of  $7.6 \pm 3.9$  years and followed for  $27.5 \pm 9.6$  months. Mean serum phosphorus levels rapidly increased from a baseline of  $2.67 \pm 0.61$  to  $3.57 \pm 0.53$  mg/dL after 3 months ( $p < 0.001$ ) and remained stable thereafter. This was in parallel with a decrease in urinary phosphate loss. Mean serum alkaline phosphatase steadily decreased from mean of  $488.7 \pm 184.4$  IU/L at baseline to  $320 \pm 93$  IU/L at 12 months ( $p < 0.05$ ) and remained stable. Mean 1,25 (OH)<sub>2</sub> Vitamin D levels increased from  $48.4 \pm 14.2$  pg/mL at baseline to  $56.7 \pm 20.1$  at 24 months (NS). Hyperparathyroidism significantly improved within normal levels. Urinary calcium to creatinine levels were followed regularly (mean sample number:  $7.5 \pm 2.4$  per patient). HC (UCA/ Creat  $> 0.2$  mg/mg) which was found in 2/26 (7.7%) patients before burosumab start, resolved in one patients and persisted, albeit improved, in the second. Two new cases of HC were diagnosed after 15 and 3 months of therapy, and it was mild in the first ( $0.26 \pm 0.05$  mg/mg), and significant in the second patient ( $0.5 \pm 0.17$  mg/mg), in whom it persisted in spite of dose reduction attempts. Seven patients had NC at baseline (grade 1: 3; grade 2: 2; grade 3: 2 patients), none had deterioration or developed new NC.

**Conclusion:** Under burosumab treatment a minority of patients developed new onset HC, but with careful monitoring [including phosphate and 1,25 (OH)<sub>2</sub> Vitamin D levels] and dose adjustment there is no worsening in preexisting NC.

Fr-3MP 016

X-LINKED HYPOPHOSPHATEMIA: THE VALUE OF FEEDBACK FOCUS GROUPS TO ASSESS PATIENT AND CAREGIVER NEEDS

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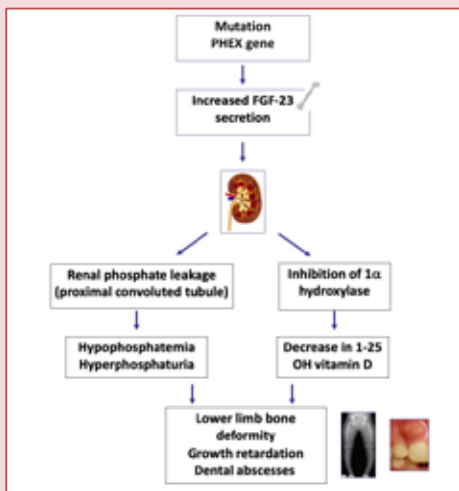
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**Background:** X-linked hypophosphatemia (XLH) is a multi-systemic disease requiring a multi-disciplinary approach. A specific antiFGF23 antibody was recently approved, thus modifying the management. We aimed to create a dedicated therapeutic education programme for XLH patients.

**Methods:** A literature search found no specific action in XLH, neither for the patients' specific needs nor for the methodology of patients' evaluation of needs. Thus, to identify the specific needs of XLH patients and their caregivers, and to understand the burden of XLH in daily life, we organised focus groups during a "XLH day" in our reference centre for rare diseases of calcium and phosphate metabolism.

**Results:** Three focus groups were organised, one for XLH children (n = 5), one for XLH adults (n = 10) and one for caregivers (parents or partner, n = 6). Each group was led by a person trained in therapeutic education (nurse, paediatric nephrologist) with another healthcare provider specialised in XLH (rheumatologist, or nephrologist). One additional person with specific XLH knowledge (clinical research associate or paediatric resident) took minutes. The duration of each session was 1.5 hours; XLH patients/caregivers were asked to answer age-adapted "open questions" on their daily life and quality of life. Used tools were paperboards and post-its. At the end of the three groups run in parallel, a global restitution was made at the end of the XLH day. Major needs were identified: knowledge of XLH, dental care and adapted physical activity, with additional questions on pain management, socio-professional adaptations and financial support in adults. Partner patients were also identified to co-build the support programme.

**Conclusion:** Assessing needs in XLH patients and caregivers using focus groups is a crucial preliminary step to target relevant issues to build a dedicated support program.



Pathophysiology of XLH.

Time	Topic / Speaker
9:30	Café et mail d'accueil, Pr Justine BACCHETTA & Dr Aurélia BERTHOLET-THOMAS
10:00	Le point de vue des orthopédistes, Dr Alice FASSER
10:30	Le point de vue du dentiste, Dr Malina TRIVICHON-FRANCE
11:00	Travaux chez l'adulte, Dr Sandrine LEMOINE & Dr Emmanuelle VIGNOT
11:30	Actualités sur le XLH, Pr Justine BACCHETTA
12:00	Le point de vue des neurobiologistes, Pr Federico DI ROCCO
12:30	Buffet convivial
13:00	Focus groupes - évaluation des besoins des patients et familles pour la construction d'un programme d'éducation thérapeutique - Modérateurs : Mélanie ROMIER & Sandrine LEMOINE - Facilitateurs : Emmanuelle VIGNOT & Sandrine JUILLARD - Modérateurs : Aurélia BERTHOLET-THOMAS & Anne JOURNOT
13:30	Activité physique adaptée, Morgane COSTALIER
14:00	Point diabétique, Charlotte GARNIER et Corélie NAUD
14:30	Conclusion de la journée

« XLH day »



Design and results



Fr-3MP 017

## THE ROLE OF MFSD12 TO CONTROL LYSOSOMAL CYSTINE LEVELS IN CYSTINOSIS

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**Aims/Purpose:** Cystinosis is caused by mutations in the CTNS gene, leading to multi-organ cystine accumulation due to the absence of a functional cystinosin. The kidneys are the first and the most severely affected organs, presenting with glomerular and proximal tubular dysfunction. The therapeutic standard, cysteamine, reduces cellular cystine levels, but does not restore kidney function and has many side effects. MFSD12 is a lysosomal cysteine transporter shown to regulate cellular cystine levels (Adelmann et al. 2020). Our aim was to investigate the role of MFSD12 in the cystinosis phenotype and the potential of its manipulation to decrease cystine levels in cystinotic proximal tubular epithelial cells (PTECs) and *ctns*<sup>-/-</sup> zebrafish.

**Methods:** Urine derived PTECs from cystinosis patients with different mutations in the CTNS gene, were evaluated for MFSD12 expression by qPCR. Next, MFSD12 was knocked out by CRISPR Cas9 gene editing in patient derived PTECs (homozygous 57kb deletion - CTNS<sup>patient</sup>) and CTNS<sup>-/-</sup> PTECs, previously made by CRISPR Cas9 (Jamalpoor et al., 2020). Knockout was done by transduction with a lentiviral delivery system (stable Cas9-sgRNA expression) or protein transduction with a Cas9-sgRNA carrying virus-like particle (VLP). MFSD12 expression and cystine levels were evaluated. Additionally, we evaluated cystine levels in a *ctns*<sup>-/-</sup> zebrafish model after *mfSD12a* morpholino injection at the one-cell stage.

**Results:** MFSD12 expression in patient derived PTECs showed no significant difference across the mutational spectrum that was assessed, when compared with control cells. Furthermore, MFSD12<sup>-/-</sup> CTNS<sup>patient</sup> and MFSD12<sup>-/-</sup> CTNS<sup>-/-</sup> PTECs were generated. In the lentiviral models, a ~76% decrease in MFSD12 mRNA was observed, as compared with ~68% in Cas9-VLP models. Cystine levels were significantly reduced in both MFSD12<sup>-/-</sup> models. Next, *ctns*<sup>-/-</sup> zebrafish were injected with *mfSD12a* translation blocking morpholino's to inhibit the translation of the MFSD12 zebrafish orthologue. These experiments are still ongoing, but pilot data already show a 2.5x decrease in cystine levels.

**Conclusion:** This study shows that cystinosis patient PTECs have comparable MFSD12 expression levels to healthy individuals. Furthermore, we show that knocking out MFSD12 gene expression reduces cystine levels in cystinotic PTECs. These results show that inactivation of MFSD12 impairs cysteine import and should be further explored as potential target for cystinosis treatment.

Fr-3MP 018  
ECVSCO: A EUROPEAN COHORT DEDICATED TO CYSTINOSIS

Aude Servais<sup>1</sup>, Gueguen Sonia<sup>2</sup>, Greco Marcella<sup>3</sup>, Elena Levchenko<sup>4</sup>, Gema Ariceta<sup>5</sup>, Julien Hogan<sup>6</sup>, Aurélie Bertholet-Thomas<sup>7</sup>, Robert Novo<sup>8</sup>, Lemoine Sandrine<sup>9</sup>, Kormann Raphael<sup>10</sup>, Katharina Hohenfellner<sup>11</sup>, Arshad Sulaiman<sup>1</sup>, Amselem Serge<sup>12</sup>, Niaudet Patrick<sup>13</sup>, RaDiCo Team<sup>12</sup>

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**Aims:** Cystinosis is a rare multisystem lysosomal storage disease due to variants in the CTNS gene, coding for cystinosine, a lysosome membrane transporter causing cystine accumulation. Specific treatment by cysteamine decreases renal and extrarenal complications frequency. The aim of this project is to describe the natural history of the disease and long-term clinical manifestations.

**Methods:** We set up a European, multi-centre, longitudinal, non-interventional cohort, ECVSCO, that uses observational study methods. 243 patients with a confirmed diagnosis of cystinosis and followed in 25 French and 5 European centers were included. Data are collected on the secure RaDiCo platform, via an e-CRF (REDCap).

**Results:** Data from 180 patients (50.0% male) were analyzed. Median age at diagnosis was 1.3 years [IQ 0.8; 1.9], with earlier diagnosis since the 1980s, but no further improvement in the 2000s. Genetic analysis was available for 174 patients: 57 (32.8%) presented with homozygous 57kb deletion in the CTNS gene, 71 (40.8%) with heterozygous 57 kb deletion associated with another variant and 46 (26.4%) with other variants. The type of variant had no impact on the age at diagnosis. Median age at cysteamine start was 1.6 years (IQ 1.0–3.0). An improvement on age at treatment start was observed after the 1990s. All but 6 patients were treated with cysteamine. 71 patients received immediate release formulation (Cystagon<sup>®</sup>) and 103 received extended release formulation (Procysbi<sup>®</sup>). Median white blood cell cystine level was correct at 1.2 nmol ½ cystine/mg protein (IQ 0.59; 2.20). The median duration of treatment was 21.5 years [IQ 11.7; 31.1]. 167 (95.9%) patients also received cysteamine ocular gel, Cystadrops<sup>®</sup>. Median age at inclusion was 19.08 years (IQ 10.43; 31.41). At that time, 104 patients (57.8%) had reached end-stage renal disease (ESRD). There was no impact of genotype on age at ESRD. Median age at ESRD was 12.9 years [IQ 9.9; 18.0]. A 5-year gain in renal survival was observed after the 1990s. 102 patients (56.7%) received a kidney transplant. Among these transplanted patients: 76 (74.5%) received 1 transplant, 23 (22.5%) received 2 consecutive transplants, and 3 (2.9%) received 3. Median eGFR in the remaining patients was 58.9 ml/min [IQ 40.4; 82.2]. Extrarenal manifestations included hypothyroidism in 61 (33.9%) patients, diabetes mellitus in 11 (6.1%), skeletal manifestations in 73 (40.5%), myopathy in 32 (17.8%), and neurological disorders in 22 (12.2%). At inclusion, 36 patients had no ESRD and no extra-renal complication.

**Conclusion:** Cystinosis is a good example of a pediatric disease with multiorgan involvement extending into adult care. More than half of patients are adults and have reached ESRD even if age at renal replacement therapy start has increased. The high frequency of extra-renal manifestations demonstrates the importance of a multidisciplinary follow up of these patients.

Fr-3MP 019

KIDNEY HEALTH IN CHILDREN WITH X-LINKED HYPOPHOSPHATEMIA: A REAL-WORLD STUDY IN GERMANY AND SWITZERLAND

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**Aims/Purpose:** X-linked hypophosphatemia (XLH) is the most frequent hereditary cause of hypophosphatemic rickets. Mutations in the PHEX gene result in elevated circulating levels of fibroblast growth factor 23 (FGF23), consecutive renal phosphate wasting and rickets. Treatment with phosphate salts and active vitamin D (conventional treatment) is associated with nephrocalcinosis in XLH patients and chronic high intake of inorganic phosphate induces proximal tubular injury in mice. Detailed analysis on kidney health and its contributing factors in XLH patients are lacking.

**Methods:** We started a prospective observational multicenter study in Germany and Switzerland to investigate the long-term outcome and its contributing factors in children with XLH treated with conventional therapy or burosumab, a fully humanized anti-FGF23 antibody. Detailed clinical and biochemical data as well as urine samples are annually obtained to assess lithogenic substances and biomarkers for kidney health and their associations e.g. with estimated glomerular filtration rate (eGFR) and nephrocalcinosis.

**Results:** Currently, 103 patients (62 girls, mean age 13 years) from 32 centers are included in the study. 14% of patients have been treated conventionally for 9.7 years, and 86% of patients have received burosumab for an average of 4.1 years with 4.5 years of conventional therapy beforehand. A reduced eGFR ( $\approx 90$  ml/min/1.73m<sup>2</sup>) and/or nephrocalcinosis was noted in 9% and 29.4% of patients, respectively. Microalbuminuria is twice as prevalent in children with XLH as in healthy children (14% vs 7%). The excretion of lithogenic substances (calcium, oxalate, glycolate) is increased in 1.8-22.8%, and the excretion of citrate is decreased in 12.3% of XLH patients when compared to healthy children. The tubular injury markers neutrophil gelatinase-associated lipocalin (NGAL) and Dickkopf-3 (DKK3) are elevated in urine of children with XLH compared to healthy individuals, and chitinase 3-like 1 (CHI3L1) is comparable to that in children with chronic kidney disease. The renal inflammation marker monocyte chemoattractant protein-1 (MCP-1) is elevated in children with XLH and epidermal growth factor (EGF) preserving the capacity of tubular cells to recover is decreased compared to healthy children. Children with XLH showed increased mean z-scores for systolic blood pressure and body mass index (BMI), but blood pressure values were not associated with BMI z-scores.

**Conclusion:** In this real-world study, children with XLH present with considerable renal comorbidity including reduced eGFR, nephrocalcinosis, elevated urinary lithogenic substances, and increased urinary kidney injury markers as well as elevated blood pressure independent of BMI. The relative contributions of conventional and burosumab treatment needs to be clarified.

Fr-3MP 020

## OXALOSIS AROUND THE WORLD: INSIGHT IN THE GLOBAL HEALTH SITUATION FOR PRIMARY HYPEROXALURIA

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**Aims/Purpose:** Primary hyperoxaluria (PH) is a rare metabolic disorder with significant morbidity and mortality if left untreated. Over the last years, the management of PH has been dramatically modified in countries having access to RNA interfering therapies. Thus, an update in the global health situation for patients with primary hyperoxalurias was preferred to highlight persistent territorial disparities and to provide health care providers with practical tools when negotiating with private insurances and public health systems. This study aims to evaluate the global health situation of patients with PH, including the access, usage and costs of diagnostic and therapeutic procedures around the world.

**Methods:** A survey is currently being conducted among physicians treating patients with primary hyperoxaluria. The survey was distributed by email via the OxalEurope and pediatric nephrology network. Further distribution of the survey will be conducted via additional networks, including the ESPN. The survey consists of 55 questions in 8 sections including personal and PH population demographics, access to diagnostic assessments and therapeutics, RNA interfering therapies, dialysis and transplantation strategies, follow-up care, national healthcare systems, and costs. The survey opened 7-3-2023 and will close on 22-5-2023. Descriptive statistics will be used to summarize differences between countries, analyzed using the latest version of SPSS and R studio. Data will be visualized using world maps and histograms.

**Results:** Over 45 responses have been obtained, indicating significant differences in available treatment options among different countries around the world. The final results of the study will be presented at the congress.

**Conclusion:** We expect the results of this study to provide insight into the current global health situation of patients with primary hyperoxaluria, highlighting significant disparities in accessibility of diagnostics and treatment options between countries. These results may provide support for global initiatives to improve management of PH patients worldwide and provide useful insights for negotiations with private insurances and public health systems regarding new therapeutics.

Fr-3MP 021

**METABOLIC REPROGRAMMING IN TUBEROUS SCLEROSIS COMPLEX CYSTIC KIDNEY DISEASE**

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**Aims/Purpose:** Kidney disease affects most patients with tuberous sclerosis complex disease (TSC) and is a leading cause of death in adulthood. Mutations in either *Tsc1* or *Tsc2* induce mTOR activation in TSC, resulting in cell growth and tumorigenesis as renal angiomyolipoma and cystic disease. However, the exact mechanisms leading to cyst formation remain poorly understood. Metabolic reprogramming is an important mechanism by which cells promote proliferation and cell growth. Here we aimed to analyze the metabolic reprogramming in TSC-associated kidney disease.

**Methods:** *Six2* Cre<sup>+</sup>/tg *Tsc1*<sup>-/-</sup> and control offspring, treated with either vehicle or rapamycin, were dissected, and kidneys were excised for metabolite extraction and analyzed by liquid chromatography/inline tandem mass spectrometry. Kidneys were also used for histology, RNA/protein extraction, and immunofluorescence.

**Results:** Whole kidney metabolome and PTCs extracted metabolome analysis from TSC mice showed significant perturbation in the arginine biosynthesis pathway. These changes were associated with increased urea cycle metabolites and the rate-limiting enzyme Argininosuccinate Synthase 1 (ASS1) expression levels. High ASS1 expression was demonstrated in kidney lysates of TSC mice compared to control mice, and ASS1 was specifically localized in cyst lining cells in the TSC kidney. Knockdown of *Tsc1* in the HK2 cell line emphasized the contribution of the *Tsc1*-mTORC1 pathway to ASS1 expression. Arginine depletion *in vivo* and *in vitro* reduced the mTOR signaling pathway, cell proliferation, and cystic kidney load.

**Conclusion:** We show that TSC kidneys exhibit a major shift in their metabolic state, associated with different metabolic pathways, mainly the arginine biosynthesis pathway. We show that dysregulated mTOR pathway in TSC PTCs induces the arginine biosynthesis pathway by over-expression of ASS1 to support the high arginine demand in PTCs. Arginine depletion ameliorates the PTCs cell signaling and cell proliferation which are major contributors to cyst development in TSC, with the potential for immediate translational and clinical impact.

Fr-3MP 022

**AORTIC DILATATION IN CHILDREN AND YOUNG PEOPLE WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE – THE ROOT CAUSE ANALYSIS STUDY**

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**Aims/Purpose:** Aortic dilatation has not been evaluated systematically in children and young people (CYP) with autosomal dominant polycystic kidney disease (ADPKD). Our objective were to (i) measure the size of the aortic root and ascending aorta; and (ii) report the prevalence, severity and determinants of aortic dilatation and compare with children without ADPKD.

**Methods:** Single centre, cross-sectional review of echocardiograms performed on CYP within a dedicated paediatric ADPKD clinic. Echocardiograms were evaluated for the presence of dilatation of the aorta at four standardised locations: the aortic valve annulus, Sinuses of Valsalva (SoV), sinotubular junction (STJ) and the ascending aorta. Dilatation was defined by a z score  $\geq 2$  ( $\approx$  99th percentile) standard deviations from the mean. None of the children were receiving anti-hypertensive medications.

**Results:** Ninety seven CYP with ADPKD, median age [IQR] of 9.3 [6.1, 13.6] years were analysed and compared with 19 normotensive controls without ADPKD. The prevalence of dilatation ranged from 5.2-17% in CYP with ADPKD, depending on anatomical location. There was no dilatation of the aortic root or the ascending aorta identified in the control group. In multivariable regression, aortic root dilatation was strongly and positively associated with cyst burden at the aortic valve annulus and SoV ( $\beta = 0.42$  and  $\beta = 0.39$ , both  $p < 0.001$ ), with age at SoV ( $\beta = -0.26$ ,  $p = 0.02$ ), SBP z-score at SoV ( $\beta = -0.20$ ,  $p = 0.04$ ) and left ventricular mass index at SoV and STJ ( $\beta = 0.24$ ,  $p = 0.02$  and  $\beta = 0.25$ ,  $p = 0.03$  respectively) following adjustment for age, sex, BMI z-score, eGFR, SBP z-score and left ventricular mass index). See Figure 1.

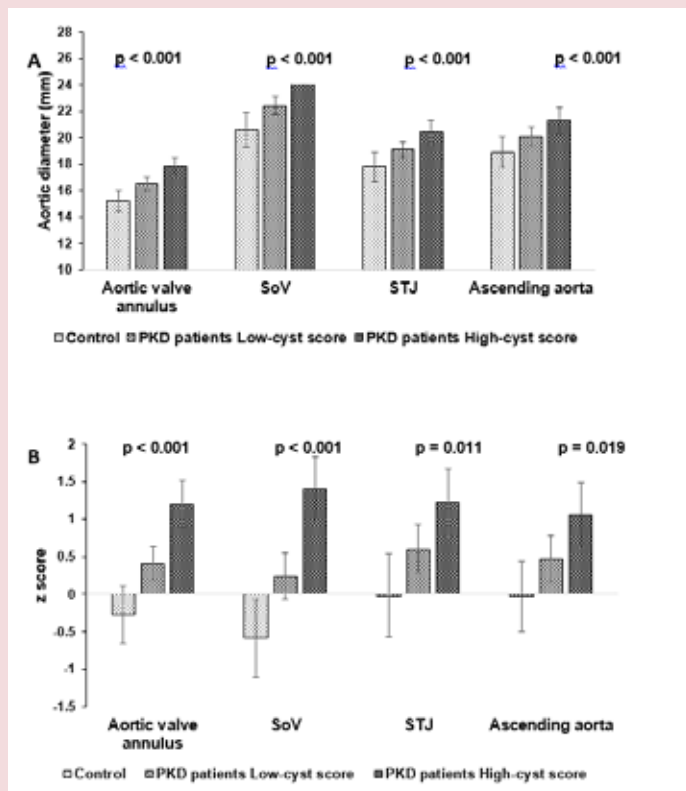


Figure 1: Aortic diameters in mm and as z-scores in 97 children and young people with ADPKD stratified by cyst burden and compared with healthy controls. Data shown as marginal means after adjustment for age, sex and SBP z-score. Error bars represent 95% confidence interval. Panel A: aortic diameters in mm; Panel B aortic diameter z-scores. P values refer to difference between groups assessed by analysis of variance.

**Conclusion:** Our data suggests increased prevalence of aortic root and ascending aortic dilatation in CYP with ADPKD when compared with healthy controls. Further studies are needed to understand the pathogenesis of this dilatation and its contribution to the unacceptably high cardiovascular morbidity in individuals with ADPKD.

Fr-3MP 023

SYSTEMIC OXALOSIS: AN OVERVIEW OF THE FINDINGS AND PREVALENCE IN PRIMARY HYPEROXALURIA

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**Aims/Purpose:** Systemic oxalosis is a severe co-morbidity that may arise in patients with primary hyperoxaluria type 1 (PH1). It is caused by precipitation of calcium oxalate crystals in organs besides the kidneys as a result of high endogenous oxalate production. In this study, we aimed to provide an overview of the prevalence, features, screening modalities and factors that play a role in developing systemic oxalosis as cohort studies are currently lacking.

**Methods:** A retrospective registry study was conducted using data from the OxalEurope registry, one of the largest registries of patients with PH1. All patients with primary hyperoxaluria and data on systemic oxalosis were identified. Data was analyzed using descriptive statistics, Chi-square tests, Mann-Whitney U tests and Kaplan Meier analyses.

**Results:** A total of 159 out of 291 (55%) screened PH1 patients were diagnosed with systemic oxalosis. In addition, 110 patients were recorded having no signs of systemic oxalosis at follow-up, however screening was not performed. Sixty-two patients had already developed systemic oxalosis at moment of diagnosis and systemic oxalosis was most often found in patients with ESKD (95%). The eyes, bones and heart are most frequently affected, nevertheless deposits occurred in many organs, as shown by obduction. Fundus photography (n = 16), X-ray (n = 43), and echocardiography (n = 59) are the modalities used most often to screen respectively the eyes, bones and heart. Patients who developed systemic oxalosis had significantly higher upper plasma oxalate levels (median 22 versus 175  $\mu\text{mol/L}$ ,  $p = 0.001$ ). Furthermore, patients with systemic oxalosis had a significant higher mortality rate compared to patients without systemic oxalosis (48 out of 142 versus 10 out of 212,  $p < 0.001$ ), which difference persisted after correcting for ESKD ( $p = 0.001$ ). Kaplan Meier analysis (Figure 1) showed that pediatric patients with ESKD tended to developed systemic oxalosis more frequently than adults ( $p = 0.001$ ).

**Conclusion:** This is the first research to systematically study and report systemic oxalosis in patients with primary hyperoxaluria type 1. Systemic oxalosis is prevalent among PH1 patients, especially when ESKD is present, and may lead to significant morbidity and mortality. Patients with systemic oxalosis have a higher mortality rate and pediatric patients may develop systemic oxalosis more frequently than adults. Given the high incidence and possible implications, we would like to make an appeal on screening all patients with systemic oxalosis. Future research should focus on reliable screening modalities for early signs of systemic oxalosis.

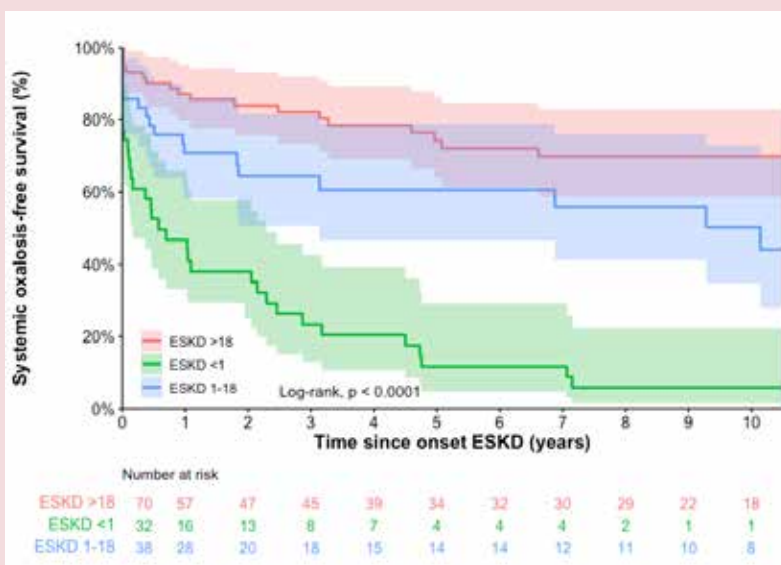


Figure 1: Kaplan Meier analysis of systemic-oxalosis free survival in patients with primary hyperoxaluria, stratified by age at onset of end-stage kidney disease (ESKD).

Fr-3MP 024

EARLY GENETIC TESTING OF CHILDREN WITH PERSISTENT HAEMATURIA ALLOWS A PRECISION MEDICINE APPROACH TO ALTER DISEASE TRAJECTORY

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**Aims/Purpose:** The differential diagnoses of persistent microscopic haematuria (MH) in childhood are broad. Our study examined the role of MH combined with genotype phenotype correlation in identifying of children at risk of end stage renal failure (ESRF) as a result of progressive inherited glomerulopathy, which may have variable age-dependent penetrance such as Alport's.

**Methods:** MH cases referred to Paediatric Nephrology who underwent genetic screening for inherited glomerulopathy between 2014–2022, were identified by retrospective analysis of electronic patient records. Analysis examined results of next generation sequencing of the COL4A3/4/5/6 /NPHS2 genes together with deep phenotyping based on clinical presentation, blood, radiological, urine investigations and renal biopsy correlated with kidney disease progression. Statistical analysis was performed using a Chi-squared test.

**Results:** 132 children (78 male, 54 female) median referral at 9.2 yrs (range 0–17 yrs) were studied. Median duration of follow up was 3.3yrs (range 0.2–12.2 yrs). Hypertension or significant renal dysfunction were rare. Pathogenic mutations primarily in COL4A genes were identified in 31% (41/132). Phenotypic analysis identified Alport's syndrome in 39% (16/41) with 9 X-linked. 59% (24/41) were Alport's carriers with 21% (5) of these X-linked. One pathogenic NPHS2 mutation was identified. Variants of unknown significance (VUS) were identified in 17 cases. 50% (18/36) cases that underwent renal biopsy had thin basement membrane disease (TBMN) with no identifiable COL4A mutation in seven. Diagnostic yield from other investigations was achieved in only 6 patients (4.5%). 78 children had a positive family history (FH) of kidney disease in which 44% had an identifiable genetic cause compared with 19.4% of children without a FH, which was statistically significant ( $p < 0.001$ ). 50% (24/48) cases with genetic/histological evidence of basement membrane abnormality exhibited MH and proteinuria at referral, and 2 developed this as a new symptom. Progression of proteinuria (new development of proteinuria during follow-up  $\pm$  ACEI start) was significantly greater in this group ( $p < 0.001$ ). 17/48 (35%) were commenced on ACEI (median 1.2 years after referral (range 0.00–9.30 yrs).

**Conclusion:** We present the largest single centre retrospective review of genetic testing in children with MH to date and provide evidence that genetic testing even if delayed, is superior to routine clinical investigations and a powerful adjunct. Significant numbers required introduction of ACEI for proteinuria management. We propose that timely genetic testing, particularly if a FH is present, may obviate the need for biopsy and more precisely identify the correct diagnosis, allowing appropriate interventions in line with a precision medicine approach.



# GUIDELINES SESSION

## Dialysis WG

Fr-3MP 0025

**THE PAEDIATRIC INTEGRATED CARE INDEX: A TOOL FOR ASSESSING AND INCORPORATING COMPLEX CARE NEEDS IN HEALTHCARE PROVISION TO CHILDREN ON PERITONEAL DIALYSIS**

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**Aims/Purpose:** Having a child on peritoneal dialysis (PD) places families and care givers under considerable strain. As healthcare providers, it can be difficult to provide equitable care without a clear understanding of their needs. Even where a family with a child on PD is recognized to be struggling, it can be challenging to provide a nuanced approach to their care to optimize outcomes, in the context of limited healthcare resources. This study aims to stratify PD patients according to complexity of their needs, in order to more effectively allocate resources where needed.

**Methods:** A cross sectional study involving 15 PD children managed by the multidisciplinary PD team in a tertiary children's hospital. The 'Paediatric Integrated Care Index (PICI) questionnaire' was used to measure complexity of patient care needs and was completed by the clinical team caring for them. It consists of five domains, each with 5 questions rated from 0-2, with higher scores indicating greater complexity. These domains relate to demographics; home care; medical complexity; functional status & psychosocial complexity. Complexity was considered low if they scored 0-16, moderate if between 17-33 and high from 34-50. Data analysis was performed using descriptive statistics.

**Results:** Median score was 11 (range 4-21). 14/15 (93.3%) scored less than 16 (low on PICI score) and one (6.6%) scored 21 (moderate). The most significant factors to score highly were non-routine interventions (surgeries, medication adjustments etc) in the medical complexity domain, followed by perception of caregiver stress related to child's needs in the psychosocial complexity domain. The most significant domain was psychosocial complexity and least significant the functional status domain. Three children (20%) known for non-adherence, achieved a score of complexity above the median, the same as those six (40%) with other comorbidities.

**Conclusion:** The PICI survey appears to be a useful exercise for caregivers of PD patients to measure complex domains that may impact care. By considering demonstrated needs, we were able to consider provision of a more personalized approach for equity of care. The psychosocial domain, more than the others, suggested further interventions were required, such as increased involvement of the psychosocial team, to better assist families in their coping strategies, to reduce caregiver stress. Despite considerable resource utilization, none of the cases analyzed reached a high level of complexity. Children with comorbid conditions and those who are non-adherent demonstrate increased support needs. This tool adopts a holistic and structured approach in assessing domains that may impact on ability to manage PD, that can be used to optimize the delivery of effective, tailored high-quality care. The PICI scoring should be evolved to also incorporate patient and caregiver perceptions.

Fr-3MP 026

## ANTIBIOTIC PROPHYLAXIS AT THE TIME OF THE PERITONEAL DIALYSIS CATHETER INSERTION

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**Aims/Purpose:** The use of Antibiotic prophylaxis at the time of peritoneal dialysis (PD) catheter insertion is not a well-studied topic. The ISPD guidelines recommend that systemic prophylactic antibiotics should be administered immediately prior to catheter insertion. Our literature review found only a handful of randomised trials in adults that suggest a reduction in early peritonitis rates with antibiotic prophylaxis versus no treatment. Without high-quality research there is no clear directive on the choice of antibiotics or duration of treatment, and there are wide variations in practice. There is also no data in children, in whom the risk of peritonitis at the time of PD catheter insertion can be higher.

**Methods:** We distributed a survey to all renal centers across the UK and members of the European Society for Paediatric Nephrology Dialysis working group investigating the current practice of antibiotic and antifungal prophylaxis at the time of PD catheter placement.

**Results:** 35 centres responded to the survey and all of these use antibiotic prophylaxis. 32.4% of centres use antibiotics based on local sensitivities whilst the others use broad spectrum antibiotics. 21/35 (60%) use only one antibiotic whilst others use a combination protocol. With the exception on one centre, the antibiotic regimens selected offer a degree of both gram-negative and gram-positive cover. 26/35 (74.3%) centers prescribe a STAT dose of antibiotic prior to insertion while 9/35 (25.7%) use a longer course ranging from 24 hours to 7 days of antibiotics post catheter insertion. 88% give the first antibiotic IV but 12% of centers use intraperitoneal antibiotics. 96.2% of centers do not use anti-fungals. Across the centers the rate of early peritonitis (defined as peritonitis within 4 weeks of PD catheter insertion) varied: 7 centers estimate 1 case, 2 centers estimated 2 cases and 2 centers estimated 2-4 cases of early peritonitis over a 12-month period.

**Conclusion:** Our data highlight significant variations in antibiotic choice, route, and duration. There is a need for rationalising antibiotic use and standardisation of practise. The next step will be to develop clinical practice recommendations on antibiotic prophylaxis at the time of PD catheter insertion based on local sensitivities and through collaboration with pediatric nephrologists, dialysis nurses, microbiologists, and pharmacists.

Fr-3MP 027

ACUTE AMINOGLYCOSIDE OVERDOSE: MANAGEMENT AND RISKS

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**Aims/Purpose:** Aminoglycosides have a narrow therapeutic range and therapeutic drug monitoring (TDM) is widely used to prevent nephro- and ototoxicity during prolonged therapy. However, the management and risks of an acute overdose of aminoglycosides are less well-known. We describe the case of a young child who received an amikacin overdose together with an overview of management strategies and toxicity risks, based on a literature review.

**Methods:** A systematic literature search for cases of acute aminoglycoside overdoses was performed in PubMed and Embase.

**Results:** Case. An amikacin dose of 125 mg/kg (recommended dose: 15 mg/kg q24h) was accidentally administered to a girl of five months old with pyelonephritis and normal renal function. On the advice of the Belgian Poison Center and the pediatric nephrologists, she was started on intermittent hemodialysis. Hemodialysis was initiated seven hours after administration and continued for four hours until subtherapeutic trough plasma levels were reached. Amikacin levels showed a rapid decline before the start of (half life: 1.6 h) and during (half life: 1 h) hemodialysis. No toxic effects were observed during follow-up. Literature review. 22 cases on acute aminoglycoside overdoses have been published. Most cases involve children (15), the majority being neonates (10). Various treatment strategies have been applied: supportive therapy (intravenous hydration, monitoring of the vital signs and renal function, and aminoglycoside TDM), hemodialysis, peritoneal dialysis, and exchange transfusion. From these interventions, intermittent hemodialysis is most effective at removing aminoglycosides from the body. Nine out of the 22 patients (40%) experienced nephro-, oto- and/or neurotoxic effects. These patients included three adults with severe renal or hepatic impairment and four neonates. The incidence of toxicity did not differ between patients on supportive therapy and those treated with hemodialysis.

**Conclusion:** Because of their low molecular mass, small volume of distribution, and low protein binding, aminoglycosides are efficiently removed from the body by extracorporeal treatments. However, scientific evidence on the added value of hemodialysis above supportive therapy for acute aminoglycoside overdoses is scarce and mainly based on expert opinion, except in patients with pre-existing renal impairment. When hemodialysis is preferred, it is advisable to start as fast as possible with high-flux intermittent hemodialysis. The risk of toxicity from an acute overdose appears to be low in patients without comorbidities and a normal renal clearance.

Fr-3MP 028

USING HOMEMADE PERITONEAL DIALYSIS FLUIDS ALLOWS SAVING LIVES OF CHILDREN WITH SEVERE ACUTE KIDNEY INJURY IN A LIMITED-RESOURCE SETTING

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**Aims/purpose:** Peritoneal dialysis (PD) is the easiest kidney replacement therapy (KRT) modality to use in children for the treatment of acute kidney injury (AKI) in a limited- resource setting. However, access to this treatment is very limited due to many barriers including the high cost of commercially prepared PD fluids. This study aimed to describe the 5-year experience of the first pediatric acute peritoneal dialysis program using locally prepared fluids in the Democratic Republic of Congo (DRC).

**Methods:** This is a retrospective review of epidemiology, clinical features and outcomes of children admitted and treated for AKI from January 2018 to February 2023 at the University Hospital of Kinshasa, the DRC. PD catheters were inserted manually at the bedside by a trained physician and PD fluids were prepared locally by adding 50% dextrose to lactated ringer's solution following ISPD guidelines.

**Results:** A total of 305 children (175 boys and 130 girls) were admitted and treated for AKI. The median age was 7 years (1.5 months – 16 years). The leading causes of AKI were severe malaria (148/305; 48.5%), sepsis (62/305; 20.3%) and HUS (48/305; 15.7%). Dialysis was indicated in 218 of 305 children (71.5%) and PD was performed in 205/218 (94.0%). The main indications for starting PD were uremia mostly associated with encephalopathy (181/218; 83.0%) and prolonged anuria (111/218; 50.9%). PD catheters used were Romsons (156/205; 76.1%), Tenckhoff (32/205; 15.6%) and nasogastric tubes 17/205 (8.3%). Catheter obstruction and peritonitis were observed in 54/205 (26.3%) and 29/205 (14.1%), respectively. Catheter obstruction was encountered at a much lower rate with Tenckhoff (3/32; 9.4%) compared to Romsons (43/156; 27.6%) (OR 0.27, 95CI 0.08–0.94, p = 0.039). As for peritonitis, it was found in a higher proportion with Romsons (27/156; 17.3%) compared with Tenckhoff (2/32; 6.3%), although this trend was not statistically significant (p = 0.062). The median duration of PD was 6 days (1–20 days). Overall survival was 75.1% of patients (154/205) and the mortality was 24.9% (51/205), mainly due to late transfer.

**Conclusion:** This first PD program has significantly improved the outcome of children with AKI in a setting where most would die without access to PD. In addition, the results showed that locally prepared fluids associated with bedside PD catheter insertion can be used safely in a limited-resource setting and effectively save the lives of many children presenting with severe AKI.

Fr-3MP 029

**SERUM METABOLIC PROFILE IS ASSOCIATED WITH PERITONEAL DIALYSIS VINTAGE AND PERITONITS EPISODES IN PEDIATRIC POPULATION: PRELIMINARY RESULTS OF A PERSPECTIVE STUDY**

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**Aims/Purpose:** Peritoneal dialysis (PD) is a main renal replacement treatment for children and adolescents with end stage kidney disease (ESKD). Peritoneal fibrosis is a major complication in long-term PD patients. PD vintage and peritonitis episodes are known to increase the risk of developing peritoneal fibrosis. Aim of the present study is to record the serum metabolic profile of PD patients in relation to peritonitis episodes.

**Methods:** Serum samples from 15 patients undergoing PD were analyzed. Patients were divided into subgroups, based on PD duration (3 groups, first:  $\leq$  1 year on PD, second: 1-5 years on PD, and third:  $>$  5 years on PD) and peritonitis episodes (3 groups, first: no episodes, second: 1-2 episodes and third:  $\geq$  3 episodes). Regarding metabolic technologies used, two targeted Liquid Chromatography - Mass Spectrometer (LC-MS) methodologies were used for the determination of 107 metabolites, in total. All samples were analyzed by a hydrophilic interaction LC coupled to MS (HILIC-MS / MS) method previously developed and validated in our laboratory for the simultaneous determination of amino acids and their derivatives in biological fluids. Also, high flow analysis was carried out (LC quadrupole Time-of-Flight analysis - High performance LC / MS).

**Results:** A total of 107 metabolites were identified but only the statistically significant correlations with the highest absolute correlation coefficient are described ( $p < 0.001$ ). Grouping the patients by number of peritonitis episodes cytosine, riboflavin, glutamic acid, methylxantine and malate found to differentiate between the three groups ( $p < 0.05$ ). Regarding the PD vintage B1 sarcosine, succinate and B2-CDP were shown to differ significantly.

**Conclusion:** Known metabolites which are involved in the inflammation process based on the literature, were further investigated in our study and showed a statistically significant difference that further establish their role. Our results are the preliminary results of an ongoing prospective study. Limitation of the study, is the small sample of patients, which does not allow safe clinical interpretation. In any case, metabolomics seems to be a useful tool for the study and identification of biomarkers in patients with ESKD on PD.

Fr-3MP 030

INVESTIGATING CONCORDANCE OF KIDNEY CARE CODING BETWEEN UK RENAL REGISTRY DATA AND HEALTH RECORDS FOR CHILDREN WITH ESTABLISHED KIDNEY FAILURE

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**Purpose:** Electronic health records (EHRs) such as Hospital Episode Statistics (HES) and the Patient Episode Database for Wales (PEDW) are widely used in epidemiological and clinical research and offer an opportunity to investigate rare diseases and their management. To do so however requires an assessment of data quality to ensure research validity. Currently, studies that validate the use of hospital records for chronic kidney disease surveillance are lacking for children. Our aim was to examine the concordance of hospital records with UK Renal Registry (UKRR) data for children receiving kidney replacement therapy (KRT) in England and Wales.

**Methods:** The study population was children aged under 16 years starting KRT between 2000–2020. We compared hospital records to UKRR data ("gold standard") for the timing and detail of key nephrology events including date of first nephrology review, KRT start, transplant and death (where applicable). For key events, the timing of incident codes in HES/PEDW relative to dates in the UKRR dataset were calculated. In addition, we described the presence of lesser stages of CKD coding and their timing relative to the UKRR-defined KRT start date.

**Results:** During the study period, 1976 children (59% male) commenced KRT in England and Wales and had linked HES/PEDW data; 46 patients (2%) did not have linked data available. Generally, there was good agreement between UKRR and HES/PEDW records for key dates relating to KRT start, modality and transplantation. At KRT start, 1530 children commenced dialysis (n = 635 haemodialysis and n = 895 peritoneal dialysis) and 492 (23%) received a pre-emptive transplant; 1386 (91%) and 400 (81%) respectively were coded as such in the EHR. Overall, 72.3% of patients had an initial KRT modality code within 90 days of KRT start, as defined using UKRR data, with the highest proportion of coding in this timeframe noted for transplant recipients (n = 395, 80.3%). Relative to the UKRR record, date of transplant and death in the EHR were highly concordant (91% and 100% coded within a month of UKRR date, respectively) while date of first nephrology review and dialysis start were more variably timed (figure 1). Of those with data, most children had evidence of coding for kidney failure or stage 5 chronic kidney disease in HES/PEDW within a month of KRT start (50%); few children (n = 246) had evidence of lesser CKD stage codes in their hospital record prior to KRT start.

**Conclusion:** EHRs demonstrate reasonable concordance of important dates relating to KRT start, kidney transplantation and death compared to UKRR-held records, however timing of events such as first nephrology review and CKD progression may be less reliable. Data from EHRs have the potential to reliably supplement observational research examining access and outcomes of dialysis and kidney transplantation.

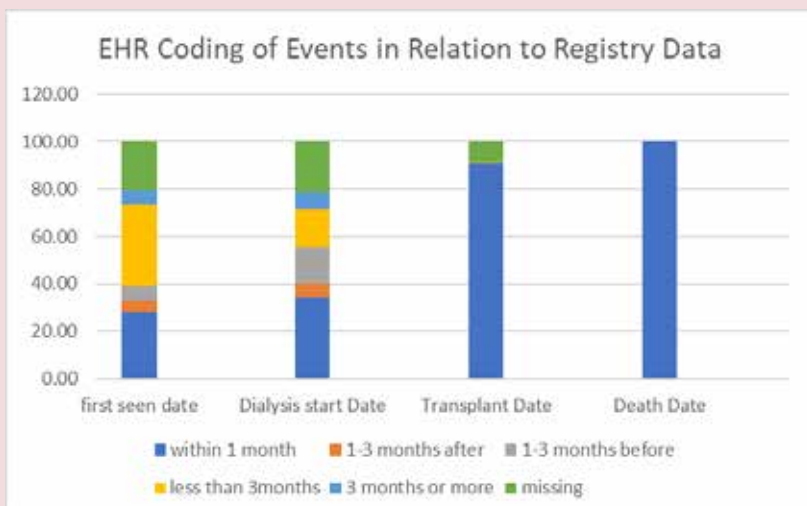


Figure 1: Timing of coding for key events in HES/PEDW relative to dates in the UKRR dataset.

Fr-3MP 031

FRENCH PEDIATRIC NEPHROLOGISTS ARE IN CRISIS: THE CONSEQUENCES OF PARADOXICAL INJUNCTIONS

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**Background:** French pediatrics, whether inside or outside the Public Hospital, is in crisis: lack of beds, transfers of children, degraded procedures, deprogramming of “non-urgent” care, child psychiatry in pain. The “Assises de la Pédiatrie et de la Santé de l’Enfant” were officially launched on 7/12/22 to cover a wide range of subjects allowing for a sustainable evolution of children’s care and health. However, the quality of life at work of pediatricians is not a primary objective of this initiative. We aimed to assess the quality of life at work and the working time of French pediatric nephrologists.

**Methods:** An anonymous declarative questionnaire was sent through the mailing list of the French Society of Pediatric Nephrology in January 2023. The results were processed anonymously and confidentially in collaboration with the Unité Mixte de Recherche Epidémiologique et de Surveillance Transport Travail Environnement.

**Results:** A total of 50 questionnaires were analyzed (out of 99 members). Among the respondents, 62% were women and 22% worked part-time. French pediatric nephrologists work an average of 61 hours per week however; despite the fact that almost 25% of the respondents were officially working part-time the 75th percentile of weekly working hours was 66 hours. Despite the clear law on safety rest after night shifts, 14% of respondents did not take their safety rest after night shifts. Of note, over the last 6 months, 28% of respondents had worked more than 15 days of weekends and 68% of respondents had more than 21 on-call nights. In total, 68% declared that their work was rather bad for their own health, 48% had signs of anxiety (10% moderate, 4% severe) and 44% signs of depression (24% moderate, 2% severe).

**Discussion / Conclusion:** French senior pediatric nephrologists work an average of 61 hours per week, despite a crystal-clear European law (48 hours per week, maximum). Strong signals have to be sent for the quality of working life and working hours of pediatric nephrologists if we want to obtain again a strong and ambitious pediatric service, and to respond to our mission of caring for all children in due time without exhausting healthcare providers.



Fr-3MP 032

**ETELCALCETIDE IMPROVES SYSTOLIC CARDIAC FUNCTION, MYOCARDIAL FIBROSIS AND IMPAIRED CARDIOMYOCYTE CONTRACTILITY IN MICE EXPOSED TO CHRONIC HIGH PHOSPHATE LOAD**

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**Aims/Purpose:** Phosphate stimulates the synthesis of parathyroid hormone (PTH) and fibroblast growth factor 23 (FGF23) and is associated with increased cardiovascular morbidity and mortality. In the secondary analysis of the EVOLVE trial, cinacalcet significantly decreased PTH and FGF23 levels in hemodialysis patients, and the latter was associated with a lower rate of cardiovascular events and death. Intravenous administration of etelcalcetide (etl) resulted in a reduction of FGF23 and a slower progression of left ventricular (LV) hypertrophy in hemodialysis patients. In the present study, we investigated the therapeutic effects of etl on the heart in mice with elevated FGF23, PTH and serum phosphate levels due to chronic high phosphate load.

**Methods:** To induce hyperphosphatemia and FGF23 and PTH levels, male C57BL/6 mice were fed a 2% high phosphate diet (HPD) for six months. After four months, half of the mice on HPD were additionally treated with 1 mg/kg body weight/day etl via osmotic minipumps for the last two months and compared with mice receiving a vehicle during HPD or a 0.8% normal phosphate diet. Cardiac function was assessed by echocardiography and Millar catheter, parameters of mineral metabolism were determined, and hearts were analyzed by histology, qPCR and Western blot. In addition, isolated adult mouse cardiomyocytes (AMCM) were stimulated with phosphate, FGF23 or PTH ± etl and contractility and calcium handling were measured using the IonOptix system.

**Results:** EtI decreased HPD-induced FGF23 and PTH levels by 80% and 75%, respectively, and significantly reduced serum calcium levels, but had no effect on persistent hyperphosphatemia and increased phosphaturia. Mice receiving HPD showed a dilated LV with decreased anterior and posterior wall thickness and increased LV diameters and volumes, reduced ejection fraction and fractional shortening, and impaired cardiac contractility. EtI effectively reduced HPD-induced LV dilation and systolic dysfunction and improved contractility in vivo. On the tissue level, etl reduced the development of HPD-induced cardiac fibrosis, but had no effects on cardiomyocyte hypertrophy. Ex vivo stimulation of AMCM with phosphate induced a pro-found decrease in cardiomyocyte shortening velocity and amplitude, a delay in relaxation, and a decrease in the velocity of intracellular Ca<sup>2+</sup> increase and a diminished Ca<sup>2+</sup> amplitude. EtI treatment ameliorated phosphate-induced restriction of single cardiomyocyte contractility, but did not return calcium parameters to baseline levels. Incubation of AMCM with FGF23 and PTH, respectively, had no effect on either contractility or calcium handling.

**Conclusion:** Administration of etl effectively prevents the HPD-induced pathological cardiac phenotype characterized by dilative cardiomyopathy and fibrosis, which may be at least partly due to improved cardiomyocyte contractility.

Fr-3MP 033

KIDNEY DISEASES IN UKRAINIAN CHILD REFUGEES; DATA FROM 13 POLISH TERTIARY PAEDIATRIC NEPHROLOGY CENTRES

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**Aims/Purpose:** The Russian invasion of Ukraine on 24 February 2022 resulted in a massive influx of refugees into the European Union, mainly to neighbouring Poland. A significant number of them were children. A preliminary analysis was performed on rate and causes of hospitalization in all 13 tertiary paediatric nephrology centres.

**Methods:** Basic data was collected from all 13 tertiary paediatric nephrology centres in Poland on the number of hospitalisations of children of refugee status in the period 24th February to 31st December 2022. The cause of kidney disease was classified according to ICD-10 and grouped to the following categories: CKD, UTI, glomerulopathies, CAKUT, hypertension, kidney stones and tubulopathies, AKI, intoxications and kidney transplant complications.

**Results:** Among the 1 573 000 registered persons for Temporary Protection 550 000 were children below 18 years of age. This constituted 6,67% of the total child population (= 18 years age) at the end of 2022. Among 17 359 hospitalizations in the analysed period 428 admissions were refugee children at 13 nephrology centres in Poland. This constituted 2.47% (428 / 17,359) of all hospitalisations noted in these tertiary care centres. The final diagnosis related to kidney diseases was documented from 329 patients. They included: CKD (23.6%), UTI (23.3%), glomerulopathies (22.8%), CAKUT (12.6%), kidney stones disease and tubulopathies (9.6%), hypertension (3.7%), intoxications (1.7%) and KTx complications (1.7%) and AKI (1.1%). Among the hospitalised cohort there was a vulnerable group of 31 children requiring KRT (12 on PD, 10 on HD, and 9 after kidney transplantation). The majority of these children had been actively transferred from Ukraine to Poland at the beginning of war. They represent approximately 20% (12/60) of HD children, 18% (10/56) of children on PD and 4% (9/233) of children with a kidney Tx under the care of Polish paediatric nephrology units.

**Conclusion:** The massive influx of refugees children in Poland since the beginning of Ukrainian war in 2022 has had a significant impact on the majority of paediatric nephrological centres. Hospitalisation rate for severe kidney diseases of refugees constitutes approximately 2.5% of all hospitalisations. 19% of the paediatric dialysis population and 4% of the kidney Tx cohort are Ukrainian children.

Fr-3MP 034

THE ROLE IN CLINICAL PRACTICE OF SERUM CREATININE AND CYSTATINE C BASED EQUATION FOR ESTIMATION OF GLOMERULAR FILTRATION RATIO, A DOUBLE EDGE SWORD?

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**Aims/Purpose:** Currently, there is no consensus on the most appropriate equation for the estimation of glomerular filtration ratio (eGFR) in the pediatric setting. The most widely used equation is the Schwartz, but it has some flaws due to the serum creatinine (sCr) limitations due to muscular mass dependence and its use in certain age groups (e.g patients < 2 years of age and > 16 years of age). Recently, the CKiDU25 combined sCr and cystatin C (cysC) equation (1) has been proposed for the eGFR in patients < 25 years old. We evaluated the impact of this equation in the staging of chronic kidney disease (CKD) and the identification of eGFR reduction.

**Methods:** We compared the eGFR estimated with the CKiDU25 equation to the eGFR obtained with the Schwartz's equation (patients < 16 years) and the CKD-EPI equation (patients > 16 years) in patients from 2 to 18 years old. Results are expressed with median (IQR) and were compared using Mann-Whitney U test with significance levels for p-value < 0.05.

**Results:** From November 2022 to February 2023, we enrolled 45 patients followed in our center with normal or slightly reduced eGFR (CKD stage I/II), 31 under 16 years old and 14 over 16 years old. 22/45 (48%) patients had a reduced eGFR with the CKiDU25 equation. Among patients < 16 years old, 5/31 (16.6%) had normal eGFR according to Schwartz's equation (median eGFR 96, IQR 93-101) and were reclassified as early stages of CKD (stage I-II, median 86.5, IQR 84.5-87, p-value < 0.05). In addition, 2/31 (6.4 %) patients who were previously classified as stage I-II of CKD were reclassified as CKD stage IIIa. Interestingly, 1/45 (2.2%) patient with a previous CKD stage I-II using Schwartz's equation had a normal eGFR using the CKiDU25 equation. Considering patients > 16 years, 9/14 (64.3%) were reclassified: in particular, 8/9 (88%) patients with normal eGFR using CKD-EPI equation (median eGFR 124, IQR 121-130), were reclassified by CKiDU25 as early stages of CKD (CKD stage I-II, median eGFR 79, IQR 63-89, p-value < 0.05). In this group, no patients were reclassified as moderate-advanced forms of CKD.

**Conclusion:** We conducted a study on a new equation that combines and targets the pediatric and young adult population. We found that this equation resulted in a discrepancy in the eGFR values of 48% of our study group when compared to previous creatinine-based eGFR equations. Specifically, the CKiD U25 formula showed a higher rate of detecting eGFR-based CKD than previously used equations. This finding could be a useful tool for pediatric nephrologists to identify CKD in patients with suspected kidney disease at an early stage. However, it could also lead to over-medicalization of patients. Our observations highlight the importance of a multiparametric approach and the need for systematic guidelines to determine a fair follow-up schedule for young patients with kidney disease.

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Fr-3MP 035

REFINING KIDNEY SURVIVAL IN 383 GENETICALLY CHARACTERIZED PATIENTS WITH NEPHRONOPHTHISIS

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**Aims/Purpose:** Renal ciliopathies comprise a group of rare hereditary disorders accounting for 10% of end-stage kidney disease (ESKD) in children with nephronophthisis being one of the main representatives. Up to date, variants in up to 24 genes have been identified causative for an NPH phenotype. Despite the improved molecular understanding, prediction of individual kidney prognosis remains a major challenge. This again reflects a major psychological burden for affected individuals. To overcome this burden, we assessed differences in genotype-specific kidney survival, the impact of mutational severity and the influence of clinical characteristics on the decline of kidney function.

**Methods:** Data was obtained from three independent sources: the network for early onset cystic kidney diseases clinical registry (n = 105), an online survey sent out to the European Reference Network for Rare Kidney Diseases (n = 60) and a systemic literature search (n = 218).

**Results:** 383 individuals were available for analysis: 116 NPHP1, 101 NPHP3, 81 NPHP4 and 85 NPHP11/TMEM67 patients. Kidney survival differed between the four cohorts with a highly variable median age at onset of ESKD: NPHP3, 4.0 years (IQR 0.3–12.0); NPHP1, 13.5 years (IQR 10.5–16.5); NPHP4, 16.0 years (IQR 11.0–25.0) and NPHP11/TMEM67, 19.0 years (IQR 8.7–28.0). Kidney survival was significantly associated with the underlying variant type for NPHP1, NPHP3 and NPHP4. Multivariate analysis for the NPHP1 cohort revealed growth retardation (HR 3.5) and ACEI treatment (HR 2.8) as two independent factors associated with an earlier onset of ESKD. At the same time arterial hypertension was associated with an accelerated GFR decline.

**Conclusion:** The present study represents one of the largest of its kind, addressing kidney survival in genetically determined NPH cohorts. The presented data enable clinicians to better estimate individual kidney prognosis and thereby facilitate personalized counselling.

Fr-3MP 036

MORTALITY, MORBIDITY AND CARE TRAJECTORIES OF DIALYSED CHILDREN WITH CKD5 BEFORE THE AGE OF 5 YEARS IN FRANCE

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**Aims/Purpose:** The younger a pediatric patient with CKD5 the more difficult is the patient management on dialysis. The objective of this study was to analyze morbidity and mortality of dialysed children with a comparison of those older and younger than 2 years.

**Methods:** All children with a dialysis onset (hemodialysis HD or peritoneal dialysis PD) before the age of 5 years between 01/01/2008 and 31/12/2020 in France have been included. We have extracted the demographic and mortality data from the national registry REIN and the hospitalizations data from the SNDS database. We have described 4 patient care trajectories during dialysis: 'optimal', 'simple', 'complicated', and 'severe' depending on the morbidity and mortality using the following parameters: death, switch of dialysis modality, hospitalizations in the intensive care unit, hospitalization for specific complications.

**Results:** 262 children under 5 years have been included, 151 under 2 years and 111 over 2 at dialysis onset, 66% boys among the patients < 2 years vs. 44% in the ≥ 2 years group and mainly genetic nephropathies (47% < 2 yrs, 41% ≥ 2 yrs) or CAKUT (34% < 2 yrs, 17% ≥ 2 yrs). Patients < 2 yrs suffered more often from malnutrition (12% vs. 4%), and had a gastric tube feeding (70% vs. 36%) compared to those ≥ 2 yrs. 70% were started on PD vs. 42% of those ≥ 2 yrs. In one third of patients < 2 yrs the dialysis modality was changed during follow up vs 17% of patients ≥ 2 yrs ( $p = 0.05$ ). Hospitalisation in the intensive care unit and specific complications such as high blood pressure, sepsis, electrolyte disturbances were similar in both groups. Peritonitis was the main reason for hospitalizations (39%). Patients < 2 yrs were more often hospitalized for hypovolemia (15% vs. 5%,  $p = 0.03$ ) and for malnutrition (14% vs. 4%,  $p = 0.05$ ). Mortality on dialysis was 7% in those < 2 yrs, 3% in ≥ 2 yrs,  $p = 0.06$ , and the mean waiting time before first kidney graft was higher in patients < 2 yrs (27 months (20, 36), vs. 17 (9, 26),  $p = 0.001$ ). Patients in 'severe' trajectory were younger (11 months; (5, 31) vs. 35; (15.5, 43.5)), had more co-morbidities (3% vs. 17%), and a lower percentage of successful kidney graft (86% vs. 63%) compared to the 'optimal' trajectory respectively.

**Conclusion:** Morbidity and care trajectories during dialysis in children under 5 yrs clearly impact the percentage of successful kidney graft and seem to be highly related to younger age.

# GUIDELINES SESSION

## Transplantation WG

Fr-3MP 037

## DARATUMAMAB FOR POST-TRANSPLANT RECURRENCE OF STEROID RESISTANT NEPHROTIC SYNDROME

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**Aims/Purpose:** Post-transplant recurrence of steroid resistant nephrotic syndrome occurs in up to 50% of patients and is a major cause of graft loss. There is currently little consensus regarding the best management for SRNS recurrence. Plasma exchange (PE) or Immunoabsorption of immunoglobulins (IA), combined to rituximab are the most common strategies. However, complete remission or sustained remission are not always achieved. Long Lived Plasma Cells (LLPC) may be responsible of refractory forms of autoimmune diseases and targeting CD38 on plasma cells with Daratumumab (DARA) may be an additional option in the treatment of post-transplant recurrence.

**Methods:** This is a retrospective multicentre study in France. We identified all children with post-transplant recurrence of SRNS, unsuccessfully treated with PE and/or IA and B-cell depletion, that secondarily received 1 to 4 infusions of Daratumumab 1g/1.73m<sup>2</sup>.

**Results:** Five patients were included. Median age at INS onset was 5.9 years and median delay to End-Stage-Renal Disease was 1.4 years. One patient had experienced, under IA, a transient remission on native kidneys. Four patients underwent a first renal transplant and one patient a second graft. All patients experienced early recurrence. Four patients went into complete remission after PE and/or IA, combined to high dose steroids and calcineurin inhibitors, but relapsed when sessions were spaced, despite B-cell depletion with rituximab and/or Ofatumumab or Obinutuzumab. After reintensification, PE and/or IA were successfully stopped within 1 month following 1 to 4 weekly infusions of Daratumumab. The fifth patient was completely resistant to IA and B-cell depletion with Obinutuzumab. Proteinuria began to decrease one week after the 4th infusion of Daratumumab, at 3 months post transplantation. IA were discontinued at D147 and she remains in complete remission at 2 years of follow-up.

**Conclusion:** We report on five patients, resistant to standard-treatment of recurrent SRNS, who achieved complete and/or sustained remission after the addition of the anti CD38 antibody, daratumumab. Post-transplant recurrence of SRNS is a dramatically challenging situation. These results identify that targeting both CD20 positive B cells and plasma cells is a novel strategy for the treatment of post-transplant recurrence and suggest that the addition of daratumumab should be considered in refractory recurrent SRNS.

Fr-3MP 038

PLASMA-LYTE-148 VERSUS STANDARD INTRAVENOUS FLUID IN CHILDREN RECEIVING KIDNEY TRANSPLANTS (PLUTO): A PRAGMATIC, OPEN-LABEL, RANDOMISED CONTROLLED TRIAL

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**Aims/Purpose:** Many paediatric kidney transplant recipients experience acute electrolyte and acid-base disturbances including hyponatraemia, hyperkalaemia, hyperchloraemia and metabolic acidosis. Smaller recipients of deceased donor kidneys are most at risk [1]. Plasma-Lyte-148 is an isotonic, gluconate-acetate buffered intravenous fluid. There is a physiological basis to expect that Plasma-Lyte will reduce electrolyte and acid-base abnormalities in children following kidney transplant. A perceived risk of hyperkalaemia from the potassium content of Plasma-Lyte concerned some paediatric nephrologists, although adult transplant recipients experience less hyperkalaemia with Plasma-Lyte compared to 0.9% sodium chloride. We conducted the PLUTO trial to determine whether clinically significantly abnormal plasma electrolyte levels in paediatric kidney transplant recipients would be reduced with the use of Plasma-Lyte compared to standard intravenous fluids.

**Methods:** PLUTO was an open-label randomised controlled trial comparing Plasma-Lyte-148 to current intravenous fluids in paediatric kidney transplant recipients, conducted in 9 UK centres. The trial protocol has been published [2]. Participants randomised to the intervention received Plasma-Lyte-148 intraoperatively and postoperatively; control arm participants received standard intravenous fluid. The primary outcome measure was acute hyponatraemia within 72 hours post-transplant. Secondary outcomes included symptomatic hyponatraemia, fluid overload, graft function, hyperkalaemia, acidosis, hyperglycaemia, hypomagnesaemia, hyperchloraemia and excessive rate of change in plasma sodium. A modified intention-to-treat analysis, with an additional per-protocol analysis of the primary outcome were used. A mixed logistic regression model adjusting for donor type, patient weight and transplant centre was used. The trial was registered (ISRCTN 16586164; EudraCT 2019-003025-22) and funded by the National Institute for Health and Care Research (NIHR200512).

**Results:** 238 patients were screened, of whom 144 participants were randomised and 138 transplanted between 8 June 2020 and 9 August 2022. Protocol adherence to randomised fluid was complete in 115/138 (83%) participants. Data collection and cleaning were completed 24 February 2023. Analysis is progressing.

**Conclusion:** PLUTO will provide novel data on the impact of Plasma-Lyte-148 on acute electrolyte and acid-base imbalance in children receiving kidney transplants. Results will be shared at the ESPN congress.

References

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Fr-3MP 039

HIGH RESOLUTION PERIPHERAL QUANTATIVE COMPUTED TOMOGRAPHY (HR-pQCT) IN TEENAGERS UNDERGOING A FIRST RENAL TRANSPLANTATION: EVOLUTION BETWEEN BASELINE AND 6 MONTHS

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**Aims/Purpose:** Mineral bone disorders associated to chronic kidney disease (CKD-MBD) frequently persist after renal transplantation (R-Tx) and are associated with significant morbidities. Risk factors include pre-existing CKD-MBD, immunosuppressive therapies and post-Tx hypophosphatemia. We aim at evaluating bone by biomarkers, DXA and HR-pQCT at the time of RTx and 6 months after Tx.

**Methods:** The TRANSOS study (NCT02729142) is a single-center prospective study. Here we present the sub-group of patients included below 18 years of age. They were matched on a 1:1 basis on gender, puberty and age with healthy controls (HC) from the VITADOS cohort (NCT01832623). Results are presented as median (range). Non-parametric tests were performed.

**Results:** At a median age of 15 (13-16) years, a total of 19 patients (6 girls, 7 pre-emptive R-Tx, 8 steroid-sparing immunosuppressive strategies) underwent a first R-Tx, with PTH levels of 70(33-103, normal range 5.5-38.4) pg/mL. Six months after R-Tx, six (31%) patients displayed acidosis, 10 (53%) had persistent hyperparathyroidism (but always  $\leq 2N$ ) and five (26%) had increased FGF23 levels; 11 (58%) received phosphate supplementation. When comparing HC and patients at the time of R-Tx, HC had significantly higher whole body bone mineral content Z scores and lean body mass on DXA, but bone parameters assessed with HR-pQCT were not significantly different. Six months after R-Tx, patients displayed significantly impaired trabecular parameters at radius compared to baseline; results were not different at the weight-bearing tibia, neither were cortical parameters at both sides. Results were similar in patients with/without steroid-sparing immunosuppression.

Biological parameters	At R-Tx		6 months post R-Tx		Healthy controls	
	Median	Range	Median	Range	Median	Range
Bicarbonate (mmol/l)	22*	(19-23)	22	(20-23)	27	(25-28,2)
Phosphate (mmol/l)	1.56* <sup>#</sup>	(1.34-1.83)	1.25	(1.11-1.42)	1.31	(1.11-1.45)
ALP (U/l)	156	(92-279)	188	(100-204)	150	(90-210)
PTH (pg/ml)	70* <sup>#</sup>	(33-103)	39	(27-41)	17	(14-23)
FGF23 (RU/ml)	838* <sup>#</sup>	(343-1825)	118	(76-165)	50	(40-62)
B-Crosslaps (pg/ml)	3704* <sup>#</sup>	(2609-4545)	2769	(1790-3276)	1421	(971-1734)
Osteocalcin (µg/L)	352* <sup>#</sup>	(271-393)	92	(65-137)	59	(38-81)

\*p = 0.05 when comparing HC and patients at baseline; <sup>#</sup>p = 0.05 when comparing patients at baseline and 6 months post RTx

**Conclusion:** Our cohort provides reassuring results concerning bone health in teenagers receiving a first renal Tx, but trabecular bone microarchitecture impairment is observed 6 months post transplantation, likely due to corticosteroids.

Fr-3MP 040

CURRENT PRACTICES IN THE MANAGEMENT OF CHILDREN WITH FAILING KIDNEY ALLOGRAFTS: PRELIMINARY RESULTS FROM ESPN CKD-MBD, DIALYSIS AND TRANSPLANT WORKING GROUPS

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**Introduction:** The lifetime of kidney allografts in children is limited due to several factors. Children with complex medical and psychosocial problems are transplanted even at a very young age, with upto 15% receiving second or even third kidney transplants before transitioning to adult services. Medical management of children with failing kidney allografts is poorly understood even in adult patients and varies across different centres in Europe. The aim of this study is to describe the cohort of children with a failing kidney allografts and provide insight into the different management practices across Europe.

**Methods:** An initial survey was sent to all members of the across ESPN CKD-MBD, Dialysis and Transplant Working Groups to determine the number of patients under 21 years of age, with a failing kidney allograft (defined as an eGFR < 30 ml/min/1.73m<sup>2</sup>). A 2- year retrospective observational review of all children identified to have a failing kidney allograft was then undertaken. Data were collected through the CERTAIN registry and included demographics, underlying aetiology, and allograft, cardiovascular, immunological, and CKD-MBD surveillance. Children with at least one-year follow-up were included.

**Results:** Preliminary analysis identified 67 patients (19 female) with a failing kidney allograft from 17 centres across Europe. Figure 1 represents percentage of these children developing allograft loss years following transplantation. 54% (36/67) had CAKUT as the underlying aetiology. 25% (16/63) of first allograft recipients were transplanted pre-emptively. Mean age at transplant was 9.3 years (SD = 5.5). Mean number of mismatches at transplant were 2.8 (SD = 1.4). At last follow-up biochemical markers for surveillance of allograft CKD are described in Table 1.

	Mean	SD
eGFR ml/min/1.73m <sup>2</sup>	19.9	7.4
BMI kg/m <sup>2</sup>	21.2	5.3
Plasma urea mg/dL	112.2	42.3
Haemoglobin g/dL	10.9	1.5
Serum bicarbonate mmol/L	22.4	4.7

80% (54/67) patients were on anti-hypertensive medication(s), 45% (30/67) were on iron supplements and 67% (46/67) were on vitamin D analogue(s) and bicarbonate supplements. All patients remained on maintenance immunosuppression with 55% (37/67) on three, 42% (28/67) on two and 3% (2/67) on one agent.

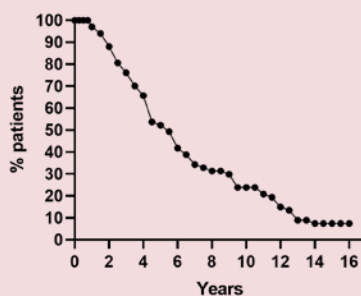


Figure 1.

**Conclusion:** Management of children with failing kidney allografts is complex, poorly understood and highly variable across Europe. This study is the first step towards understanding this cohort and developing future directions in research to attenuate kidney allograft failure.

Fr-3MP 041

CORRELATION BETWEEN CLINICAL OUTCOMES AND QUALITY OF LIFE OF PAEDIATRIC KIDNEY TRANSPLANT RECIPIENTS

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**Aims/Purpose:** Kidney transplantation is the preferential kidney replacement therapy (KRT) for children with renal failure with well reported physiological and psychosocial advantages over dialysis. There is an abundance of literature regarding clinical outcomes (CO's) associated with KRT but a scarcity of data assessing the impact of these CO's on quality of life (QoL). This study aimed at identifying correlation between CO's and the effect on QoL of paediatric kidney transplant recipients (pKTR).

**Methods:** Patients attending outpatient clinics were offered the opportunity to complete a standardised age-appropriate QoL questionnaire (PedsQL TMv3.0) during clinic attendances in April 2022. Inclusion criteria were pKTR at least three months post-transplant of a single organ (kidney). Questionnaire responses were pseudo-anonymised with QoL scores subsequently matched to individual clinical outcome dataset. The Cronbach alpha co-efficient was calculated for each section of the questionnaire to ensure there was reliable as opposed to error variance

**Results:** Of the 46 patients approached to take part, 36 (25% of total post-transplant cohort) met inclusion criteria and completed the questionnaire. The mean patient age and timing post-transplantation were 12.8 years and 5.2 years, respectively. CAKUT (42%) and nephrotic syndrome (22%) were the most common primary renal diagnosis. There was no statistically significant correlation between QoL and number of clinic attendances ( $p = 0.373$ ) or number of medications ( $p = 0.739$ ). There was a statistically significant difference in beliefs regarding the impact of medications on physical appearance between adolescents with a history of rejection and those without ( $p = 0.044$ ).

**Conclusion:** QoL is subject and patient specific. Clinicians must identify factors impacting QoL and work collaboratively to lessen their impact. Surprisingly medication burden or number of clinic attendances was not shown to affect QoL in this cohort. Adolescents often struggle with compliance, our study has shown a link between history of allograft rejection and a belief that medications negatively impact appearance. At a time of significant social pressures it is important that we address the psychosocial impact of post-transplant medications on self-esteem and positive body image.

Fr-3MP 042

TRENDS IN OUTCOMES OF PAEDIATRIC KIDNEY TRANSPLANTATION

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**Aims/Purpose:** To investigate trends over time in patient and graft survival after paediatric kidney transplantation (KT) and to identify predictors of graft survival.

**Methods:** Patient data were extracted from a prospective registry of all paediatric KT procedures performed at a single centre between 01/01/1984 and 31/12/2022. Patient and death-censored graft survival were estimated and compared across transplantation periods using Kaplan-Meier methods and log-rank tests. Cox proportional hazard regression models were used to identify predictors of graft survival probabilities.

**Results:** A total of 181 paediatric KT procedures were analysed (170 patients, 58% male). Median age at KT was 13.1 years (interquartile range [IQR]: 10.0–15.7). Comparing recipient, donor and KT baseline characteristics across transplantation periods (1984–2003 vs 2004–2022) living donor KT increased from 1% to 13% ( $p = 0.001$ ) and KT with 6/6 HLA-A, B, DR mismatches increased from 2% to 23% ( $p = 0.001$ ). Over a median follow-up of 17.5 years (IQR: 10.2–26.7; range: 0.3–39.2), 8 (5%) patients died (all had been transplanted in 1984–2003). Overall, patient survival rates at 1, 5, 10, 15, and 20 years were, respectively, 100%, 99%, 98%, 96%, and 96%. Median graft survival was 25.6 years. Graft loss occurred in 63 (35%) cases, primary non function in 11 (6%), and delayed graft function in 34 (19%). Graft loss significantly decreased from 51% among patients transplanted in 1984–2003 to 18% among those transplanted in 2004–2022 ( $p = 0.001$ ), in parallel with an improvement in 1-, 5-, 10-, and 15-year graft survival rates among patients transplanted in 1984–2003 (89%, 82%, 69%, and 58%) compared with those transplanted in 2004–2022 (96%, 90%, 85%, and 70%;  $p = 0.04$ ). In univariate analyses, paediatric donors and induction therapy with anti-thymocyte globulin were significantly associated with improved graft survival (HR 0.44, 95% CI 0.26–0.74,  $p = 0.002$ ; HR 0.47, 95% CI 0.24–0.85,  $p = 0.013$ ; respectively). In a multivariable Cox proportional hazards regression model adjusted for age, sex, donor age and induction therapy with anti-thymocyte globulin, the year of transplantation was an independent predictor of improved graft survival (HR 0.97; 95% CI 0.94–0.99;  $p = 0.03$ ).

**Conclusions:** Outcomes after paediatric KT have improved overtime, with a 3% decreased hazard of graft loss with each more recent year of transplantation, adjusting for age, sex, donor age, and induction therapy with anti-thymocyte globulin.

Fr-3MP 043

RENAL ALLOGRAFT SURVIVAL FOR (RE)TRANSPLANTATED CHILDREN IN ADULthood; AN ERA REGISTRY STUDY FROM 1978 TO 2019

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**Background:** Knowledge regarding renal allograft survival in (re)transplanted European children followed from childhood into adulthood including factors affecting these outcomes is lacking.

**Methods:** Using ERA Registry data, we investigated all patients on kidney replacement therapy (KRT) who received their first kidney transplant (KT) before 20 years of age between 1978 and 2019. Graft survival after first, second and third KT were analysed together with their risk factors, using Kaplan-Meier survival analysis and multivariable Cox regression models.

**Results:** Among 10,012 paediatric KT recipients, 8601, 1962 and 412 received at least one, two and three KTs. Graft survival at 10 years was 65.7% for first, 53.7% for second and 49.5% for third KTs. Factors associated with increased graft failure rates were primary disease of glomerulonephritis or recurrent disease as cause of kidney failure for first KT recipients (aHR 1.24, 95%CI 1.12-1.37 and aHR 1.24, 95%CI 1.13-1.37, respectively). Patients whose first KT lifespan was between 0-30 days or > 5 years had lower graft failure rates for their second KT compared to patients whose KT survived between 1-5 years (aHR 0.79, 95%CI 0.64-0.98 and aHR 0.73, 95%CI 0.61-0.88, respectively). Similar results were found for third KT recipients whose second KT survival was > 5 years (aHR 0.61, 95%CI 0.41-0.92). Patients who were transplanted for the first and second time before 2007 had 1.5-2x higher graft failure rates compared to patients who received their KT between 2016 and 2019. Pre-emptive KT recipients had lower graft failure rates compared to patients who received dialysis > 1 year for first and second KT (aHR 0.89, 95%CI 0.81-0.98 and aHR 0.63, 95%CI 0.51-0.78, respectively). Patients who received a living donor (LD) KT had lower graft failure rates for first and second KT (aHR 0.77, 95%CI 0.7-0.84 and aHR 0.71 (0.6-0.85, respectively). Second LD KT recipients had survival advantage compared to having a second deceased donor KT.

**Conclusions:** Graft outcomes after pediatric kidney (re)transplantation have improved significantly over time for all recipient subgroups, especially for patients with LD KT, longer previous KT lifespan and pre-emptive KT. Patients with GN and recurrent diseases showed the poorest outcomes, highlighting the requirement for further research.

Fr-3MP 044

EVALUATION OF CUMULATIVE EFFECT OF STANDARD TRIPLE IMMUNOSUPPRESSION ON THE PREVENTION OF DE NOVO DONOR SPECIFIC ANTIBODIES (DNDSA) PRODUCTION IN CHILDREN AFTER KIDNEY TRANSPLANTATION – A RETROSPECTIVE AND PROSPECTIVE STUDY

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The presence of de novo Donor Specific Antibodies (dnDSA) is associated with the inferior graft outcome. Standard immunosuppression is expected to prevent the dnDSA production in low-risk patients.

**Aims/Purpose:** Evaluation of a cumulative effect of a triple immunosuppression (CNI/ MMF/Pred), as well as TAC CO concentration and TAC CO coefficient of variation on the incidence of dnDSA production

**Methods:** Overall, 67 transplanted patients were evaluated, belonging to the retrospective (dnDSA tested for-cause; n = 29) and prospective (dnDSA tested by protocol; n = 38) group, regarded as being at low/moderate immunological risk.

**Results:** In the retrospective group, the eGFR value at first dnDSA detection (median interval - 4.0 years post-transplant) was 41 mL/min/1.73m<sup>2</sup>; 55% of patients presented biopsy-proven cAMR, and 41% lost the graft within next 2.4 years. Patients from the prospective group presented 97% graft survival and eGFR of 76 mL/min/1.73m<sup>2</sup> at 2 years follow-up. In prospective group the overall incidence of dnDSA progressively increased from 8% at 3; 11% at 6; 16% at 12, to 21% at 24 months. Overall incidence of acute (T cell) rejection was 18%. None of the patients from a prospective group developed cAMR, however the probability of the eGFR decrease > 30% from baseline was higher in dnDSA(+) patients (log rank p = 0.012). Median value of a Vasudev score (a cumulative value of exposure to the immunosuppressive drugs combined in a triple protocol) within 2 years of follow-up was numerically higher in dnDSA (-) vs dnDSA (+) patients (5.3 vs 4.1; NS), however not significantly different. Median value of all TAC CO evaluated during 1–24 months (overall n = 145) post-transplant was 7.9 in dnDSA (-) vs. 7.1 ng/mL in dnDSA (+) patients (p = 0.008). Variability of TAC CO (a coefficient of variation) was numerically higher in DSA(-) vs DSA(+) patients from a prospective group, however not significantly different (31 vs 29; p = 0.56). The median value of all TAC CO evaluated during 1–24 months post-transplant in prospective group (overall n = 181) and within 2-years preceding appearance of dnDSA in retrospective group (overall n = 145), was significantly higher among dnDSA (-) vs all dnDSA (+) patients (7.4 vs 6.0 ng/mL; p < 0.0001).

**Conclusion:** The major factor determining the dnDSA production was a lower exposure to tacrolimus, while not to the combined triple immunosuppression. Variability of TAC CO concentration was similar in dnDSA(+) and dnDSA (-) patients.

Fr-3MP 045

**SAFETY AND IMMUNOGENICITY OF HPV VACCINATION IN IMMUNOCOMPROMISED GIRLS: THE PRIMAVERA CLINICAL TRIAL (NCT 01687192)**

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**Background:** Human papillomavirus (HPV) infection is found in about 30% of adolescent girls with solid organ transplant and autoimmune diseases can induce subsequent neoplasia. The aim of this trial was to determine the safety and immunogenicity of the quadrivalent HPV vaccine (HPV-6, -11, -16, and -18) in clinically stable immunocompromised girls.

**Methods:** This prospective, open-label, single arm, phase 2 study was conducted in a national hospital-based research program and included clinically stable adolescent girls aged 9-17 years who were receiving immunosuppressive therapy. Participants received the quadrivalent HPV vaccine in intramuscular injections on Day 0 Month 2 and Month 6. Anti-HPV-6, -11, -16, and -18 neutralization titers determined using a pseudovirion-based neutralization assay were measured in serum before (month 0) and at months 7, 18 and 36 post vaccination. Anti-HPV T cell response was also studied at M7 and M18.

**Results:** A total of 37 girls receiving immunosuppressive therapy (median age 13.1 years, 17 kidney transplant recipients, 11 liver transplant recipients, 9 autoimmune diseases) were included. After vaccine series completion (n = 36), 30 of 35 patients (85.7%, 95% CI 72.3-94.2) developed antibody responses to HPV-16 and -18 types. Immunogenicity persisted at month 36. Geometric mean antibody levels for each HPV type were higher at months 7 and 18 than at baseline and greater for HPV-18 than -16. No serious adverse events were reported and mild, local adverse events were reported in 7 cases.

**Conclusions:** Treatment with the HPV vaccination in immunocompromised girls was followed by adequate antibody responses against HPV-16 and -18 types in 85% and no serious adverse events. HPV vaccination may be safely administered to girls post organ transplantation or autoimmune disease to reduce HPV infection and related neoplasia.

Fr-3MP 046

**TORQUE-TENO VIRUS LOADS MAY PREDICT OPPORTUNISTIC VIRAL INFECTIONS IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS DURING POST-TRANSPLANT FOLLOW-UP**

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**Aims/Purpose:** Kidney graft rejection by alloimmunity remains the major cause of late graft failure in children and adolescents with kidney transplantation (KTX). Immunosuppressive regimens, however, must be carefully balanced against a substantially increased risk for infectious complications. Plasma loads of the non-pathogenic Torque Teno virus (TTV) were shown to reflect adult and pediatric patients individual immune status during follow-up after solid-organ transplantation. This study aimed at the investigation of potential associations and the predictive capability of TTV plasma loads with major opportunistic viral infections (e.g., cytomegaly virus [CMV]) during follow-up of pediatric KTX patients.

**Methods:** We included all children and adolescents with a post-transplant time of  $\geq 3$  months after KTX at the Medical University of Vienna in this study. Every four to eight weeks viral loads (TTV, CMV, Epstein-Barr virus [EBV], BK polyomavirus [BKV]) were routinely measured from plasma and/or urine by quantitative PCR. Generalized poisson mixed models and mixed effects logistic regression for  $\log_{10}$  TTV loads with  $\log_{10}$  EBV, CMV, and BKV loads were calculated with fixed effects accounting for potential confounders (age, time after KTX), alongside Receiver Operating Characteristics (ROC).

**Results:**  $N = 72$  KTX recipients, being 65% male, at median 12 years (IQR 8-16), 19 months post KTX (IQR 3.3-6), with a HLA-mismatch of 3 (IQR 2-3), 63% living donors, all with basiliximab induction, and mainly triple immunosuppressive maintenance therapy (mostly tacrolimus, mycophenolate, steroids), and a median eGFR of 96 ml/min/1.73m<sup>2</sup> (IQR 76-134) were included in this study. TTV loads significantly predicted CMVemia above plasma loads of  $10^3$  c/mL 4 to 8 weeks before occurrence (OR 2.56,  $p = 0.002$ ) after adjustment for potential confounders. Prediction of the first CMVemia above the same threshold resulted in a sensitivity of 88% and a specificity of 79% for TTV. Furthermore, TTV loads were able to significantly predict BKVuria ( $p = 0.02$ ) above urine loads of  $1.7 \times 10^9$  c/mL for the next visit and BKVemia above plasma loads of  $10^4$  c/mL on the same visit ( $p = 0.005$ ). Associations with EBV were not significant.

**Conclusion:** This is the first study to demonstrate significant predictive capability of TTV plasma loads for the occurrence of clinically relevant viral infections (CMV, BKV) above clinically relevant cut-offs 4 to 8 weeks later during follow-up of pediatric KTX patients.



Fr-3MP 047

ASSESSMENT OF PRE-TRANSPLANT MEMORY T CELL PHENOTYPES IN CHILDREN ASSOCIATED WITH COSTIMULATION BLOCKADE RESISTANT REJECTION IN ADULTS

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**Aims/Purpose:** Despite improved patient and graft outcomes with costimulation blockade, increased early acute rejection has hindered the widespread use of belatacept (CTLA-4lg) for kidney transplant. The Emory group has previously reported lower pre-transplant frequencies of CD28+CD4+ effector memory T cells (CD4+TEM: CCR7- CD45RA-) with decreased functional capacity in adults that were subsequently free from early rejection on belatacept. Our preliminary data of unstimulated PBMCs collected from children on dialysis (n = 30) or healthy children (n = 18) allowed us to demonstrate that similar T cell phenotypes are also detectable. A subset of children on dialysis accumulates CD4+ TEM cells that have lost CD28 expression, a phenotype reminiscent of adults with decreased risk for early rejection on belatacept. We aimed to determine if the stable-like phenotype detected in children with ESRD (CD28low CD4+ effector memory T cells) represents dysregulated and/or senescent T cells with decreased functional capacities.

**Methods:** We analyzed flow cytometry data of PBMCs collected from 17 children on dialysis at the Children's Healthcare of Atlanta. We examined expression of markers of costimulation (CD28), activation (HLA-DR), intracellular cytokine production (IL2, TNFα) and cytotoxicity (Perforin) on CD4+TEM in different in vitro stimulation conditions: 1) unstimulated 2) unspecific TCR stimulation (CD3/CD28) or 3) allogenic stimulation (using MLR = mixed lymphocyte reaction) for 72h.

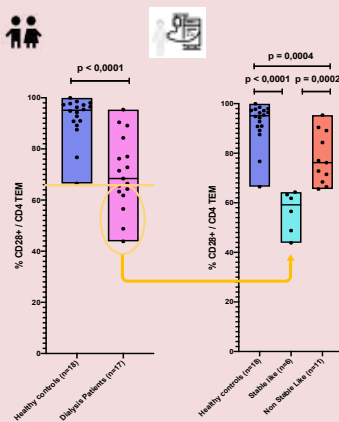


Figure 1: 6/17 dialysis patients had CD28+CD4+TEM frequencies below the minimum value (68%) observed in healthy children in our preliminary data.

n (%)	Stable like	Non stable-like	p value
Number of patients	6	11	
<b>Demographics</b>			
Age (years, median (min - max))	13.2 (8.3 - 17.4)	15.2 (11.5 - 18.5)	0.428
Male gender	0 (0)	6 (54.5)	<b>0,034</b>
<b>Ethnicity</b>			
Afro-American	4 (66.8)	8 (72.7)	>0,999
White	1 (16.6)	2 (18.2)	
Other	1 (16.6)	1 (9.1)	
<b>ESRD etiology</b>			
CAKUT	4	5	>0,999
Autoimmune GN	2	4	>0,999
Genetic nephropathy	0	1	
Unknown	0	1	
Time on dialysis (months)	26.3 (4.2 - 56.3)	21.2 (8.6 - 35.6)	0.793
Prior exposure to IS treatment	2 (33.3)	4 (36.4)	>0,999

Figure 2: Stable like (CD28<sup>low</sup>CD4+TEM) and non-stable like patients' characteristics.

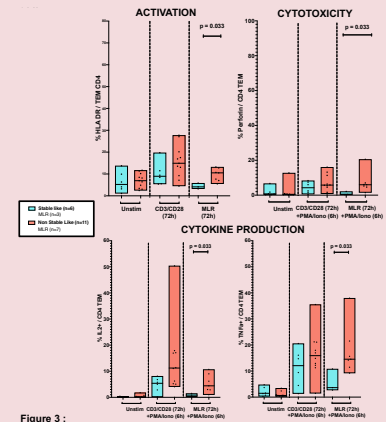


Figure 3:

Figure 3: Following stimulation, stable-like patients had significantly lower frequencies of CD4+TEM cells bearing activation markers, cytotoxicity markers and intracytoplasmic cytokine production to the rest of the dialysis patients.

**Results:** 6/17 dialysis patients had CD28+CD4+TEM frequencies below the minimum value (68%) observed in healthy children in our preliminary data (Figure 1). Patients' characteristics are summarized in Figure 2. We saw no difference between stable- and non stable-like CD4+TEM functional capacities at baseline or after a stimulation as strong as CD3/CD28. However, following allogenic stimulation, patients with the stable-like phenotype had significantly lower frequencies of CD4+TEM cells bearing activation markers, cytotoxicity markers and intracytoplasmic cytokine production compared to the rest of the dialysis patients (Figure 3).

**Conclusion:** A subset of children on dialysis accumulates CD4+ TEM cells that have lost CD28 expression and show decreased functional capacities in response to allogenic stimulation. Further studies are needed to confirm the association of this phenotype with rejection and support its use as a biomarker to stratify the risk of rejection under belatacept in pediatrics.

Fr-3MP 048

## INFECTION RELATED HOSPITALIZATIONS IN YOUNG VERSUS OLDER CHILDREN UNDERGOING KIDNEY TRANSPLANTATION AND ITS CLINICAL DETERMINANTS

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**Aims/Purpose:** Children undergoing kidney transplantation (KTX) are prone to infections which may result in septic complications, and need for hospitalization. The impact of patients age and immunosuppressive protocols used is uncertain.

**Methods:** Here we analyzed the outcome of 255 children (< 18 years) who underwent KTX in our center between 2005 and 2022. The number, type and treatment of infections, and number and duration of infection related hospitalizations and immunosuppressive medication within the first 3 years after KTX were assessed. Outcome in young (age < 3 year, n = 47) versus older (age ≥ 3 years, n = 208) children in relation to immunosuppressive regime was compared by Two factorial ANOVA or Friedmann Test.

**Results:** Children aged less than 3 years at the time of KTX had a significantly higher number of hospital stays (mean ± SD, 0.34 ± 0.41 vs 0.18 ± 0.35) and significantly higher number of days in hospital (2.63 ± 3.67 vs 1.4 ± 3.1) when compared to older children (each p < 0.001). Antibiotic-treated outpatient infections occurred more frequently in young (0.16 ± 0.15) compared to older (0.12 ± 0.3) children (p = 0.003). In terms of immunosuppressant combinations, multiple registrations per patient were possible due to changes of the regime. The data were referred to the month of follow-up. No significant differences in hospitalization rate, duration and number of outpatient infections per follow up month was shown for Tacrolimus (TAC) + Mycophenolate mofetil (MMF) (n = 81), Cyclosporine A (CsA) + MMF (n = 52), CsA + Everolimus (EVR) (n = 157) and TAC + EVR (n = 46).

**Conclusion:** Children aged less than 3 years at the time of KTX are significantly more prone for infections requiring antibiotic treatment and hospitalization compared to older children. No significant difference was identified with respect to the immunosuppression combinations chosen within and between age groups.

# SYMPOSIUM 4

# Hypertension

Sa-3MP 049

COMPARISON OF PERFORMANCE DURING COMPUTERIZED COGNITIVE ASSESSMENT IN PEDIATRIC PATIENTS WITH PRIMARY HYPERTENSION AND HEALTHY CONTROLS

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**Aims/Purpose:** The impact of primary hypertension (PH) on cognitive functions in children and adolescents remains poorly defined. The aim of our study was to compare non-verbal cognitive performance of pediatric patients with PH and healthy controls (HCs). A statistical analysis of the data was carried out using IBM SPSS v26. Methods of descriptive and analytical statistics were applied.

**Methods:** We conducted a cross-sectional study at Vilnius University Hospital Santaros Klinikos between December 2021 and March 2023 by enrolling patients aged 6–17 years with PH and age and height-matched HCs. PH was diagnosed according to the European Society of Hypertension guidelines. Both groups completed a computerized (CANTAB, Cambridge Cognition Ltd) evaluation for attention and processing speed (Match to Sample Visual Search, MTS), sustained attention (Rapid Visual Information Processing, RVP), reaction speed (Reaction Time Task, RTI), visual memory and new learning (Paired Associates Learning, PAL), spatial planning (Stockings of Cambridge, SOC) and working memory (Spatial Working Memory, SWM, and Spatial Span, SSP).

**Results:** The study sample consisted of 50 patients with PH (78.0% male, aged  $13.9 \pm 3.2$  years) and 31 HCs (54.8% male, aged  $13.2 \pm 2.7$  years). The median time of response to a target stimulus was higher in the PH group in two of the selected tasks ( $226.1 \pm 42.5$  vs  $251.7 \pm 63.6$  seconds,  $t = -2.173$ ,  $p = 0.033$  [RTI] and  $1923.5 \pm 508.0$  vs  $2257.4 \pm 791.5$  ms,  $Z = -2.089$ ,  $p = 0.037$  [MTS]). Patients with PH also performed worse on the paired associates learning task ( $9.8 \pm 11.2$  vs  $4.2 \pm 3.8$  incorrect attempts,  $Z = -2.916$ ,  $p = 0.004$  [PAL]). The latter differences remained after adjustment for sex. Results of the aforementioned tests were not associated with patient body mass index, blood uric acid, cholesterol or triglyceride concentrations ( $p > 0.05$ ). There was no statistically significant difference between group performance in tasks of sustained attention, spatial planning and working memory.

**Conclusion:** Our data suggests impairments in reaction and processing speed, visual memory and new learning among children and adolescents with PH. The results of the study should be confirmed within a larger study sample and include assessment of verbal cognition.

Sa-3MP 050

**CHILDREN'S CYSTIC KIDNEY DISEASES: DATA FROM LITHUANIAN UNIVERSITY OF HEALTH SCIENCES DEPARTMENT OF CHILDREN DISEASES**

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**Aims/Purpose:** To determine the cause and progression of chronic kidney disease (CKD) among children diagnosed with cystic kidney diseases in our outpatient clinic.

**Methods:** A retrospective cohort study was conducted, analyzing the registration data of outpatient clinic between the years 2011 and 2021. Inclusion criteria were children consulted by a pediatric nephrologist and diagnosed with a cystic kidney disease. We analyzed the included patients' medical data, determining the diagnosis, age at diagnosis, presence and progression of CKD at diagnosis and after 1, 5, and 10 years.

**Results:** A total of 139 children were consulted for cystic kidney diseases during the study period. 75 children were diagnosed with nonspecific cystic kidney disease or uncomplicated single cysts. No patients in this group developed CKD during the study period. 31 children were diagnosed with a multicystic dysplastic kidney (MDK), 14 (45.2%) were boys. 14 (45.2%) were diagnosed under 12 months of age, 9 (29%) at an age of 1–9 years and 8 (25.8%) at an age of 10–17 years. None had CKD at diagnosis, 1 patient (3.2%) developed stage 2 CKD within 5 years after diagnosis with no further progression during the study period. 24 children were diagnosed with autosomal dominant polycystic kidney disease. 10 (41.7%) were boys, 7 (29.3%) were diagnosed under 12 months of age, 8 (33.3%) at an age of 1–9 years and 9 (37.5%) at an age of 10–17 years. None developed CKD. 9 children had autosomal recessive polycystic kidney disease (ARPKD), all diagnosed in infancy. 7 (77.8%) were boys. At diagnosis, 2 (22.2%) had CKD, stages 3 and 4, the latter patient developed stage 5 within 10 years. One patient with no CKD at diagnosis developed stage 5 within 1 year. At 5 years from diagnosis, one patient had newly developed CKD stage 2 and one CKD stage 3. 4 patients did not develop CKD during the study period, most likely due to insufficient data (single visits without long-term monitoring).

**Conclusion:** Most cystic kidney diseases in children are self-limiting and do not result in CKD. Only 3.2% of children with MDK had a reduction in glomerular filtration rate, confirming the unilateral presentation of the disease and good compensation in children with a single functioning kidney. Although rare, ARPKD represents most of the CKD burden in children with cystic kidney diseases.

Sa-3MP 051  
HYPERTENSION IN CHILDREN – IMAGING PROTOCOL FOR SUSPECTED RENOVASCULAR HYPERTENSION

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**Aims/Purpose:** The authors propose a diagnostic imaging algorithm to best identify children being evaluated for hypertension who may have renovascular disease (RVD) as a cause of secondary hypertension.

**Methods:** After a dedicated clinical assessment (according to literature 43% children referred for high blood pressure were found to be normotensive), mode-B ultrasound (MBUS) is suggested as a first-line approach unless the patient has high clinical suspicion of renovascular disease in which case proceeds directly to renal Doppler ultrasound (RDUS). MBUS aims to access renal artery stenosis visualized on B-mode, aortic calibre, renal vein patency, the presence of unilateral small kidney / difference in kidney length or the existence of other causes of hypertension such as signs of chronic renal disease or renal/suprarenal masses. RDUS assessment is recommended in high suspicion patients (as per ESPR Abdominal Imaging Task Force definitions) and in case of a positive MBUS. Further imaging is performed accordingly and is included in the suggested algorithm. The proposed algorithm was retrospectively tested in a database of 85 patients who were referred to a tertiary paediatric hypertension service for evaluation of sustained high blood pressure. Patients underwent MBUS and/or RDUS as part of their investigation to identify underlying renovascular disease.

**Results:** Seventy-five out of the 85 (88%) children underwent MBUS, 57 (67%) underwent RDUS and 7 (8%) CT or MRA. MBUS was positive in 6 of 9 with confirmed renovascular hypertension, representing a sensitivity of 67% (and specificity of 82%). RDUS was performed on 57 patients and was positive in 5 of 9 with confirmed RVD, attaining a sensitivity of 67% and specificity of 82%. Based on the proposed algorithm only 33/85 (39%) of RDUS would have been indicated [25/33 (76%) because of high clinical suspicion and 8/33 (24%) as positive mode-B ultrasound]. All the patients with confirmed renovascular hypertension would have had RDUS evaluation as per the algorithm. Adequate patient selection as per proposed algorithm would reduce RDUS by 28%.

**Conclusion:** MBUS may be sufficient in many patients with hypertension and may provide alternative diagnosis (other causes of hypertension). In high risk patients for renovascular hypertension RDUS may be the appropriate initial test and may direct further work-up. However, RDUS has high specificity but low sensitivity and therefore is not ideal as screening for RVD.

IMAGING PROTOCOL FOR HYPERTENSION IN CHILDREN

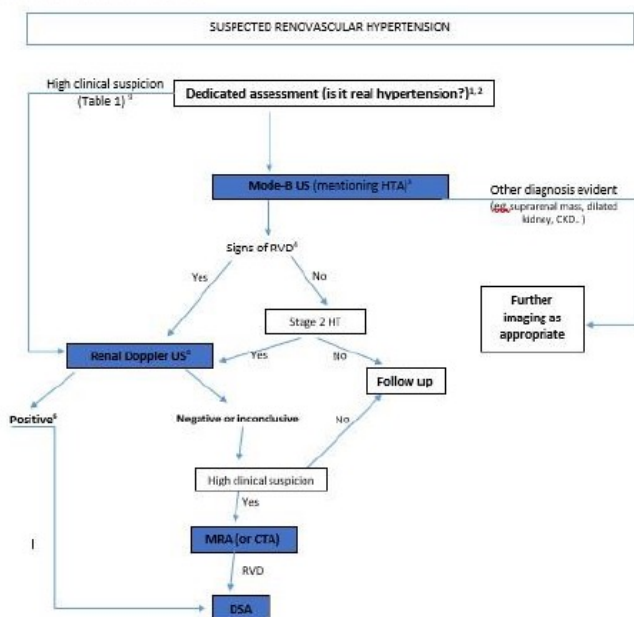


Table 1 - High clinical suspicion of renovascular disease (table from *Riccabona Pediatric Urogenital Radiology 2018 Spring*)

Extremely high blood pressure at presentation
Antihypertensive treatment
Hypertension not controlled on one or two drugs
Unacceptable adverse effects of antihypertensive drugs
Secondary symptoms (e.g., neurological symptoms, cardiac failure)
Syndrome associated with renovascular disease
Neurofibromatosis type 1
Williams syndrome
Tuberous sclerosis
Evidence of large vessel vasculitis
History of renal trauma or radiation
Umbilical artery catheterization
Renovascular thrombosis
High renin levels
Abdominal bruit
Renal transplant

ADAPTED FROM *Pediatr Radiol* 2011; 41:939–944 (Recommendations from the ESPR Abdominal (GI and GU) Imaging Task Force together with ESUR paediatric urogenital imaging working group)

Algorithm testing results at the power point presentation

Sa-3MP 052

THE GROWING PREVALENCE OF HYPERTENSION ASSOCIATED WITH OBESITY IN CHILDHOOD: TIME TO ACT EARLY

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**Purpose:** Primary hypertension in childhood is defined as persistently raised blood pressure (BP) ( $\geq$  95th percentile) without a secondary cause [1]. Increasing evidence suggests obesity as risk factor for hypertension in childhood [2]. This study aimed to understand the prevalence of obesity in children with primary hypertension.

**Methods:** 10-year single centre retrospective review of all patients less than 18 years of age, referred to a tertiary hypertension service was undertaken. Children with no secondary cause found for their hypertension were included. Longitudinal data was collected using electronic patient records.

**Results:** 84 patients (44 female) were included. Mean age at referral was 12 years (IQR 10–14, range 0.5–18). 74% (n = 62) of children with no secondary cause of hypertension were overweight at the time of referral (BMI  $\geq$  85th centile) and 68% (n = 57) of these were obese (BMI  $\geq$  95th centile) [3]. Investigations at referral and follow-up are summarised in Table 1. 30% (n = 25) were on antihypertensive medication(s) at referral. A further 49% (n = 41) were commenced on anti-hypertensives after review in hypertension clinic. 76% (n = 64) received dietary and lifestyle advice for weight management. 86% (n = 72) of the patients were seen at follow up. Median follow up duration was 30 months (IQR 16–50, range 8–138).

TAB. 1

Investigations	At referral	At follow up	P-value
BMI $\geq$ 85th centile	74%	67%	0.168
BMI $\geq$ 95th centile	68%	58%	0.09
Office BP $\geq$ 95th centile	76%	50%	0.0003
Average ambulatory BP $\geq$ 95th centile	41%	18%	0.0009
Mild to moderate LVH	19%	18%	0.436
Retinal changes	4%	1%	0.12
Proteinuria (Urine albumin creatinine $\geq$ 4mg/mmol)	2%	2%	0.5

**Conclusion:** Early intervention including dietetic and lifestyle advice can help reduce office and ambulatory blood pressure in children with primary hypertension. Our study contributes to growing evidence that obesity in the paediatric population is a risk factor for developing hypertension and of further consequence to cardiovascular health.

References

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# SYMPOSIUM 5

## Diagnostics



SA-3MP 053

**BIALLELIC VARIANTS OF THE PLANAR CELL POLARITY GENE CELSR3 ARE IMPLICATED IN CONGENITAL AND DEVELOPMENTAL CENTRAL NERVOUS SYSTEM ANOMALIES AND URINARY TRACT MALFORMATIONS**

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**Purpose:** CELSR3 codes for a planar cell polarity protein. We investigated CELSR3 as a candidate gene for congenital and developmental anomalies of the central nervous system (CNS) and urinary tract malformations (UTM).

**Methods:** We describe 17 individuals from 15 independent families with biallelic putative pathogenic variants in CELSR3. We performed genotype-phenotype correlations and computational simulation of the 3D protein structure. We investigated the embryonic role of CELSR3 in human embryonic tissues and examined the function of the zebrafish (zf) ortholog *celsr3* during early neuronal and urinary tract development.

**Results:** Affected individuals presented with an overlapping phenotypic spectrum comprising CNS anomalies (11/17), combined CNS anomalies and UTM (4/17), and UTM only (2/17). The computed CELSR3 protein structure suggests the position of the identified variants to be implicated in phenotype diversity. Immuno-detection of CELSR3 in the human embryonic urinary tract and transient suppression and rescue experiments of *celsr3* transcripts in fluorescent zf reporter lines suggest an embryonic role in CNS and urinary tract formation.

**Conclusion:** The presented human genetic data, computational simulation of protein structure, and functional analysis in zf larvae suggest biallelic variants in CELSR3 to be implicated in a novel syndrome mainly affecting the CNS and urinary tract.

Sa-3MP 054

A HOMOZYGOUS TBC1D31 VARIATION AS A POTENTIAL NOVEL CAUSE OF AUTOSOMAL RECESSIVE CONGENITAL ANOMALIES OF THE KIDNEY AND URINARY TRACT

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**Aims/Purpose:** Congenital anomalies of the kidney and urinary tract (CAKUT) is one the leading causes of end-stage kidney disease in children. Until now, more than 180 monogenic causes of isolated or syndromic CAKUT have been described. Nevertheless, these genetic factors can explain only about 10 % of CAKUT cases; incomplete penetrance and variable expressivity are often observed.

**Methods:** We described monozygotic twins and a sibling with CAKUT from a consanguineous pedigree in whom no disease-causing mutation was found in already known genes; therefore the family was subjected to research. Monozygotic twins had unilateral kidney dysplasia and bilateral high grade vesicourethral reflux, whereas their sibling showed mild hydronephrosis. None of them had extrarenal findings. Whole-exome sequencing (WES) was performed in monozygotic twins, one affected girl, and their parents. 3D protein modelling and molecular dynamics (MD) simulations were performed to predict pathogenicity of variation.

**Results:** WES identified a total of 39.218, 39.815, 39.325, 39.784 and 39.954 variants for the samples. Filtering steps following Integrative Genomics Viewer (IGV) (The Broad Institute, Cambridge, MA) visualization revealed two homozygous rare missense variants (i.e. TBC1D31 and AGAP4) that were not detected in Genome Aggregation Database (gnomAD) in homozygous state. Among them, TBC1D31 NM\_145647.4: c.187C > G (p.Gln63Glu) variant was classified as “disease causing”, “deleterious” or “damaging by four different variant effect prediction methods (i.e., SIFT, PolyPhen2, MutationTaster and CADD) and therefore was selected for further evaluation with in silico methods. The causative homozygous rare missense variant is located at the glutamine residue at position 63, which is completely conserved among different species until the level of *R.norvegicus*. Protein Modelling and Gibbs Free Energy Calculation of TBC1D31 p.Gln63Glu variant showed decreased protein stability and predicted as “Destabilizing” with all four different protein stability prediction tools upon point mutations. In the MD simulations, p.Gln63Glu variant was shown to be associated with the alterations of atomic interactions in the protein structure.

**Conclusion:** Our study identified a homozygous missense variant in TBC1D31 as a potential novel monogenic cause of isolated CAKUT in childhood thereby expanding its genetic spectrum.

Sa-3MP 055

**CALCINEURIN INHIBITORS IN MENDELIAN STEROID RESISTANT NEPHROTIC SYNDROME: AN INTERNATIONAL RETROSPECTIVE STUDY**

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**Aims/Purpose:** While calcineurin inhibitors (CNI) constitute the first line immunosuppressants for children with non-genetic steroid resistant nephrotic syndrome (SRNS), their use is not recommended for those with monogenic SRNS due to inferior response rates according to previous studies assessing response to immunosuppression in SRNS. However, no studies to date have specifically addressed the role of CNI in monogenic SRNS. We aimed to assess the frequency of response to CNI in monogenic SRNS, their impact in long term kidney survival as well as factors associated with achievement of response.

**Methods:** We retrospectively collected data of children aged 0-18 years with genetically proven monogenic SRNS treated with a CNI for at least 3 months via the use of questionnaires disseminated via the ESPN and IPNA mailing lists. More specifically, demographic, clinical, laboratory, genetic, histopathological and treatment-related information were collected at various time points (ie, at clinical diagnosis, time of CNI initiation, 6, 12, 24 months from treatment initiation and last visit available). Variant pathogenicity was reviewed by a dedicated geneticist and only patients with a pathogenic genotype were included in the analysis. Response to treatment (complete or partial) was assigned as per IPNA SRNS Clinical Practice Recommendations.

**Results:** 141 patients from 37 international paediatric nephrology centers were finally included. At 6 months from CNI initiation and at last visit, 27.6% and 22.5%, respectively, demonstrated either complete or partial response ("at least partial response"). Median observation time between CNI initiation and last visit was 42.1 months (IQR 20.1- 65.6) and was comparable between patients with no response and at least partial response (42.3 vs 41.6 months;  $p > 0.05$ ). Children with at least partial response at 6 months were less likely to progress to kidney failure at last visit versus non-responders (hazard ratio [95%CI] 0.25, [0.10- 0.62];  $P = 0.003$ ) and results were similar for the subgroup of those with a follow-up of at least 2 years (HR [95%CI] 0.35, [0.14- 0.91];  $P = 0.03$ ). Higher serum albumin at CNI onset was the only factor associated with higher likelihood of response at 6 months (odds ratio [95% CI] 1.16, [1.08- 1.24];  $p < 0.001$ ).

**Conclusion:** CNI can be considered as a treatment option in monogenic SRNS on a case-by-case basis since achievement of response is associated with a favorable long term kidney outcome.

Sa-3MP 056

OFATUMUMAB PROVIDES A SAFE AND EFFECTIVE ALTERNATIVE IN RITUXIMAB FAILURE?

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**Aims:** Ofatumumab (OFA) may offer superior efficacy to Rituximab (RTX) due to its stronger binding affinity for the CD20 receptor with similar safety profile. Limited paediatric studies in multidrug resistant nephrotic syndrome (MDRNS) reveal similar therapeutic results between OFA and RTX. However we propose that in cases of allergy and RTX failure (including antibody resistance), a single dose of OFA confers a suitable, safe and effective alternative.

**Methods:** Retrospective report of 3 MDRNS patients treated with OFA (2018 to 2023) for RTX failure or allergy. OFA was administered as a single test dose 300mg/m<sup>2</sup> and then full dose 750mg/m<sup>2</sup> 2 weeks later.

**Results:** Summarised in table below.

**Conclusions:** OFA should be considered in refractory MDRNS and in cases of allergy as there is little to no cross reactivity. A multicentre paediatric clinical trial would ideally serve to prove this is a wider context.

		Male 13 years old	Male 17 years old	Female 7 years old
At presentation	Diagnosis	Secondary SRNS	Secondary SRNS	Primary SRNS
	Age	20 months	8 years old	4 years old
Treatment received before OFA		<ul style="list-style-type: none"> <li>- Prednisolone (oral &amp; IVMP)</li> <li>- Cyclophosphamide (oral)</li> <li>- Levamisole</li> <li>- Tacrolimus</li> <li>- MMF</li> <li>- RTX</li> <li>- LDL apheresis</li> </ul>	<ul style="list-style-type: none"> <li>- Prednisolone (oral &amp; IVMP)</li> <li>- Tacrolimus</li> <li>- MMF</li> <li>- RTX</li> </ul>	<ul style="list-style-type: none"> <li>- Prednisolone (oral &amp; IVMP)</li> <li>- Tacrolimus</li> <li>- MMF</li> <li>- RTX</li> </ul>
Reason for OFA		- No response to RTX after 3 years	- No response to RTX after 5 years	- Allergy to RTX
Date of 1st OFA cycle (2 <sup>nd</sup> doses)		05/2021	07/2018	02/2021
Creatinine (µmol/l)	Before 1st OFA	65	44	44
	After 1st OFA	42	41	41
Plasma Albumin (g/L)	Before 1st OFA	13	19	31
	After 1st OFA	29	35	36
uPCR (mg/mmol)	Before 1st OFA	2732	2844	1138
	After 1st OFA	1610	6	354
Current treatment		<ul style="list-style-type: none"> <li>- Tacrolimus</li> <li>- MMF</li> <li>- OFA</li> </ul>	- OFA	<ul style="list-style-type: none"> <li>- Tacrolimus</li> <li>- MMF</li> <li>- LD Prednisolone</li> <li>- OFA</li> </ul>
Total OFA cycles given		4	5	2
Side effects of IS/INS prior to OFA		- PRES (IVMP), CVC sepsis, right atrial thrombus	- Hypogammaglobinaemia (before anti-CD-20) - Aseptic meningitis	- Chest infections (Azathioprine and IgG prophylaxis)
Latest bloods (2023)	Creatinine (µmol/l)	57	73	53
	p.Albumin (g/L)	32	46	28
	uPCR (mg/mmol)	95.7*	10	478**

SRNS; steroid-resistant nephrotic syndrome, IVMP; intra-venous methylprednisolone, MMF; mycophenolate mofetil, uPCR; LDL; low density lipoprotein, RTX; rituximab, pPCR; urine protein/creatinine ratio, LD; low dose, OFA; ofatumumab, IS; immunosuppression, INS; idiopathic nephrotic syndrome, PRES; posterior reversible encephalopathy syndrome, CVC; central venous catheter

\* partial tubular protein leak

\*\* progressive increase before planning next OFA dose

# SYMPOSIUM 6

# Management Dilemmas

Sa-3MP 057

DECREASED INCIDENCE OF POST-ACUTE COVID-19 ACUTE TUBULO-INTERSTITIAL NEPHRITIS: EFFECT OF VACCINATION IN CHILDREN

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**Aims/Purpose:** COVID-19 is a complex multisystem disease, frequently associated with kidney injury. We recently reported acute tubulointerstitial nephritis (aTIN) without or with uveitis (TINUs) as novel forms of post-acute COVID-19 syndrome in children (Avramescu et al., *Kidney int* 2023). Indeed, between April-2020 and March-2021, we observed a 3-fold and 12-fold increase in aTIN and TINUs incidence respectively, compared to pre-pandemic years. The 48 affected children were mostly adolescents, with a median age at diagnosis of 14.7 years (9.4-17.6). All patients had impaired kidney function with a median eGFR of 31.9 ml/min/1.73 m<sup>2</sup> at diagnosis that rose to 86.0 ml/min/1.73 m<sup>2</sup> at one-year follow-up, while 32% patients had CKD. No patient had concomitant acute COVID-19 at onset of kidney disease. All 16 children tested had high anti-N IgG titers and one had anti-S IgGs. Moreover, COVID-19 ELISpot was positive in the 5 tested children. SARS-CoV-2 RNA was detected by PCR in 2 kidney samples supporting a direct link between SARS-CoV-2 and aTIN/TINUs. The aTIN/TINUs incidence declined after the 1st pandemic wave. This led us to examine whether the vaccination campaign, that was launched on June-2021 for children > 12 yrs in France, may have played a role.

**Methods:** We conducted a French nationwide retrospective cohort study. We included all consecutive children diagnosed with aTIN or TINUs of undetermined cause between April-2022 and March-2023. Patients with an undisputable cause of aTIN (medication, infection, sarcoidosis, Sjogren), were excluded from the study.

**Results:** 14 children were diagnosed with aTIN (n = 10) or TINUs (n = 4) in France between April 2022-March 2023, compared to 16 between April 2021-March 2022 and 48 between April 2020-March 2021. Of the 14 included children, 2 were vaccinated (14%) and 12 were not. In contrast, 64% of aged-matched children in the general population had received a complete vaccination scheme (p < 0.0002). The clinical presentation and outcome were similar to that of patients diagnosed with post-acute COVID-19 aTIN/TINUs during the 1st pandemic wave.

**Conclusions:** aTIN and TINUs are novel forms of post-acute COVID-19 syndrome in children, unique in their exclusive kidney and eye involvement, and distinctive N+/S- serological profile. The aTIN/TINUs incidence declined after the 1st pandemic wave. The vaccination campaign, herd immunity and emergence of new variants might have contributed to this trend. 12/14 children diagnosed between April 2022-March 2023 were not vaccinated and the vaccination rate was significantly lower in this series than in the aged-matched controls. We therefore advocate for vaccination in children and their household, as this may protect them from acute and post-acute manifestations of COVID-19. Our data should also raise awareness that post-COVID-19 aTIN/TINUs may be responsible for chronic kidney damage in adolescents and compromise future kidney function.

Sa-3MP 058

WORLDWIDE VIEW OF ACCESS TO TREATMENT AND INVESTIGATIONS IN NEPHROPATHIC CYSTINOSIS: A 2022 PERSPECTIVE

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**Aims/Purpose:** Nephropathic cystinosis (NC) is a rare inherited lysosomal storage disease, leading to early kidney failure and extra-renal comorbidities. Its prognosis strongly relies on early diagnosis and treatment by cysteamine. Developing Economies [DiE] face many challenges when treating patients for rare and chronic diseases, as demonstrated in our first survey of 2011 [1]. The aim here is to update knowledge on the access to investigations and treatment in DiE, and to assess for potential persistent inequalities between DiE and Developed Economies [DeE] when managing patients with NC.

**Methods:** In this international cross-sectional study, a questionnaire including 43 general items on demographics, access, price and reimbursement of genetic and biological analyses, treatment and follow-up was sent by e-mail to pediatric and adult nephrology centers worldwide between January and September 2022.

**Results:** A total of 109 centers completed the survey, coming from 49 countries and managing in total 741 patients: 43 centers were coming from 30 different DiE and Economies in transition (TrE), whereas the other 66 centers were coming from 19 DeE. In 2022, the access to genetics was 63% in DiE and 100% in DeE, whereas intra leukocytes cystine levels was available for 30% of DiE patients, and for 94% of DeE patients. This represents a major improvement in DiE compared to 2011, when genetics was performed only in 23% patients and intra leukocytes cystine levels wasn't available. The access to cysteamine therapy has also extended in DiE: oral cysteamine access has increased from 53 % in 2011 to 63% of patients, and cysteamine eyes drops from 21% in 2011 to 63% in 2022. However, inequalities and difficulties in DiE remain : delayed form of cysteamine can be delivered to only 7% vs 74% of patients from DiE and DeE, respectively. Refund is still very limited in DiE where most of patients cannot be reimbursed.

**Conclusion:** Over the last decade, access to investigations (namely genetics and intra leukocytes cystine levels) and to cysteamine therapy have improved in DiE. However, discrepancies remain with DeE: access to delayed cysteamine is extremely limited, and reimbursement of therapies and investigations is still profoundly insufficient in DiE, limiting their current use.

References

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Sa-3MP 059

FPC FUNCTION REQUIRED TO SUPPRESS FORMATION OF CYSTIC EPITHELIA IN ARPKD

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**Aims/Purpose:** Loss of ciliary protein function leads to defective control of epithelial morphogenesis and/or homeostasis in hereditary polycystic kidney diseases. To address molecular aspects of epithelial function, genetically modified canine renal tubular epithelial cells, MDCK, provide a well-defined model. In 3D culture, monolayered epithelial spheroids with apicobasal polarity and controlled water and ion transport can be used to analyze consequences of protein expression and pharmacological intervention. Here, we employed epithelial cell clones deficient for the protein fibrocystin (FPC), the cause of ARPKD, to study the impact of FPC cytoplasmic domain expression on cAMP/Src-induced cyst formation.

**Methods:** We used pl-MDCK, sub-cloned principal-like cell lines, with CRISPR/Cas9-based genetic knockout (KO) of *Pkhd1* / FPC and corresponding controls. Cells were grown in matrigel to allow formation of epithelial spheroids within 3 days. Forskolin (Fsk) treatment was employed to induce cAMP-mediated cyst growth mimicking disease conditions. The proportional lumen, i.e. the ratio of lumen to spheroid area, provided a biological readout to detect the enhanced water / ion transport across the barrier that is characteristic of cystic epithelia. Cellular signals known to stimulate cyst formation were modulated by viral expression of the FPC C-terminal domain and/or interventional treatment.

**Results:** In *Pkhd1*-KO cell lines, enhanced cAMP levels resulted in massive lumen expansion of epithelial spheroids with no increase in cell number, and thus, occurred independent of cell proliferation. The observed cyst induction was sensitive to inhibition of Src kinase and was accompanied by activation of STAT3 as indicated by a rise in its phosphorylation on Y705. To address the contribution of FPC to cyst signaling, expression of a membrane-bound FPC C-terminal protein domain was studied, and its processing and intracellular localization determined. Controlled expression of the FPC cytoplasmic domain in *Pkhd1*-KO cell lines suppressed the Fsk-induced increase of proportional lumen / cyst formation, and furthermore, reduced both phosphorylation of STAT3 and transcript levels of STAT3 target genes, *SOCS3* and *c-myc*.

**Conclusion:** In FPC-deficient pl-MDCK cells, cyst formation stimulated by high cAMP levels is associated with enhanced Src/STAT3 signaling. Expression of the FPC cytoplasmic domain can correct control of the epithelial barrier in *Pkhd1*-KO and inhibit cyst growth *in vitro*. Therefore, expression of FPC domain constructs can lead to a gain-of-function and limit cyst promoting signals, a proposed cellular function of FPC protein. Application of FPC mimetics could become a useful strategy to attenuate disease progression in ARPKD.



Sa-3MP 060

RAPIDLY PROGRESSIVE AUTOSOMAL POLYCYSTIC KIDNEY DISEASE: RISK FACTORS DURING CHILDHOOD AND EARLY ADULTHOOD

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**Background and Aims:** Autosomal dominant polycystic kidney disease (ADPKD) is the most common genetic kidney disease and is characterized by genetic complexity and phenotypic variability. The age of reaching kidney failure (KF) is variable and covers the complete age-spectrum. There is an unmet need for early biomarkers to differentiate between rapid and slow progressors. The PROPKD score identified hypertension before the age of 35 years as a risk factor for rapid kidney function decline. We aim to identify earlier risk factors for rapid disease progression by studying a population of ADPKD patients who reached kidney failure (KF) before the age of 40y.

**Method:** This multicentric retrospective study focusses on a unique population (n = 200) of ADPKD patients who reached KF before 40y. Kidney failure (KF) was defined as CKD5 or start of Kidney Replacement Therapy (KRT), whichever came first. Longitudinal data on childhood history, comorbidities and kidney function were collected. Life table and Proportional Hazards analysis were used to assess associations between clinical parameters and time to KF.

**Results:** Median age of ADPKD diagnosis was 22.3 (16.5 – 28.6) and median age of KF onset was 36.2 years (32.9–38.7 years). Forty-seven patients were genotyped (23.5%) of which 38 patients (81.0%) were PKDIT and 8 (17.0%) were PKDINT and only 1 patient (2.1%) was PKD2. Median age at first urological event was 27.0 (20.7 – 32.0) years. 71 patients (35.5%) had history of UTI's, 67 patients (33.5%) had hemorrhagic cysts on abdominal imaging, 66 patients (33.0%) presented with gross hematuria and 40 patients (25.0%) presented with kidney stones. . There was a high prevalence of hypertension (N = 128, 64.0%). Four patients (N = 4/128, 3.1%) had a very early diagnosis of hypertension before the age of 10 years. Hypertension-onset before the age of 18 years correlated with a significantly faster progression (UV HR: 2.07 (1.32 – 3.25)).

**Conclusion:** This study describes a unique cohort of ADPKD patients with rapid disease progression. Hypertension at young age (= 18) correlated with rapid disease progression, suggesting that ambulatory blood pressure in children might be useful to identify patients at risk for rapidly progressive ADPKD.

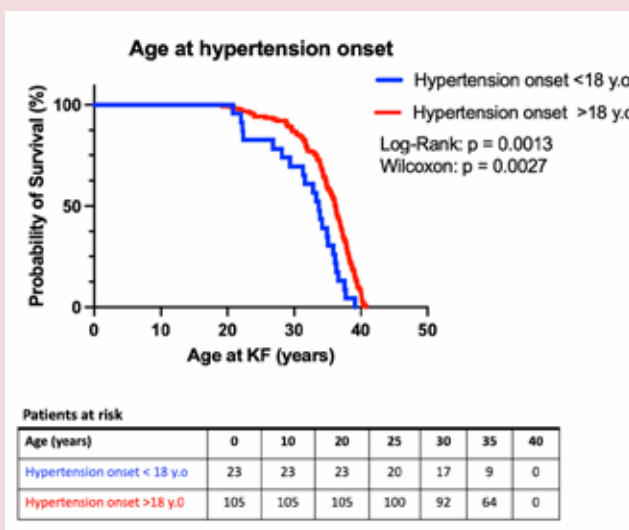


Figure: Survival analysis with endpoint defined as age of KF between patients with ADPKD and hypertension onset before or after 18 years old.

# GUIDELINES SESSION

## CAKUT WG

Sa-3MP 061

HOW WELL DO WE PREDICT RENAL DYSPLASIA? COMPARISON BETWEEN PRENATAL ULTRASOUND AND POST NATAL RENAL SCINTIGRAPHY

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**Purpose/ Aims:** Congenital anomalies of the kidneys and urinary tract (CAKUT) are among the most diagnosed congenital malformations. As urinary tract dilatations or obstructive uropathies can be easily diagnosed and interpreted, the renal parenchymal appearance and the future renal function estimation is based on subjective evaluation including parenchymal thickness and echogenicity. The aim of our study was to assess the accuracy of prenatal estimation of renal dysplasia and reduced renal function compared to objective post-natal renal scan.

**Methods:** A retrospective cohort study was conducted in a single tertiary referral center. Cases diagnosed prenatally with CAKUT, maintained follow-up in the paediatric nephrology institute, and underwent a renal scan - comprised the study group. Prenatal scans were revised and classified for the risk for dysplasia and future renal function according to the renal parenchymal appearance (thickness, echogenicity, cysts). Cases that demonstrated intra-uterine renal failure were excluded. Renal scan was performed on a need basis in selected cases. The possibility for renal dysplasia was compared to post-natal renal scan results (mild and severe dysplasia).

**Results:** 58 cases fulfilled all inclusion criteria and comprised the study group. A total of 116 kidneys were evaluated (all children included in the study had two kidneys). 34 kidneys were estimated prenatally as dysplastic kidneys, of them 24 kidneys (70%) were found to have features of dysplasia according to renal scan. 82 kidneys were estimated prenatally to have normal function, of them 26 kidneys (30%) were found to have dysplasia according to renal scan. The sensitivity, specificity, PPV, and NPV for prenatal classification of renal dysplasia were 76%, 84%, 70.5%, and 68.3%, respectively. Final diagnosis included ureteropelvic junction obstruction in 34 cases, vesicoureteral reflux in 9 cases and other diagnoses as posterior urethral valve, ureterocele, ureterovesical junction obstruction in the remaining cases.

**Conclusions:** Estimation of kidney function during the prenatal period is an important challenge and may influence decisions regarding pregnancy. Although post-natal renal scintigraphy is not performed routinely, the presented results shed light on the prenatal ability to predict renal dysplasia in cases of CAKUT. Estimating renal parenchyma is subjective and operator dependent, and the predictive value is currently sub-optimal even in a tertiary referral center. Creation of objective tools may improve the predictive ability of prenatal ultrasound to predict post-natal renal function.

Sa-3MP 062

URINARY TRACT INFECTIONS CAUSED BY EXTENDED-SPECTRUM B-LACTAMASES (ESBL)-PRODUCING PATHOGENS. A SINGLE CENTER EXPERIENCE

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**Aims/Purpose:** The global spread of antimicrobial-resistant microorganisms, particularly extended-spectrum beta-lactamases (ESBLs), has become a worldwide problem with serious consequences on the treatment of infectious diseases. Urinary tract infections (UTIs) are the most common ESBL-related bacterial infections in children and constitute a therapeutic challenge for pediatricians. The aim of the study was to investigate the epidemiological data, frequency, trends and susceptibility patterns of UTI caused by ESBL-producing enterobacteriaceae in children.

**Methods:** Children, 15 days – 16 years old, hospitalized between 01/01/2012 and 31/12/2019 suffering from enterobacteriaceae-associated UTIs with ESBL phenotype. Urine culture was obtained based on age-related recommendations. Identification and susceptibility testing was done by the API system and the antimicrobial disc diffusion method.

**Results:** A total of 36 positive urine cultures due to ESBL-producing pathogens were obtained from 35 patients (16 boys), while, one patient had 2 UTI episodes in which *Klebsiella pneumoniae* and *Escherichia coli* were isolated, respectively. The mean age of children was 43.38 months, while 63.63% had antecedent history of UTI and 40% had receiving chemoprophylaxis during UTI episode, most commonly trimethoprin+sulfamethoxazole. In addition, 20% of patients had vesicoureteral reflux, while 40% had congenital anomalies of the kidney and urinary tract. Overall, the strains isolated were *Escherichia coli* (58.3%), *Pseudomonas aeruginosa* (16.7%), *Klebsiella pneumoniae* and *Enterobacter cloacae* (each 8.3%, respectively), and one strain of *Proteus mirabilis*, *Enterobacter aerogenes* and *Citrobacter freundii* (each 2.8%, respectively). The overall susceptibility tests of the 36 ESBL-producing pathogens showed that resistance was: trimethoprin+sulfamethoxazole (77.8%), quinolones (41.2%), nitrofurantoin (33.3%) and aminoglycosides (26.3%). Noteworthy is the fact that all strains were sensitive to carbapenems, either meropenem or imipenem.

**Conclusion:** *Escherichia coli* strains were the most common uropathogen among those with an ESBL phenotype, but other less common enterobacteria also showed high rates. In this study, carbapenems were the most reliable treatment option, while quinolones and aminoglycosides showed high resistance.

Sa-3MP 063

DESCRIPTIVE ANALYSIS OF A PEDIATRIC POPULATION WITH HORSESHOE KIDNEY: A RETROSPECTIVE MULTICENTER OBSERVATIONAL STUDY

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**Aims/Purpose:** Horseshoe kidney (HSK), the most common fusion defect of the kidneys, consists of two distinct functioning kidneys on both sides of the midline which are fused together at one of the poles by an isthmus of functioning renal parenchyma or fibrous tissue. Children with HSK are often asymptomatic, thus the condition is identified incidentally and has historically been associated with a good prognosis. However, complications such as infections, hypertension, nephrolithiasis, impaired renal function, and urinary tract obstruction can develop. The objective of our study was to evaluate the incidence and spectrum of renal complications and extra-renal diseases and syndromes in children with HSK.

**Methods:** The medical records of 353 children with a diagnosis of HSK followed at 15 different Italian pediatric nephrology clinical units between 2012 and 2022 were retrospectively reviewed and the results were compared with the data in the literature.

**Results:** We enrolled 124 girls (35.2%) and 229 boys (64.8%). HSK was prenatally diagnosed in 71 patients (20.1%), 70 patients (19.8%) received an erroneous prenatal diagnosis, while HSK was incidentally found postnatally in 120 patients (34.4%). The isthmus was parenchymatous in 96% of cases, involving the lower poles in 91% of patients. Aspects of hypo-dysplasia were present in at least one kidney in 95 patients (26.9%). Comparing our data with the literature, we found that HSK children had a better renal outcome than reported: urinary tract infection was detected in 96 patients (26.4% vs 41.4%), 17 patients developed proteinuria (4.8% vs 14.6%), hypertension was diagnosed in 12 patients (3.4% vs 9.8%), 6 patients developed some degree of CKD (1.7% vs 7.3%), none were in ESRD. Conversely, an increased risk of nephrolithiasis was documented, with 21 patients experiencing at least one episode of nephrolithiasis (5.9% vs 3%). Genito-urinary tract anomalies were present in 138 patients (39.1%): VUR was found in 32 patients (9.1% vs 9.7%), SGPU in 6 patients (1.7% vs 1.6%), hypospadias in 11 patients (3.1% vs 1.1%). Seventy-three patients (20.6%) had extrarenal diseases or syndromes. Cardiovascular (8.2% vs 5.3%) and bone (4.5% vs 14.2%) anomalies were the most common. Turner syndrome was the most common (6 patients) followed by VACTERL syndrome (4 patients).

**Conclusion:** We can confirm that HSK is associated with a favorable prognosis and a lower risk of developing complications than described in the literature; the presence of hypo-dysplasia plays a fundamental role in the outcome of these patients as it is detectable in 100% of CKD, 80% of hypertensive and 50% of proteinuric patients. Furthermore, the high percentage of incidental diagnoses suggests that this condition is still underdiagnosed, which probably further reduces the effective prevalence of complications in the outcome of these patients.

Sa-3MP 064

CHRONIC KIDNEY DISEASE-MINERAL BONE DISORDER AFFECTS ALL SKELETAL SITES UNIFORMLY NORMAL O FALSE FALSE FALSE EN-GB X-NONE X-NONE

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**Aims/Purpose:** Abnormal bone mineralisation is known to occur early in children and young people with CKD, causing bone mineral density (BMD) decrease, disproportionate fracture burden and bone disease. Serum biomarkers are only moderate predictors of BMD, and no radiological imaging has yet proven a useful adjunct in assessing BMD in young people with CKD. Multiple body sites have been used in dual energy X-ray absorptiometry (DXA) and peripheral quantitative computed tomography (pQCT) studies to assess BMD. It is not known if CKD-related changes in BMD affects different skeletal sites uniformly. Our aim was to examine multiple trabecular and cortical sites in young people with CKD and compare the BMD and the rate of change in BMD.

**Methods:** We performed a multi-centre cross-sectional study: 69 participants on dialysis and 18 in CKD4-5 (n = 87 total), aged 5 to 30 years old [median 13.97 (IQR 10.8 to 16.2)]. Patients under 30 yrs of age were studied as bone mineral accretion may continue up to 30 yrs when peak bone mass is achieved. Participants underwent hip and lumbar spine (LS) DXA [for areal BMD (aBMD)], tibial and radial pQCT (for volumetric cortical and trabecular BMD) of non-dominant limbs. Thirty-eight participants attended a follow up visit 1.4 years later (IQR 1.2, 1.7).

**Results:** Three different trabecular sites (radius 4%, tibia 3%, 4% length) were significantly different from each other [233.5 (196.6, 288.4) vs 224.7 (197.7, 252.9) vs 212.9 (184.3, 251.8) mg/cm<sup>3</sup> respectively, p < 0.0001] (Fig 1). The difference was more pronounced between the cortical sites (Radius 66%, Tibia 38%) [1010 (941.1, 1080) vs 1098 (1044, 1150) mg/cm<sup>3</sup>, p < 0.0001] and DXA LS vs hip sites [0.90 (0.75, 1.15) vs 0.87 (0.70, 1.02) g/cm<sup>2</sup>, p < 0.0001]. Bland-Altman analysis showed there was only moderate correlation of measurements within the trabecular loci (R2 0.11-0.22, p = 0.002) and cortical sites (R2 0.19, p < 0.001). At follow up, there was no difference between annualised radial and tibial trabecular BMD change -0.60 (-18.22, 11.41) vs -0.37 (-8.46, 10.03) mg/cm<sup>3</sup>/yr or cortical BMD change 4.55 (-19.46, 33.23) vs 6.71 (-8.06, 13.56) mg/cm<sup>3</sup>/yr, indicating that changes in BMD uniformly affect both skeletal sites (Fig 2). There was also no difference between annualised DXA lumbar spine and hip aBMD change 0.02 (-0.03, 0.06) vs 0.01 (-0.02, 0.05)g/cm<sup>2</sup>/yr, p = 0.72).

**Conclusions:** There are significant BMD differences between upper and lower limb trabecular and cortical bone compartments. These may be partially explained by normal anatomy and weight bearing. In a young cohort with CKD and on dialysis the rate of annualised change in different bone compartments is uniform. Any longitudinal BMD assessments need to take into account the heterogeneity present in the literature, and use one site for measurement consistency.

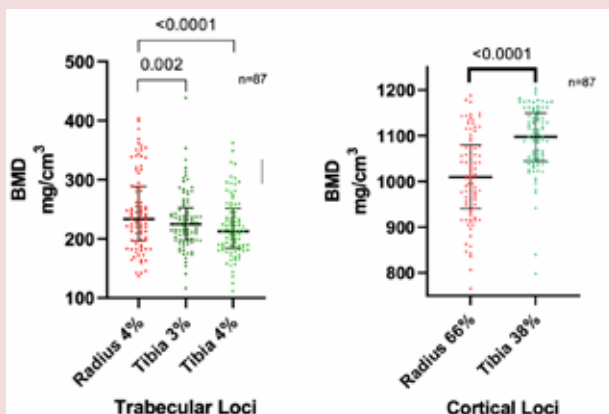


Figure 1: Trabecular and Cortical BMD at radial and tibial sites.

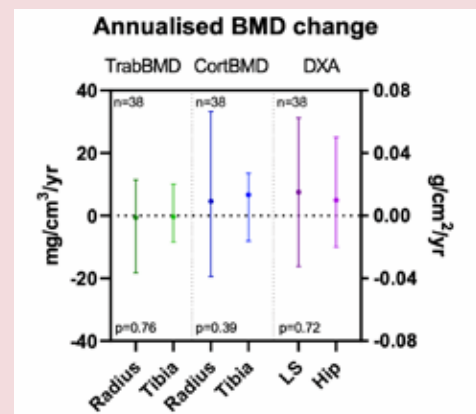


Figure 2: Annualised BMD change.

Sa-3MP 065

KIDNEY VOLUME NORMATIVE VALUES IN CHILDREN AGED 0-18 YEARS – PRELIMINARY RESULTS OF MULTICENTER STUDY

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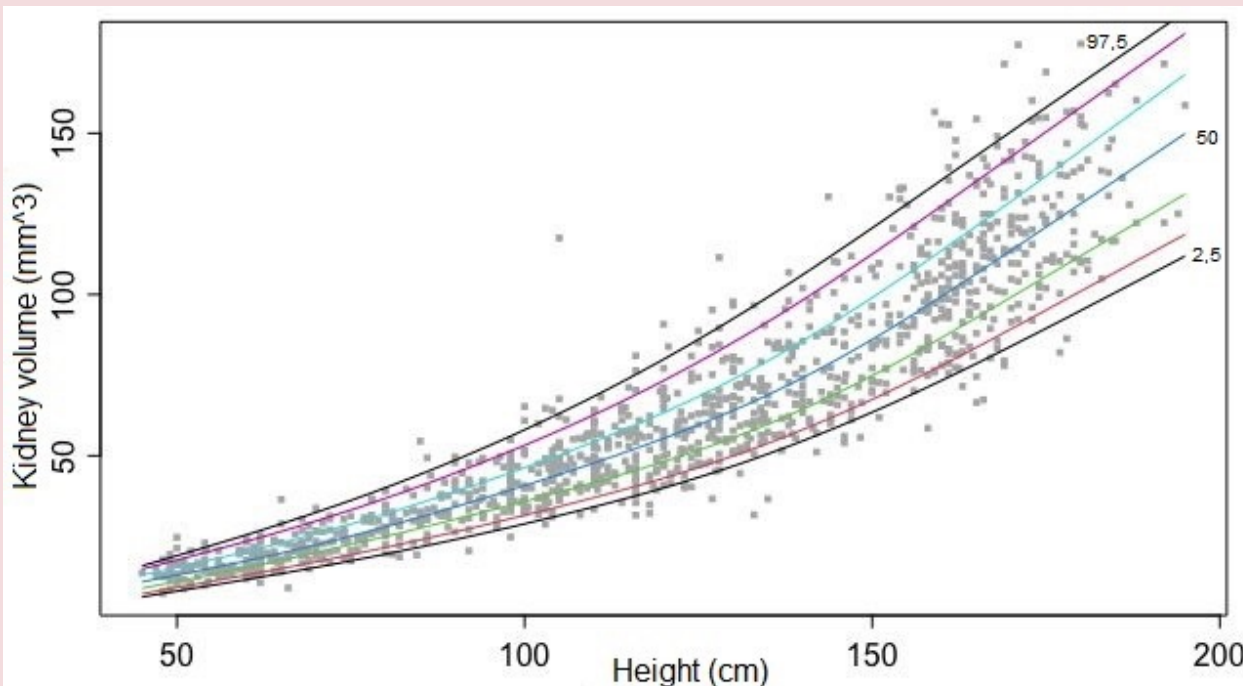
**Introduction:** Kidney volume (KV) assessment is particularly important in conditions such as polycystic kidney disease. The most widely used KV norms, published in 1985, are based on the German study including 325 patients aged 0-16 years with no kidney function assessment.

**Objectives:** The aim of the study was to develop ultrasound-based normative values of KV in European healthy children and adolescents aged 0-18 years.

**Methods:** Our study already included 1160 patients aged 0-18 years (551 boys; 48%), with normal glomerular filtration rate, no history of urinary tract infections, no kidney abnormalities on abdominal ultrasound, recruited in schools and kindergartens as well as in pediatric units in Poland, Czech Republic and Lithuania. The examination was conducted in accordance with the standards of the Polish and European ultrasound societies.

**Results:** Kidney volume (mean  $\pm$  SD) increased progressively from  $18 \pm 6$  mm<sup>3</sup> in infants to  $114 \pm 25$  mm<sup>3</sup> in 18 years old. Based on the ultrasound measurements, KV nomograms (including 2.5th; 10th; 25th; 50th; 75th; 90th and 97.5th percentiles) for patients aged 0-18 years were developed using quantile regression. There were no sex-related or side-related (left or right) differences in KV. Out of anthropometric parameters height was the most significant predictor of KV ( $r = 0.95$ ), followed by body surface area ( $r = 0.94$ ), age ( $r = 0.91$ ), and body mass index ( $r = 0.68$ ;  $p = 0.001$  in all). We also developed a formula to calculate the average KV (50th percentile) using the patient's height.  $KV = \text{EXP}(\text{LN}(\text{height in cm}) * 1.77 - 4.44)$  and cut-off points for small [ $< 2.5$ th percentile;  $KV = \text{EXP}(\text{LN}(\text{height in cm}) * 1.85 - 5.18)$ ] and enlarged kidney [ $> 97.5$ th percentile;  $KV = \text{EXP}(\text{LN}(\text{height in cm}) * 1.71 - 3.74)$ ].

**Conclusions:** The main determinant of kidney volume was statural height. Our results, based on a largest pediatric cohort to date, can serve as reference values in clinical practice and research studies.



# GUIDELINES SESSION

## Glomerular Diseases WG



Sa-3MP 066

LEVAMISOLE SUPPRESSES ACTIVATION AND PROLIFERATION OF HUMAN T-CELLS BY THE INDUCTION OF A P53-DEPENDANT DNA DAMAGE RESPONSE

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**Purpose:** Levamisole (LMS) is used in the treatment of idiopathic nephrotic syndrome (INS). The pathogenesis of INS remains unknown, but points towards an immunological basis of the disease. LMS increases the relapse-free survival in INS patients treated with corticosteroids with few side effects. While LMS has been hypothesized to exert an immunomodulatory effect, its mechanism of action remains unknown. To provide insight into the working mechanism of LMS, we studied its immunomodulatory activity on in vitro cultured human T-cells.

**Methods:** Human T-cells were isolated from buffy coats and activated with anti-CD3/anti-CD28. To determine the affected signaling pathways during LMS treatment, RNA sequencing was performed. Differentially expressed genes were verified on protein level by flow cytometry and western blot analysis. The effects of LMS on T-cell activation, proliferation, toxicity and cell cycle were assessed by flow cytometry. T-cell specific cytokine production was measured by multiplex immunoassay. Finally, the DNA damage response was assessed through analyzing  $\gamma$ H2AX-positive foci by using fluorescence microscopy.

**Results:** Treatment with 1 mM LMS decreased T-cell activation and proliferation, shown by decreased CD69 expression and Celltrace dilution, respectively. LMS decreased proliferation and activation in CD4<sup>+</sup> and CD8<sup>+</sup> T-cells. This was supported by the reduction of cytokines production associated with activation: IL-2, TNF- $\alpha$  and IFN- $\gamma$ . Contrastingly, IL-4 and IL-13 production was increased in LMS-treated T-cells. RNA sequencing confirmed the suppressive effects of LMS on proliferation as numerous genes involved in cell cycle progression were downregulated. Genes associated with p53 activation and cell cycle arrest were upregulated by LMS. LMS increased the expression of p-p53 and the p53 target Fas. There was no basal increase of apoptosis in LMS-treated T-cells, but treatment with Fas ligand increased the amount of cleaved caspase-3, alluding to a sensitizing effect of LMS for apoptosis through the activation of p53. With cell cycle analysis, LMS induced a mid S phase arrest and overexpression of p-CHK1, indicating replication stress. Finally, expression of nuclear  $\gamma$ H2AX-foci was increased in T-cells treated with LMS, confirming increased DNA damage.

**Conclusion:** Our in vitro findings indicate that LMS acts as an immunosuppressive drug directly affecting T-cell activation and proliferation by a p53-dependant DNA damage response.

Sa-3MP 067

APOLIPOPROTEIN L1 LOCALIZATION IN ENDOPLASMIC RETICULUM TRIGGERS CALCIUM FLUX LEADING TO KIDNEY DYSFUNCTION

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**Background:** Apolipoprotein L1 (APO1) risk variants (G1 and G2) have been known to provide protection against African trypanosome parasites. However, this is accompanied by a significant increased risk of developing kidney disease in human with the homozygous (G1/G1 and G2/G2) or compound heterozygous (G1/G2) form of these risk variants. Nevertheless, the mechanisms leading to the kidney damage remain poorly understood, with little or no consensus on the pathophysiological mechanism. Yet, it has been shown that the APO1 risk toxicity is dependent on the haplotype background.

**Methods:** Using site-directed mutagenesis, we introduced the APO1 risk variants as well as the haplotype backgrounds (EIK and KIK) mutations into an APO1 reference (EMR) GO pCDNA3.1 plasmid tagged at the C-terminal with GFP. These constructs were then transiently transfected into human embryo kidney (HEK) 293T cells for 24 hours. Subcellular localization of the APO1 was visualized using Confocal microscopy (63x), while cell viability was measured using Resazurin dye. To understand the effect of APO1 on calcium ion flux, changes in intracellular calcium concentration were monitored using ratiometric Fura-2-acetoxymethyl ester based fluorimetry. Ionomycin was used to release intracellular calcium stores.

**Results:** Transiently transfection of HEK 293T cells with APO1 results in the localization of APO1 to the endoplasmic reticulum and mitochondria. This leads to an increased basal calcium flux activity, which is both risk variants and haplotype dependent. This effect was maintained upon stimulation with ionomycin. In addition, transfection of HEK 293T cells results in decreased cell viability in a haplotype dependent manner, with the reference (EMR) haplotype having less cytotoxicity when compared to the other haplotypes (EIK and KIK). Similarly, the cytotoxicity was more pronounced in the risk variants, when compared to the GO.

**Conclusion:** We propose that APO1 channel activity results in the flux of calcium ion from the calcium stores, predominately the endoplasmic reticulum and this event precedes cell death.

Sa-3MP 068

THE FRENCH 2022 EPIDEMIC OF SHIGA-TOXIN PRODUCING *ESCHERICHIA COLI* O26: H11 : CHARACTERISTICS AND OUTCOME OF PATIENTS

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**Background:** An outbreak of Shiga toxin producing *Escherichia coli* associated hemolytic uremic syndrome (STEC HUS) occurred in France between January and April 2022. Consumption of frozen pizzas was surprisingly identified as the vehicle of infection. We report the clinical and biological characteristics of the patients, and the outcome at one and three months follow-up.

**Methodology:** Patients with STEC HUS linked to the *E.coli* O26H11 outbreak were identified using the national network of pediatric STEC HUS of the Santé publique France Institute, and The French National Reference Centre (CNR) for enterohaemorrhagic *Escherichia coli*. Data were analyzed from the patients hospital records.

**Results:** 49 pediatric cases of STEC HUS linked to the outbreak cluster were identified. The outbreak peaked in February 2022. Median age was 74 months (range 9-213). Most of them (81%) presented with diarrhea, 8 had received prior antibiotherapy. Two patients died within the first month, one from cardiac failure and one from neurologic injury. 33 (67%) patients required dialysis. Twenty (40%) had an extra renal manifestation: central nervous system for 16, cardiac involvement for 17 (13 isolated troponin elevation, 2 severe cardiac failure, 2 needed pericardial drainage). Eculizumab infusion was performed for 12 patients, and 2 had plasma exchanges. At one-month follow-up, 5 patients were still hospitalized (mostly for neurological indication) and 13 patients had a glomerular filtration rate below 80 ml/min/1.73m<sup>2</sup> and 12 had hypertension. Epidemiological investigations identified the frequent consumption of a specific brand frozen pizza. Samples of pizza crust and flour used by the brand were tested positive for STEC.

**Conclusion:** The 2022 STEC HUS outbreak with *E. coli* O26: H11 strain is the largest one to date in France. Patients were older, with a high rate of dialysis requirement, neurologic and cardiac involvements. The short term outcome was favorable in most cases but marked by an important rate of renal and neurological sequelae. The patients age in this outbreak points out the need to extend the protective measures aiming to prevent STEC infections to older children. Although flour presents a known STEC risk, frozen pizzas are a surprising vehicle of contamination. Further investigations are ongoing to understand sources of contamination and persistence of STEC in home-cooked matrices such as raw pizza dough and genomics characterization of the O26 H11 strain.

Sa-3MP 069

IMMUNOGLOBULIN LEVELS IN CHILDREN TREATED WITH IMMUNOSUPPRESSIVE AGENTS FOR STEROID-DEPENDENT OR FREQUENT RELAPSING NEPHROTIC SYNDROME

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**Aim:** A significant proportion of children with idiopathic nephrotic syndrome [INS] require long-term immunosuppressive therapy [IMS]. With the introduction of biological drug – Rituximab [RTX] concerns have risen about treatment associated hypogammaglobulinemia and its consequences. Little is known about the prevalence of hypogammaglobulinemia in INS children on standard IMS therapy. The aim of this study is to calculate the incidence of hypogammaglobulinemia in an unselected cohort of children treated for INS.

**Methods:** A cross sectional analysis of serum IgG, IgM, IgA levels was performed in 64 prevalent children [23 females and 41 males] with INS at a single tertiary care center. Mean age at analysis was 11.6 [4.7–18 ] years. All children had received prolonged IMS, of which 36/ 64 had received RTX. Samples for serum immunoglobulin levels were collected in complete remission of INS and following B cell reconstitution in RTX treated subjects. The study was supported by an unrestricted grant provided by European Society for Paediatric Nephrology.

**Results:** The mean serum IgG levels in the total cohort was:  $7.65 \pm 2.42$  g/L, IgM:  $1.08 \pm 1.53$  g/L and IgA:  $1.18 \pm 0.84$  g/L. A decreased for age serum IgG was noted in 50% [32/63] of children, low IgM in 22.4% [11/49] and low IgA in 35.3% [18/51]. The mean serum levels of immunoglobulins in children treated with RTX versus those on standard IMS therapy did not differ statistically: IgG [ $7.13 \pm 2.6$  vs.  $8.34 \pm 1.79$ ;  $p = 0.06$ ], IgM [ $1.08 \pm 1.81$  vs.  $1.06 \pm 0.47$ ;  $p = 0.07$ ] and serum IgA [ $1.27 \pm 0.98$  vs.  $1.03 \pm 0.46$ ;  $p = 0.616$ ]. Among the RTX treated group, low for age IgG was present in 55.5% [20/36], low IgM in 26.4% [9/34] and low IgA in 44.1% [15/34]. Among the group on standard IMS therapy, low for age IgG was present in 44.4% [12/27], IgM in 13.3% [2/15], IgA 16.6% [3/18]. The differences in hypogammaglobulinemia rates between RTX treated subjects and those on standard IMS were not statistically significant.

**Conclusions:** Hypogammaglobulinemia is a common finding in children with INS on long term immunosuppressive therapy. Hypogammaglobulinemia is observed not only in children treated with RTX but also in those on standard IMS.

Sa-3MP 070

RISK OF RELAPSE AFTER SARS-COV-2 VACCINATION IN CHILDREN WITH IDIOPATHIC NEPHROTIC SYNDROME

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**Aims/Purpose:** Vaccination against SARS-CoV-2 has drastically reduced COVID-19 morbidity and mortality. Nevertheless, the temporal association between SARS-CoV-2 vaccination and relapse in patients with idiopathic nephrotic syndrome (INS) has been reported, despite the real risk is unknown.

**Methods:** We performed a retrospective observational study to evaluate the risk of relapse in all INS children eligible for SARS-CoV-2 vaccination (age > 5 years). Children were classified as vaccinated or unvaccinated controls. The risk of relapse was assessed in a 120-days period starting from the first dose in vaccinated patients and in a comparable randomly selected timeframe in the unvaccinated control population.

**Results:** A total of 156 INS children were enrolled, including 91 vaccinated (44 females, median age 12.8 years) and 65 controls (24 females, median age 9.5 years). During the 120-day study period, relapses were documented in 5/91 vaccinated and 11/65 unvaccinated patients, with a total of 5 and 13 relapses, respectively. The rate of INS relapse in children undergoing or not SARS-CoV-2 vaccination was not statistically different at 30 (1/91 vs 2/65,  $p = 0.39$ ), 60 (4/91 vs 4/65,  $p = 0.62$ ) and 90 (4/91 vs 10/65,  $p = 0.05$ ) days after vaccination. In contrast, the relapse rate was significantly lower in the vaccinated group at 120 days (5/91 vs 13/65;  $p = 0.014$ ). The results were confirmed after correcting for age and sex (OR 0.27).

**Conclusion:** SARS-CoV-2 vaccination does not increase the risk of relapse and can be safely performed in children with INS.

# GUIDELINES SESSION

## CKD MBD WG

Sa-3MP 071

GASTROSTOMY TUBE FEEDING IMPROVES WEIGHT BUT NOT HEIGHT IN YOUNG CHILDREN WITH CHRONIC KIDNEY DISEASE

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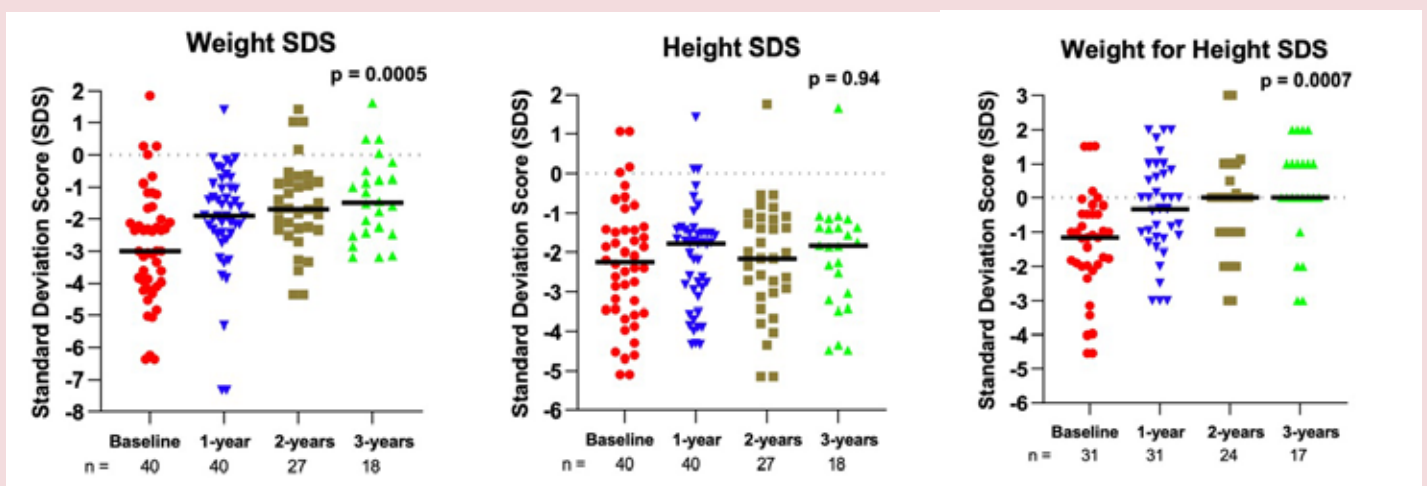
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**Aims/Purpose:** Gastrostomy tube (GT) feeding is often used to promote growth in children with chronic kidney disease (CKD) who require long-term feeding support. However, some studies suggest that GT feeding increases the risk of obesity, which is becoming more prevalent in the paediatric CKD population, mirroring the global trend. Obesity may have negative effects on CKD by increasing the risk of cardiovascular disease, worsening kidney function, and potentially causing non-alcoholic fatty liver disease (NAFLD). The aim of our study is to explore a relationship between gastrostomy feeding and obesity in children with CKD.

**Methods:** This is a single centre study in patients with CKD stages 2-5 and on dialysis at a tertiary children's renal unit. Data on anthropometry, biochemistry, and nutritional composition of feeds were collected from the time of GT insertion for 3 years or until transplantation.

**Results:** 40 children (18 female) were included. 19 children were on peritoneal dialysis, 8 on haemodialysis, 8 with CKD stages 4- 5, and 5 with stage CKD 3. The median (interquartile range [IQR]) age of patients at GT insertion was 1.26 (0.61 to 3.58) years. The median duration of gastrostomy feeding was 5.32 (3.05-6.31) years. Children showed a significant increase in weight ( $p = 0.0005$ ), weight-for-height ( $p = 0.0007$ ) and BMI ( $p = 0.0001$ ) z-scores. (Figure 1). Although not significant, the median height SDS increased into the normal range (from -2.29 to -1.85). According to the WHO definition of childhood obesity, no child was obese. No child had transaminitis implying that none of the children had NAFLD. Weight z-score and the percentage energy intake of estimated average requirements (EAR) from feeds had a positive correlation ( $p = 0.02$ ), as did BMI z-score and the percentage fat of total energy intake ( $p = 0.001$ ). At 1-year follow up, protein/energy ratio correlated with weight ( $p = 0.009$ ), height ( $p = 0.01$ ), weight-for-height ( $p = 0.009$ ), and urea ( $p = 0.05$ ). Height SDS and weight-for-height SDS correlated more closely with eGFR both at baseline ( $p = 0.005$  and  $p = 0.03$ , respectively) and at 12-months ( $p = 0.04$  and  $p = 0.05$ ), rather than with any nutritional parameter.

**Conclusion:** These findings suggest that GT feeding improves weight and BMI z-scores without leading to obesity. No significant improvement in height z-score with G-tube feeding was found, which calls for the consideration of other factors such as growth hormone therapy in addition to nutritional optimisation.



Sa-3MP 072

**SERUM METABOLIC PROFILE IS ASSOCIATED WITH CLEARANCE ADEQUACY IN PEDIATRIC PERITONEAL DIALYSIS POPULATION: PRELIMINARY RESULTS OF AN ONGOING PERSPECTIVE STUDY**

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**Aims/Purpose:** Peritoneal dialysis (PD) is a common renal replacement therapy for children with end stage renal disease. Long-term use of the method may result in peritoneal fibrosis and insufficient clearance. Purpose of the present study was to investigate the metabolic profile of the patients and its correlation with the adequacy of creatinine clearance with the ultimate goal of identifying potential biomarkers that could predict early peritoneal dysfunction.

**Methods:** Serum samples from 15 patients undergoing PD were analyzed. Patients were divided into subgroups, based on Creatine Clearance (CrCl) (3 groups, CrCl: < 50, 50-80, > 80 L/1.73m<sup>2</sup>/week). Statistically significant correlations with the highest absolute correlation coefficient are described. Regarding metabolic technologies used, two targeted Liquid Chromatography - Mass Spectrometer (LC-MS) methodologies were used for the determination of metabolites. All samples were analyzed by a hydrophilic interaction liquid chromatography coupled to mass spectrometry (HILIC-MS / MS) method previously developed and validated in our laboratory for the simultaneous determination of amino acids and their derivatives in biological fluids. Also, high flow analysis was carried out (LC quadrupole Time-of-Flight analysis - High performance LC / MS).

**Results:** A total of 13 metabolites were found to differentiate between the three groups. Specifically, grouping the patients by CrCl, kynurenine, glucuronic acid, HIAA, pyroglutamic acid, succinate, NAG and deoxycytidine found to differentiate significantly between the three groups (p = 0.05). Based on the literature, kynurenine has a known role in kidney disease and succinate is also a known marker for inflammation. In addition, the remaining studied metabolites (glucuronic acid, HIAA, pyroglutamic acid, NAG and deoxycytidine) also appear to be involved in inflammation and oxidative stress pathways. Of note, follow-up of our patients highlighted that patients with satisfactory dialysis adequacy but with the presence of increased concentration of specific biomarkers in the serum progressively over a period of 6 months developed loss of clearance.

**Conclusion:** Our results is a strong indication that specific serum metabolic profile may be associated with the current status and possibly predictive of the future status of this population. Metabolomics technologies seems to could play a crucial role in the early diagnosis of peritoneal dysfunction.



Sa-3MP 073

DIETARY PHOSPHATE EDUCATIONAL MATERIALS FOR PAEDIATRIC CHRONIC KIDNEY DISEASE: IS INCONSISTENT MESSAGING REDUCING THEIR IMPACT?

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**Aims:** Controlling dietary phosphate intake is integral to the management of children with chronic kidney disease (CKD). The practical implementation of this is not well described. We aimed to review phosphate educational materials (PEMs) used in paediatric CKD and evaluate their quality and content.

**Methods:** Written text PEMs, requested from paediatric renal dietitians in the UK and internationally, were screened to exclude duplications, those intended for adults or not focused on phosphate (P). The quality of the PEMs was assessed using validated suitability (Suitability Assessment of Materials [SAM]) and readability (Flesch Reading Ease [FRE] and Flesch-Kincaid [FK] Grade Level) instruments. 48 codes were derived for format, appearance, target audience, resource type and content, and independently reviewed by 3 dietitians, aiming for intercoder reliability (ICR) = 80%.

**Results:** Of the 63 PEMs obtained 37 were paediatric-focused (28 written, 2 pictorial, 1 video, 1 app, 4 games, 1 recipe booklet). Of the 28 written PEMs, 32% were aimed at caregivers, 25% children and 43% unspecified. 75% included a production date, with 24% produced < 2 years ago, 57% 2- < 5 years, 9.5% 5-10 years and 9.5% > 10 years ago. The median FRE test score was 68.2 (IQR 61.1-75.3) and median FK reading grade level was 5.6 (4.5-7.7). 54% of written PEMs were rated “superior” (≥ 70 rating), 38% “adequate” (40-69) and 8% “not suitable” (≤ 39). Low scoring PEMs lacked a summary (12%), cover graphics (35%) or had irrelevant illustrations (50%). An ICR of 87% was achieved. Over ½ PEMs were limiting higher P foods in agreement with the Paediatric Renal Nutrition Taskforce (PRNT), but > ⅓ restricted legumes and wholegrains (Figure 1). P additives were mentioned in 89% of PEMs. Over ⅓ of the PEMs had inaccuracies and < ⅓ included practical advice (Table 1).



Figure 1: Inclusion of specific dietary advice in PEMs.

Domain	Category	Sub-category	% PEM
Background		Introduction	68
		Consequences	89
		Blood levels	11
Dietary advice	Additives	General	89
		Role	71
		Label reading	75
	Natural phosphate	Sources	68
		Sources	93
		High/low lists	46
		Portion sizes	71
		Alternatives	64
	Practicalities	Recipes	7
		Meal ideas	29
		Cooking tips	18
		Helpful links	14
		Explanation	
	Practicalities		71
			36

Table 1: Content analysis of written PEMs (%)

**Conclusion:** The written paediatric PEMs were pitched at an appropriate literacy level for adults (median FK grade 5.7, “aged 10-11 years”; FRE 68.2, “easily understood by a 13-15-year-old”) and ½ rated superior (by SAM). The inclusion of relevant illustrations would improve this. In contrast to the advice from the PRNT, > ⅓ were not limiting eggs, fish with bones, P raising agents or seeds and > ⅓ continued to limit wholegrains and legumes.

Sa-3MP 074

**CHRONIC HIGH PHOSPHATE LOAD CAUSES LEFT VENTRICULAR DILATION ASSOCIATED WITH IMPAIRED CARDIOMYOCYTE CONTRACTILITY AND INCREASED FIBROSIS IN MICE**

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**Aims/Purpose:** Patients with chronic kidney disease show elevated serum phosphate levels, which contribute to an increased cardiovascular (CV) mortality. In western countries, the consumption of processed food leads to an increased intake of inorganic phosphate, which could therefore magnify the CV risk for the general population as well.

**Methods:** To investigate the CV effects of chronic phosphate excess, male C57BL/6 mice were fed a 2% inorganic phosphate diet (HPD) or a 0.8% phosphate control diet (Ctrl) for six months. Cardiac function was examined using echocardiography and functional catheter analyses. Blood and urine were collected and cardiac tissue was isolated for histological, molecular biological and bulk RNAseq analyses. Contractility and Ca<sup>2+</sup> handling were determined in isolated phosphate-stimulated adult mouse cardiomyocytes (AMCM) using IonOptix system.

**Results:** HPD resulted in increased serum phosphate levels and enhanced renal phosphate excretion, which was associated with slowly progressive kidney disease. Echocardiography showed that HPD fed mice developed a dilated cardiac phenotype with increased left ventricular (LV) volumes, enlarged LV internal diameters and reduced ejection fraction. Pressure volume loop analyses observed enhanced preload and decreased contractility in HPD fed mice. Bulk RNAseq of total heart tissue and subsequent IPA pathway analyses indicated significant changes in the expressions of genes involved in LV dilatation, impaired cardiac contractility, as well as increased fibrosis in mice on HPD compared to Ctrl. On the cellular level, HPD mice showed an increase in cardiomyocyte cross-sectional area and cardiomyocyte length and histological analysis confirmed enhanced perivascular and interstitial fibrosis. Ex vivo stimulation of AMCM with phosphate reduced cytosolic Ca<sup>2+</sup> contents and the total Ca<sup>2+</sup> amplitude compared to control, and contractility measurements observed longer systolic sarcomere length and reduced shortening amplitude, indicating impaired contraction. Moreover, the shortening and return velocities were smaller due to phosphate stimulation and consequently cardiomyocytes took longer for relaxation.

**Conclusion:** Our data suggest that HPD in mice leads to hyperphosphatemia and a dilated cardiac phenotype with impaired Ca<sup>2+</sup> handling, reduced contractility and increased fibrosis. Thus, chronic high phosphate load could be a risk factor for CV disease progression in humans with and without CKD.

Sa-3MP 075

HIGH PHOSPHATE DIET INDUCES TERTIARY LYMPHOID STRUCTURES IN THE KIDNEY OF MICE

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**Aims/Purpose:** Tertiary lymphoid structures (TLS) are immune cell aggregates developing in non-lymphoid tissues by various stimuli such as chronic inflammation. In their basic functions, they resemble secondary lymphoid organs and can initiate adaptive immune responses. The development of TLS has already been described for autoimmune diseases of the kidney such as lupus nephritis, membranous glomerulonephritis or IgA nephritis, but their exact origin, function and trigger remain unclear. Here we identify high phosphate as a new factor for the development of TLS in murine kidneys.

**Methods:** C57BL/6 male mice received a 0.8% control diet (Ctrl) or a 2% high phosphate diet (HPD) for six months. To enhance the phosphaturic hormone fibroblast growth factor 23 (FGF23) in the setting of normal and high serum phosphate level, C57BL/6 mice were injected an Fgf23 expressing adeno-associated vector (AAV-Fgf23) and fed a Ctrl or HPD for six months. As a model for X-linked hypophosphatemia with increased circulating FGF23 levels, male B6.Cg-PhexHyp/J (Hyp) mice were used. Kidney tissue of all mice was investigated by histology, qPCR and protein analyses.

**Results:** After 2 months of HPD immune cell clusters and a significant induction of mRNA levels of venous markers and cell adhesion molecules were observed. Perivascular TLS could be detected in the corticomedullary zone and in the cortex after 3 months of HPD, which consisted of large aggregates of CD45R+ B cells and CD3+/CD8+ T cells, scattered proliferating B cells, podoplanin+ fibroblastic reticular cell networks, increased accumulation of collagen III and LYVE+ lymphatic vessels. After 4 months of HPD, large proliferating B cell clusters, high endothelial venules, follicular dendritic cells, plasma cells and increased IgD synthesis indicated fully matured TLS. Transcriptional analyses revealed an induction of classical TLS markers such as Cxcl12 and Cxcl13 in HPD kidney tissue, which could be confirmed histologically. Importantly, TLS only occurred in kidneys, but not in the heart, nor the liver of HPD mice. Compared with AAV-Fgf23 mice on Ctrl diet, only AAV-Fgf23 mice on HPD developed fully matured TLS, whereas hypophosphatemic Hyp mice did not develop TLS at all.

**Conclusion:** Our data show that HPD causes chronic inflammation in the kidney and induces a de novo formation of fully matured perivascular TLS. This is most likely due to direct effects of phosphate and independent of FGF23.

# INNOVATIONS AND INDUSTRY

## SYMPOSIUM AND BEST PITCHES

Sa-3MP 076

PREDICTORS OF HYPERKALAEMIA IN PEDIATRIC PATIENTS ON DIALYSIS: MULTICENTER PROSPECTIVE OBSERVATIONAL STUDY

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**Aims/Purpose:** Hyperkalaemia management is of vital importance in children on dialysis. Aim of the study was to investigate the predictors of hyperkalaemia in pediatric patients receiving maintenance hemodialysis (HD) or automated peritoneal dialysis (PD).

**Methods:** This is a multicenter prospective cross-sectional observational study on potassium and sodium balance in patients < 18 years receiving chronic HD or PD. We focused here on serum potassium (sK), measured at the beginning of a mid-week HD session or during the morning clinic visit for those on PD. Hyperkalaemia was defined as sK  $\geq$  5 mEq/L according to the recommendations of the Pediatric Renal Nutrition Taskforce (Desloovere et al, *Pediatr Nephrol* 2021). The following parameters were considered: age, dialysis vintage, urine output on a 24-h urine collection; dietary K, sodium, energy and protein intake (assessed by three-day dietary diary); systolic and diastolic blood pressure (BP), measured by 24h ABPM in children > 5 years and median office BP in younger patients; biochemical parameters (urea, creatinine, sodium, phosphate, hemoglobin, bicarbonate and albumin) and medications, in particular renin-angiotensin-aldosterone system (RAAS) antagonists and  $\beta$ -blockers (BB).

**Results:** We enrolled 41 patients (31 HD, 10 PD), median age 13.3 (IQR 10.6-15.8) years. Median sK was 4.7 (IQR 4.4-5.0) mEq/L, hyperkalaemia was diagnosed in 15 patients (36.6%). Median K intake was 0.9 (IQR 0.6-1.2) mEq/kg/day. 21 patients (51%) received either RAAS antagonists or BB, specifically 11/15 patients (73.3%) with hyperkalaemia and 10/26 (38.5%) with normokalaemia ( $p = 0.03$ ). Compared with patients with K = 5 mEq/L, those with hyperkalaemia were older, had lower K intake and higher urea values. No significant differences were observed for the other parameters under study. A backward stepwise multivariable model, including all the parameters with a  $p < 0.15$  at the univariable analysis, showed that the only predictors of hyperkalaemia were age ( $\beta = 0.42$ ,  $p = 0.01$ ), serum urea ( $\beta = 0.02$ ,  $p = 0.06$ ) and treatment with RAAS antagonists or BB ( $\beta = 2.2$ ,  $p = 0.02$ ).

**Conclusion:** Main predictors of hyperkalaemia in pediatric patients on dialysis are age, urea and treatment with RAAS antagonists or  $\beta$ -blockers, while K intake was not significantly associated with sK. Reconsidering antihypertensive treatment may be important in facing hyperkalaemia in this population.

Sa-3MP 077

## PERSISTENT KIDNEY ABNORMALITIES AND THEIR ASSOCIATION WITH GENETIC RISK FACTORS IN A LARGE COHORT OF AFRICAN SICKLE CELL ANEMIA CHILDREN

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**Aims/Purpose:** Kidney abnormalities are common in sickle cell anemia (SCA) children. Glomerular hyperfiltration (GHF) and albuminuria are the most frequent early markers of kidney damage. However, little is known about their persistence in african children with SCA. Our study aimed to determine the prevalence of persistent kidney abnormalities and to assess their association with genetic risk factors in a large cohort of SCA children living in Kinshasa, the Democratic Republic of Congo (DRC).

**Methods:** We prospectively recruited 618 steady-state children with SCA, diagnosis based on Hb electrophoresis, aged 2–18 years, from March 2021 to December 2022. All participants were genotyped for the  $\beta$ -globin gene, APOL1 risk variants (RVs) and HMOX1 GT-dinucleotide repeats. APOL1 high-risk genotype (HRG) was defined by the presence of 2 RVs (G1/G1, G2/G2, G1/G2) and HMOX1 long repeat by the presence of  $\geq 25$  repeats. Albuminuria was defined as urinary albumin-to-creatinine ratio (ACR)  $\geq 30$ mg/g. The original Schwartz formula was used to estimate the glomerular filtration rate (eGFRcr). Decreased eGFR was defined as eGFRcr  $< 60$ ml/min/1.73 m<sup>2</sup>; and GHF as eGFRcr  $\geq 180$  ml/min/1.73m<sup>2</sup> for children between 2–10 years of age and  $> 140$  ml/min/1.73m<sup>2</sup> for children more than 10 years of age. Participants with kidney abnormalities at the first measure were invited for a repeated measure at least three months later. Persistent GHF and persistent albuminuria were the main outcome parameters.

**Results:** 585 participants (male gender 278; 47.5%) were confirmed to have SCA with the  $\beta$ -globin gene sequencing. At baseline, 234/585 (40.0%) participants had kidney abnormalities: GHF 171/585 (29.2%), albuminuria 80/585 (13.7%) and decreased eGFR 15/585 (2.6%). After a median duration of 5 months (interquartile range 4–9), the repeated measure was performed in 176/234 (75.2%) available participants, among whom 130 had baseline GHF and 57 had baseline albuminuria. Persistent GHF and albuminuria were present in 28.5% (37/130) and 38.6% (22/57), respectively. All participants with a baseline decreased eGFR normalized their GFR without any treatment. In multivariate analysis, APOL1 HRC was significantly associated with persistent albuminuria (aOR 3.5, 95CI 1.1–11.4, p = 0.033), while HMOX1 long repeat was not associated with any persistent kidney abnormality.

**Conclusion:** This study reveals that single screening overestimates the rate of kidney disease in children with SCA. Repeated tests are indicated before starting expensive renoprotective treatment among SCA children in a resource-constrained area. APOL1 RVs emerged as the major genetic determinant of persistent kidney abnormalities.

Sa-3MP 078

## NATIONAL CLINICAL OUTCOMES IN CHILDREN WITH MULTI-ORGAN TRANSPLANTS: AN UPDATE FROM THE UNIQUE STUDY

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**Aims/Purpose:** Due to advances in modern medicine, children with previously fatal conditions are now surviving much longer and are presenting as transplant candidates. Generation Alfa of paediatric transplant candidates brings an increasing number of children requiring multiple different solid-organ transplants (MSOT). However, there is very limited data on their long-term clinical outcomes. The UNIQUE study is a UK national study that aims to gain a better understanding of the long-term clinical outcomes in patients who have received a MSOT during childhood in the UK in the last 20 years.

**Methods:** Clinical outcomes data was analysed for all children who received a kidney and at least one other solid-organ transplant as a child in 2000–2021 in the UK. Clinical outcomes were extracted from the national NHS Blood and Transplant (NHS BT) registry and included patient and graft survival, graft function, rates of rejection and post-operative complications at 1, 5 and 10 years post-transplant.

**Results:** 92 children were on the NHS BT Registry as having MSOTs in the UK in 2000–2021. The types of transplant were heart/heart-lung and kidney n = 15 (simultaneous n = 1 and sequential n = 14), liver and kidney n = 72 (simultaneous n = 53 and sequential n = 19), pancreas and kidney n = 4 (simultaneous n = 4) and multivisceral n = 1. All 92 patients had their clinical outcomes analysed using quantitative analysis. The mean follow up time following patients receiving their first kidney transplant was 7.9 years. Patient survival was 98%, 93% and 89% at 1, 5 and 10 years post-transplant with the highest patient survival rate being in those receiving a kidney and liver transplant or kidney and pancreas transplant. Kidney graft survival was 91%, 83% and 77% at 1, 5 and 10 years post-transplant and similarly, the highest graft survival rate was in those receiving a kidney and liver transplant. Graft function was excellent and was comparable to single-organ transplant recipients as reported in the literature. Patients also had fewer episodes of acute rejection compared to the rates reported in the literature for single-organ transplant recipients. In patients receiving both a kidney and a liver, clinical outcomes were significantly better (incl. higher patient and graft survival and lower rates of rejection) in patients with simultaneous liver and kidney transplants as opposed to sequential liver and kidney transplants.

**Conclusion:** UK national data shows that paediatric MSOT recipients have excellent long-term clinical outcomes.

Sa-3MP 079

PRELIMINARY OUTCOMES OF THE TIMING-STUDY: PATIENTS' AND CLINICIANS' PERSPECTIVES ON ADPKD & FAMILY PLANNING

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**Aims/Purpose:** Autosomal Dominant Polycystic Kidney Disease (ADPKD) is the most common monogenic kidney disease encompassing cyst growth, hypertension and progressive loss of kidney function leading to end-stage kidney disease (ESKD). Due to the possibility of genetic transmission and pregnancy complications, family planning can be complex. Reproductive options are, amongst others, accepting the risk, preimplantation genetic testing (PGT) or prenatal diagnosis (PND). For early disease detection in children at risk of ADPKD different policies exist. A guideline on reproductive care for patients with ADPKD is lacking. To gain insight in the experiences, perspectives and wishes regarding family planning and reproductive care, we conducted a focus group study in ADPKD patients and their clinicians.

**Methods:** Focus group discussions with ADPKD patients (men, women, with/without pursued PGT-trajectory) and their physicians (gynecologists, (pediatric) nephrologists, geneticists) were held. Purposive sampling identified participants with a variety of backgrounds. Recordings were transcribed verbatim and inductive thematic analysis was performed following grounded theory. Consensus discussion identified preliminary themes.

**Results:** In total, nine focus groups (n = 31 participants, 16 patients, 15 physicians) were held. This preliminary report is on four focus groups (n = 14 participants), among adult nephrologists, geneticists, men that pursued PGT-trajectory and women that have not. Six themes were identified. First, 'timely information', emphasized by patients and clinicians, to ensure informed decision-making for patients and persons at risk. Second, 'personal choice', patients expressed factors influencing decision-making and a need for autonomy herein. Third, 'considering patients' perception of quality of life' in reproductive care. Fourth, 'guidance in family planning process' with all groups identifying complexity of multidisciplinary care. Communication, responsibility and multidisciplinary collaboration were important topics. Fifth, screening 'minors at risk' encompassed ambivalent opinions. Lastly, reproductive care is threatened by 'inequity', with patients and clinicians experiencing inequity in accessibility of care, regional differences and financial aspects.

**Conclusion:** This is the first qualitative study on perspectives of patients with ADPKD and physicians focusing on reproductive care. Inequity was reported. Minors at risk are often not in physicians' sight and ambivalent thoughts on screening exist. Care improvements should focus on providing timely information on family planning and informed decision-making. Multidisciplinary collaboration is needed to provide optimal care for these patients. Furthermore, physicians outed a wish for a practice recommendation on the management of life cycle care for patients with ADPKD.



Sa-3MP 080

UPDATE ON A GLOBAL ANTI B CELL STRATEGY WITH OBINUTUZUMAB AND DARATUMUMAB WITH DIFFICULT TO TREAT STEROID DEPENDANT NEPHROTIC SYNDROM

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**Aims/Purpose:** Steroid-Dependent Nephrotic Syndrome(SDNS) is a challenging situation B cell depletion with rituximab targets CD20+ B-cells and enables sustained remission after oral drugs discontinuation, but fails to maintain long-term remission following B cell recovery. Autoreactive long-lived plasma cells, not targeted by anti-CD20 antibodies, might play a role in the pathogeny of refractory auto-immune diseases and be a therapeutic target. We report on a global anti B cell strategy with anti CD20 and antiCD38 antibody in patients with difficult to treat SDNS.

**Methods:** This is an update on a monocentric retrospective study including patients with difficult to treat steroid dependent nephrotic syndrome treated after failure of one or several attempts at B cell depletion, at Robert-Debré Hospital, Paris, between June 2018 and February 2020, with an infusion of Obinutuzumab (OBI 1000mg/1.73m<sup>2</sup>) at D0 and Daratumumab (DARA 1000 mg/1.73m<sup>2</sup>) at D15. Oral immunosuppressors were discontinued within 6 weeks, and biological monitoring was performed monthly until B cell recover.

**Results:** Sixteen patients were included. Median age at INS onset was 3.1 years (IQ1.9 ; 6) and at treatment 10.9 years (IQ 10.3; 13.9). Median time to CD20+ B-cell repletion was 9.2 months (IQ 8.2; 11). Median follow-up was 45.9 months (IQ 38.8; 48.9). 14/16 patients relapsed with a median relapse free survival after Obinutuzumab of 23.2 (Q 11; 27) month. Two patients were still in remission at 54.7 and 45.2 months after Obinutuzumab. In comparaisou with prior B-cell depletion course, probability of remission after OBI-DARA at 6, 12 and 24 months after treatment was 100% Vs 63.8%, 75% Vs 38.9% and 56.25 Vs 11.1% respectively. Regarding tolerance, no serious adverse event was reported. Regarding hypogammaglobulinemia, 4 had low IgG at baseline, 15 during follow-up and 8 remained low at last follow up or received intravenous polyclonal immunoglobulins. Median time to IgG level recovery was 16.6 months (Q 7.5; 19.1). Five patients had low or undetectbale IgA level baseline, All had low IgA during follow up and 7 recovered at last follow up, with a median time to recovery of 10.8 months (IQ 9.8; 13.4). Three patients had low IgM at baseline. 15 during follow up and 11 recovered at last follow-up with median time to recovery of 20 months (IQ 14,8; 33).

**Conclusion:** The combined anti-B cell strategy with Obinutuzumab and Daratumumab was not able to interrupt the course of SDNS. However patients experienced a longer relapse-free survival compared to prior rituximab courses with a good tolerance profil. It is impossible to conclude if this results from the combined CD20 and CD38 targeting or just from the effect of the second generation anti CD20 Obinutuzumab.

Sa-3MP 081

GENE-ENVIRONMENT INTERACTIONS ARE A RELEVANT MECHANISM IN THE AETIOLOGY OF CONGENITAL SOLITARY FUNCTIONING KIDNEY

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**Aims/Purpose:** Congenital solitary functioning kidney (CSFK) is an anomaly which is part of the CAKUT (congenital anomalies of the kidney and urinary tract) spectrum and predisposes to kidney injury. The aetiology is complex and includes both genetic and environmental factors. The role of gene-environment interactions (GxE), although shown to be relevant for other congenital anomalies, has not yet been investigated. Therefore, we performed a genome-wide GxE analysis to explore the role of these interactions in the aetiology of CSFK.

**Methods:** In the AGORA data- and biobank, genome-wide single-nucleotide variant (SNV) data and questionnaire data on prenatal exposure to environmental risk factors were available for 381 CSFK patients and 598 healthy controls. Six of these risk factors were selected for the current study. Using a two-step strategy, we first selected SNVs independently ( $r^2 \leq 0.6$ ) associated with any of the environmental factors ( $p$ -value  $\leq 1 \times 10^{-5}$ ) in the combined set of patients and controls. We subsequently used logistic regression to calculate the  $p$ -values for interactions between the SNVs and relevant environmental factors. Interactions with a  $p$ -value below the Bonferroni-corrected threshold, based on the number of SNVs selected for each environmental factor in step one, were considered statistically significant and those with a  $p$ -value  $< 0.05$  suggestive.

**Results:** In step one, 7 to 40 SNVs were identified per environmental exposure, resulting in Bonferroni-corrected  $p$ -value thresholds between 0.0013 and 0.0071 for step two. Only the interaction between rs3098698 and maternal overweight/obesity reached statistical significance in step two ( $p = 0.0016$ , threshold 0.0045). This SNV results in lower expression of the ARSB gene, which is considered to lead to lower activity of the insulin receptor. Whereas maternal overweight/obesity did not result in an elevated risk of CSFK in children carrying this variant (odds ratio (OR) 0.6, 95% confidence interval (CI) 0.3-1.3), it did increase the risk for children without the variant (OR 1.9, 95% CI 1.3-2.6). Eight other GxE interactions had a  $p$ -value  $< 0.05$ , of which two were also biologically plausible and warrant further study.

**Conclusion:** Interactions between genetic factors and environmental exposures are likely to contribute to the aetiology of CSFK. To determine their role in the aetiology of CSFK and other CAKUT, large studies combining data on genetic and environmental risk factors are warranted.

Sa-3MP 082

METABOLIC ACIDOSIS AND ALLOGRAFT DYSFUNCTION IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS

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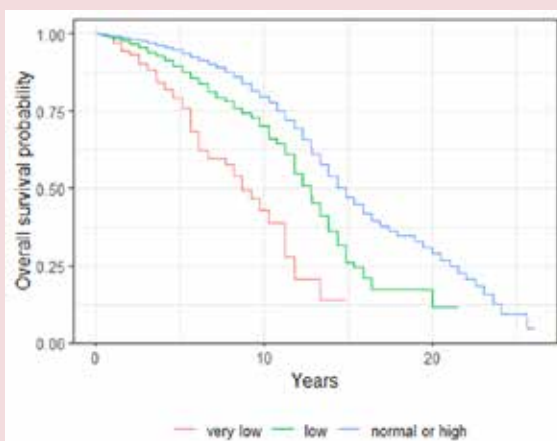
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**Aims/Purpose:** Little is known about the risk factors for metabolic acidosis (MA) and its association with kidney allograft function in children. We investigated the relationship between MA over time and allograft outcome in pediatric recipients.

**Methods:** This registry study from the Cooperative European Paediatric Renal Transplant Initiative (CERTAIN) collected laboratory measures at baseline (pre-transplant), months 1, 3, 6, 9 and 12 post-transplant, and every 6 months thereafter. Survival analysis for a composite endpoint of graft loss or estimated glomerular filtration rate (eGFR)  $\leq 30$  mL/min per 1.73m<sup>2</sup> or a  $\geq 50\%$  decline from baseline eGFR at month 3 post-transplant was performed. First, unadjusted cumulative probabilities of allograft dysfunction with categorized serum bicarbonate (HCO<sub>3</sub><sup>-</sup>)  $< 18$  mmol/L, 18–22 mmol/L or  $> 22$  mmol/L as time-varying covariate were visualized. Next, association of HCO<sub>3</sub><sup>-</sup>  $< 18$  mmol/L with allograft outcome was investigated using the conventional stratified Cox proportional hazards models and further verified using marginal structural models with time-varying covariates.

**Results:** We report on 1911 patients (61% boys), of whom 1704 with a first graft, from 49 centers in 17 European countries. The unadjusted cumulative probabilities of allograft dysfunction with time-varying covariates HCO<sub>3</sub><sup>-</sup>  $< 18$  mmol/L and 18–22 mmol/L were associated with time to composite endpoint as compared with HCO<sub>3</sub><sup>-</sup>  $> 22$  mmol/L (see Figure). Within 5 years of transplantation, the composite endpoint was achieved in 547 (28.6%) grafts, of which 45 (2.3%) were allograft losses. The prevalence of HCO<sub>3</sub><sup>-</sup>  $< 18$  mmol/L at various time-points was 1.5–3.9%. In the conventional Cox proportional hazards models adjusted for potential confounders including time-varying rejection and systolic blood pressure Z score, HCO<sub>3</sub><sup>-</sup>  $< 18$  mmol/L (hazard ratio [HR], 2.67; 95% confidence interval [CI], 1.86 to 3.84) was associated with the composite endpoint. Marginal structural models showed similar results (HR, 2.18; 95% CI, 1.37 to 3.48) suggesting that the association of HCO<sub>3</sub><sup>-</sup>  $< 18$  mmol/L with graft dysfunction is independent of eGFR decline.

**Conclusion:** Severe MA with HCO<sub>3</sub><sup>-</sup>  $< 18$  mmol/L, is an independent risk factor for allograft dysfunction even in the presence of rejection or systolic hypertension.



HCO<sub>3</sub><sup>-</sup>  $< 18$  mmol/L  
HCO<sub>3</sub><sup>-</sup> 18–22 mmol/L  
HCO<sub>3</sub><sup>-</sup>  $> 22$  mmol/L  
HCO<sub>3</sub><sup>-</sup> 18–22 mmol/L vs.  $> 22$  mmol/L  
HR 2.07; 95% CI 1.72 to 2.48 (P = 0.001)  
HCO<sub>3</sub><sup>-</sup>  $< 18$  mmol/L vs.  $> 22$  mmol/L  
HR 4.67; 95% CI 3.27 to 6.66 (P = 0.001)

Sa-3MP 083  
GENETIC DETERMINANTS OF RENAL SCARRING IN INFANTS WITH FEBRILE URINARY TRACT INFECTION

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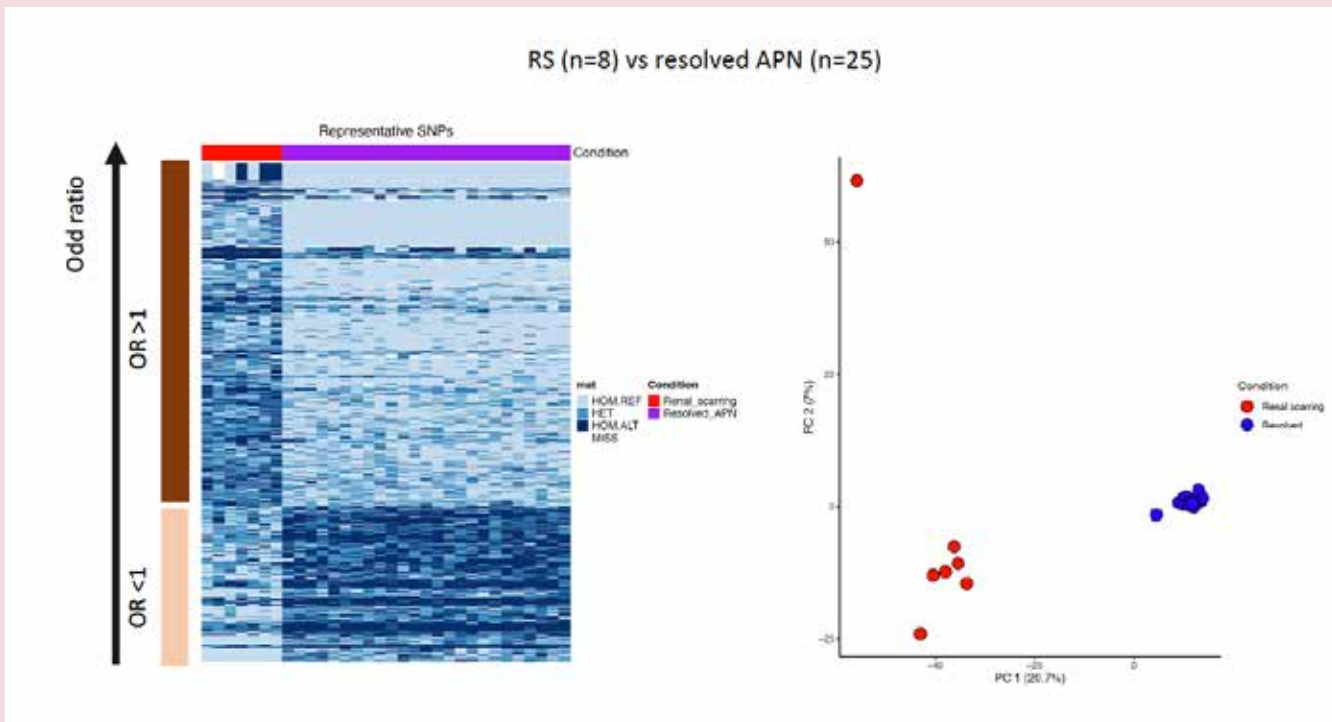
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**Aims/Purpose:** To identify genetic variants in infants with renal scarring with the purpose of presenting an individualized management strategy of infants at risk of long-term complications after febrile urinary tract infection (UTI).

**Methods:** In a Swedish multicenter study, we included infants < 1 year of age presenting with a first episode of UTI. Infants were treated in pediatric emergency units, with clinical data first reported after the initial evaluation, and with a second report after further management and new findings one year after infection. A 99mTc-dimercaptosuccinic acid (DMSA) scan was used to identify acute pyelonephritis (APN) (1st DMSA < 7 days post infection), renal involvement (time independent 1st DMSA) and renal scarring (RS) (2nd DMSA > 6 months post infection). DNA was obtained from peripheral blood and analyzed by exome genotyping. Bioinformatic analysis including allelic frequency test and calculation of odds ratio (OR) were used to identify disease associated genetic variants.

**Results:** Of 1087 infants with febrile UTI, RS was diagnosed in 58/135 examined with a 2nd DMSA. RS was more common in children with recurrent UTI compared to those without UTI recurrences (43.1% vs 23.4%) and in infants with vesicourethral reflux (VUR) grade 3–5 (85.7%, 65.2%, 77.8% respectively) than in VUR 1–2 (0% and 42.9%). Infants without VUR were also diagnosed with RS (36.7%). DNA association analysis were performed by comparing significant SNPs ( $p < 0.005$ ) to 2nd DMSA outcome by allelic frequency test. The variants were sorted on the base of OR and presented in a heatmap that demonstrates a genetic segregation where the alternative alleles are more frequently found in the renal scarring group. Principal component analysis (PCA) further demonstrated the genetic differences between infants with renal scarring and those with resolved APN.

**Conclusion:** In this nationwide study of genetic susceptibility to renal scarring after febrile UTI in infancy, we identified a genetic profile associated with renal scarring dominated by mitochondrial genes.



Sa-3MP 084

MOLECULAR FINDINGS IN A GROUP OF PATIENTS WITH PRIMARY HYPOMAGNESEMIA AND SALT-LOSING TUBULOPATHY

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**Aims/Purpose:** Disturbed Na<sup>+</sup> reabsorption in the distal convoluted tubule (DCT) is associated with hypomagnesemia and hypokalemic alkalosis. Most of the Mg<sup>2+</sup> delivered from the loop of Henle is reabsorbed in the DCT, so this segment plays an important role in maintaining Mg<sup>2+</sup> homeostasis. The aim of our study was to analyse the molecular findings in a group of patients with renal salt-losing tubulopathies associated with hypomagnesemia.

**Methods:** 38 patients from 35 families with hypokalemia and hypomagnesemia of renal origin. Initial study with NGS panel with 44 genes (including SLC12A3, CLCNKB, SLC12A1, KCNJ1, BSND, KCNJ10, FXVD2, CLCN5, CLDN16, CLDN19, ATP1A1, KCNJ10, CNNM2, HNF1B). Exome sequencing in those cases where no molecular alteration was found. MLPA for the search of gross deletions in the CLCNKB and the SLC12A3 genes.

**Results:** The most common diagnosis were Bartter syndrome type 3 (BS3, 16/38 patients) and Gitelman syndrome (GS, 14/38 patients). In addition, 3/38 patient carried a heterozygous pathogenic variant in RRAGD, 1/38 carried a heterozygous pathogenic variant in CLCN5, 1/38 patient carried a heterozygous pathogenic variant in HNF1B, and 1/38 patient carried a homozygous pathogenic variant in BSND. Finally, in 2/38 patients no molecular alterations were found. Mean serum Mg<sup>2+</sup> levels were similar in BS3 and GS patients ( $1.47 \pm 0.21$  &  $1.46 \pm 0.16$  mg/dL;  $p = 0.9$ ) but significantly lower in RRAGD patients ( $1.06 \pm 0.25$  mg/dL,  $p < 0.05$ ). Mean serum K<sup>+</sup> levels were significantly lower in BS3 patients than GS and RRAGD ( $2.1 \pm 0.67$  vs.  $2.92 \pm 0.62$  vs.  $3 \pm 0.34$  mEq/L,  $p < 0.05$ ).

**Conclusion:** Mutations in different genes are associated with salt losing tubulopathies with hypomagnesemia, mostly SLC12A3 (GS) and CLCNKB (BS3). Potassium levels are lower in BS3 patients, indicating a stronger activation of the renin-angiotensin system. Although it is not universal, Mg<sup>2+</sup> levels can be low in BS3 patients due to the ubiquitous expression of the ClC-Kb channel in the loop of Henle and in the DCT. Other less frequent primary tubulopathies affecting the DCT can present with hypomagnesemia and mimic Bartter and Gitelman syndromes.

Sa-3MP 085

NEPHROCALCINOSIS: THE PUZZLE IS ALMOST COMPLETE WITH WHOLE EXOME SEQUENCING

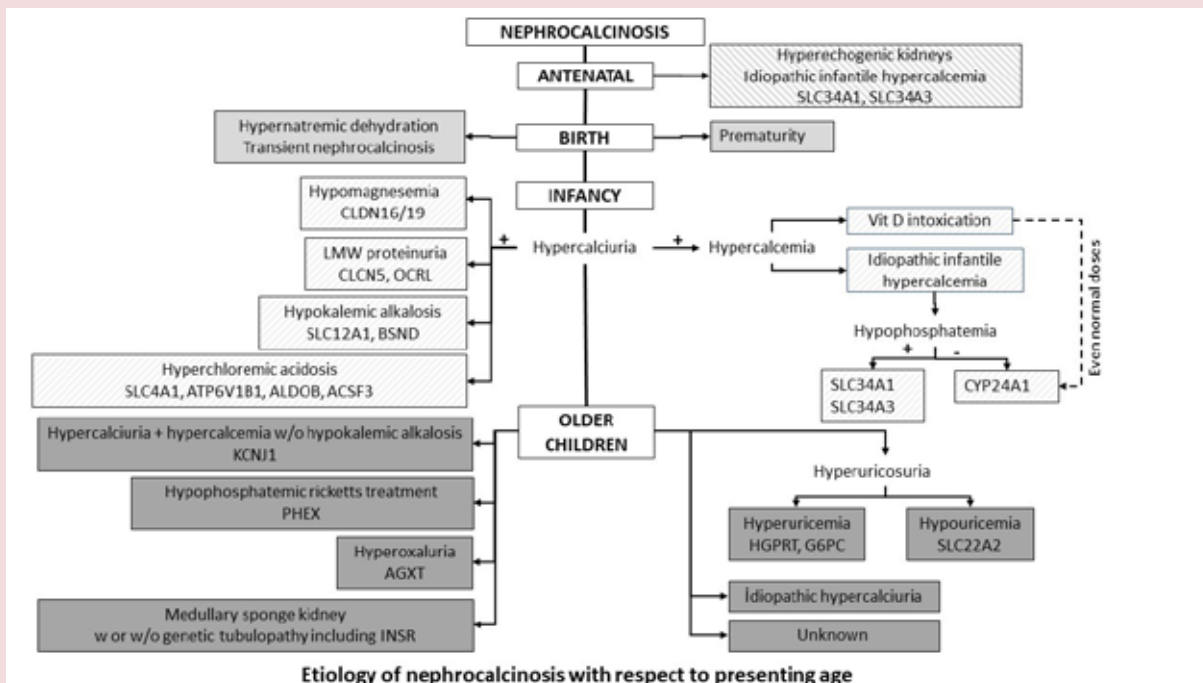
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**Background:** A monogenic etiology has been identified in up to 30% of patients with childhood-onset isolated nephrolithiasis or nephrocalcinosis by detailed genetic examinations. We aimed to determine the etiology of nephrocalcinosis only with respect to presenting age in childhood. We also aimed to create an algorithm for the diagnostic approach to children with nephrocalcinosis.

**Patients and Methods:** We obtained clinical data, pedigree information, blood and urine laboratory tests and DNA samples for genetic analyses from children including newborns presenting with nephrocalcinosis on renal ultrasound. Subjects with a potential secondary cause of nephrocalcinosis such as use of loop diuretics, high dose vitamin D, calcitriol or steroids were also included to demonstrate the rate of genetic causes among all cases of nephrocalcinosis. Gene panel sequencing was performed in children with an obvious cause of primary nephrocalcinosis like Bartter syndrome, whereas whole exome sequencing was performed in other cases.

**Results:** There were 59 cases with nephrocalcinosis. Eight cases had a secondary cause: 2 premature, 2 high dose vitamin D treatment, 2 congenital adrenal hyperplasia (CYP21A2) with steroid treatment, and 2 hypophosphatemic rickets (PHEX) with calcitriol and calcium treatment. One newborn has transient nephrocalcinosis due to hypernatremic dehydration. The diagnoses in the remaining 50 children were idiopathic infantile hypercalcemia (13: 8 SLC34A1, 2 SLC34A3, 3 CYP24A1), renal tubular acidosis (8: 2 ATP6V1B1, 1 SLC4A1, 3 G6PC, 1 ALDOB, 1 ACSF3), Bartter syndrome (6: 4 SLC12A1, 1 BSND, 1 KCNJ1), familial hypomagnesemic hypercalciuric nephrocalcinosis (2: CLDN16 and CLDN19), Dent's disease (3), Lowe syndrome (1), Lesch-Nyhan syndrome (2), renal hypouricemia (1: SLC22A2), primary hyperoxaluria (2: AGXT), medullary sponge kidney (3: all had hypercalciuria and one had INSR mutation), idiopathic hypercalciuria (2), and undefined (6). Presenting of children and approach to diagnosis was summarized in figure 1.



**Conclusion:** Among 50 cases of primary nephrocalcinosis 76% was determined to have a genetic cause. Most patients with idiopathic infantile hypercalcemia and other tubulopathies presented during the first 2 years of life.

# SYMPOSIUM 7

## Complement Mediated Disorders

Su-3MP 086

HEMOLYTIC UREMIC SYNDROME: FIRST DAYS IN THE INTENSIVE CARE. CREATININE OR CYSTATIN?

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**Aims/Purpose:** Hemolytic uremic syndrome (HUS) is a thrombotic microangiopathy that affects various organs; with predominance on kidney, gastrointestinal and central nervous system. This clinical and anatomopathological entity is classically characterized by the sudden onset of hemolytic anemia, acute renal compromise, and thrombocytopenia. It is currently classified as Shiga toxin-associated HUS (STEC-HUS) and atypical HUS (due to pneumococcus invasive infection, altered complement regulation, altered cobalamin metabolism or secondary to other causes). This study aims to describe the clinical, analytical and therapeutic characteristics of the patients admitted with HUS in the Pediatric Intensive Care Unit of a tertiary hospital in Spain.

**Methods:** Retrospective, descriptive and analytical study by reviewing the medical records of patients with HUS admitted in the Pediatric Intensive Care Unit of a tertiary hospital in Barcelona, Spain the last 14 years. Glomerular filtration rate (GFR) is estimated with the modified Schwartz 2009 equation using plasma creatinine determinations, and with the Pottel 2017 equation using plasma cystatin C determinations. A Pearson correlation coefficient was computed to assess the relationship between both equations.

**Results:** 10 cases were studied. 4 were STEC-HUS and 6 atypical HUS (5 of which secondary to pneumococcus invasive infection). Age:  $35 \pm 30^{*}29$  (17-108) months. Sex: 5 girls, 5 boys. All of them required admission to the intensive care unit of our center during a mean stay of  $26.6 \pm 9.90$  (13-48) days. At diagnosis, all of them presented microangiopathic hemolytic anemia, thrombocytopenia, and acute renal failure (AKI III). Mean hemoglobin on admission:  $5^{*}04 \pm 1^{*}10$  ( $3^{*}0-6^{*}4$ ) g/dl, platelets:  $16.200 \pm 6.646$  (8.000-29.000) uL, C3 levels:  $68^{*}47 \pm 1^{*}10$  ( $3^{*}0-6^{*}4$ ) mg/dl, C4 levels:  $11^{*}05 \pm 4^{*}02$  ( $2^{*}77-19^{*}10$ ) mg/dl, haptoglobin:  $0^{*}09 \pm 0^{*}06$  ( $0^{*}06-0^{*}26$ ) g/l, creatinine:  $2.03 \pm 1.8$  (0.42-6.05) mg/dL, GFR Schwartz-2009  $27.97 \pm 22.24$  (8-77) ml/min/1.73m<sup>2</sup>, cystatin:  $2^{*}13 \pm 1.52$  (0.58- 5.49) mg/dl and GFR Pottel-2017  $60.37 \pm 41.88$  (16-151) ml/min/1.73m<sup>2</sup>. The correlation between both equations is  $r(6)$ : .73, p.019. The mean GFR estimated using cystatine C was 2.16 times higher than GFR estimated using creatinine the day of admission. Minimum glomerular filtration rate during admission:  $25^{*}41 \pm 14^{*}36$  (7<sup>9</sup>-58) ml/min/1.73m<sup>2</sup>. One month after admission: creatinine:  $0.53 \pm 0.12$  (0.33-0.75) mg/dL, GFR Schwartz-2009  $76 \pm 20.12$  (45-106) ml/min/1.73m<sup>2</sup>, cystatin:  $1.29 \pm 0.35$  (0.86-1.77) mg/dl and GFR Pottel-2017  $71,9 \pm 18.99$  (49-102) ml/min/1.73m<sup>2</sup>. The correlation between both equations is  $r(9)$ : .79, p.003. The mean GFR estimated using cystatine C was 0,95 times lower than GFR estimated using creatinine the day of admission. Among the 5 patients affected by pneumococcal HUS, only one was vaccinated against pneumococcus. Among the other 5 patients, all were vaccinated except one. The polyagglutination study shows exposure of the T antigen in all atypical pneumococcal HUS. Regarding the treatment carried out: 90% needed hemodiafiltration, 30% orotracheal intubation and 100% non-invasive respiratory support. All needed transfusion of blood products: mean transfusion of red blood cells:  $4.70 \pm 2.62$  (2-9) units and platelets:  $2.40 \pm 1.26$  (1-5) units. When we compare between groups (STEC-HUS and atypical HUS) the following results are significant: C3 levels on admission was lower in atypicals ( $55^{*}23 \pm 7.64$ ) vs STEC-HUS ( $88^{*}32 \pm 6^{*}41$ ) (p = 0.05) and hospital stay was shorter in STEC-HUS ( $17^{*}75 \pm 3^{*}40$ ) vs atypical HUS ( $32^{*}50 \pm 8^{*}06$ ) days (p = 0.005). At discharge, the glomerular filtration rate improved to  $77.87 \pm 21.48$  (46-119) ml/min/1.73m<sup>2</sup>. 40% have sequelae at discharge: 1 patient proteinuria, 2 arterial hypertension, 1 chronic kidney disease. No patient dies.

**Conclusion:** The C3 value on admission is significantly lower in atypical HUS vs. in STEC-HUS. Patients with atypical HUS require a longer hospital stay. Atypical HUS due to pneumococcus in our register, compared to the literature, presents a low number of sequelae and no mortality. The GFR estimation equations that use creatinine and cystatin have a similar correlation both on the day of admission and the month of admission, but the difference between them is much greater on the day of admission. On the day of admission, Cystatin C equations estimated a GFR 2,16 times higher than the ones using creatinine. On the month of admission, Cystatin C equations estimated a GFR 0,95 times lower than the ones using creatinine.





Su-3MP 087

## CLINICAL CHARACTERISTICS AND OUTCOME OF PATIENTS WITH ATYPICAL HEMOLYTIC UREMIC SYNDROME: BELGIUM COHORT OF THE GLOBAL AHUS REGISTRY

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**Objectives:** To describe the baseline characteristics and management of a large longitudinal cohort of Belgian patients with atypical hemolytic uremic syndrome (aHUS) enrolled in the global aHUS registry. Belgium has the highest number of patients enrolled per inhabitant within the global aHUS registry (10 per million inhabitants).

**Methods:** The Global aHUS Registry (NCT01522183) is an observational multicenter study designed to collect disease characteristics of patients with aHUS irrespective of treatment modality. Enrollment is open to all patients with a clinical diagnosis of aHUS, with no requirement of identified complement gene variants/ autoantibodies. Patients with evidence of Shiga toxin or with an ADAMTS13 activity  $\leq$  5% (if performed) were excluded.

**Results:** As of December 26, 2022, 121 patients (44 pediatric, and 77 adults) were enrolled in the Global Registry from the 7 Belgian academic hospitals and one reference center for pediatric nephrology. In the pediatric group, there was an equal number of males and females, whereas in adult patients there were more female (62%). The disease first presented at a median (IQR) age of 4 years (0.7-7.7) in children and 39 years (28-47) in adults, with a positive familial history in 16% and 13%, respectively. In this Belgian cohort, 49 patients had a past medical history of kidney failure (40%), 33 (27%) patients had received kidney transplant and 63 (52%) were treated with eculizumab. The proportion of patient tested for  $\geq$  5 complement genes and anti-CFH antibody was 57% (69/121), higher compared to other country cohorts. Of those patients with available genetic data, 56/69 (81%) had a pathogenic / likely pathogenic variant in  $\geq$  1 aHUS-associated gene (CFH, C3, CFB, CFI, MCP, THBD, or DGKe) or anti-complement factor H (CFH) antibody. The most frequent complement abnormalities detected were CFH and CD46 gene variants and anti-CFH antibodies. Preselected precipitating factors potentially linked to the clinical manifestation of aHUS, including transplant, pregnancy, malignancy, autoimmune disease, and malignant hypertension, was noted in 21/77 (27%) adult patients and in 3/44 (7%) children.

**Conclusions:** Overall, our results were consistent with previous global and local aHUS registry data published. Given the high proportion of patients tested and detected with complement abnormalities in Belgium, this cohort from the global aHUS registry may be a valuable source to better understand the natural history of the disease and management of aHUS patients.

Su-3MP 088

MANAGEMENT AND OUTCOME OF ATYPICAL HEMOLYTIC UREMIC SYNDROME IN CHILDREN SINCE THE MARKETING OF COMPLEMENT INHIBITORS: A NATIONWIDE STUDY

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**Aims/Purpose:** 55-70% of atypical hemolytic uremic syndromes (aHUS) are caused by pathogenic variants of complement genes or by anti-Factor H autoantibodies (complement-mediated aHUS), or by DGKE variants. In the remaining patients, the underlying cause remains elusive. Complement inhibitors have revolutionized the prognosis of complement-mediated aHUS. The objectives of this study were to evaluate the outcome of aHUS in a large pediatric cohort and the medical practices since the marketing of eculizumab in 2011.

**Methods:** In this French nationwide multicenter retrospective study, we enrolled 78 consecutive children diagnosed with aHUS, between 2011-2018, of whom 60% had an identified underlying etiology.

**Results:** 45/78 (57%) received eculizumab at onset and 55/78 (71%) during follow-up. At last visit, the median eGFR was 114 ml/min/1.73m<sup>2</sup> (IQR [97-131]) and did not differ between patients who received eculizumab at 1st episode and the others. One patient died and 5 (6%) had CKD5. The kidney and patient survivals were significantly higher than that of the historical French cohort (2000-2008; Frémeaux-Bacchi et al., JASN 2013). At initial presentation, 38% children with complement-mediated HUS had diarrhea including 2 shigatoxin+. Children with complement-mediated aHUS significantly had deeper thrombocytopenia and less hyperleukocytosis, lower C3 and CD46 levels than their counterparts. 18 patients relapsed (23%), including 12 after eculizumab withdrawal. The total number of relapses was significantly higher in the complement-mediated group. At last follow-up, 39/53 (64%) patients were off eculizumab without any disease activity.

**Conclusion:** This study reports improved kidney prognosis and survival in pediatric aHUS since the use of eculizumab compared with historical studies. Some patients did not receive eculizumab at all, others only during a relapse, and the majority stopped treatment at some point during follow-up. The outcome did not differ among these patients, even with variants at high risk for relapse. Moreover, the efficacy of eculizumab must be weighed against the risks of infection, the costs, complications of venous access and the consequences on quality of life. Altogether, this leads us to propose a personalized treatment considering the severity of flares, the sequelae, and the individual risk of subsequent relapses.

Su-3MP 089

OUTCOME IN CHILDREN WITH IGA VASCULITIS WITH NEPHRITIS TREATED WITH ORAL IMMUNOSUPPRESSIVE TREATMENT IN COMBINATION WITH STEROIDS

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**Aims/Purpose:** IgA vasculitis (IgAV) is the most common vasculitis in children. IgAV long-term prognosis depends on kidney involvement or IgA vasculitis with nephritis (IgAVN). Corticosteroids are widely used for patients with IgAVN. However, about 30% of patients present chronic kidney disease at the end of corticosteroids, raising thus the question of others immunosuppressives treatments (IMS) efficiency in IgAVN. The aim of this study is to assess the role of IMS in combination with steroids on IgAVN outcome. We also evaluate risk factors associated with poor renal outcome and IMS impact on histological lesions.

**Methods:** All children with IgAVN diagnosed between 2000 and 2019 and treated with IMS in combination with steroids in French pediatric nephrology units were retrospectively included. The outcomes of patients treated with IMS and steroids were compared with those treated only with steroids matched for age, proteinuria, eGFR and histological features. The primary endpoint was IgAVN remission defined as a proteinuria  $\leq$  30 mg/mmol without renal failure.

**Results:** 51 children with a median age of 8.5 years treated with mycophenolate mofetil, cyclophosphamide, calcineurin inhibitors or azathioprine in combination with steroids were included. 30 patients (58.8%) were in remission at the end of a median follow-up of 4.70 years (2.64–7.06). 38 patients treated with IMS and steroids were matched with 38 patients treated with steroids alone for age, proteinuria, eGFR and histological features. IgAVN remission proportion was not significantly different between both groups. Older patients, tubular atrophy and a longer delay between renal involvement and IMS onset were significantly associated with the absence of remission. We did not find any IMS impact on histological lesions in 21 patients with repeated biopsy. Proteinuria significantly decreased during IMS treatment.

**Conclusion:** 41.2% of children with IgAVN treated with IMS present a persistent renal disease at the end of a 4.7-year follow-up. The benefit of IMS in IgAVN could not be established based on our findings. Prospective studies are thus required to determine IMS efficiency in IgAVN.

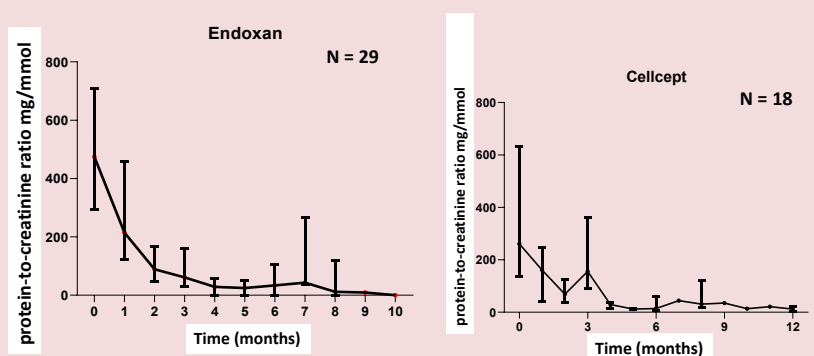
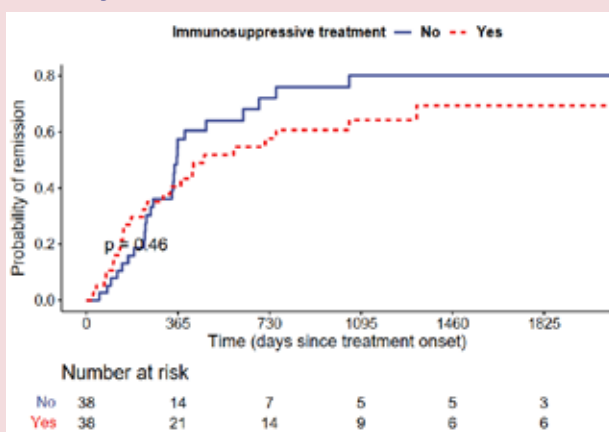


Figure 1: Proportion of IgAVN remission in patients treated with IMS and steroids compared with patients treated with steroids alone.

Figure 2: evolution of protein-to-creatinine ratio mg/mmol in patients treated with mycophenolate mofetil and cyclophosphamide.

# SYMPOSIUM 8

## Critical Care Nephrology

Su-3MP 090  
ACUTE KIDNEY INJURY IN PATIENTS WITH CYSTIC FIBROSIS

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**Aims/Purpose:** Cystic fibrosis (CF) is a multisystem disease caused by mutations in the CFTR (cystic fibrosis transmembrane regulator protein) gene and is inherited in an autosomal recessive manner. Pulmonary involvement is the most important cause of morbidity and mortality. Although the kidneys are not one of the primary organs affected in patients with CF, the incidence of renal involvement has increased over the years as life expectancy has increased. Different types of renal involvement have been described in patients with CF, including urinary stone disease, nephrocalcinosis, acute kidney injury (AKI), glomerulonephritis, tubulointerstitial nephritis, vasculitis, amyloidosis, and diabetic nephropathy. The aim of this study is to determine the incidence of AKI and its risk factors in CF patients.

**Methods:** This retrospective, single-center study included a total of 153 genetically confirmed CF patients who were followed up between 2022 and 2023 at the Department of Pediatric Pulmonology, Cerrahpaşa Medical Faculty, Istanbul. Demographic characteristics, clinical features, medications (inhaled and systemic nephrotoxic drugs, radiocontrast agents, immunomodulatory drugs), presence of colonization, hospitalizations (number and duration), and serum creatinine levels were retrospectively recorded from the files of patients. Acute kidney injury was defined as > 1.5-fold increase in serum creatinine.

**Results:** The mean age of patients was  $9.8 \pm 6.5$  years, and the male-to-female ratio was 1.2/1.0. Forty-one patients (27%) had been hospitalized within the past year, and AKI occurred in 28 patients (18%). There were no differences between patients with and without AKI in terms of age, sex, use of radiocontrast agents or immunomodulatory drugs; however, patients with AKI had a higher hospitalization rate (54% vs. 21%,  $p = 0.001$ ), more frequent hospitalizations ( $1.2 \pm 1.6$  vs.  $0.3 \pm 0.7$ ,  $p < 0.001$ ), higher prevalence of colonization (64% vs. 30%,  $p = 0.001$ ), and higher use of systemic nephrotoxic (54% vs. 19%,  $p = 0.001$ ) and inhaled nephrotoxic drugs (61% vs. 38%,  $p = 0.022$ ) than patients without AKI. In logistic regression analysis, colonization was found to be an independent risk factor for AKI ( $p = 0.0037$ ).

**Conclusion:** Acute kidney injury is not uncommon in patients with CF. The presence of respiratory colonization appears to be an important risk factor for AKI. Hospitalization and use of nephrotoxic medications are other risk factors that may contribute to the occurrence of AKI. Early diagnosis and treatment of all these factors may improve renal survival in this patient group.

Su-3MP 091

**ACUTE UNTOWARD EFFECTS OF MAINTENANCE HEMODIALYSIS IN CHILDREN. FINDINGS FROM THE INTERNATIONAL PEDIATRIC HEMODIALYSIS NETWORK (IPHN)**

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**Aims:** To assess frequency and risk factors of acute untoward effects of maintenance hemodialysis (HD) in children

**Methods:** Analysis of 910 patients, 0-21 (median 12.1, IQR 12.9; 9.0-15.9) years on chronic HD(F), prospectively followed in the IPHN.

**Results:** Untoward side effects (intradialytic hypotension (IDH), seizures, cramps, vomiting) within the past 4 weeks were reported in 27% of 6 monthly updates in 218 patients (24%). Patients who experienced adverse events were younger (11.9 vs. 13.1 years;  $p < 0.0001$ ) and were longer on HD (2.0 vs 1.6 years;  $p < 0.0001$ ). They had lower urine output (236 vs. 388 ml/m<sup>2</sup>/24h;  $p < 0.0001$ ), higher interdialytic weight gain (IDWG; 4.1% vs. 3.2%;  $p < 0.0001$ ), associated with higher UF rates (296 vs. 239 ml/h/m<sup>2</sup>;  $p < 0.0001$ ). In multivariable analysis younger age and lower urine output remained significant predictors of any of the reported adverse event. IDH was the most common side effect, reported in  $0.72 \pm 1.87$  sessions per 4 weeks. IDH was less prevalent in patients with body volume monitoring ( $0.34 \pm 1.13$  versus  $0.78 \pm 1.95$  episodes per 4 weeks;  $p < 0.0001$ ) and was not influenced by antihypertensive treatment. IDH frequency was higher in HD vs. HDF ( $0.82 \pm 0.72$  vs  $0.49 \pm 0.40$ ,  $p < 0.0001$ ) and correlated positively with IDWG ( $r = 0.13$ ,  $p < 0.0001$ ), log PTH ( $r = 0.09$ ,  $p < 0.0001$ ), dialysis vintage ( $r = 0.04$ ,  $p = 0.01$ ) and inversely with urine output ( $r = -0.12$ ,  $p < 0.0001$ ) and age ( $r = -0.09$ ,  $p < 0.0001$ ), but not with dialysate sodium concentration ( $r = 0.015$ ,  $p = 0.4$ ). In multivariable analysis lower pre-dialysis systolic BP-SDS (OR 0.9, 95%CI 0.86-0.96), younger age (OR 0.96, 95%CI 0.94-0.98,  $p = 0.001$ ), HD vs. HDF modality (OR 1.44, 95%CI 1.15-1.8), high ultrafiltration rate (OR 1.03, 95%CI 1.01-1.05) and low urine output (OR 0.8 95%CI 0.66-0.96,  $p = 0.02$ ) predicted frequency of IDH.

**Conclusions:** Acute dialysis complications are reported in one fourth of the children on maintenance HD. IDH, a complication associated with worse cardiovascular outcome may be prevented by use of HDF instead of HD and lowering of ultrafiltration rates.

Su-3MP 092

FACTORS AFFECTING THE DEGREE OF ACUTE KIDNEY INJURY IN PEDIATRIC EARTHQUAKE VICTIMS WITH CRUSH SYNDROME IN THE FIRST WEEK FOLLOWING RESCUE

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**Aims/Purpose:** Acute kidney injury due to crush syndrome in earthquake victims is a complex and difficult condition to manage, especially in the first days. On February 6, 2023, millions of people in Turkey and Syria were affected by the Kahramanmaraş earthquake. Crush syndrome developed in 97 children earthquake victims who applied to our hospital from our region where the earthquake had a devastating effect.

**Methods:** Clinical and laboratory findings of the victims with crush syndrome were analyzed within the first week.

**Results:** Fifty-three (54.6%) of the children were female and 44 (45.4%) were male. The mean age was  $10.91 \pm 4.68$  years. The mean time under the rubble was  $31.52 \pm 24.03$  hours. Thirty-six (37.1%) patients had a single extremity injury, while 44 (45.3%) patients had more than one extremity injury. Fasciotomy was performed in 14 (14.4%) patients and amputation was performed in 24 (24.7%) patients. Twenty-two patients (22.7%) required kidney replacement therapy (KRT). Hemodialysis was applied to 16 (72.7%) of them, and hemodiafiltration was applied to 6 (27.2%) of them in the pediatric intensive care unit. KRT requirement was evaluated according to creatinine phosphokinase (CPK) values. KRT was not required in patients with CPK values under 10,000 IU/L. Ten (21.2%) patients in the group with CPK values between 10,000–50,000 IU/L, six (60%) of patients in the group with CPK values between 50,000–100,000 IU/L, and six (66.6%) of patients in the group with CPK values 100,000 IU/L and above required KRT. The requirement of KRT was found to be significantly higher in groups with higher CPK values ( $p < 0.001$ ). We used the rule of nines to measure body surface area crushed and found the mean percentage of body crush in patients who required KRT was  $39.96 \pm 11.35\%$ , while it was  $14.74\% \pm 13.02\%$  in those who did not require KRT ( $p < 0.001$ ). The mean time under the rubble of victims who required KRT was  $30.12 \pm 19.09$  hours, while the mean time under the rubble of the victims who did not require KRT was  $31.00 \pm 25.46$  hours ( $p = 0.895$ ). There was a moderate correlation between the percentage of body area crushed and serum albumin, creatinine and CPK levels at admission ( $r = -0.375$ ,  $p < 0.001$ ,  $r = 0.410$ ,  $p < 0.001$  and  $r = 0.421$ ,  $p < 0.000$ , respectively). According to daily CPK levels, a moderate correlation was found between the rate of decrease in CPK and time under the rubble on day five ( $r = 0.322$ ,  $p = 0.14$ ).

**Conclusion:** Clinical findings can help in predicting the need for KRT in patients with crush syndrome. The requirement of KRT was seen in patients with a CPK level of 10,000 IU/L and above. Time under the rubble is not a prognostic factor of requirement of KRT for the patients with crush syndrome. Many factors other than the time to be rescued from the rubble could also contribute on acute kidney injury.

**Su-3MP 093**

**10 YEARS EXPERIENCE IN THE USE OF CUFFED-TUNNELED CENTRAL VASCULAR CATHETERS IN PAEDIATRIC HAEMODIALYSIS**

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**Introduction:** An adequate vascular access is essential for the performance of an effective haemodialysis. The use of cuffed-tunnelled central venous catheters (CCVC) as vascular access in paediatrics may be an option when a short duration of haemodialysis is expected.

**Aim:** Describe the characteristics of our haemodialysis patients and their vascular accesses in the last 10 years.

**Methods:** We retrospectively reviewed the medical records of patients undergoing haemodialysis in our unit from 2012-2022.

**Results:** 105 patients (62% male) with mean age of 8.15 years (23% younger than 3 years) received haemodialysis during this period. The most frequent underlying primary renal disease was congenital kidney and urinary tract anomalies (48%). All of them used CCVC as vascular access. The median time on haemodialysis was 8.5 months. 73 patients are currently transplanted. Haemodialysis is still being performed in 9% of our patients. Four patients died, none of them due to haemodialysis complications. 181 CCVC were used, 60% of the patients required a single catheter. The preferred vascular access was the right internal jugular vein (90% of cases). The catheters used in 146 cases were made of silicone (Perm-cath), the rest were made of polyurethane (Split-cath). 145 complications were described, affecting 106 of the CCVC. In seventy-two percent of the cases of complications, CCVCs required replacement for this reason. The most frequent complications were mechanical (45%), almost equal to infections (42%), whereas thrombotical events represented only 11% of the complications. The complication rate was 1 complication per 10 catheter/month, with a probability of remaining complication-free at 6 and 12 months of 76 and 52% respectively.

**Conclusions:** The vascular access preferentially used in our unit are CCVCs. In our series, their use allows adequate dialysis with a low complication rate. The median duration of haemodialysis in our sample is lower than 1 year.



# SYMPOSIUM 9

## ESPN/ERA and ERKNet Registries

**Su-3MP 094**  
**EUROPEAN SURVEY ON LONG-TERM PAEDIATRIC HAEMODIALYSIS**

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**Aims/Purpose:** Children requiring long-term hemodialysis (HD) are fortunately rare. We aimed to describe the legal rules and organisation of paediatric HD in European countries.

**Methods:** With the support of ESPN, we have created an online questionnaire for a national representative from each country.

**Results:** We received a response from 36 countries (Albania, Austria, Belarus, Belgium, Bosnia and Herzegovina (BH), Bulgaria, Croatia, Czechia, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Malta, Moldova, Montenegro, North Macedonia, The Netherlands, Norway, Poland, Portugal, Romania, Russia, Serbia, Slovakia, Slovenia, Sweden, Switzerland, Turkey, United Kingdom (UK) and Ukraine). We observed a great heterogeneity in the organisation of pediatric HD across Europe. Finland has the highest ratio of centers per inhabitants: one center per less than one million, compared to countries with one per more than five millions (Austria, Belarus, Bulgaria, Greece, Italy, Serbia and UK). Currently in 28% of the countries (Albania, Austria, Belarus, Croatia, Czechia, Germany, Moldova, Poland, Portugal, and Serbia), a child cannot be “legally” dialysed in an adult centre before the age of 18 year. On the contrary, 11% of the countries (Denmark, Malta, Norway and Russia) allowed HD of children in adult centers with no lower age limit. In 19% of countries, the law allows HD of children in adult centers from the age of 5 to 16 years: 5 in Ukraine, 8 in France, 10 in Latvia, 14 in BH, 15 in Slovakia and 16 in Greece and Montenegro. In 42% of the countries (Belgium, Bulgaria, Finland, Hungary, Ireland, Italy, Lithuania, The Netherlands, North Macedonia, Romania, Slovenia, Sweden, Switzerland, Turkey and UK) there is no legal framework specifying a minimum age. If children are haemodialysed in an adult center, legislation requires a paediatrician to be part of the medical team in 42% of countries (Croatia, Denmark, France, Germany, Greece, Lithuania, Malta, Moldova, Montenegro, North Macedonia, Portugal, Romania, Russia, Slovakia and Turkey), while this requirement does not exist in 28% (Belgium, Bulgaria, Czechia, Ireland, Latvia, Poland, Slovenia, Sweden, UK and Ukraine) or is not specified in 28% (Albania, Austria, Belarus, BH, Finland, Hungary, Italy, The Netherlands, Norway, Serbia and Switzerland). There is a legal framework in 44% of the countries regarding the minimum number of doctors per center (1 to 3), in 53% of the countries regarding the maximum ratio of the number of patients per nurses (1 to 6) and in 25% per auxiliary nurses (1 to 4) during a HD session. 72% of the countries must provide urgent HD session out of the hours.

**Conclusion:** Our work could serve as a basis for discussing legal and practical organisation of pediatric HD in our European countries.

We would like to thank all colleagues who have already participated in the survey and members of EPDWG.

Su-3MP 095

CUFFED-TUNNELED CENTRAL VASCULAR CATHETERS FOR HAEMODIALYSIS AND ASSOCIATED INFECTIONS: 10 YEARS EXPERIENCE IN ONE SINGLE PAEDIATRIC CENTRE

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**Introduction:** The use of cuffed-tunneled central venous catheters (CCVC) as vascular access for haemodialysis in paediatrics is common clinical practice in our setting. Its management is not free of complications. Infections are of special relevance given their high morbidity and risk of vascular access failure.

**Aims:** Describe infectious complications, as well as their influence on survival of vascular access in our patients.

**Methods:** We retrospectively reviewed the medical records of patients carriers of CCVC undergoing haemodialysis in our unit in the period from 2012–2022.

**Results:** 181 CCVC were used during this period in 105 patients (60% patients required a single catheter). 63 infectious complications were recorded in 60 catheters over 10 years: 25 catheter-related bacteraemia, 28 exit site infections and 10 tunellitis. The infection rate was 1.42/1000 catheter-days with a probability of remaining infection-free at 6 and 12 months of 82% and 64% respectively. 32% of infectious events resulted in vascular access replacement. Catheter-related bacteraemia was the most frequent infectious cause of failure (20% failures in the sample). There was no case of mortality related. *Staphylococcus aureus* was the most frequent isolated micro-organism (36 occasions), followed by *Staphylococcus epidermidis* (12) and *Pseudomonas aeruginosa* (6). Seventy percent of the S.Aureus related cases were nasal carriers. Median catheter survival in the infection group in our sample was lower (10.7 months vs. 15.66 months in the absence of infection), although this difference was not statistically significant ( $p = 0.14$ ).

**Conclusions:** Infectious complications related to CCVC are an important cause of CCVC failure, leading in our sample to decreased catheter survival. Our infection rate was similar to that reported in the literature. We observed a higher rate of S. Aureus nasal carriers in those patients with infectious complications.

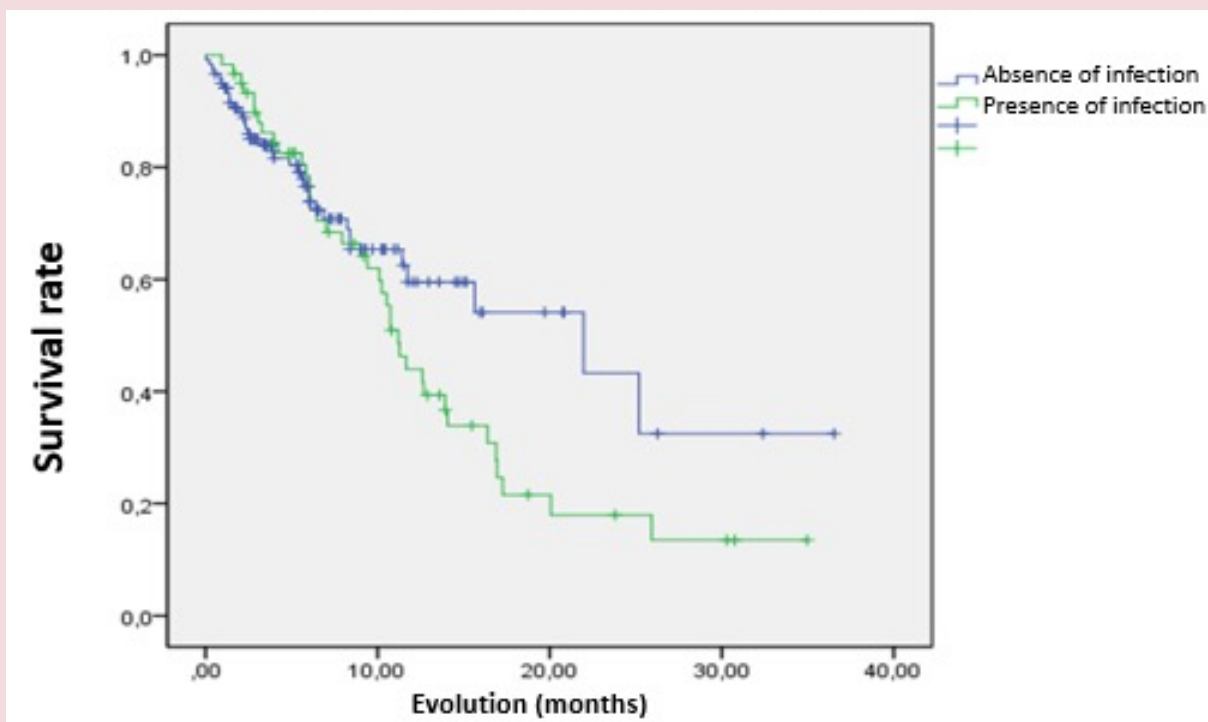


Figure: CCVC survival depending on the presence of infectious complications

**Su-3MP 096**

**AN UPDATE ON THE CHARACTERISTICS, TREATMENT HISTORY AND SURVIVAL OF 18-YEAR OLDS WHO STARTED KIDNEY REPLACEMENT THERAPY DURING CHILDHOOD: AN ERA REGISTRY ANALYSIS**

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**Aims/Purpose:** Young adults starting kidney replacement therapy (KRT) during childhood form a challenging population due to the transition from paediatric to adult nephrology care. We aimed to investigate characteristics, treatment and survival of patients who turned 18 years during the period 2008–2019, after initiation of KRT in childhood.

**Methods:** Data was collected from 20 European countries/regions providing individual patient data to the European Renal Association (ERA) Registry. Patient characteristics and treatment history were assessed by age at start of KRT and period of their 18th birthday. Cox regression was used to calculate 5-year patient survival from that date. Besides, we calculated expected remaining lifetime at 18 years, stratified by treatment modality.

**Results:** We included 2861 patients. The number of patients turning 18 was stable over time, varying from 142.2 per million age-related population (pmarp) in 2008–2011 to 137.2 pmarp in 2016–2019. Most patients were 10–14 years at KRT start and hypoplasia/dysplasia was the most common cause of kidney failure. Peritoneal dialysis was the most common treatment at start of KRT, yet in the oldest age group (15–17 years) it was haemodialysis. Of patients turning 18 between 2008–2011, 26% had a pre-emptive transplant which increased to 32% in 2016–2019 (15% and 20% from living donors, respectively). When reaching 18 years, 82% of patients had a functioning transplant. The overall unadjusted 5-year patient survival after their 18th birthday was 97.5% (95% CI 96.9–98.2). For transplant patients it was 98.4% (95% CI 97.8–98.9) and for dialysis patients 93.5% (95% CI 91.1–95.9). The average life expectancy at 18 years was 65 years for kidney transplant patients and 42 years for dialysis patients.

**Conclusion:** Patient characteristics of adult survivors of paediatric KRT remained stable during the past decade. Yet, the total number of patients reaching 18 years and the percentage of patients with a functioning kidney transplant (82% vs 60%) were higher in 2008–2019 compared to a previous ERA Registry study [1]. Survival has improved in both treatment modalities comparing with the previous study, but the discrepancy between patients with a functioning graft and those on dialysis remains huge [1]. Further research will focus on KRT patients transitioning from childhood to adulthood. To this end we aim to merge data from the paediatric ESPN/ERA Registry and the ERA Registry.

**References**

1. Kramer A, Stel VS, Tizard J, et al. Characteristics and survival of young adults who started renal replacement therapy during childhood. *Nephrology Dialysis Transplantation* 2009; 24: 926–933.

Su-3MP 097

**DETERMINING THE ROLE OF MEMBRANE BOUND COMPLEMENT REGULATORY PROTEINS (MCRPS) AS PAEDIATRIC RENAL TRANSPLANT BIOMARKERS IN ANTIBODY-MEDIATED REJECTION (ABMR)**

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**Aim/Objectives:** The accurate and prompt diagnosis of ABMR in pKTR is vital in allowing the early initiation of treatment to prevent renal allograft dysfunction and loss. The important role of complement activation in renal transplant immunology and rejection has been debated, especially when some pKTR can have circulating peripheral donor specific antibodies for years. There is evidence that it is as a critical mediator of inflammation and injury to allografts undergoing ABMR and particularly the classical pathway leading to C4d deposition and that is something that is evaluated in ABMR classification. Membrane-bound complement regulatory proteins (mCRPs), such as CD46, CD55, and CD59, are expressed throughout the body to prevent over-activation of the complement system. Pro-inflammatory factors such as spleen tyrosine kinase (Syk) and C3d promote leucocyte recruitment and activation, and enhance the immune response. There are limited data in the paediatric population identifying the presence and deposition of specific complement pro-inflammatory and inhibitory factors in suspected ABMR. We looked to investigate if there are dynamic markers that could monitor the degree of complement activation, that could subsequently be used either as treatment targets or monitoring tools. We know that under complement attack, membrane complement regulatory proteins show dynamic expression on both endothelial and epithelial cells.

**Hypothesis:** Dynamic complement regulator expression in ABMR could be used as a tool to monitor complement involvement

**Methods:** Retrospective, single-centre study of percutaneous renal transplant biopsies from 54 pKTR with donor-specific antibodies (DSA) and a histological diagnosis of ABMR. Following the optimization of the above antibodies, the tissue materials of these 54 patients were retrieved from GOSH archives for IHC staining with CD46, CD55, CD59, SYK and C3D. The renal tissues were formalin-fixed-paraffin-embedded (FFPE) and sectioned at 3 microns thickness. The slides were then scored using a semi-quantitative scoring system on strength of staining: 0 = no significant staining, 1+ = patchy staining and 2+ = strong staining; and location = glomerular capillaries, proximal or distal tubules. We used placenta as our positive controls, with all antibodies showing strongly positive staining (2+) and non ABMR renal tissue to assess baseline level of mCRP expression.

**Results:** CD55, which is one of the proximal complement regulators, showed no evidence of staining in any of the 54 biopsies, compared to patchy staining observed in the controls. And for the other proximal regulator CD46, there was positive staining in 32 of the 54 biopsies (58%) which was mainly confined to the proximal and distal tubules. However, conversely, CD59, which was one of the terminal regulators, there was positive staining in 96% biopsies, in the peritubular capillaries, proximal and distal tubules. Looking at the pro-inflammatory factors, Syk showed positive staining in all biopsies and C3d in 87% biopsies. For syk, this was mainly confined to the distal tubule. And for c3d, patchy staining in the proximal and distal tubules and stronger staining in the glomerulus. This suggests there is some complement activation in ABMR.

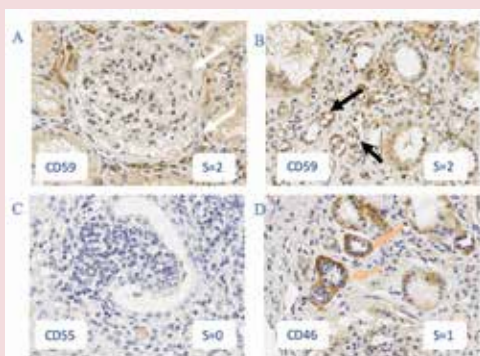


Figure 1: Renal biopsy staining for complement factors in pKTR diagnosed with ABMR. Selected section of biopsy slide stained for CD59 in glomeruli (A) and in peritubular capillaries (B). Selected section of biopsy slide stained for CD55 in glomeruli (C) and CD46 in proximal and distal tubules (D). White arrows indicate glomeruli, black arrows indicate peritubular capillaries, green arrows indicate proximal and distal tubules. Semi-quantitative scores (0-2) indicated in the lower right corner.

**Conclusion:** Our results suggest that these mCRPs demonstrate varying degrees of expression and location in kidneys undergoing ABMR, which could provide important information in diagnosing, classifying and treating ABMR. Our results also show possible stronger natural protection against terminal complement by CD59 compared to proximal regulators CD46 and CD55. One possible explanation is that, in response to increased complement activation, there is increased expression of mCRPs, in which case future studies looking at the role of complement blockade would be warranted. Or alternatively, there is decreased expression of mCRPs as a response to increased complement activation, possibly due to immunosuppression or transplant physiology. In this case, mCRPs could be used as a monitoring tool to show increased risk of ABMR. Looking ahead, we are looking to validate these results in a larger study, co-staining for other segments of nephron and identifying if our results are heterogeneous or homogeneous. Where does this leave us, our pilot study suggests that membrane bound complement regulatory proteins show variability in their expression and location in pKTR undergoing ABMR. And as such, further addressing their role and the wider role of complement in ABMR is warranted.

# WORKING GROUP SESSION

## CAKUT and CKD

Su-3MP 098

**BENEFITS OF VITAMIN D SUPPLEMENTATION IN CHILDREN WITH CHRONIC KIDNEY DISEASE: A SYSTEMATIC REVIEW**

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**Aims/Purpose:** Chronic kidney disease (CKD) is an irreversible, debilitating kidney disease which might be caused by either anatomical or functional abnormality of kidney. Its prevalence was found to be about 18 out of 1 million children. Vitamin D deficiency is commonly found in this population, worsened by inability to metabolize vitamin D optimally due to the deteriorating function of kidney. Vitamin D deficiency might worsen kidney function, thus, vitamin D supplementation is commonly given to lessen further complication. However, up until now, there is still not much information regarding the benefits of vitamin D supplementation in children with CKD. This systematic review was made to find out and

**Methods:** The literature search was done from 4 databases (Google Scholar, Pubmed, ScienceDirect, and SpringerLink) using combinations of keywords (“CHILDREN” OR “PEDIATRIC”) AND (“CHRONIC KIDNEY DISEASE” OR “CKD”) AND (“VITAMIN D SUPPLEMENTATION”). The making of this systematic review was based on guidelines from Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA). Our review included articles published in the last 10 years (2012–2022) in English, on children aged 0–18 years with CKD who had vitamin D supplementation.

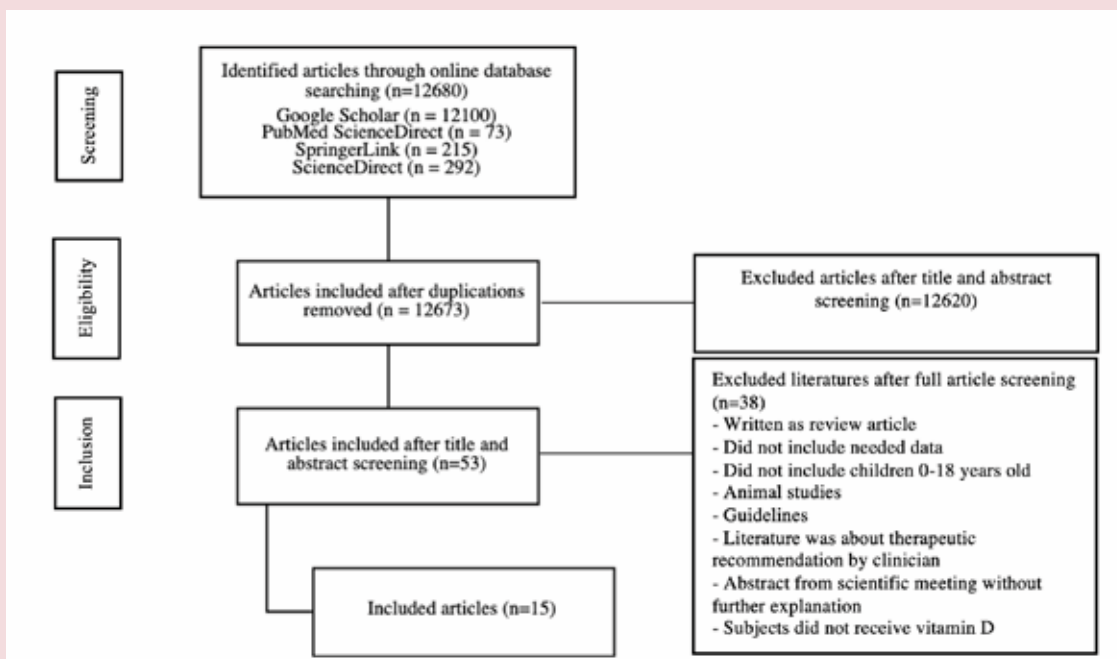


Figure 1: Journal articles search flow diagram

**Results:** Twenty two articles were included in this study. Five articles found that inactive form of vitamin D can increase the value of serum vitamin D. It was also found that the value of vitamin D serum was affected by eGFR/CKD stage; the higher the eGFR, the higher the value of serum vitamin D and vice versa. Supplementation did not affect PTH value, but secondary hyperparathyroidism happened slower when given to patients with lower stage of CKD. Klotho and sclerostin value was also lower in patients who received vitamin D supplementation at lower stage of CKD. Arterial stiffness and heart deformity was also improved. Erythropoietin injection was also found to be more effective in children who received vitamin D supplementation.

**Conclusion:** Vitamin D supplementation in children with CKD is suggested to be done routinely due to its many benefits. It was found to be able to improve the overall condition and also hinder the progressivity and complication that might happen in children with PKG. Despite several guidelines of vitamin D supplementation are already available, further studies are still needed to determine the most effective dose, route of administration, and forms of vitamin D supplementation.

Su-3MP 099

SODIUM ZIRCONIUM CYCLOSILICATE FOR CONTROLLING ACUTE AND CHRONIC HYPERKALEMIA: EXPERIENCE IN PAEDIATRIC CHRONIC KIDNEY DISEASE AND DIALYSIS

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<sup>1</sup>Nephrology, <sup>2</sup>Pharmacy, Great Ormond Street Hospital, London, United Kingdom

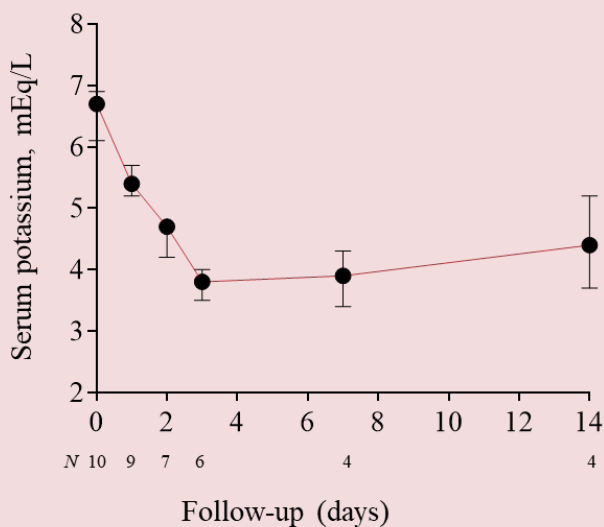
**Aims/Purpose:** Sodium zirconium cyclosilicate (SZC) is safe and effective for the treatment of hyperkalemia in adults with chronic kidney disease (CKD); reports of use in children is limited. The role of prolonged therapy with SZC to relax dietary potassium (K<sup>+</sup>) restrictions in CKD patients with hyperkalemia has not been examined.

**Methods:** We conducted a retrospective chart review of patients 6-mo–18-yr with CKD stage 5 and on dialysis (5D) administered SZC for sustained hyperkalemia (K<sup>+</sup> > 5.5 mEq/L; at least 2 values 48-hr apart) from July 2020 to March 2023. Patients received SZC (0.5–5 g; age-based), titrated based on serum K<sup>+</sup> levels, either short-term (< 30 d) or long-term (> 30 d). Dietary restrictions were liberalized where feasible. Blood pressure and serum electrolytes were serially recorded on follow-up.

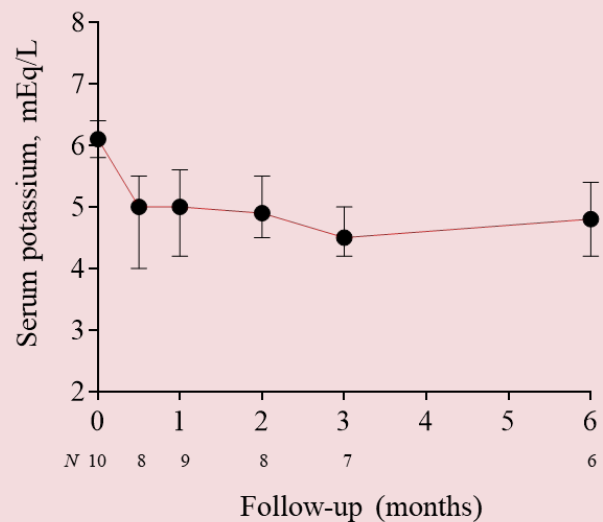
**Results:** Twenty patients with median age 10.8 (3.9, 13.4) yr, were treated with SZC for acute hyperkalemia (short-term) or long-term. Ten were on hemodialysis, 6 on peritoneal dialysis and 4 on conservative management of CKD. Short-term SZC, for 5 (3, 19) days in 10 patients, facilitated safe management of dialysis catheter insertions by 2–27 days (n = 5), management of access dysfunction (n = 4), and allowed palliation (n = 1). Serum K<sup>+</sup> levels decreased from median 6.7 (6.1, 6.9) mEq/L to 4.4 (3.7, 5.2) mEq/L (P < 0.001; Fig a); hypokalemia (serum K<sup>+</sup> 3.2 mEq/L) was observed at 72-hr in two patients. Long-term SZC for 5.3 (4.2, 10.1) months in another 10 patients achieved a significantly decline in serum K from 6.1 (5.8, 6.4) mEq/L to 4.8 (4.2, 5.4) mEq/L (P < 0.001; Fig b). The strategy allowed liberalization of diet (n = 5), and was useful in patients with poor compliance to dietary restriction (n = 3), or where restrictions were not possible (n = 1), and facilitated delayed initiation of dialysis by 63 and 120 days (n = 2). SZC was well tolerated, without serious adverse events; levels of serum sodium and blood pressure did not show statistically significant increase during follow-up.

**Conclusion:** Prolonged use of SZC is safe and efficacious to maintain normokalemia in children with CKD 5/5D. Treatment with SZC allowed patients to relax dietary K<sup>+</sup> restriction or to keep a safe serum K level in those who were non-adherent to dietary restrictions. Studies to examine the routine use of a potassium binder to improve nutritional status in children with CKD are required.

a



b





Su-3MP 100  
LESSONS OF WAR: CHILDREN'S NEPHROLOGICAL CARE IN UKRAINE

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<sup>3</sup>First medical Union of Lviv, Lviv, Ukraine, <sup>4</sup>Dnipro State Medical University, Pediatrics, Dnipro, Ukraine, <sup>5</sup>Lviv Medical University, Lviv, Ukraine, <sup>6</sup>Institute of Hereditary Pathology of the National Academy of Sciences of Ukraine, Lviv, Ukraine, <sup>7</sup>National Pirogov Memorial Medical University, Vinnytsya, Ukraine

**Aims/Purpose:** Analysis of changes in the provision of paediatric nephrological care during the war in Ukraine.

**Methods:** An analysis of the indicators of medical care for children with kidney disease was carried out in Ukraine from February 2022 to March 2023. We also used direct interview methods and a summary presentation of the results according to the SWOT analysis.

**Results:** During the period of martial law, 3.5 (47%) children out of 7.4 million left the country, and out of 2296 children with CKD, more than 1300 (57%) emigrated. Out of 124 doctors providing paediatric nephrological care, 76 (61%) remained in Ukraine. The entire territory of Ukraine was divided into 4 zones (red, yellow, green and grey). Children's nephrology departments in 4 regions were closed and evacuated, which led to a violation of the availability of care for children. The overall nephrological morbidity did not increase significantly, either for acute or chronic diseases. There was a shortage of medicines, which led to the active use of humanitarian rituximab instead of hormone therapy for nephrotic syndrome. The number of kidney transplants increased by 72%. **STRENGTHS:** support by the EU and Ukrainian government, the solidarity of people, the return of medical staff to their jobs after emigration, state support, and stimulation of knowledge expansion. **WEAKNESSES:** emigration of qualified personnel, the unpredictability of the situation and shortage of medicines and supplies, the inability to provide RR therapy for all patients, the worsening condition of chronic patients, stress on doctors, parents and children. **OPPORTUNITIES:** rapid introduction of modern technologies, development of new approaches, humanitarian communication, strengthening contacts with colleagues. **THREATS:** blackout, lack of water, heat, communication, strengthening the destructive factor of war, depletion of moral and material resources, war weariness, the political split of society

**Conclusion:** The war led to the formation of previously known difficulties and the emergence of unexpected challenges, but in certain issues, it potentiated the accelerated development of knowledge and skills that are useful for sick children.

Su-3MP 101

ACUTE KIDNEY DISEASE – THE SILENT CONTINUUM OF KIDNEY INJURY

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**Aims/Purpose:** Epidemiology and outcome of acute kidney disease (AKD) in children following an acute kidney injury (AKI) episode from a large East European database.

**Methods:** We conducted a multiyear, single-center, retrospective observational study in the ‘Louis Turcanu’ Emergency County Hospital for Children in Timisoara, Romania. Data were extracted from the electronic data base between first of January 2014 until 31 December 2021. The study cohort included 128036 patients (aged 1 day to 18 years). The inclusion criteria was AKI diagnosis according to KDIGO criteria. Kidney damage with duration between 7 days and 90 days was defined as acute kidney disease (AKD) according to the 2021 KDIGO Consensus Conference. Out of the 2199 AKI patients, 390 had AKD. The study was performed in accordance with the Ethics Code of the World Medical Association and the Hospital’s Ethics Committee.

**Results:** The incidence of in-hospital acquired AKD was 3/1000 hospital admissions. The mean age was  $827.8 \pm 1774.5$  days, 52.8 % were boys and 57.2% came from urban area. AKD was dependent of: lower age ( $p < 0.001$ ), lower body weight ( $p < 0.001$ ), intrinsic cause of kidney injury ( $p < 0.0001$ ) and severe AKI ( $p < 0.0001$ ). The presence of sepsis, hypovolemic shock, mechanical ventilation, critical illness and nephrotoxic drugs generated an OR of AKD of 3.5 (CI 2.7 – 4.5,  $p < 0.0001$ ), 1.78 (CI 1.06 – 2.97,  $p = 0.027$ ), 3.73 (CI 2.94 – 4.72,  $p < 0.0001$ ), 2.37 (CI 1.73 – 3.25,  $p < 0.0001$ ) respectively 2.07 (CI 1.54 – 2.78,  $p < 0.0001$ ). Renal replacement therapy was associated in 72% AKD children (OR 12.44, CI 5.16 – 30,  $p < 0.0001$ ). The mortality in our AKD cohort was 17% with a relative risk of death of 1.6 (CI 1.25 – 2.09,  $p = 0.0002$ ). AKD doubled hospital stay, from  $17.55 \pm 17.27$  days in AKI non-AKD patients to  $36.08 \pm 21$  days.

**Conclusion:** AKD is a continuum of kidney injury in hospitalized pediatric patients with high mortality and longer hospital stay. Our results provide new information about AKD outcomes in hospitalized AKI pediatric population.

Su-3MP 102

DETERMINATION OF RENAL PARENCHYMAL CHANGES IN PRETERM-BORN CHILDREN BY MRI-DERIVED RADIOMICS – A MACHINE LEARNING STUDY

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**Aims/Purpose:** Preterm-born children are prone to both low number and hypertrophy of the nephrons. These abnormalities cannot be demonstrated non-invasively. Magnetic resonance imaging (MRI)-based radiomics is a new method that defines a large number of features of an image providing quantitative data on textural features that the naked eyes fail to detect. In this study, we aim to evaluate whether MRI-based radiomics image features can differentiate early renal parenchymal changes in preterm-born children.

**Methods:** This case-control cross-sectional study included MR images of 50 preterm-born and 27 term-born children as a control group. Renal parenchyma segmentation was performed by an experienced radiologist blinded to clinical data using coronal T2-weighted images. A total of 106 MRI-derived textural features were extracted from each region of interest. The dataset was randomly divided five times into training and test sets (ratio 4:1), and the least absolute shrinkage and selection operator (LASSO) algorithm was applied to the test set to select the most relevant features. Selected feature subsets were used to train and optimize different supervised machine learning classifiers.

**Results:** There were no significant differences between the preterm and control groups considering age ( $11.5 \pm 1.9$  vs  $11.7 \pm 2.6$  years) or sex (58% vs 52% female). The mean gestational age of the preterm group was  $31 \pm 2.5$  weeks and birth weight was  $1.4 \pm 0.4$  kg. MRI-based kidney volume did not differ significantly between the preterm and control groups ( $122 \pm 16$  cm<sup>3</sup>/m<sup>2</sup> vs  $128 \pm 18.0$  cm<sup>3</sup>/m<sup>2</sup>,  $p = 0.17$ ); however, 13 of 106 MRI-based textural parameters in the preterm group were significantly different from the control group ( $p < 0.05$  for all). Of these parameters, five were independently associated with the preterm-born kidney as follows: the preterm group had significantly (1) higher median signal intensity on T2-weighted images ( $p = 0.025$ ), (2) lower gray level size zone matrix (GLSZM) small zone emphasis ( $p = 0.032$ ), (3) higher GLSZM small zone gray level emphasis ( $p = 0.033$ ) and higher (4) gray level run length matrix (GLRLM) long run high gray level emphasis ( $p = 0.030$ ), indicating coarser texture, and (5) lower GLSZM normalized zone size non-uniformity ( $p = 0.020$ ), indicating non-uniform texture. The support vector machine (SVM) algorithm demonstrated the best accuracy in predicting preterm kidney with an AUC of 0.88.

**Conclusion:** MRI-based radiomics reveal that the kidneys of the preterm-born infants have a coarser and non-uniform texture compared with those of term-born kidneys in the first decade of life. Artificial intelligence-assisted evaluation of MRI derived parameters may foresee the risk of chronic kidney disease in preterm-born children in the future.

Su-3MP 103

HIGH INORGANIC PHOSPHATE INTAKE CAUSES RENAL PHOSPHATE WASTING BY PIT-2/ERK1/2 MEDIATED DOWNREGULATION OF NPT2A

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**Aims/Purpose:** Fibroblast growth factor 23 (FGF23) and parathyroid hormone (PTH) are major regulators of renal phosphate (Pi) handling downregulating the sodium-phosphate cotransporters NPT2a (SLC34A1) and NPT2c (SLC34A3) in proximal tubule (PT) cells by activation of FGFR1/Klotho and PTHR-mediated ERK1/2 signalling pathway, respectively. In bone cells in vitro, high extracellular phosphate activates ERK1/2 via PiT-1 and PiT-2, but yet, it is unclear whether high phosphate concentrations can be sensed by PT cells of the kidney as well and phosphate thereby regulates its own excretion.

**Methods:** C57BL/6 male mice were fed with a 2% high inorganic phosphate diet (HPD) or a 0.8% control phosphate diet (Ctrl) for six months, renal PT cells were isolated and RNAseq was performed. Phosphate metabolism and signaling pathway regulating phosphate transporters were determined by qPCR, immunoblot and histology. To normalize FGF23 and PTH levels, mice on HPD were additionally treated with a calcimimetic agent and renal phosphate handling was compared to mice on Ctrl and HPD without calcimimetic supplementation. Renal PT cells were stimulated in vitro with phosphate or FGF23 + the phosphate transporter inhibitor foscarnet and the activation of downstream ERK1/2 signaling was examined.

**Results:** HPD in mice resulted in elevated intact FGF23 and PTH levels associated with reduced tubular reabsorption and increased fractional excretion of phosphate, but serum phosphate levels were still enhanced compared to Ctrl. RNAseq analysis observed downregulation of Fgfr1, Kl, Slc34a1 and Slc34a3, and interestingly, upregulation of Slc20a2 in isolated PT cells of HPD-fed mice compared to Ctrl. Immunoblot analyses of total renal tissue showed reduced Klotho protein levels while Fgfr1 was not altered in the HPD group. However, NPT2a protein was reduced in isolated brush boarder membrane (BBM) vesicles of HPD-fed mice and immunofluorescence (IF) staining revealed internalization of NPT2a from the apical BBM due to HPD. qPCR of total renal tissue further confirmed RNAseq data showing a significant upregulation of Slc20a2 in the HPD group. Concomitant treatment of HPD-fed with calcimimetic significantly lowered plasma FGF23 and PTH levels, but urinary phosphate excretion was still enhanced. In cultured PT cells in vitro, stimulation with high phosphate induced ERK1/2 phosphorylation and Slc20a2 mRNA levels and downregulated Slc34a1. The phosphate-mediated Slc20a2 upregulation and ERK1/2 phosphorylation was blocked by foscarnet co-treatment.

**Conclusion:** Chronic high Pi intake results in renal phosphate wasting caused by Pi-induced PiT-2/ERK1/2 signaling resulting in downregulation of NPT2a, while the phosphaturic actions of FGF23 are partly weaned-off by renal FGF23 resistance due to Klotho deficiency.

Su-3MP 104

ETELCALCETIDE AMELIOREATES THE PROGRESSION OF HIGH PHOSPHATE DIET INDUCED TUBULAR INJURY IN MICE

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**Aims/Purpose:** The phosphate intake in western countries exceeds by far the recommended dietary consumption and may impact kidney health. We have recently shown that a chronic high phosphate diet (HPD) resulted in increased serum phosphate, fibroblast growth factor 23 (Fgf23) and parathyroid hormone (PTH) levels, and enhanced phosphaturia in healthy mice. In addition, mice exhibited proximal tubular injury, tubulointerstitial fibrosis and inflammation and perivascular tertiary lymphoid structures (TLS) in the corticomedullary zone. Activation of the calcium-sensing receptor (CaSR) with calcimimetics was shown to stabilize podocyte function in proteinuric humans and mice. The CaSR is also expressed in the tubular system and therefore, we hypothesized that treatment with calcimimetics may ameliorate HPD induced tubular damage in mice.

**Methods:** To investigate whether calcimimetic treatment positively affects kidney health, we induced kidney disease in male C57BL/6 mice by the use of a 2% HPD in comparison to a 0.8% phosphate control diet (Ctrl). After four months of dietary intervention, one HPD-fed group was concomitantly treated with 1 mg/kg body weight/day etelcalcetide (KP-2326) for further two months. At the end, blood and urine were taken and kidneys were harvested for histological and transcriptional analysis.

**Results:** Concomitant treatment of HPD-fed mice with etelcalcetide significantly reduced albuminuria and lowered plasma intact Fgf23 and PTH levels, but urinary phosphate excretion and serum phosphate levels were still enhanced compared to Ctrl. The enhanced tubular injury score caused by HPD and the transcription levels of kidney injury marker Kim-1, encoded by *Havcr1* were reduced by etelcalcetide treatment. The mRNA expression of monocyte chemoattractant protein-1, encoded by *Ccl2*, regulating infiltration of monocytes and macrophages, and the macrophage specific marker *Adgre1* were significantly lower in etelcalcetide treated HPD group compared to HPD vehicle. Etelcalcetide treated HPD fed mice still developed fully matured perivascular TLS in the kidneys, which were characterized by clustered CD3<sup>+</sup> T cells, CD45R<sup>+</sup> B cells, and IgD secreting CD138<sup>+</sup> plasma cells and podoplanin<sup>+</sup> cell networks. However, the number of TLS found in this group was lower compared to the vehicle treated HPD group.

**Conclusion:** Treatment with etelcalcetide reduces the progression of tubular injury in mice on HPD. The persistent maturation of TLS despite etelcalcetide treatment suggests that hyperphosphatemia per se is able to promote local kidney inflammation in this setting.

Su-3MP 105

NEW TREATMENTS, NEW CHALLENGES: NEPHROTOXICITY ASSOCIATED TO NAXITAMAB IN PATIENTS WITH HIGH-RISK NEUROBLASTOMA

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**Aims/Purpose:** Neuroblastoma is the most common extracranial solid tumor in children, harboring a poor survival for those with high-risk (HR) tumors. Naxitamab (hu3F8) is a humanized monoclonal anti-disialoganglioside (GD2) antibody approved for the treatment of patients older than 1-year with refractory/relapsed HR-neuroblastoma limited to bone and/or bone marrow. First naxitamab (DanyelzaR) infusion was in 2017 in our institution and since then a large experience has been acquired with its use through several clinical trials as well as an expanded named patient access program. Our objective is to describe the renal toxicity profile associated to naxitamab in patients with HR-neuroblastoma

**Methods:** Retrospective descriptive study including 244 patients (41% female -101- and 59% male -143-) treated with naxitamab (either on monotherapy or associated to chemotherapy) from June 2017 to December 2022 in whom renal involvement and/or hypertension (HT) was evaluated.

**Results:** Mean age of the cohort was 8 years, presenting nephrotoxicity of some type up to 26.6% (n = 65): HT (11.9%), acute renal damage (ARD 10.2%) and proteinuria (5.3%), developing all during the infusion or the first 3 cycles. In the case of HT only in 6 patients an 24-hours Ambulatory Blood Pressure Monitoring (ABPM) was performed, observing: 2 nocturnal-HT, 2 diurnal-HT without specific-pattern, and 2 disautonomic-pattern. Among the ARD, all cases were tubular except for one patient who presented clinical-analytical pattern of acute tubule-interstitial nephritis (AIN) and another who presented thrombotic microangiopathy (TMA) with subsequent confirmation of heterozygous CFHR1-CFHR4 deletion. Eight of them (32%) had potential confounding factors (previous chemotherapy, ibuprofen or radiotherapy). Among patients with proteinuria (none in the nephrotic range): 38% tubular, 38% glomerular and 23% mixed. Two patients presented ARD + AHT and 3 a combination of AHT + ARD + proteinuria. All patients received prior chemotherapy and 2 developing chronic renal damage (CKD stage 2 and 3)

**Conclusion:** Short-and long-term follow-up, the systematic performance of ABPM, and the use of early markers of renal damage, could lead to a more efficient management of complications derived from this new treatment. Previous studies of our group in mice explain the involvement of the myelin sheaths of the autonomic nervous system with this drug, which could explain the dysautonomic pattern of blood pressure presented.

Su-3MP 106

X-LINKED FILAMINOPATHY IN A PATIENT WITH CONGENITAL ANOMALIES OF THE KIDNEY AND URINARY TRACT

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**Introduction:** X-linked filaminopathies are a diverse group of orphan diseases caused by mutations in the FLNA gene which encodes the cytoskeletal actin-binding protein filamin A. This protein widely expressed in the body and performs various functions: embryonic development, neuronal migration, maintenance of connective tissue integrity, and vascular development. Pathogenic variants in this gene cause a wide range of genetic syndromes with signs of organ and tissue damage – from skeletal dysplasia, cardiovascular disease, gastrointestinal and renal abnormalities to brain damage. One of the wide spectrum disorders of a group X-linked filaminopathies is frontometaphyseal dysplasia (FMD; OMIM 305620).

**Material and Methods:** We describe a clinical case of X-linked FMD identified by Next Generation Sequencing (NGS).

**Results:** Case report: a 11-year-old boy with congenital anomalies of the kidney and urinary tract: bilateral megaureter, neurogenic bladder, CKD3A was examined. In addition, the patient had congenital heart disease: atrial septal defect, valvular pulmonary artery stenosis and secondary chronic cicatricial-granular stenosis of the larynx. Skeletal anomalies included craniofacial abnormalities – coarse facies prominent supraorbital ridges, high-degree scoliosis, valgus deformity of the lower extremities. Pronounced short stature of mixed genesis, multiple congenital developmental features. NGS analysis (exome panel, Illumina, NextSeq 550) found a nonsynonymous heterozygous variant in the FLNA gene: c.3557G > A (p.S1186L, rs137853312). The discovered variant is a known pathogenic mutation and is registered in the ClinVar (ID: 11761) and HGMD (ID: CMO30671) databases. The identified mutation was confirmed by Sanger sequencing, genetic testing of the parents was carried out, the p.S1186L heterozygous mutation was found in the patient's mother.

**Conclusion:** The use of modern genetic methods makes it possible to identify rare hereditary syndromes and make an accurate diagnosis, which is very important for choosing the right management of patient.

Su-3MP 107

LACTOBACILLUS RHAMNOSUS PL1 AND LACTOBACILLUS PLANTARUM PM1 VERSUS PLACEBO AS A PROPHYLAXIS FOR RECURRENCE TRACT INFECTIONS IN CHILDREN: A RANDOMISED CONTROLLED TRIAL

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**Background:** Urinary tract infections (UTIs) are one of the most common bacterial infections in children. In children < 7 years of age, the prevalence of one episode of symptomatic UTI has been estimated at 3-7% in girls and 1-2% in boys, whereas 8-30% of them will have one or more episodes of UTI. Probiotics appear to have a role in reducing uropathogen colonization, virulence, and the need for antibiotics in UTIs. There is limited clinical evidence to support the role of probiotics in preventing recurrent UTIs.

**Aims:** The main aim of this study is to determine whether probiotics (containing *Lactobacillus rhamnosus* PL1 and *Lactobacillus plantarum* PM1) therapy are effective in preventing UTI in children compared to placebo.

**Method:** A superiority, double-blind, randomized, controlled trial is being conducted. 54 patients aged 3 to 18 years with recurrent UTIs in the year before the research (defined as  $\geq 2$  episodes of UTI with acute pyelonephritis/upper UTI; or 1 episode of UTI with acute pyelonephritis and  $\geq 1$  episode of UTI with cystitis/lower UTI; or  $\geq 3$  episodes of UTI with cystitis/lower UTI) were randomly assigned to receive a 90-day prophylaxis arm (probiotic containing *L. rhamnosus* PL1 and *L. plantarum* PM1) or a 90-day placebo arm. Study duration 9 months (3 months intervention and 6 months follow-up).

**Results:** The study groups did not differ in age, sex, diagnosis, renal function, or risk factors for UTI. An intention-to-treat analysis was performed. The study groups had a similar number of recurrences of UTI, fewer episodes of UTI, and fewer days of antibiotic therapy than before the intervention. There were no statistically significant differences in the decrease in UTI episodes between groups.

**Conclusions:** A multifactorial effect has an impact on the decrease of recurrent UTIs. The administration of probiotics in the prevention of UTI requires further research.

Keywords: Recurrent UTI, Children, Probiotics, Prophylaxis, RCT, *Lactobacillus rhamnosus* PL1, *Lactobacillus plantarum* PM1



Su-3MP 108

EVALUATION AND FOLLOW-UP OF URINARY TRACT INFECTION AND RENAL SCAR FREQUENCY IN PEDIATRIC PATIENTS WITH PRIMARY VESICoureTERAL REFLUX

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**Aims:** Vesicoureteral reflux (VUR) is the most common congenital anomaly of the urinary tract in children. VUR, recurrent UTIs, and a delay in initiating antibiotic treatment are the risk factors for renal scarring and reflux nephropathy. However, the factors affecting renal scarring in patients with VUR are increasingly questioned, and the clinical effect and treatment of VUR are controversial. Our aim in this study is to reveal the clinical, laboratory, and imaging findings, follow-up, and treatment options of patients who were followed up with the diagnosis of primary VUR in the Department of Pediatric Nephrology of Ondokuz Mayıs University between 01.01.2010 and 31.12.2021 and to determine the factors affecting the prognosis.

**Methods:** 263 patients, 0–18 years, with the primary VUR, were retrospectively examined.

**Results:** 40.7% were male, and 59.3% were female. The mean admission age was  $3.80 \pm 3.80$  years (median 3.08 years), and the mean follow-up period was  $3.99 \pm 3.23$  years (median 3.12 years). One hundred fifty patients had high-grade reflux (57.03%) (80 of them male) and 113 patients (42.97%) had low-grade reflux (only 27 of them male). Urinary tract infection (UTI), with a ratio of 79.1%, was the most common cause of admission, the second one was antenatal HN (17%). One hundred thirty seven patients (52.09%) had renal scar formation in DMSA scan. While there was no statistically significant difference in terms of gender and reflux degree between those with and without renal scar ( $p = 0.947$  and  $p = 0.642$ ), GFR was found to be lower in patients with renal scar ( $p = 0.041$ ). Also renal scar was higher in patients who did not use prophylactic antibiotics ( $p = 0.041$ ). Proteinuria was found in 7 and hypertension was found in 8 of the patients with renal scar, but there was no statistically significant difference compared to patients without renal scarring. In terms of treatment, while 42.6% of the patients were followed conservatively, endoscopic and/or open surgery was performed in 57.4% of the patients. Patients with recurrent UTI, renal scars and female gender underwent surgery more frequently ( $p < 0.001$ ,  $p < 0.001$ , and  $p = 0.032$  respectively).

**Conclusion:** Primary VUR causes recurrent urinary tract infections, renal parenchymal scar, and chronic kidney disease. Our study shows GFR is significantly lower in children with renal scarring, also low GFR and renal scarring are not associated with increased reflux. The use of prophylactic antibiotics, a very controversial issue in recent years, has also been examined and shown to reduce renal scarring in our study. Since our study group consisted mostly of high-grade reflux patients, prophylactic antibiotics may be beneficial for kidney function in the long term, especially in high-grade reflux patients.

Keywords: vesicoureteral reflux, renal scar, urinary tract infection.

Su-3MP 109

PREFERENTIAL CLINICAL EQUATIONS TO ESTIMATE GLOMERULAR FILTRATION RATE IN CHILDREN WITH CHRONIC KIDNEY DISEASE STAGES 3-5: INFLUENCE OF SEX AND ANTHROPOMETRIC VARIABLES

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**Aims/Purpose:** The estimation of the Glomerular Filtration Rate (eGFR) is essential in the evaluation of pediatric chronic kidney disease (CKD) patients. With this study, we intended to compare eGFR by different equations using serum creatinine (Cr) and/or Cystatin C(CysC) with the 24h Creatinine Clearance (24h CrCl) in stage 3-5 CKD patients and to evaluate the relationship with sex and anthropometric variables.

**Methods:** We conducted a retrospective study on pediatric patients with CKD stage 3-5, based on 24h CrCl and according to KDIGO criteria, in a Pediatric Nephrology Unit of a tertiary hospital. The eGFR was calculated using CKiD-Cr, CKiD CysC, CKiD-Cr/CysC, Zapitelli-CysC and Zapitelli combined Cr/CysC formulas.

**Results:** 61 patients were included, with median age 13(8.1-16.3) years, 68.9%(n = 42) males and median BMI 18.2 (16.2-23.6) kg/m<sup>2</sup>. 18 patients (11%) were overweight/obese (BMI z-score > +1). Most of the patients (65.6%, n = 40) had Congenital Anomalies of Kidney and Urinary tract (CAKUT) as the cause of CKD. The median eGFR (ml/min/1.73m<sup>2</sup>) was: CKiD-Cr 15.1 (13.3-25.4); CKiD-CysC 21.9 (18.9-27.8), CKiD-Cr/CysC 18.2 (15.8-26.4); Zapitelli-CysC 21.6 (18.4-27.8) and Zapitelli-Cr/CysC 15.3 (12.7-23.4). The median 24h CrCl (ml/min/1.73m<sup>2</sup>) was 19.9 (14.6-305). Based on 24h CrCl, 27.9% (n = 17), 45.9% (n = 28) and 26.2% (n = 16) of patients were classified into stages 3, 4 and 5 CKD. Correlations between eGFR by all formulas and 24h CrCl proved to be strong and statistically significant (p = 0.001), especially between 24h CrCl and CKiD-Cr (r = 0.871), CKiD-Cr/CysC (r = 0.926), and Zapitelli-Cr/CysC (r = 0.906) vs. CKiD-CysC (r = 0.640) and Zapitelli-CysC (r = 0.640). In stages 4-5 CKD patients, the correlations remained strong and statistically significant, although those between 24h CrCl and eGFR by CysC equations were lower than those calculated for stage 3 CKD (CKiD-CysC (r = 0.595 vs. 0.715) and Zapitelli-CysC (r = 0.477 vs. 0.715)). The 24h CrCl-eGFR difference (mean ± SD, mL/min/1.73m<sup>2</sup>) found for the different formulas: CKiD-Cr 2.11 ± 6.19; CKiD-CysC 0.04 ± 10.18, CKiD-Cr/CysC 1.35 ± 5.64; Zapitelli-CysC 0.07 ± 10.08 and Zapitelli-Cr/CysC 4.32 ± 5.93. Male sex was associated with a statistically significant superior 24hCrCl-eGFR difference in the CKiD-Cr and CKiD-Cr/CysC formulas, while CKD etiology-CAKUT was shown to increase the difference in the cystatin-based formulas.

**Conclusion:** eGFR monitoring plays an important role during the follow-up of CKD, namely in later stages of the disease. In the present sample, 24h CrCl showed a statistically significant correlation with all studied equations, being stronger for Cr-based and combined formulas compared to cystatin-based formulas, and this difference in correlation is even more evident in later-stages CKD. Our results support the possible influence of demographic variables on the 24hCrCl-eGFR difference.

Su-3MP 110

ESTIMATED GLOMERULAR FILTRATION RATE USING CYSTATIN C: AN EARLY MARKER OF CHRONIC KIDNEY DISEASE IN NEUROGENIC BLADDER PEDIATRIC PATIENTS

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**Aims/Purpose:** Patients with neurogenic bladder (NB) can develop progressive chronic kidney disease (CKD) and early detection of estimated glomerular filtration rate (eGFR) reduction is essential to prevent morbimortality. This study aims to analyse eGFR calculated by different equations using serum creatinine (Cr) and/or cystatin C (CysC) and compare between 2 groups (1-2 vs 4-5 CKD stages) in neurogenic bladder patients.

**Methods:** A retrospective study was conducted on pediatric patients with NB and CKD divided in two groups (stages 1 and 2 vs 4 and 5), based on CKiD-Cr formula, from a Pediatric Nephrology Unit of a tertiary hospital. The eGFR was calculated using CKiD CysC, CKiD-Cr/CysC, Zapitelli-CysC and Zapitelli combined Cr/CysC formulas.

**Results:** The first group included 50 patients, with a median (P25th-75th) age of 14.2 (9.0-16.7) years, 48% (n = 24) female, with a median height of 142 (119.8-154.3) cm, a median body mass index (BMI) of 20.5 (15.5-26.7) kg/m<sup>2</sup>, 58% (n = 29) had myelomeningocele and 76% (n = 38) were classified as stage 1 CKD. The median eGFR (ml/min/1.73m<sup>2</sup>) calculated by different formulas was: CKiD-Cr 108.1 (89.2-129.6); CKiD-CysC 77.1 (59.7-87.7), CKiD-Cr/CysC 86.6 (67.4-98.1); Zapitelli-CysC 83.3 (63.3-95.7) and Zapitelli combined- Cr/CysC 101.4 (75.5-121.2). When compared to CKiD-Cr, all the CysC-based formulas showed significantly lower values of eGFR (p < 0.01). In patients on wheelchair or orthosis, with more muscle atrophy (54%, n = 27), the eGFR by CKiD-Cr equation was higher (p < 0.01), which was not observed with CKiD-CysC formula (p = 0.640). In the other group, 24 patients were evaluated, with a median age of 12.9 (9.1-16.4) years, 58.3% female, with a median height of 137.8 (11.3-144.5) cm, a median BMI of 17.7 (15.3-19.2) kg/m<sup>2</sup>, 58.3% (n = 14) had myelomeningocele and 70.8% (n = 17) were classified as stage 4 CKD. The median eGFR (ml/min/1.73m<sup>2</sup>) calculated by different formulas was: CKiD-Cr 12.4 (8.3-20.9); CKiD-CysC 19.1 (15.6-23.8), CKiD-Cr/CysC 15.9 (11.7-20.3); Zapitelli-CysC 18.6 (14.9-23.6) and Zapitelli combined- Cr/CysC 11.9 (8.5-17.5). When compared to CKiD-Cr, CKiD-CysC and CKiD-Cr/CysC equations showed significantly higher values of eGFR (p < 0.01), but that did not occur with Zapitelli combined-Cr/CysC (p = 0.068). There were no differences in eGFR by CKiD-CysC (p = 0.588) and CKiD-Cr (p = 0.879) regarding independent gait capacity and muscle mass.

**Conclusion:** In pediatric patients with NB and poor muscle mass Cr-based formulas can overestimate eGFR and delay the diagnosis and correct staging of CKD. In the group with early CKD (stages 1 and 2) CysC-based equations seem to be more reliable in assessing kidney function. In more advanced stages (4 and 5) the same did not happen, either with CKiD-Cr or CKiD-CysC, which shows a more valuable role for cystatin as an early marker of CKD.

Su-3MP 111

INTERLEUKIN-10 INFLUENCES THE RECRUITMENT OF IMMUNE CELLS IN THE NEONATAL MOUSE MODEL OF OBSTRUCTIVE UROPATHY

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**Aims/Purpose:** Urinary tract obstruction during renal development leads to inflammation, interstitial leukocyte infiltration, tubular cell death (apoptosis and necrosis), and interstitial fibrosis. Interleukin-10 (IL-10) is an anti-inflammatory cytokine, produced mainly by monocytes/macrophages and regulatory T-cells. IL-10 inhibits the innate and adaptive immune response. A protective, anti-inflammatory and antifibrotic effect of IL-10 after unilateral ureteral obstruction (UUO) was shown in the adult mouse kidney. We studied the role of IL-10 in the neonatal mouse kidney with UUO.

**Methods:** Newborn transgenic mice (IL10<sup>-/-</sup>) and wildtype-mice (C57BL/6; WT) were subjected to either UUO or sham operation at day 2 of life. Whole kidneys were harvested at day 3, 7, and 14 of life. The kidneys were analyzed for recruitment of leukocyte subpopulations (FACS analysis), inflammation (Luminex Assay for chemokines and cytokines), programmed cell death, proliferation, and fibrosis (immunohistochemistry and western blot analysis).

**Results:** Neonatal IL10<sup>-/-</sup> mice showed a reduced infiltration of neutrophils, CD11bhi macrophages, type 1 dendritic cells, and T-cells in the neonatal UUO kidney in comparison to WT. Following UUO IL10<sup>-/-</sup> mice showed a reduction of pro-inflammatory chemokine and cytokine concentration in the kidney (IP-10, IL-1 $\alpha$ , MIP-2 $\alpha$ , IL-17A) in comparison to WT. Additionally, IL10<sup>-/-</sup> mice displayed less necroptosis in the neonatal UUO kidney. Immunohistochemical staining of  $\alpha$ -SMA and collagen did not show differences in interstitial fibrosis between IL10<sup>-/-</sup> and WT UUO kidneys.

**Conclusion:** Contrary to expectations, neonatal UUO kidneys of IL10<sup>-/-</sup> mice showed no stronger upregulation of inflammation and fibrosis in comparison to WT. Additionally, we observed reduced recruitment of immune cells in the absence of IL-10. These results indicate a different role of IL-10 in the neonatal UUO model compared to the adult one. Further studies are needed to clarify how IL-10 regulates immune responses after neonatal UUO in detail.

Su-3MP 112

EARLY VERSUS LATE NEPHRECTOMY IN CHILDREN WITH CONGENITAL NEPHROTIC SYNDROME OF THE FINNISH TYPE

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**Aims/Purpose:** Congenital nephrotic syndrome of the Finnish type (CNF) is a genetic disorder leading to massive proteinuria and oedema. The only available treatment is nephrectomy and kidney transplantation (KTx). We compared the outcome of infants with undergoing nephrectomy before 1-year of age followed by peritoneal dialysis (Group 1, n = 13) to those with delayed nephrectomy and short period of hemodialysis (Group 2, n = 10) prior to KTx.

**Methods:** A total of 23 infants were recruited. The key clinical data including laboratory results, growth, thromboembolic events, transplantation related complications, and eating habits after transplantation were collected.

**Results:** There were no statistically significant difference in the baseline patient demographics between the groups. Patients in group 1 were significantly younger at nephrectomy compared to group 2 (278 vs. 408 days,  $p = 0.007$ ). The time on dialysis was significantly longer in group 1 than in group 2 (261 vs. 36 days,  $p < 0.001$ ). The occurrence of thromboembolic events or septicemia before transplantation did not differ between the groups. The age at KTx did not differ between the groups. Patients in group 1 were heavier at the time of KTx than patients in group 2. The length of the patients either before or after KTx did not differ between the groups. Importantly, patients in group 1 had significantly more often eating problems and need for tube feeding than patients in group 2 after KTx. The dependency on nasogastric tube at discharge, 3 months, and 6 months post-KTx were 100%, 92%, and 69% in group 1 and 90% ( $p = 0.244$ ), 50% ( $p = 0.022$ ), and 20% ( $p = 0.019$ ) in group 2, respectively. Neurocognitive development was considered normal before KTx and 12 months after the KTx in 30.8% and 84.6% of the patients in group 1, while the respective figures in group 2 were 80% ( $p = 0.019$ ) and 90% ( $p = 0.704$ ), respectively.

**Conclusions:** CNF patients with delayed nephrectomy and shorted dialysis time do not present increased risk for thrombosis, infections, or growth problems compared to patients with early nephrectomy below the age of one year. On the contrary, patients with delayed nephrectomy appears to have less eating problems and their neurocognitive development is better probably due to avoidance of peritoneal dialysis. However, these results should be interpreted with caution due to the small number of patients.

Su-3MP 113  
ALPORTS SYNDROME: ARE WE ACE-ING THE MANAGEMENT

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**Aims/Purpose:** Alports syndrome (AS) is a heterogeneous condition with phenotypic and genotypic variations. Management and practice has varied over the years. Recent guidance recommends early diagnosis with gene sequencing, and earlier use of Angiotensin Converting Enzyme inhibitors (ACEi) [1,2]. There has also been a change in nomenclature and classification [3]. We reviewed how practice has evolved in our unit.

**Methods:** Retrospective data including demographics, clinical presentation, genetic mutation and management was collected for all patients with AS < 18 years since 2002.

**Results:** A cohort of 41 patients was identified. All presented with haemato-proteinuria with 40% having a positive family history. The mean age at presentation was 6 years. The cohort was 61% male 39% female. Of the cohort, 21% underwent a renal biopsy. Very few patients had genetics sent prior to 2013, 2 reflecting challenges in accessibility. All patients are now genetically confirmed as AS. Time to genetic diagnosis was 4-144 months (mean 24 months). 68% of patients had a pathogenic variant in COL4A5, 39% of which were females. Other genetic mutations included compound heterozygotes (12%), autosomal recessive, (7%) and heterozygous genetic variants (12%). Accurate nomenclature was not documented in 58% of clinical correspondence. Female pathogenic variants in COL4A5 were still labelled as "carriers" in 36% (which wrongly implies a milder phenotype). Within the cohort, 65% were on ACEi. Applying the new guidance, a further 7% of would currently qualify for ACEi with a mean protein creatinine ratio in the untreated cohort of 13 mg/mmol. New guidance uses micro albuminuria threshold (Albumin Creatinine Ratio (ACR) 30mg/mg) to initiate therapy; however ACR is not routinely sent in our centre.

**Conclusion:** Early diagnosis and intervention is recommended to delay progression to renal failure in patients with AS. Our data highlights the importance of reviewing current practice in light of recent guidance.

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Su-3MP 114

BONE IMPAIRMENT IN ATYPICAL HEMOLYTIC AND UREMIC SYNDROME TREATED BY LONG TERM ECULIZUMAB

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**Aims/Purpose:** Atypical Hemolytic Uremic Syndrom (aHUS) is a thrombotic microangiopathy (TMA) often related to complement dysregulation. Dysregulation in factor H (FH) is detected in 10% of cases, and associated with high risks of relapses and complications. Treatment involves lifelong therapy by eculizumab, a terminal complement blockade antibody, whose long-term effects are not yet described.

**Methods:** We collected intriguing data from 2 pediatric patients with FH deficiency receiving long-term eculizumab and displaying a peculiar bone phenotype, including pain, deformations and lysis.

**Results:** The first patient is a 11 years-old girl, presenting aHUS with FH deficiency since the age of 3 months, treated by long-term eculizumab, with near-normal renal function (eGFR 78 mL/min/1.73m<sup>2</sup>). She displays bone pain, for which X-Rays and MRI were performed, describing multifocal osteochondritis with deformities of ankles, wrists and knees of unknown etiology. A bone biopsy was performed for clinical purposes, finding no histological signs of TMA. It revealed numerous active osteoblasts with high mineralization rate confirming active bone formation, and many areas of bone resorption, corresponding to a very remodeling bone. Immunofluorescence showed C3d accumulation (as compared to healthy bone from controls). These findings could be consistent with a side effect of eculizumab therapy, as the C3d accumulation could result from the downstream blockage of complement C5. Bone architecture alterations could also be due to the absence of FH, as described in mouse models FH<sup>-/-</sup>, which however could not explain C3 accumulation. The second patient is a 10 years-old girl, diagnosed with aHUS at 11 days of age with genetic mutation of FH, treated by long term eculizumab. She also displays mechanical bone pains, for which bone scintigraphy described a surprising hypofixation of wrist and ankle. MRI was normal, and bone mineral density was low (Z-score: -2.6 for age at lumbar spine, and -1.2 at left femoral neck).

**Conclusion:** We reported here on 2 cases of aHUS teenagers with FH deficiency receiving long term eculizumab and presenting bone disorders. They could possibly be attributed to the long-term treatment by eculizumab, to the C3 accumulation or the absence of FH.

Su-3MP 115

**CARDIOVASCULAR OUTCOMES IMPROVE IN CHILDREN WITH RENOVASCULAR HYPERTENSION FOLLOWING ENDOVASCULAR AND SURGICAL INTERVENTIONS**

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**Aims/Purpose:** Renovascular hypertension (RVH) is a common cause of hypertension in children. It is caused by renal artery stenosis reducing the blood supply to the renal parenchyma and activating the renin-angiotensin-aldosterone axis, often leading to cardiac remodelling. This is a longitudinal observational study that aims to describe the occurrence of hypertensive changes and their severity and also any improvement in cardiac remodelling after successful endovascular and/or surgical intervention in children with RVH.

**Methods:** All patients with RVH referred to our centre, who had received at least one endovascular intervention, were included. Data was collected by retrospective database review over a 22-year period. We assessed oscillometric blood pressure as well as eight echocardiographic parameters pre- and post-intervention: intraventricular septal diameter (IVSD), posterior wall diameter (PWD), left ventricular internal diastolic diameter (LVIDD), fractional shortening (FS), Relative Wall Thickness (RWT), Left Ventricular Mass (LVM) and Left Ventricular Ejection Fraction (LVEF).

**Results:** 152 patients met inclusion criteria and had on average two endovascular interventions. Six children presented in frank heart failure. 54.4% achieved normal blood pressure (BP) control after intervention. Average z-scores improved in IVSD, PWD and FS; LVM and RWT also improved. PWD saw the greatest reduction in mean difference in children with an abnormal (z-score reduction of 0.25,  $p < 0.001$ ) and severely abnormal (z-score reduction of 0.23,  $p < 0.001$ ) z-scores between pre- and post-intervention echocardiograms. 45.9% of children had a reduction in prescribed antihypertensive medications.

**Conclusion:** Our study reports improvement in cardiac outcomes after either endovascular or surgical intervention. This is evidenced on BP control and echocardiogram changes in which almost half achieved normalisation in systolic BP readings and reduction in the number of children with abnormal echocardiographic parameters.



Su-3MP 116

RAPID COMPLIMENT INHIBITION WITH THE C5 INHIBITOR CROVALIMAB: TIMING ANALYSIS USING ANIMAL MODEL AND COMPOSER TRIAL DATA

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**Aims/Purpose:** Atypical haemolytic uremic syndrome (aHUS) is currently treated with the complement C5 antibodies eculizumab and ravulizumab. Although effective at inhibiting complement-mediated thrombotic microangiopathy (TMA) and improving renal function, regular IV infusion dosing regimens can be burdensome, particularly in paediatric patients (pts). Crovalimab (crova) is a novel C5 antibody, engineered for small volume subcutaneous (SC) self injection every 4 weeks (Q4W), in a weight-based dosing regimen.

The 4-part, adaptive Phase I/II COMPOSER trial (NCT03157635) evaluated crova in pts with paroxysmal nocturnal haemoglobinuria (PNH), which is a disease driven by uncontrolled complement activation. In COMPOSER, crova maintained disease control and was well tolerated after a median exposure of 3 yrs. Crova is currently being evaluated in adult and paediatric pts with aHUS, either treatment-naïve or switching from another complement inhibitor, in the ongoing Phase III single-arm COMMUTE-a (NCT04861259) and COMMUTE-p (NCT04958265) trials. Due to the rapidly progressing nature of aHUS, pts experiencing a TMA require rapid suppression of complement activation upon diagnosis. Data from in vivo models and COMPOSER were used to determine the time to complete complement inhibition after first crova IV dose.

**Methods:** This study assessed the PK and PD of crova in cynomolgus monkeys after a single IV. Four animals per group were evaluated with single 4 mg/kg IV and 20 mg/kg IV doses. Part 2 (n = 10) and Part 4A (n = 8) of COMPOSER enrolled pts with PNH who were naïve to complement inhibition. Part 2 pts received crova 375 mg IV on Day (D) 1, 500 mg IV on D8, 1000 mg IV on D22 and 170 mg SC weekly from D36 for 20 wks. Part 4A pts received an optimised crova dosing regimen of 1000 mg IV on D1, 340 mg SC on D2, 8, 15 and 22, and 680 mg SC Q4W from D29 onwards for 20 wks. Crova concentration, free C5 and complement activity were measured using validated assays.

**Results:** Compared with baseline values in cynomolgus monkeys, a single crova IV dose of 4 mg/kg reduced mean free C5 concentration by 99.6% and terminal complement activity by 81.4%, within 5 mins of administration. In treatment-naïve pts from COMPOSER Parts 2 and 4, mean free C5 concentration dropped to below 1 µg/ml, indicating a high level of target engagement within 1-6 hrs from first IV dose (Fig. 1). Also, inhibition of terminal complement activity was reached within 1 hr, with values near or below the LLOQ (10 U/ml; Fig. 2). Complete complement blockade was generally maintained long term, up to Wk 20, in both Parts 2 and 4, regardless of dose.

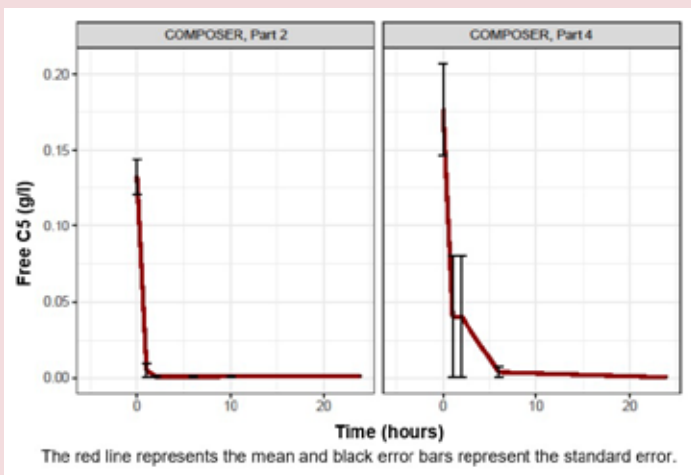


Figure 1: Mean free C5 in treatment-naïve patients with PNH.

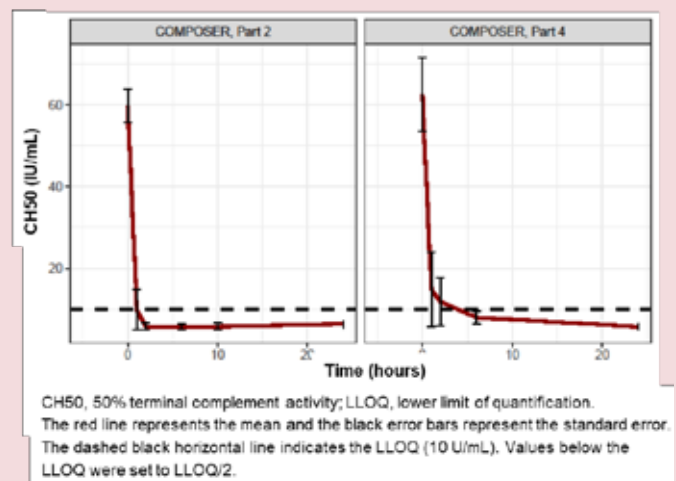


Figure 2: Mean terminal CH50 in treatment-naïve patients with PNH.

**Conclusion:** Crova induced a complete, rapid and sustained blockade of terminal complement activity within hrs of first dose. The dosing schedule of crova included an initial IV loading dose, allowing for a rapid onset of action, followed by a convenient long-term SC maintenance regimen.

Su-3MP 117

## RAPID DETECTION OF HETEROZYGOUS CARRIER OF AGT FOR AUTOSOMAL RECESSIVE RENAL TUBULAR DYSGENESIS IN TAIWAN

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**Aims/Purpose:** Recurrent mutation of homozygous E3\_E4 del:2870bp deletion+9bp insertion in the AGT gene responsible for autosomal recessive renal tubular dysgenesis (ARRTD) is frequently reported in Taiwan, but the exact prevalence of heterozygosity is still unknown. The rapid detection of this mutation may help in the prevention of recurrent ARRTD.

**Methods:** This study was aimed to investigate the prevalence of heterozygosity of E3\_E4 del:2870bp deletion+9bp insertion of AGT in Taiwan and develop a simple and rapid method to detect this mutation. Three thousand health, ten heterozygous parents, and five homozygous Taiwanese were enrolled to define this mutation and determine their prevalence by using TaqMan probe-based real-time polymerase chain reaction (RT-PCR). We designed and validated the mutation detection plate, and tested its feasibility in newly diagnosed ARRTD patients.

**Results:** The recurrent mutation-based TaqMan assays were fully validated with excellent sensitivity and specificity in genetic diagnosed patients and healthy subjects. The prevalence of heterozygosity of E3\_E4 del:2870bp deletion+9bp insertion of AGT is 1.0% in Taiwan. The probability that this haplotype occurred independently in all index cases was of  $1.52 \times 10^{-5}$ , suggesting a founder effect. The blood pressures of heterozygous subjects were significantly lower than those in wild-type subjects after adjusting the age and sex. Compared to homozygous individuals, serum AGT concentration was significantly increased in heterozygous carriers. The serum Ang I and Ang II concentrations were not different between heterozygous carriers and wild-type subjects.

**Conclusion:** The prevalence of heterozygosity of E3\_E4 del:2870bp deletion+9bp insertion of AGT in Taiwan is high and can be rapidly identified by TagMan probe-based RT-PCR.

# WORKING GROUP SESSION

## Dialysis and Transplantation

Su-3MP 118

## EARLY STEROID WITHDRAWAL REDUCES PREVALENCE OF HYPERTENSION IN CHILDREN FOLLOWING KIDNEY TRANSPLANTATION

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**Introduction:** The prevalence of hypertension following kidney transplantation (KT) in children is 49–84%. KT recipients have an increased mortality, with cardiovascular disease accounting for a significant proportion of deaths. We hypothesise that using early steroid withdrawal immunosuppressive regimen (ESW) improves prevalence of hypertension both early and medium to longer term following KT.

**Methods:** This cross-sectional, case-control study compared BP values in children over the age of 5 who had undergone KT. Children at 2 tertiary nephrology centres who received steroid maintenance (SM) and ESW regimens underwent 24 hour ambulatory blood pressure monitoring (ABPM). Patients under 5 years and who did not attend or had inadequate ABPM study were excluded. Mean systolic and diastolic blood pressure values were compared to assess the prevalence of hypertension and blood pressure control dependent on immunosuppressive regimen. Hypertension was defined as a mean blood pressure above the 90th centile in patients under 13 years and above 125/75 mmHg for patients 13 years and above. For patients on anti-hypertensive medication, values above the same parameters were used to define uncontrolled hypertension.

**Results:** The SM group (n = 42) were 65% male with a mean follow up period of 5.6 years (range 0.5–14 y). The ESW group (n = 50) were 75% male with a mean follow up duration of 4.7 years (range 0.5–12 y). Significantly fewer patients with an overweight or obese BMI were observed in the ESW group (8% v 51% p = 0.0001). Anti-hypertensive medication was used in 37% and 20% of patients in the SM and ESW groups respectively. Patients with SM when compared with ESW group had significantly higher rates of uncontrolled hypertension (43% v 5%) (p = 0.05); with uncontrolled systolic hypertension 23% vs. 4% (p = 0.05) and uncontrolled diastolic hypertension in 28% vs. 10% respectively (p = 0.05). Overall prevalence of hypertension was 17%, 0% and 3% at < 1, 1–3 and > 3 years post transplantation for patients treated with ESW respectively. For patients treated with SM, hypertension was observed in 50%, 30% and 16% at < 1, 1–3 and > 3 years.

**Conclusions:** Prevalence of hypertension assessed using ABPM was significantly reduced both early and longer term following KT who were initiated on an ESW. Blood pressure control was significantly better in patients on anti-hypertensive treatment when using ESW. Patients on SM treatment were significantly more likely to be overweight or obese. ESW may reduce long term cardiovascular risk by improving rates of obesity and hypertension in paediatric kidney transplant recipients.

Su-3MP 119

**A QUALITATIVE STUDY: EXPLORING PATIENT, FAMILY AND CLINICIAN PERSPECTIVES ABOUT THE PSYCHOSOCIAL FACTORS INFLUENCING ACCESS TO KIDNEY TRANSPLANTATION AND TRANSPLANT OUTCOMES FOR CHILDREN**

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**Aims/Purpose:** Kidney transplantation is often seen as the optimal form of kidney replacement therapy for children and young people (CYP) with stage 5 Chronic Kidney Disease (CKD5). Psychosocial factors have been cited to delay their access to a kidney transplant, however it is unclear what these factors are. We undertook a multi-centre qualitative study that explored the range of psychological and social factors that CYP, their carers and their paediatric nephrology multi-disciplinary team (MDT) perceived to influence how soon a CYP with CKD5 accesses a kidney transplant. This included factors that were perceived to influence kidney transplantation outcomes or deemed important to patients and their families in terms of their quality of life (QoL).

**Methods:** Semi-structured interviews were conducted with CYP, their carers and their paediatric nephrology MDT across 8 tertiary paediatric nephrology units in the United Kingdom. These interviews were reviewed for pertinent themes using thematic Analysis following the approach of Braun and Clarke.

**Results:** A total of 37 interviews were conducted with 13 families and 18 members of the paediatric nephrology MDT. The majority of participating families identified as White (57%), followed by Black (22%) or Asian (21%). The following themes were deemed important to accessing kidney transplantation and post-transplant outcomes: health beliefs; relationship with and trust in healthcare; support networks; family relationships; socioeconomic circumstances; culture and race; and mental health and coping strategies. Some of these factors influenced how clinicians, CYP or their family viewed the CYP as a suitable transplant candidate. Other factors influenced why families opted for living or deceased donation. Specific challenges from living with CKD5 and living through the COVID-19 pandemic were also discussed due to their impact on QoL and accessing a kidney transplant.

**Conclusion:** There are a wide range of psychosocial factors that are perceived to influence a CYP's access to kidney transplantation. Longitudinal and prospective studies are needed to fully assess the relationship between these psychosocial factors and a CYP's access to, and outcomes of, kidney transplantation.

Su-3MP 120

NEPHROLOGICAL FOLLOW-UP OF PEDIATRIC EARTHQUAKE VICTIMS: A SINGLE CENTER EXPERIENCE

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**Aims/Purpose:** We retrospectively analyzed the nephrological status of victims who were admitted to the Pediatric Nephrology Clinic of our hospital in Izmir, after Kahramanmaraş earthquake happened in March 6, which can be defined as the disaster of the century

**Methods:** Age, gender, time spent under debris, number of crushed extremities, presence of amputation or fasciotomy, presence of acute kidney injury, creatinine kinase (CK) levels and prognosis of all patients were evaluated. 5% dextrose and 0.45% NaCl solution were given as 1500 cc/m<sup>2</sup>/day if the CK levels of the children were between 1000–3000 U/L, and as 3000 cc/m<sup>2</sup>/day for those with CK levels > 3000 U/L. If the bicarbonate value in blood gas is < 25, alkalization was achieved by applying NaHCO<sub>3</sub> treatment to 50 mEq/L. If the CK values fall below 3000 U/L in the follow-up, the amount of fluid is halved and stopped below 1000 U/L. If blood gas pH is > 7.50 and/or bicarbonate ≥ 30, alkalization treatment was discontinued, if 25–30 it was halved.

**Results:** A total of 33 pediatric patients were followed up in the Pediatric Nephrology Clinic. 48.5% were girls, 51.5% were boys. The children were between 2 and 16 years old, with a mean age of 9.0 ± 3.9 years. The mean stay under the rubble (was unknown in one patient) was 27.2 ± 26.8 hours. CK values were known to be > 10,000 U/L in 3 patients before admission, but CK values returned to normal at our admission. The CK values of 23 patients were > 1000 U/L at the time of admission. Six patients had acute kidney injury at admission. 4 patients received HD and/or HDF treatment. The CK values returned to normal in a mean of 4.89 ± 2.33 days in the patients who received fluid and alkalization treatments. Serum creatinine values of all patients normalized in the follow-up.

**Conclusion:** Even in the case of concomitant acute kidney injury in crush syndrome developing after an earthquake, full recovery can be achieved with aggressive fluid and alkalization treatment.

Su-3MP 121

TREATMENT OF PERITONEAL DIALYSIS EXIT SITE GRANULOMA WITH SODIUM CHLORIDE POWDER VERSUS COPPER SULPHATE – A SINGLE CENTER EXPERIENCE

Azilawati Hanim Binti Ghozali, Yok Chin Yap, Jia Vi Tham, Amalina Binti Nasari, Azlina Binti Abu Bakar, Sarah Sabiha Binti Roslan, Nor Athika Edora Binti Yusof, Wan Zuraini Binti Wan Abdullah, Nur Amira Binti Roslan

*Hospital Tunku Azizah Kuala Lumpur, Pediatric Nephrology Unit, Kuala Lumpur, Malaysia*

**Aims:** Peritoneal dialysis (PD) exit site granuloma is a common complication associated with PD. In our center, it was the standard practise to treat PD exit site granuloma using copper sulphate until January 2021 when the supply of copper sulphate became limited. There are studies demonstrated the effectiveness of sodium chloride (NaCl) in treating umbilical granuloma, however there is no published study on the use of NaCl in treating PD exit site granuloma [1,2]. The hyperosmolarity of NaCl causes shrinkage of granuloma through dessicant effect [3]. Therefore we improvised the use of pharmaceutical NaCl powder which widely available as an alternative treatment for PD exit site granuloma. This is a pilot study that compares the efficacy of NaCl powder as a new treatment of PD exit site granuloma against historical treatment cohort that used copper sulphate, in terms of duration of granuloma resolution, frequency of granuloma recurrence and treatment complications.

**Methods:** Data on pediatric PD patients (less than 18 year old) from January 2019 to December 2020 who were treated with copper sulphate and data from January 2021 to December 2022 for patients who were treated with NaCl powder were reviewed. The copper sulphate was applied once, whereas NaCl powder was applied daily for 3 consecutive days. Statistical analysis was perform with SPSS 29.

**Results:** A total number of 17 PD patients with exit site granuloma were reviewed. 9 (53%) received copper sulphate and the remaining 8 (47%) received NaCl powder. Copper sulphate group has longer duration on PD compared to NaCl group (26 months vs 15 months,  $p = 0.26$ ). Both modalities had similar efficacy in terms of granuloma resolution within 3 days of treatment (55.6% in copper sulphate vs 50% in NaCl powder,  $p = 0.32$ ). Rate of granuloma recurrence within 3 months is higher in copper sulphate group in which 7 of 9 patients vs only 4 of 8 patients in NaCl powder group (77.7% vs 50%,  $p = 0.29$ ). In terms of granuloma complications between copper sulphate group vs NaCl group, 3 of 9 patients vs 2 of 8 patients had concurrent exit site infection (33.3% vs 25%,  $p = 1.00$ ) and 3 of 9 patients vs 2 of 8 patients had peritonitis (33.3% vs 25%,  $p = 1.00$ ) which is not statistically significance. None of the patients experienced adverse effects such as skin irritation or PD catheter erosion in this study.

**Conclusion:** NaCl powder is a safe and widely available compound that can be used as an alternative treatment for PD exit site granuloma.

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Su-3MP 122

TURKISH SOCIETY OF PEDIATRIC NEPHROLOGY – FEBRUARY 6<sup>TH</sup> EARTHQUAKES DISASTER MANAGEMENT

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**Aims/Purpose:** 10 cities in the southeastern part of Türkiye hit by devastating earthquakes (EQ) in the early hours of Monday 6 February 2023. This unprecedented disaster has affected a huge area and over 13 million people. More than 50.000 people have been killed and many more have been injured. We herein present the actions of Turkish Society of Pediatric Nephrology (TSPN) during first days of EQ.

**Methods:** TSPN took responsibility from the early hours of the disaster and became a part of the effort with other stakeholders. An emergent response was important not only for disaster victims but also for patients with chronic diseases in need of uninterrupted medical care.

**Results:** A rapid communication was established with the disaster area. The Crush Syndrome Initial Guide for children was created. Another guideline was created with the cooperation of the Turkish Neonatology Association for newborns. Needs such as pediatric nephrologist, dialysis machines, catheters, dialysis supply and medications were determined and replaced with the coordination of Disaster and Emergency Management Presidency (AFAD) and Ministry of Health officials. Ten volunteer pediatric nephrologists served in the earthquake zone with shifts. In order to maximize efforts, TSPN worked in cooperation with the Turkish Society of Nephrology, Turkish Pediatric Association and the Istanbul branch of TSPN. Meetings were organized for increased awareness on EQ preparedness and EQ-related medical and psychological problems. A meeting was held with the participation of the European Society for Paediatric Nephrology (ESPN) Disaster Taskforce and online free registration support was granted for pediatric nephrologists who worked in the EQ zone. The International Society of Nephrology (ISN) Renal Disaster Group and the German Nephrology Association also expressed their willingness for support. A web-based data collection system was created and the first results are being analyzed.

**Conclusion:** TSPN worked with the national/international collaborative effort to save lives and to decrease crush injury and its morbidities. Renal disaster preparedness needs much more attention and work on it.



Su-3MP 123

## HYPONATREMIA AS AN ACUTE KIDNEY INJURY PREDICTOR FACTOR AMONG CRITICALLY ILL CHILDREN

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**Aims/Purpose:** Hyponatremia in hospitalized children and adults has been shown to be an independent prognostic factor for risk-adjusted mortality. It is a common electrolyte abnormality observed in critically ill children. The aim of our study was to evaluate hyponatremia as an acute kidney injury predictor factor among critically ill children

**Methods:** The total of 97 children staying in pediatric intensive care unit of our hospital has been included in the study. Among them, 31.9% (N = 31) of children has been hospitalized with acute respiratory failure due to respiratory tract infection, 27.8% (N = 27) has had history of seizures/epilepsy during current hospitalization, 40.2% (N = 39) has been diagnosed with sepsis. Only children who have presented normonatremia (sodium level 135 – 145 mEq/l) on the day of admission to the intensive care unit, has been qualified for the study. Mild hyponatremia was defined as a serum sodium 130–134 mEq/L, moderate hyponatremia as a serum sodium of 125–129 mEq/L, and severe hyponatremia as a serum sodium < 125 mEq/L. Acute kidney injury stage was determined by pediatric KDIGO scale.

**Results:** 65% of children included in the study (N = 63) has developed hyponatremia during intensive care unit hospitalization period. Stage 1 of AKI developed in 22.7% (N = 22) children, stage 2 in 4.1% (N = 4) of children with hyponatremia. Among our patients no one has developed stage 3 of acute kidney injury and no one has required dialysis. Among the children with normonatremia, only 8.7% (N = 9) has developed stage 1 of acute kidney injury and no one has developed more severe stage. We have noticed, that all children with hyponatremia has been staying in intensive care unit longer than 7 days. The average length of stay in intensive care unit among the children with normonatremia included in our study has been 5,3 days. We didn't notice the correlation between severity of hyponatremia and grade of acute kidney injury stage among the children included in our study.

**Conclusion:** Clinicians should be aware of the increased risk for acute kidney injury in children staying in the intensive care unit who develops hyponatremia. It's modifiable risk factor for this condition, as well for the prolonged stay at the intensive care. However, in our study we could not determine, whether hyponatremia is a causal factor in the development of acute kidney injury or early marker of kidney injury.

Su-3MP 124

EVALUATION OF CHILDREN WITH KIDNEY TRANSPLANTATION IN TERMS OF CHRONIC KIDNEY DISEASE-MINERAL BONE DISORDER

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**Aims/Purpose:** Chronic kidney disease (CKD)-mineral bone disorder (CKD-MBD) is an important problem that causes increased comorbidity such as bone pain, fractures and growth retardation. Although the disorders detected in the CKD process partially improve after transplantation, bone mineral disorders are an important cause of mortality and morbidity in kidney transplant recipients. Osteoprotegerin (OPG) has important effects on osteoclastic differentiation and proliferation and plays a protective role against osteoporosis. In our study, it was aimed to evaluate renal transplant patients in terms of CKD-MBD, to show the effects of renal transplantation on mineral bone disorder by comparing them with patients receiving dialysis treatment, and to determine the relationship between OPG, Fibroblast growth factor-23 (FGF-23) and CKD-MBD.

**Methods:** 31 kidney transplant patients and 25 dialysis patients (14 hemodialysis, 11 peritoneal dialysis) were included in the study. Anthropometric measurements, biochemical parameters and bone mineral density (BMD) measurement values of the patients were recorded from the patient's files. FGF23 and OPG serum levels were measured by ELISA.

**Results:** While the parathormone (PTH) value was high in 96% of the patients receiving dialysis, the PTH value was found to be high in 54.8% of the kidney transplant patients. Height standard deviation score (SDS) of the dialysis group was found to be significantly lower than the transplant group. It has been shown that 17% of the patients have osteoporosis and 27.7% of them have osteopenia. It was found statistically significant that the BMD value of the dialysis group was lower than the transplant group ( $p = 0.025$ ;  $p < 0.05$ ). There was no difference between the kidney transplant and dialysis groups in terms of FGF23 and OPG levels. No correlation was found between FGF-23 value and GFR, PTH, ALP, phosphorus, OPG levels ( $p > 0.05$ ). A positive correlation was found between OPG and BMD value in the dialysis group ( $r = .518$ ,  $p < 0.05$ ). A positive correlation was found between OPG and height SDS in the transplant group ( $r = .599$ ,  $p < 0.01$ ). There was no statistically significant relationship between OPG and GFR, FGF-23, PTH, ALP values ( $p > 0.05$ ).

**Conclusions:** Relatively improved CKD-MBD in kidney transplant patients showed the protective role of early renal transplantation for bone mineral disease. The positive correlation of OPG levels with BMD value and height SDS value suggests the protective effect of OPG from osteoporosis.

Su-3MP 125  
VARICELLA VACCINATION: THE LASTING IMPACT

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**Aims/Purpose:** Varicella vaccination is recommended in paediatric patients prior to solid organ transplant [1] if there has been a lack of natural infection. Immunosuppressed patients are at risk of severe disseminated disease [2]. However, the long-term effect of vaccination in immunocompromised patients is limited. In the UK, the two vaccine brands are propagated in the MRC-5 cell line which has the HLA type: A\*02:01, 29:02, B\*07:02, 44:02, C\*05:01, 07:02. We report our experience with varicella vaccine associated HLA antibodies in prospective paediatric renal transplant patients.

**Methods:** A retrospective, single centre, review of the transplant immunology data of 15 paediatric patients, all of which had received a varicella vaccine since January 2018. Patients received one of the two UK licensed varicella vaccines (Varilrix or Varivax.)

**Results:** Nine patients showed evidence of sensitization to alloantigens present in the varicella vaccine cell line, albeit three of these patients had a history of transfusion, also a known potential sensitizing event. The calculated reaction frequency (cRF) specific to the cell line HLA type used within the varicella vaccine varied between 33–64% (mean cRF:53%).

**Conclusion:** Vaccinations have been previously reported in the literature to be a potential stimulus to HLA antibody formation [3]. We report six patients (40% of the cohort) with no prior sensitizing events, developing HLA specific antibodies to HLA types on the varicella vaccine cell line. These have resulted in high cRFs, exclusion of potential donors and increasing waiting times to transplant. HLA-A2 is the most commonly present HLA type within the Caucasian population. It is displayed on the varicella vaccine cell line, with potential sensitisation to this HLA-antigen reducing the donor pool by 50% [4]. Although a small cohort, it raises a pertinent question for children with limited donor options, as deceased donor waiting times for paediatric patients in the UK continue to increase. Alternative strategies of varicella vaccination need to be considered and increased vigilance in using live vaccines in patients awaiting transplantation.

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Su-3MP 126

**DRIED BLOOD SPOT SAMPLING FOR THERAPEUTIC DRUG MONITORING AND ASSESSMENT OF KIDNEY FUNCTION IN CHILDREN WITH KIDNEY DISEASE**

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**Aim/ Purpose:** Therapeutic drug monitoring (TDM) and assessment of kidney function requires venous blood sampling which is inconvenient especially in young children and requires travelling to the clinic. Dried blood spot sampling (DBS) may be a useful alternative.

**Methods:** A total of 89 children (female 38%) requiring TDM and assessment of kidney function after kidney transplantation (79%) or treatment for glomerular diseases (21%) were enrolled in this prospective single center study. The mean age (range) was 13.4 years (5.7–18.1). The values for Cyclosporine A (CsA), Tacrolimus (TAC) or Everolimus (EVR) and creatinine were determined from capillary blood from the fingertip or earlobe via a dry blood card (DBS) and from standardized venous serum sample taken in parallel and analyzed by standard techniques (STANDARD). An online survey for children and parents was conducted to analyze pain perception, feasibility and satisfaction with the measurement method.

**Results:** There were no significant differences between the values measured by the two methods for all parameters (mean  $\pm$  SD): Creatinine ( $-1.7 \pm 14.5 \mu\text{mol/l}$ ), EVR ( $0.1 \pm 1.2 \mu\text{g/L}$ ), TAC ( $0.3 \pm 1.1 \mu\text{g/L}$ ) and CsA ( $2.8 \pm 9.8 \mu\text{g/L}$ ). The Bland Altman plot showed sufficient accuracy for DBS measurement compared to STANDARD. The questionnaire was returned by 29 of 50 patients. The finger prick was preferred to the ear prick. All families indicated that they have a stable internet connection at home for conducting televisits in future. The main hope of the patients was to have more time for school and to avoid the stress of a long journey to the treatment center when using home DMS.

**Conclusion:** DMS is a reliable method for TDM and assessment of kidney function in children with kidney diseases and is superior compared with the standard venous blood collecting with respect to the burden for patients and families and may allow adequate telemedicine consultations in these patients.

Su-3MP 127

**DONOR-DERIVED CELL-FREE DNA (DD-CFDNA) AS A NON-INVASIVE BIOMARKER OF KIDNEY ALLOGRAFT REJECTION IN PEDIATRIC KIDNEY TRANSPLANTATION**

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**Aims/Purpose:** Rejection remains the first cause of allograft loss in pediatric kidney transplant (pkTx) recipients. Detection of rejection currently relies on kTx biopsies performed either because of allograft dysfunction with the risk of late diagnosis or per surveillance protocols allowing early detection of subclinical rejection but resulting in many unnecessary biopsies. Dd-cfDNA was reported as a new non-invasive biomarker with the potential to improve rejection detection and guide biopsy indications. We aim to assess the association of dd-cfDNA levels with biopsy results in a large cohort of pediatric kTx recipients.

**Methods:** All pediatric kTx patients with at least one dd-cfDNA assessment at the time of a biopsy at a single pediatric transplant center were included. Clinical, biological and histological data were collected from medical reports. Dd-cfDNA were retrospectively measured from plasma samples biobanked at the time of allograft biopsy between 2015 and 2020 or collected in patients who received regular dd-cfDNA testing as part as clinical care between 2021 and 2022.

**Results:** 170 cfDNA measurements in 132 pkTx recipients were available at the time of a biopsy, including 100 performed for surveillance. Mean age at biopsy was 16 years with a median time from kTx of 21 [11;38] months. Median eGFR was 62 [48;83] mL/min/1.73m<sup>2</sup>, median UPCr 0,21 [0,14;0,36] g/g, and 20% had DSA at the time of the biopsy. Biopsy findings included: 109 normal, 30 borderline, 15 TCMR, 11 AMR and 5 mixed rejections. Median cfDNA level was 0,64 [0,31;1,80] %. We found a strong association between cfDNA levels and active tubule-interstitial and microvascular Banff lesions (Figure 1). cfDNA levels were significantly increased in cases with rejection (Figure 2). Using the proposed cut-off of 0.5%, performances of the test to detect rejection were Se 84%, Spe 51%, PPV 33%, NPV 92%. Among the borderline cases, 17 (57%) had cfDNA > 0.5%.

**Conclusion:** We confirm in the largest pediatric kTx cohort to date, the association of dd-cfDNA levels with allograft rejection and its potential interest as a non-invasive biomarker in children. Further studies are needed to assess the added value of dd-cfDNA monitoring to the current standard of care and its ability to reduce unnecessary surveillance biopsies and improve outcomes.

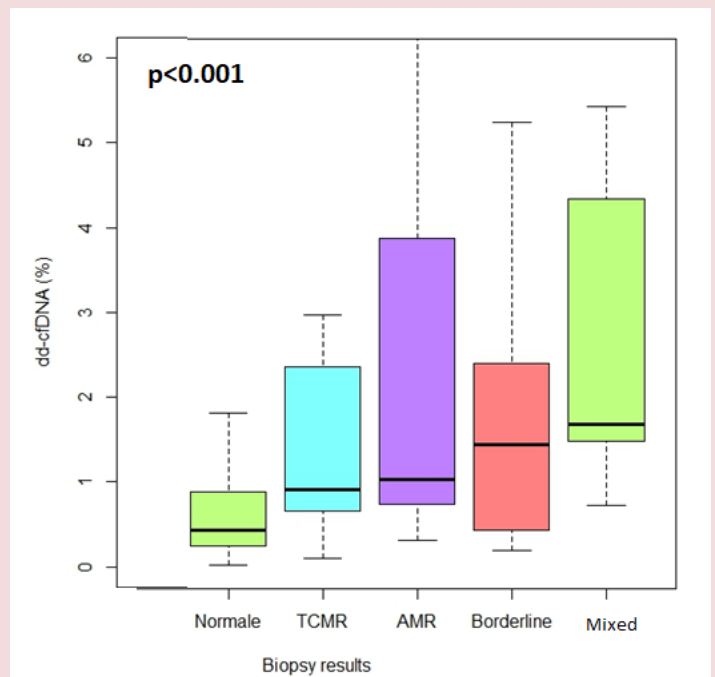
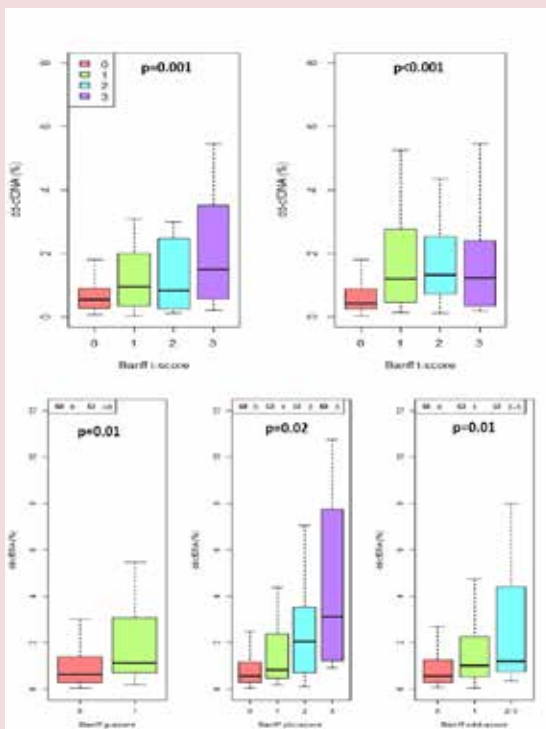


Figure 1: Association between dd-cfDNA levels and active tubule-interstitial and microvascular Banff lesions

Figure 2: Association between dd-cfDNA levels and biopsy results.

Su-3MP 128

### EBV INFECTION IN KIDNEY TRANSPLANT PATIENTS: ANALYSIS OF A SINGLE CENTER EXPERIENCE

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**Backgrounds:** Pediatric solid organ transplant (SOT) recipients commonly present Epstein-Barr virus (EBV) DNAemia. EBV is related to post-transplant lymphoproliferative disease (PTLD), a potentially fatal complication which occurs in 1-20% of SOT.

**Methods:** All patients who underwent a renal transplant between 2011-2022 at Bambino Gesù Children's Hospital in Rome were enrolled in our study. A "persistent" EBV infection was defined as a blood viral load  $\geq 5000$  cp/ $\mu$ l detected for  $\geq 6$  consecutive months while an "high" EBV viral load was defined as  $\geq 100,000$  cp/ $\mu$ l detected for  $\geq 6$  consecutive months on blood.

**Results:** Of the 240 patients included, 97 (40.4%) developed a persistent EBV infection during follow-up. Among these 49 (20.4%) developed a high viral load. Primary infections evolved more frequently into persistent infections ( $p 0.002$ ) and high EBV viraemia ( $p < 0.000$ ) than reactivations. Seropositive CMV recipients less frequently developed a high EBV viral load ( $p 0.043$ ), probably because they did not experience the predisposing effect of primary CMV infection on reactivation of other herpesviruses. Patients with high EBV viral load developed more frequently coinfections from BK virus (0.025). Rituximab has been used in 14 patients, resulting in a reduction of EBV viral load  $< 5000$  cp/ $\mu$ l in almost 80% of cases with an average time of 28.7 days. The cases of PTLD in the cohort were 9, of which 6 non-destructive PTLD and 3 malignant lymphomas. The incidence of malignant lymphomas significantly reduced compared to the previous decade in our hospital, suggesting the efficacy of pre-emptive strategies.

**Conclusions:** Prevention of PTLD remains a clinical challenge. Our study identified risk factors for persistent EBV infection and high EBV viral load. Further studies are needed to identify predictive markers of PTLD and to define the real efficacy of pre-emptive strategies.

Su-3MP 129

**CLINICAL OUTCOMES AND QUALITY OF LIFE IN CHILDREN WITH METHYLMALONIC ACIDAEMIA AND END-STAGE KIDNEY DISEASE: A PROMISING FUTURE FOR CHILDREN WITH COMPLEX CONDITIONS**

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**Introduction:** Methylmalonic Acidaemia (MMA) is characterised by accumulation of methylmalonic acid in body tissues due to defects in Methylmalonyl-Coenzyme (CoA) mutase or Cobalamin (Vit B12). It leads to end stage kidney disease (ESKD) and severe neurological deficits. To minimize disease-related complications and improve quality of life, isolated Kidney (KT), Liver (LT) or Combined Liver-Kidney Transplantation (CLKT) can be considered. This is the first study reporting correlation of these transplant strategies on quality of life (QoL) and clinical outcomes.

**Methods:** This single centre, retrospective observational study, evaluated the clinical outcomes and QoL of children with MMA and ESKD, comparing transplanted and non-transplanted patients from 2015 onwards. Percentage change in serum MMA, Creatinine and e-GFR were analysed using IBM SPSS software. Statistical significance was considered at 95% confidence level ( $p < 0.05$ ). Mann Whitney U test was used to compare current clinical outcomes and QoL between transplanted and non-transplanted groups. Validated PedsQL Transplant Module and End Stage Renal Disease Module questionnaires were used. Scores were calculated and compared using a scale from 0 to 100, with higher values representing better QoL.

**Results:** This study included 5 girls and 4 boys with MMA; median age of 10 years. Transplantation was performed in 6 out of 9 children (2 KT, 2 LT, 2 CLKT); median age of 6.5 years. A statistically significant difference in mean percentage reduction in serum MMA was observed between transplant and non-transplant groups (63.21% Vs 0.18%,  $p = 0.05$ ). In the transplantation subgroups, CLKT demonstrated the highest percentage reduction in serum MMA levels (93.32%), followed by LT (58.74%) and KT (37.58%). CLKT showed the highest percentage improvement in serum creatinine (71.43%). PedsQL mean score values of 75 and 74.7 were observed in non-transplanted patients and transplanted patients respectively.

**Conclusion:** Children with MMA and ESKD benefit from transplantation, with reduced MMA-levels post-transplant and subsequently reduced toxic effects on all organs. CLKT should be considered as the first choice type of transplant in children with established ESKD. Short term follow up identified no statistically significant improvement in QoL in this cohort.

Su-3MP 130

PERFORMANCE OF CYSTATIN-BASE FORMULAS TO ESTIMATE GLOMERULAR FILTRATION RATE IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS

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**Purpose:** Pediatric GFR estimation (eGFR) formulas were developed in cohorts of CKD patients excluding transplant patients. Previous study compared the performances of various serum creatinine (sCreat)-based equations to eGFR in pediatric kidney transplant (kTx) recipients. Although cystatin C is known to improve eGFR in CKD patients, the performances of cystatin-based equations have not been systematically evaluated. This study aimed at assessing the performances of cystatin C-based eGFR equations in pediatric kTx recipients.

**Methods:** We included pediatric kTx recipients (< 18years old), who underwent plasma iohexol clearances for mGFR with concomitant serum creatinine and cystatin C assessment between January 2017 and December 2022. Performances of 8 GFR estimation formulas were assessed by calculating the bias (eGFR-mGFR), precision (root mean square error [RMSE]) and accuracy (percentage of estimates within 7.5%, 10% and 30% of mGFR) (Schwartz-bedside (= CKiDSCr = mod-Schwartz), U25 Screat 2021, S Cystatin C 2021, EKFC 2021, U25 SCystatin C 2021, U25 mean, Screat-SCystatin-BUN 2012, FAS 2016).

**Results:** 104 iohexol clearances were performed in 53 children, 62.3 % were male and the median age at measurement was 12.5 years [2.73, 18.0]. The median mGFR was 66.6 ml/min/1.73m<sup>2</sup> [10.0, 125]. Among sCreat-based formulas, we confirmed that the bedside Schwartz formula performed the best with mean bias of 4.66 and a P30 of 90% similar to what was reported in CKD cohorts. Table 1 reports the performances of 5 cystatin C-based formulas. Among them, the Full-Age-Spectrum formula (FAS) had the best performance with a bias of -1.08 and a P30 of 97%.

**Conclusion:** Although sCreat-based formulas have acceptable performances in pediatric kTx recipients, cystatin-C based formulas and especially the FAS formula presented higher performances and are likely to improve GFR estimation in this population.

Table 1: Performances of 8 formulas to estimate GFR in pediatric kidney transplant recipients

Variable	S Creat-based equations			Cystatin based equations				
	Schwartz-bedside	U25 Screat 2021	EKFC	U25 mean	Cystatin 2012	U25 cystatin	BUN 2021	FAS
Bias	4.66	2.19	5.63	-7.82	-18.33	-12.83	-5.32	-1.08
RMSE	16.48	16.73	17.47	15.33	23.08	18.19	13.96	12.25
P 30%	0.90	0.94	0.93	0.91	0.85	0.90	0.94	0.97
P 10%	0.60	0.50	0.47	0.65	0.28	0.40	0.68	0.68
P 7.5%	0.46	0.40	0.38	0.54	0.20	0.31	0.54	0.57

U25 Serum creatinine 2021, U25 Screat 2021; European Kidney Function Consortium, EKFC; Screat-SCystatin-Blood Urea Nitrogen (BUN), Full-Age-Spectrum (FAS); root mean square error RMSE; percentage of estimates within 7.5%, 10% and 30% of mGFR P30%, P10% and P7.5%

Keywords: eGFR, kidney transplant, pediatrics, cystatin, FAS



Su-3MP 131

RECURRENCE OF NEPHROTIC SYNDROME AFTER PAEDIATRIC KIDNEY TRANSPLANTATION IN EUROPE: RISK FACTORS, TREATMENT AND OUTCOME

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**Introduction:** Steroid resistant nephrotic syndrome (SRNS) is a rare disease in childhood. The treatment is challenging and many progress to end-stage kidney disease (ESKD). The aetiology of SRNS is heterogeneous: genetic, idiopathic or secondary form. Kidney transplantation is required for children with ESKD. Unfortunately, recurrent disease after transplantation is common in children with idiopathic SRNS. The aim of this study is to investigate the occurrence, risk factors, treatment and outcome of recurrent NS after paediatric kidney transplantation included in a large Europe-wide clinical registry.

**Methods:** A retrospective, multicentre cohort analysis of clinical data collected in the Cooperative European Paediatric Renal Transplant Initiative (CERTAIN) Registry was conducted. Patients (age < 18 years) with a diagnosis of congenital, infantile or SRNS, and received a kidney transplantation were included. Data were collected until February 1, 2022 with a maximum follow-up of 5 years after transplantation. NS recurrence (% of all transplantations) and risk factors (hazard ratios) were calculated.

**Results:** 80 patients were included in this study, of whom 14 (17.5%) experienced post-transplantation recurrence. Of 33 patients with a detected genetic mutation, none developed recurrent disease. Median (IQR) time to recurrence was 0 (0-3.75) months after transplantation. Prophylactic treatment did not prevent recurrence (HR 1.54,  $p = 0.42$ ). Preventive plasmapheresis was significantly more performed in the recurrence group (HR 2.4,  $p = 0.012$ ). Of the patients with recurrence, 6 (42.9%) achieved complete remission, 1 (7.1%) partial and 7 (50%) no remission. In the recurrence group three patients (21.4%) experienced graft loss, while none of the patients without recurrence did ( $p = 0.004$ ).

**Conclusion:** This study shows that recurrence of SRNS after paediatric kidney transplantation is common. It confirms earlier findings that the presence of a genetic mutation minimises the risk for recurrence. We did not find a protective effect of prophylactic treatment. No additional factors were identified as either a protective or risk factor. Graft loss occurred in the recurrence group only. Based on our results, no firm conclusions on treatment recommendations can be drawn. Currently, we are analyzing an update of collected data until February 1, 2023 with 157 patients.

**Su-3MP 132**  
**A TOXIC CAUSE OF ACUTE KIDNEY FAILURE CAN HIDE ANOTHER ONE**

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Toxics are a common cause of acute kidney injury worldwide. In teenagers, the most common toxic leading to acute kidney injury are non-steroidal anti-inflammatory drugs.

A 17-year-old girl was admitted for deterioration of general condition, vomiting, stiffness, back and abdominal pain and fever. She presented oliguria and her blood pressure was normal. Exams showed an acute renal failure with plasmatic creatinine at 1021micromol/L, urea 31 mmol/L without metabolic disorder. The ratio proteinuria/creatininuria was a 128 mg/mmol without hypoalbuminemia. She had no anemia and no thrombocytopenia. She slowly recovered a normal renal function.

Renal biopsy was performed and found severe proximal tubular lesions characterized by massive micro vacuolization without interstitial inflammation, without glomerular or vascular lesions. Histological appearance suggested a toxic tubulopathy.

A routine toxicological urinalysis didn't find any toxics, so we performed a toxicological urinalysis by mass spectrometry which found beta-blockers (acebutolol) and metformin. The patient denied taking any of these treatments, so we performed a toxicological analysis of her hair.

We cut an 8 centimeters strand of hairs which represented toxic expositions during the last 8 months.

This analysis found that she was chronically intoxicated with cocaine and that the acute renal failure was corresponded to a cocaine shot cut with metformin, beta-blockers (acebutolol), levamisole.

The aim of this case report is to raise awareness of the importance of going further in the research toxics in acute renal failure when one toxic is found but not understood. The development of new and multiples techniques of toxicological analysis can help the nephrologist to find the toxic in charge of acute renal failure and facilitate the patients care.

Su-3MP 133

## SHIGA TOXIN-MEDIATED HEMOLYTIC UREMIC SYNDROME IN ICELANDIC CHILDREN

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**Aims/Purpose:** Hemolytic uremic syndrome (HUS) is a form of thrombotic microangiopathy (TMA) characterized by hemolytic anemia, thrombocytopenia and acute kidney injury (AKI). The aim of this work was to study the outcomes of Shiga toxin-producing *E. coli* (STEC) enteritis and STEC-HUS in Icelandic children aged 0-17 years in the period 2010-2020.

**Methods:** Patients were identified by retrospectively searching: a) a centralized national microbiology database for STEC enteritis, and b) the national electronic health record systems for ICD-10 codes indicative of bacterial enteritis, HUS, AKI, chronic kidney disease (CKD), dialysis and kidney transplantation. Medical records were reviewed to confirm STEC infections, HUS and clinical outcomes. Complete HUS (cHUS) was defined as TMA with AKI, and incomplete HUS (iHUS) as TMA with kidney involvement without AKI. The Kidney Disease: Improving Global Outcomes classification system was used for the diagnosis and staging of AKI and CKD. Estimated glomerular filtration rate (eGFR) was calculated using the modified Schwartz method.

**Results:** Of the 34 confirmed STEC-infections, 22 (65%) were traced to a 2019 outbreak caused by the O26 serotype. Vomiting in infected patients predicted progression to HUS ( $p = 0.04$ ). Thirteen (38%) progressed to HUS (7 cHUS and 6 iHUS) at the median age of 3.5 (0-12) years. Three (43%) children needed peritoneal dialysis for the treatment of AKI for a median of 23 (range, 15-35) days. At 3 months following the HUS diagnosis, 9 patients had CKD stages I-III. No deaths occurred from HUS in the study period. Acute extrarenal complications included central nervous system (CNS) involvement in 5 (71%) children with cHUS, pancreatitis and hyperglycemia in 2 cases, transient respiratory failure in 1 case and 1 episode of peritonitis in a child on peritoneal dialysis. The median time from the onset of gastrointestinal symptoms to HUS diagnosis during the STEC outbreak was 7.5 (range, 1-15) days.

**Conclusion:** A spectrum of kidney involvement was observed in our HUS population; only half of the cases developed AKI while the other affected children did not and were managed as outpatients. Vomiting in STEC infected patients predicted the development of HUS. CNS involvement was the most common and serious extrarenal HUS complication. The relatively common development of CKD and other chronic HUS associated health problems underlines the need for long-term nephrology follow-up.

Su-3MP 134

POPULATION PHARMACOKINETICS OF PREDNISOLONE IN SALIVA AND PLASMA IN CHILDREN WITH FIRST ONSET STEROID-SENSITIVE NEPHROTIC SYNDROME

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**Aim:** Prednisolone has been the cornerstone of treatment for first onset steroid-sensitive nephrotic syndrome (SSNS) in children, but is associated with marked side-effects. Therapeutic drug monitoring (TDM) using saliva would be a patient-friendly alternative to optimise personalised treatment. To assess the feasibility of saliva for TDM, we aimed to describe the pharmacokinetics (PK) of prednisolone in plasma and saliva of children with first onset SSNS.

**Methods:** Children (age 2–16 years) with SSNS participating in a randomised, placebo-controlled trial were all treated with an 18-week tapering schedule of prednisolone (60 mg m<sup>-2</sup> on alternate days). Five serial plasma and saliva samples were collected at 4 and 8 weeks after first onset. A non-linear mixed effect model (NONMEM) was used to estimate the PK parameters of unbound prednisolone and the saliva-to-plasma ratio.

**Results:** From 45 (85%) children, plasma (n = 109) and saliva (n = 275) samples were available for population PK analysis. Based on unbound plasma concentrations, clearance (CL) and volume of distribution (Vd) were 67 mL/h and 114 L, respectively. Absorption rate (Ka) could not be estimated and was fixed to 0.8/h. Concentration profiles in saliva parallel the profile in plasma. The saliva-to-plasma ratio (SPR) was 0.72. There was moderate inter-individual variability for CL and SPR with values of 44% and 24%, respectively. This variability could not be explained by patient characteristics or clinical parameters. Goodness-of-fit plots and prediction-corrected visual prediction checks confirmed the robustness of the results.

**Conclusions:** A population model was developed describing of unbound prednisolone in plasma and saliva in children with SSNS. Saliva proved to be a reliable and patient-friendly alternative to determine prednisolone concentrations in children with SSNS, although a minimum of one plasma sample would still be needed due to inter-individual variability in the SPR. This opens up opportunities for further research to TDM of prednisolone in these patients.

Su-3MP 135

**MENSTRUAL DISORDERS IN PATIENTS AFFECTED BY IDIOPATHIC NEPHROTIC SYNDROME**

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**Aims/Purpose:** Secondary amenorrhea is defined by the cessation of previous regular menstruation for at least 3 months or previously irregular menses for 6 months. Oligomenorrhea is the lack of menstruation for intervals longer than 45 days in adolescents. To date, no data have been reported regarding the association between idiopathic nephrotic syndrome (INS) and menstrual disorders (MD).

**Methods:** We performed a monocentric study, enrolling all female INS patients who had their menarche before disease onset. Data were retrospectively collected about the occurrence and duration of MD since the beginning of INS, hormon replacement therapy, type of INS and immunosuppressive therapies.

**Results:** Among 182 female patients affected with INS, only 10 had their menarche before INS onset and were enrolled. Five (50%) reported MD after the onset, amenorrhea in 3 and oligomenorrhea in 2 cases. All patients with MD were affected by severe INS, requiring prolonged immunosuppressive therapies. Amenorrhea was more common in multi-drug resistant patients. In most patients (4/5) MD started at INS onset. Only one required hormon replacement therapy, in the other cases MD resolved spontaneously. The characteristics of enrolled patients are summarized in table 1.

Table 1: IS:immunosuppressive; MDRNS:multi-drug resistant nephrotic syndrome; SDNS:steroid-dependent nephrotic syndrome; IRNS:infrequent relapses nephrotic syndrome; PDN:prednisone; FK:Tacrolimus; OFA:Ofatumumab; CSA:Cyclosporine; RTX:Rituximab; CVC:Cyclophosphamide

AMENORRHEA/OLIGOMENORRHEA					
	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Type of disease	MDRNS	MDRNS	SRNS	SRNS	SDNS
IS therapy at the MD onset	PDN, FK, OFA	PDN, CSA, FK, OFA	PDN, FK, MMF	PDN, MMF, FK	PDN
Timing of MD	INS onset	INS onset	INS onset	5 months after onset	During second relapse
Type of MD	amenorrhea	amenorrhea	amenorrhea	oligomenorrhea	oligomenorrhea
Duration of MD (months)	28	84 (ongoing)	17	3	5
Hormon replacement therapy	No	Yes	No	No	No
IS therapy at MD resolution	None	Not applicable	FK, MMF	FK, MMF	None
NO MD					
	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Type of disease	SDNS	SRNS	IRNS	MDRNS	IRNS
IS therapy	PDN, FK, MMF, RTX	PDN, MMF, FK, RTX	PDN	PDN, CVC, FK	PDN

**Conclusion:** Our data suggest that MD, particularly secondary amenorrhea, are common in post-menarchal INS patients. According to our data it is not possible to ascertain if MD are secondary to immunosuppressive drugs or related with the disease itself. Multicenter studies are needed to define incidence, factors associated with MD and the need for hormonal therapy.

Su-3MP 136

**THE DAILY-LUMA STUDY: AN EXHAUSTIVE FOLLOW-UP COHORT OF PATIENTS WITH PRIMARY HYPEROXALURIA TYPE I TREATED WITH LUMASIRAN IN FRANCE**

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**Aims/Purpose:** Lumasiran is the first RNA interference (RNAi) therapy approved for the treatment of primary hyperoxaluria type 1 (PH1), a rare genetic recessive disease caused by mutation in the AGXT gene inducing hepatic overproduction of oxalate. Patients present with nephrocalcinosis, kidney stones, and ultimately develop kidney failure and systemic oxalosis. Lumasiran was approved by the EMA in November 2020. Industry-sponsored clinical trials have provided information on its efficacy and safety. However, they do not provide data on long-term efficacy, safety and patients' management in a real life setting.

**Methods:** As part of the post-marketing follow-up of lumasiran, the French authorities requested a quasi-exhaustive retrospective and prospective follow-up over 5 years of adult and pediatric patients receiving lumasiran patients, asking that at least 80% of such patients are included in this nation-wide registry. Thus, the main objective of the DAILY-LUMA study is to monitor the evolution of PH1 parameters (amongst them urinary and plasma oxalate, evolution of renal function, transplantation policies, side effects), through a standardized clinical, biological and radiological follow-up. Data from patients who have been treated under the temporary French authorization for use (since January 2020) and until the implementation of the study will be collected, and then prospectively followed over 5 years; patients newly treated in France between 2020 and 2026 will also be included.

**Results:** To date, 73 patients (42 children, 31 adults), all genetically confirmed PH1, are treated with lumasiran in France. They all agreed to be included in this study. Data collection is in progress.

**Conclusion:** To the best of our knowledge, the DAILY-LUMA study is currently the largest cohort of patients treated with Lumasiran in real life. It will bring new insights into the long-term follow-up of patients receiving RNAi therapies for PH1, and improve our knowledge on this extra-rare disease.

Su-3MP 137

DETECTION OF ALPORT GENE VARIANTS IN CHILDREN AND YOUNG PEOPLE WITH PERSISTENT HAEMATURIA

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**Aim:** To evaluate the proportion of children and young people (CYP) with persistent microscopic haematuria (MH) identified to have a variant in the Alport genes (COL4A3, COL4A4 or COL4A5).

**Methods:** Retrospective longitudinal study of children referred to a tertiary paediatric nephrology service with persistent MH between April 2012 to 2022. Clinical characteristics including duration of MH, proteinuria, family history of MH and outcomes of genetic testing including variant characteristics were collated.

**Results:** A total of 224 children (female 51.8%) were referred over the 10-year period with persistent MH. Mean  $\pm$  SD age at presentation with persistent MH was  $7.5 \pm 4.3$  years. Targeted exome sequencing was performed in 134 children with 91 children (68%) identified to have a pathogenic or likely pathogenic variant in COL4A3, COL4A4 or COL4A5. Mean  $\pm$  SD duration of MH in children who underwent genetic testing compared to children who did not were  $2.4 \pm 2.3$  years and  $2.8 \pm 3.3$  years respectively. In children with identified variants in COL4A3, COL4A4 or COL4A5, 45/56 (80%) had a family history of MH compared to 10/21 (48%) children who did not ( $p = 0.049$ ). 52/89 (58%) children with identified variants in COL4A3, COL4A4 or COL4A5 had proteinuria along with MH compared to 6/40 (15%) children who did not ( $p < 0.001$ ). COL4A5 was the most common gene affected (Tab. 1). Missense variants affecting glycine residues were the most common pathogenic type (Tab. 2).

Table 1: Variant classification (n = 90)

Variant	Inheritance	Number (%)
COL4A5	X-linked	42 (46.7)
COL4A4	Homozygous	4 (4.4)
	Compound heterozygous	1 (1.1)
	Heterozygous	27 (30.0)
COL4A3	Homozygous	1 (1.1)
	Compound heterozygous	5 (5.6)
	Heterozygous	10 (11.1)

Table 2: Variant characteristic (n = 86)

Variant characteristic	Number (%)
Frameshift (loss of function)	4 (4.4)
In frame deletion	4 (4.4)
Missense - glycine	40 (44.4)
Missense - non-glycine	6 (6.7)
Non-sense (loss of function)	25 (27.8)
Splicing	11 (12.2)

**Conclusion:** Over two thirds of the children who underwent genetic testing had a genetic basis for MH. Genetic testing should be part of evaluation of all children with persistent MH despite a negative family history.

# WORKING GROUP SESSION

## Inherited and Glomerular Diseases



**Su-3MP 138**

**GENETIC MUTATION PATTERN AND RISK FACTORS IN CONGENITAL AND STEROID RESISTANT NEPHROTIC SYNDROME IN CHILDREN: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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**Aims/Purpose:** Genetic analysis in congenital and pediatric steroid resistant nephrotic syndrome (SRNS) has become widely implemented as it can aid in diagnosis, therapy, and prognosis. Aim of this study is to describe the overall prevalence, genetic mutation pattern, and risk factors for genetic mutations in children with congenital and SRNS.

**Methods:** A systematic literature search in Pubmed was performed with specific keywords and relevant MeSH terms. The inclusion criteria are cohort studies in children with at least 20 subjects, at least 5 genes tested, publication in English, and publication from 2010 onwards. Exclusion criteria are similar cohorts from the same center and absence of relevant/eligible data. The selection process included title screening, abstract screening, full text reading, and adding studies from the reference list. Appraisal for eligible studies was done before data extraction (Fig. 1). Available and relevant data were collected in Microsoft Excel®. Forest plot analysis was performed with Review Manager®.

**Results:** We found 17 eligible studies with 3,573 congenital or SRNS patients. Overall, 27.8% (n = 995) were found to have a mutation in a total of 51 genes. Most prevalent genes with mutations were NPHS2, WT1, NPHS1, INF2, PLCE1, COL4A5, SMARCAL1, LAMB2, LMX1B, TRPC6, and ADCY4, accounting for 85.1% of the mutations described (Fig. 2). A genetic mutation was more commonly found in girls than boys (1.2:1). With increasing age, less mutations were found (= 3 month: 71.0%, 4-12 month: 46.8%, 1-12 year: 34.2%, > 12 year: 16.2%) (Fig. 3). There are differences in overall prevalence (36.2% vs. 26.1%) and genetic mutation pattern between European and Asian subjects (Fig. 4). Meta analysis of the data show that genetic mutation prevalence was significantly higher in children with a positive family history, consanguinity, primary SRNS, calcineurin inhibitor resistancy, biopsy results with non-minimal change disease, and end-stage kidney disease. Atypical symptoms and extrarenal manifestation were not found to predict the presence of a gene mutation, but this was based on limited data (Fig. 5).

**Conclusion:** Genetic investigation shows a high yield in congenital and SRNS children and adolescents, but is declining with age. The pattern of genetic mutations seems to be different between regions. In case of limited funding, risk factors and the described prevalence of specific gene mutations may assist in deciding which analysis to perform in which patient. More good quality studies are needed for better predictions in the future.

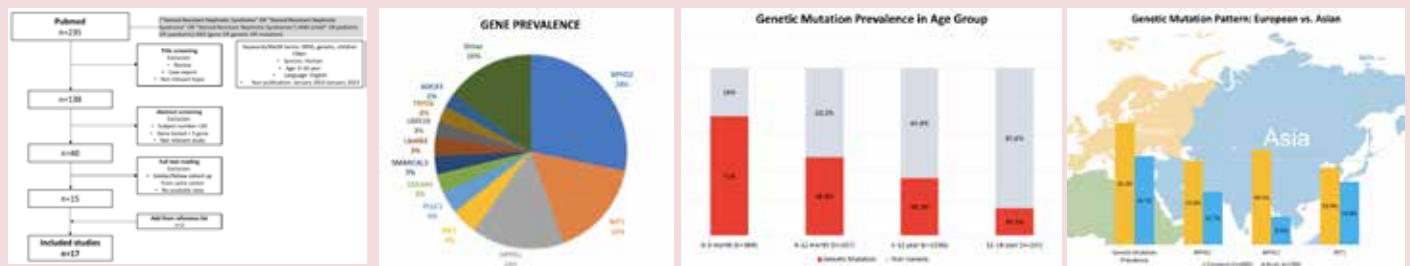


Figure 1: Flowchart searching method for systematic review.

Figure 2: Overall gene prevalence from included studies.

Figure 3: Genetic mutation prevalence in age group.

Figure 4: Genetic mutation pattern between European and Asian population.

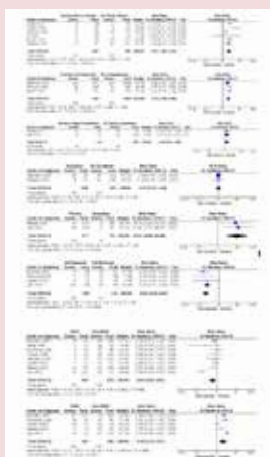


Figure 5: Meta-analysis result of various factors.

Su-3MP 139

## IGA VASCULITIS WITH KIDNEY INVOLVEMENT: CLINICAL FEATURES AND OUTCOMES

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**Objectives:** Immunoglobulin A vasculitis (IgAV) is the most common vasculitis in children. Although typically self-limiting, IgAV may result in serious complications such as kidney involvement. This study aimed to evaluate the incidence and clinical features of IgA vasculitis with kidney involvement.

**Methods:** Retrospective chart review of all patients  $\leq 18$  years of age with newly diagnosed IgA vasculitis in a tertiary care center during the period of January 2013 and December 2021. Demographic, clinical, laboratory data, incidence of renal involvement were analyzed. In addition, neutrophil, lymphocyte, platelets count, mean platelet volume (MPV) and neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) was calculated.

**Results:** 240 patients with IgA vasculitis were included. Kidney involvement at the time of presentation was identified in 21 patients (8.8%) and included isolated hematuria (7.1%) or proteinuria with hematuria (1.7%). All patients with kidney involvement had normal eGFR. Patients with kidney involvement were older ( $8.6 \pm 1.1$  vs  $5.8 \pm 0.3$  years,  $p = 0.02$ ) with male predominance (male-to-female ratio 2.5:1). During two years of surveillance after IgAV diagnosis, 11 cases (4.6%) developed indications and underwent kidney biopsy and were diagnosed with IgAV nephritis. Age was the only variable associated with increased odds of kidney involvement (OR 3.5, 95% confidence interval 1.4-8.6,  $p = 0.009$ ) at the time of presentation. None of the tested variables (neutrophil, lymphocyte and platelet count, NLR, PLR, gender, seasonality, gastrointestinal or joint involvement) were associated with kidney involvement in univariable logistic regression (all  $p < 0.05$ ).

**Conclusion:** Our study demonstrates relatively low prevalence of kidney involvement among patients with IgAV and suggests older age at diagnosis as a risk factor of kidney involvement at disease manifestation.

Su-3MP 140

## OBINUTUZUMAB AS AN ALTERNATIVE THERAPY IN FR/SDNS CHILDREN WITH ANTI-RITUXIMAB ANTIBODIES

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**Aims/Purpose:** B-cell depletion with Rituximab (RTX), a chimeric anti-CD20 monoclonal antibody, is able to maintain sustained remission in children with Frequent-Relapsing or Steroid-Dependent NS (FR-SDNS). However, up to 30 % of patients develop Anti-RTX Antibodies (ARA), that may be associated to RTX failure and/or intolerance. The second generation humanised anti-CD20 mAb Obinutuzumab (OBI) may overcome these situations. We report on efficacy and tolerance of OBI in a series of patients treated because of ARA.

**Methods:** We retrospectively screened patients with FR-SDNS and a positive testing for ARA between March 2018 and March 2023 at Robert-Debre Hospital and Armand-Trousseau Hospital, Paris, and secondarily treated with OBI (single infusion of 300 mg/1.73m<sup>2</sup>). Clinical and biological data were collected from medical charts. Primary outcome was B-cell depletion. Secondary outcomes included tolerance, persistence of ARA and relapse-free survival.

**Results:** Twenty-five patients were included (75% boys). Median age at INS onset, first RTX and OBI were 3.4, 7.7 and 8.2 years, respectively. ARA were detected after first RTX in 12 patients and after 2 to 8 infusions in the others (mean 3). At prior RTX, 7 patients (28%) presented an Infusion-Related Reaction and 2 (8%) Serum Sickness Disease at Day 8 and 10. Indication for OBI was no or short B-cell depletion < 3months in 23 patients and isolated ARA in 2. B-cell depletion was obtained in all patients after a single infusion of OBI. Infusion-Related Reactions were reported in 5 patients (20%) while no Serum Sickness Disease. At last follow-up, B-cell recovery had occurred in 21 patients after a median duration of 6.2 months (IQ 5.3-8.2). A follow-up monitoring for ARA was available in 8 patients, ARA were negative in 4 and persistent in 4.

**Conclusion:** In children with FR/SDNS and failure and/or intolerance to RTX associated to Anti-RTX Antibodies, OBI is able to induce B-cell depletion and is well tolerated. We believe that a screening for ARA should be performed in case of no or short B-cell depletion following Rituximab as it might help to personalize further treatment strategy and clear ARA.

Su-3MP 141

## LONG TERM ADULT OUTCOME OF PATIENTS WITH PEDIATRIC ONSET STEROID SENSITIVE NEPHROTIC SYNDROME (SSNS) IN THE OCCITANIE REGION

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**Aims:** Clinical presentation, treatment of short term outcome of steroid-sensitive nephrotic syndrome (SSNS) in pediatric patients have been extensively studied. By contrast, few data regarding the outcome in adulthood of these patients are available and most of them are based on small series of patients treated in the 80's. We carried out a retrospective study of the outcome in adulthood of a large cohort of patients with an pediatric onset SSNS.

**Methods:** Patients born before 1997 with a pediatric onset SSNS followed up in one of the 3 university hospital of the Occitanie area (France) were included. The identification of eligible patients was carried out by matching data from the PMSI registry, CEMARA and BAMARA rare disease registries. Clinical, and biological characteristics of SSNS, therapies used as well as the number of relapse were collected for each patient. The patient was considered cured of SSNS if there was no relapse for 4 years and/or a treatment-free period of 3 years without relapse. Patient outcomes were analysed at transition to adulthood and at last follow-up, with a target mean of 5 years of follow-up in adults. Risk factors for active SSNS and chronic kidney disease in adulthood were assessed.

**Results:** 169 patients were considered for inclusion. Median age at diagnosis was 4.8 years. 35 of them do not meet criteria of follow up to be included for analysis. Of the 134 patients included, 117 experienced at least one relapse (88%). At transition to adulthood at a median age of 20.1 years, 96 (71%) had an active SSNS. Risk factors of active disease at transition to adulthood were younger age at SSNS onset, the need of prednisolone pulses to achieve remission at first flare, as well as the use of the following immunosuppressive therapies: levamisole, cyclophosphamide, calcineurin inhibitors, MMF, or rituximab. At last follow up in adulthood (median time 7 years), of the 96 patients (median age 25.6 years old) with an active disease at transition, 14 were lost to follow up, 39 were considered as cured and 43 not. 11 patients had a chronic renal failure (8 CKD2 and 3 CKD5). No specific risk factors for the persistence of SSNS in adulthood have been highlighted.

**Conclusion:** This work has shown that the rate of active SSNS at transition to adulthood is higher than previously described in the literature. However, the evolution is favourable both in terms of renal function and in terms of cure, since almost 90% of the patients have normal renal function and 2/3 of them are considered cured at last follow-up.

Su-3MP 142

THE UTILITY OF RITUXIMAB IN STEROID SENSITIVE NEPHROTIC SYNDROME: A PRELIMINARY FEASIBILITY STUDY IN A MIDDLE INCOME COUNTRY

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**Aims/Purpose:** The use of Rituximab in steroid sensitive nephrotic syndrome (SSNS) as a steroid sparing agent is increasingly established. Nevertheless, this may be limited by its prohibitive cost. We aimed to compare costs incurred between rituximab (RTX) and cyclosporine (CSA), a commonly used steroid-sparing agent, to justify RTX utility in a middle-income setting.

**Methods:** Children with SSNS who received either RTX or CSA as steroid sparing agents and followed up for at least 12 months were included in this retrospective cohort study. Primary endpoint was the cost of healthcare one year after commencement. Data on performance of RTX over CSA (the existing standard therapy offered) include reduction in number of relapses, hospital admission, corticosteroid use and body mass index from preceding year) as well as safety (frequency of infection and medication-related adverse effects) were analysed.

**Results:** The study recruited 23 children, 12 received RTX and 11 received CSA. The RTX group was older 12.0 years (9.0-14.3) compared to the CSA group 5.7 years (3.9-10.4). The RTX group too had a longer nephrotic vintage of 6.9 years (4.9 – 10.1) compared to 1.75 years (1.25-7.6) in the CSA group. These observations reflected the local practice to reserve RTX as the last resort in managing difficult SSNS. Total healthcare cost for patients receiving RTX was observed to be lower than CSA; RM 5315.26 (4494.94 – 7846.71) versus RM 6192.58 (5604.62 – 11110.78),  $p = 0.24$ . Children who received RTX had a significant reduction in the number of relapses and hospitalisation; 64 to 20 relapses and 5 to 1.5 hospital admissions ( $p < 0.05$ ). There was also greater reduction in the amount of prednisolone used compared to the preceding year in the RTX group. There were no infusion related reactions in the rituximab group and cyclosporin was also well tolerated. One patient reported to have community acquired pneumonia in the RTX group but recovered well soon after discharge; this may be an unrelated adverse effect.

**Conclusion:** This is the first study to be carried out in a lower middle income country to compare the healthcare costs of using RTX over CSA in children with SSNS. In children with a protracted course, our data suggest feasibility and possibly better cost-benefit with RTX. The high cost of rituximab should not be an impediment to its utility in a middle income setting.

**Su-3MP 143**

**A MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE 3 STUDY (APPARENT) TO ASSESS THE EFFICACY AND SAFETY OF IPTACOPAN IN IDIOPATHIC (PRIMARY) IMMUNE COMPLEX-MEDIATED MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS**

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**Aims/Purpose:** Immune complex-mediated membranoproliferative glomerulonephritis (IC-MPGN) is a rare, fast-progressing kidney disease that may be idiopathic (primary) or secondary to chronic infection, autoimmune disorders, or monoclonal gammopathies. Idiopathic IC-MPGN has a comparable clinical course to complement 3 glomerulopathy (C3G), which is also characterized by membranoproliferative histology. Dysregulation of the alternative complement pathway is implicated in the pathophysiology of both glomerular diseases. Currently, there are no approved targeted treatments for IC-MPGN. Iptacopan (LNPO23) is an oral, first-in-class, highly potent proximal complement inhibitor that specifically binds to factor B and inhibits the alternative pathway (AP).

**Methods:** This randomized, double-blind, placebo-controlled, pivotal Phase 3 study (APPARENT; NCT05755386) is the first to evaluate the efficacy and safety of iptacopan in patients with idiopathic IC-MPGN, enrolling 68 patients (including a minimum of 10 adolescents) aged 12–60 years with biopsy-confirmed IC-MPGN, proteinuria  $\geq$  1 g/g, and estimated glomerular filtration rate (eGFR)  $\geq$  30 mL/min/1.73m<sup>2</sup>. All patients will have received maximally tolerated angiotensin-converting enzyme inhibitor/angiotensin receptor blocker and vaccination against encapsulated bacteria. Patients with any organ transplant, progressive crescentic glomerulonephritis, or kidney biopsy with  $>$  50% interstitial fibrosis/tubular atrophy, will be excluded. Patients will be randomized 1:1 to receive either iptacopan 200 mg twice daily (bid) or placebo for 6 months (double-blind period), followed by open-label treatment with iptacopan 200 mg bid for all patients for 6 months. The primary objective is to evaluate the efficacy of iptacopan versus placebo on proteinuria reduction measured as urine protein-creatinine ratio (24-h urine) at 6 months. Key secondary endpoints will assess kidney function measured by eGFR, patients who achieve a proteinuria-eGFR composite renal endpoint, and patient-reported fatigue. The safety objectives are to evaluate the safety and tolerability of iptacopan in all patients and perform cardiovascular surveillance in adolescent patients (blood pressure, heart rate, cardiac function and biomarkers).

**Results:** The study is expected to start in Q2 2023.

**Conclusion:** This study will provide evidence towards the efficacy and safety of iptacopan in idiopathic IC-MPGN.

Su-3MP 144

THE CENTURY COLD WAR: IS THE KIDNEY BIOPSY USEFUL IN CHILDREN WITH NEPHROTIC SYNDROME?

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**Aims/Purpose:** To investigate the role of histology in predicting long-term kidney outcome in children with steroid resistant idiopathic nephrotic syndrome (iSRNS).

**Methods:** We retrospectively analysed data from patients with clinically diagnosed idiopathic nephrotic syndrome, which underwent kidney biopsy from 1998 to 2020 in our Centre. Mid-term follow-up was set at 18 months. Kidney replacement therapy (KRT) was considered as long-term outcome.

**Results:** Data from 184 patients were available. Patients with steroid resistant nephrotic syndrome, or incomplete clinical data or with a genetic form of NS were excluded. The analysis of the remaining 136 patients showed the presence of focal segmental glomerular sclerosis (FSGS) pattern in 40.4%, Minimal change disease (MCD) in 47.8% and Membranous nephropathy (MN) in the remaining 11.8%. Concerning the histological-prognostic correlation, the long-term outcome was available for 81 patients: 10/34 (29.4%) of FSGS patients underwent KRT, as 4/35 (11.4%) of MCD and 1/12 (8.3%) of MN patients. These differences are statistically significant ( $p = 0.0002$ ). After 18 months from the onset of NS (mid term follow up), histology was not significantly related to proteinuria ( $p = 0.34$ ), while a higher proteinuria was associated with a higher rate of KRT ( $p = 0.002$ ). 4/13 patients (30.2%) with nephrotic proteinuria underwent KRT, while none of the 39 patients without proteinuria ( $p = 0.003$ ).

**Conclusion:** Our study shows a greater likelihood of FSGS to develop KRT in patients with steroid resistance, compared to MCD and MN, as already observed in the literature [1, 2, 3]. In contrast to other studies [1, 2], however, the proportions of FSGS and MCD within SRNS are very comparable in our population, with slight prevalence of MCD pattern. This could be a starting point to better investigate if the kidney biopsy should really still have a prognostic role in patients with SRNS. It is also important to note that about 11% of patient with clinically diagnosed iSRNS are affected by MN.

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**Su-3MP 145**

**ANTI-FACTOR B ANTIBODIES ARE PRESENT IN A SMALL PROPORTION OF PATIENTS WITH ATYPICAL HEMOLYTIC UREMIC SYNDROME**

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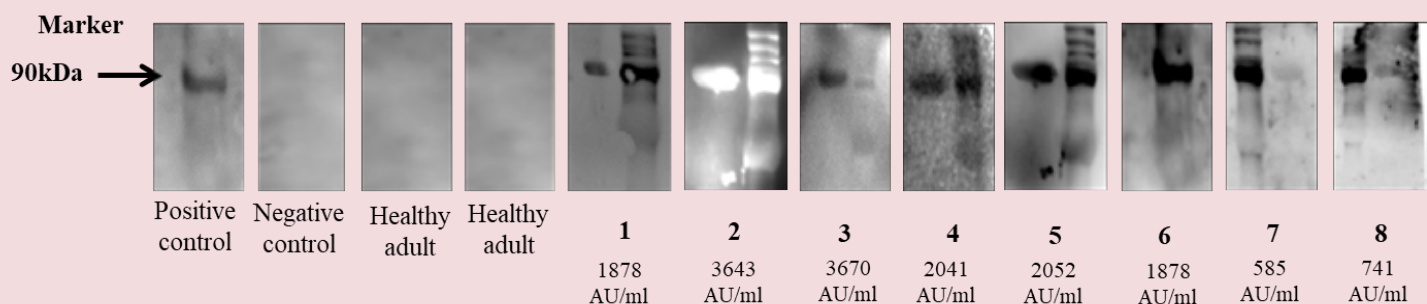
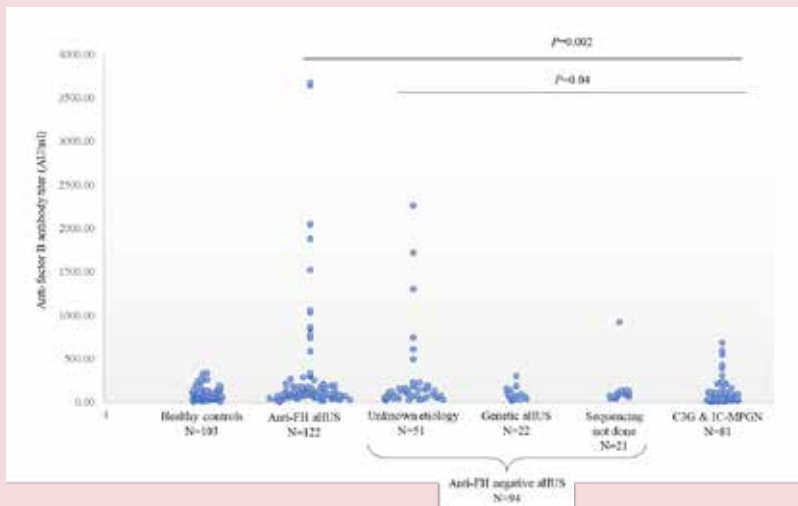
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**Aims/Purpose:** The etiology of atypical hemolytic uremic syndrome (aHUS) is not known in 30–40% patients. While anti-factor H associated aHUS comprise one-half of Indian children, anti-factor B (FB) antibodies, found to stabilize C3 convertase in C3 glomerulopathy (C3G) and immune-complex membranoproliferative glomerulopathy (IC-MPGN), are not reported in aHUS.

**Methods:** We screened consecutive samples of patients < 18-year-old, enrolled between 2015–19, from a multicenter database of aHUS and a cohort of C3G and idiopathic IC-MPGN. Blood levels of anti-FB IgG antibodies were measured by ELISA and calculated using a calibration curve obtained with serial dilutions of reference plasma, tested simultaneously at Hôpital Européen Georges Pompidou, Paris (courtesy Dr. Marie-Agnes Dragon Durey). Normative levels were based on antibody levels in 103 healthy blood donors (306.5 AU/ml; 97.5th centile). Inter-assay and intra-assay CV were 8.9% and 2.3%, respectively. Positive results were confirmed by western blot.

**Results:** Of 216 patients with aHUS, anti-FH antibodies were found in 122 (56.5%) and rare genetic variants in 22 (30.1%). The prevalence of anti-FB antibodies was 9.7% (95% CI 6.1–14.5%; n = 21) in aHUS; 11.5% (95% CI 6.4–18.5%; n = 14) in anti-FH associated aHUS, and not detected in patients with rare variants (Fig. A; western blot confirmation in patients 1–8 in panel below). Median anti-FH titers was higher in those with concomitant anti-FB antibodies (11312 AU/ml vs. 4920 AU/ml; P = 0.044). Titer of anti-FB antibodies correlated with disease severity (blood hemoglobin and platelets; P = 0.05), declined following plasma exchange (median 1045.6 AU/ml to 93.3; p = 0.001; n = 14) and increased with relapse (n = 1). While 4/64 patients with C3G (6.3%; 95% CI 1.7–15.2%) and 1/17 with IC-MPGN showed anti-FB antibodies; titers were higher in aHUS (1028.8 vs 544.8 AU/ml; p = 0.003, Fig. A).

**Conclusion:** Anti-FB antibodies are present in 6–10% patients with aHUS and C3G/IC-MPGN, with higher titers in the former. Patients with aHUS might show propensity for autoantibody generation and coexistence of multiple concurrent risk factors for aHUS. The clinical implication of detection of FB antibodies in 12% aHUS patients without other genetic or autoimmune causes requires exploration.





Su-3MP 146

THESE DEPOSITS SHOULD NOT BE TAKEN LIGHTLY

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**Aims/Purpose:** Angiogenesis is critically important in tumor growth, invasion and metastasis development. VEGF play this role, overexpressed in a wide variety of tumors, associated with progression. Bevacizumab (BVZ) is a humanized anti-VEGF monoclonal antibody widely used and studied in oncologic patients. Its short-term role in the development of renal toxicity (hypertension, proteinuria and TMA) is well known, although the pattern of renal toxicity associated with prolonged treatment is still unknown.

**Methods:** Present a case of nephrotoxicity due to prolonged use of BVZ.

**Results:** 18-year-old woman with neurofibromatosis type II started treatment with BVZ. 18 months later developed proteinuria (iPr/Cr 0.68 mg/mg) with preserved renal function. Started antiproteinuric therapy (candesartan) with good control but need to increase to maximum dose. Nephrotic proteinuria persisted and forced to change to olmesartan and later to lisinopril (both maximum doses). Despite this, developed HT needing amlodipine (maximum dose). Due to these findings BVZ was suspended on multiple occasions, worsening her underlying disease. Such decompensation together with the finding of persistent microhematuria (suspected TMA), promotes renal biopsy: glomeruli with mesangiocapillary pattern and PAS-positive pseudothrombus. Conventional IIF: IgM (+++), Kappa (+++) and Lambda (+++), deposits for C1q (+) and very focal and segmental positivity for IgG together with images of pseudothrombus impregnation for IgA. Congo red staining negative, receiving initially the diagnosis of cryoglobulinemic glomerulonephritis. While awaiting the definitive results, prednisone was started (60 mg/day) with subsequent decrease until discontinuation in the absence of response, after performing a proteinogram (normal) and cryoglobulins (negative). Electron microscopy showed electron-dense deposits at subendothelial, mesangial and paramesangial levels compatible with glomerular microangiopathy associated with chronic use of bevacizumab, and in order to improve the quality of life of the patient as an alternative, it was decided to start Brigatinib, reducing the dose of BVZ and progressive renal involvement.

**Conclusion:** The deposition of antibodies, either by immunocomplex formation or anti-BVZ antibody production, could explain the cases of difficult-to-control nephrotic proteinuria in patients with prolonged treatment with BVZ. Knowledge of the mechanisms of nephrotoxicity, as well as its long-term effects, is essential for the development of new guidelines and preventive strategies to minimize the risk and impact on the survival of these patients.

Su-3MP 147

A CHILD WITH SEMAPHORIN 3B-ASSOCIATED MEMBRANOUS NEPHROPATHY EFFECTIVELY TREATED WITH OBINUTUZUMAB

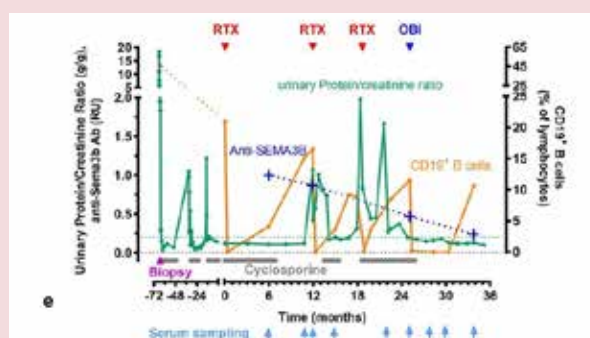
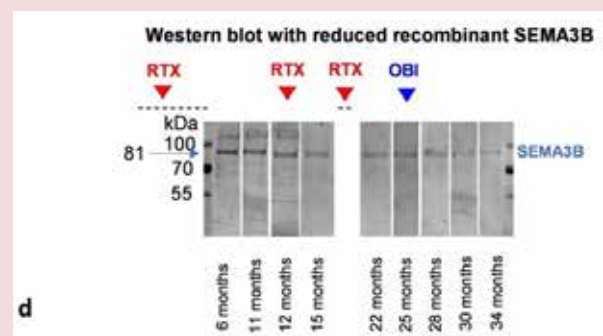
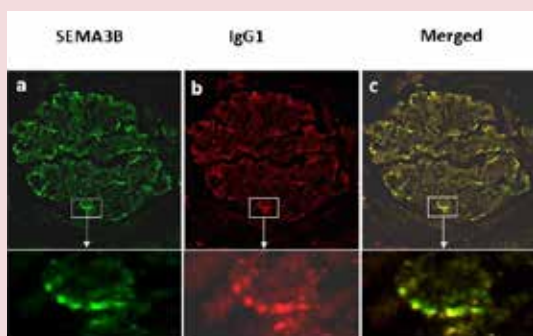
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Membranous nephropathy (MN) is a glomerular disease characterized by a thickening of the glomerular capillary wall, consequential to the presence of immune-complexes deposited in the glomerular basement membrane. Semaphorin 3B (SEMA3B) was recently described as a target antigen in a pediatric and young adult cohort of patients affected by MN. Anti-CD20 monoclonal antibody therapy is effective for this glomerulopathy, targeting the formation of specific antibodies. We report the case of a child diagnosed with semaphorin 3B (SEMA3B)-associated primary MN, effectively treated with Obinutuzumab (OBI), a novel anti-CD20 antibody. The patient presented with primary steroid-resistant nephrotic syndrome at the age of two. Renal biopsy showed thickening of the glomerular basement membrane consistent with MN, with granular pericapillary positivity for IgG (+++), IgM (+) and C3 (+), also present along the tubular basement membrane. Immunohistochemical evaluation showed SEMA3B (green) and IgG1 (red) in glomerular immune deposits in membranous nephropathy by confocal immunofluorescence microscopy analysis (figure 1.a-c). The patient responded to cyclosporine, but relapsed upon tapering of this agent. Therefore, at the age of 9 he was successfully treated with rituximab to overcome cyclosporine dependence. Rituximab infusion was characterized by an adverse reaction (headache and vomit). After 6 months a second rituximab infusion was given for CD19+ B cells reconstitution; 4 month later CD19+ B cells were reconstituted and a relapse of proteinuria occurred, requiring reintroduction of cyclosporine. OBI was then infused inducing a complete remission despite cyclosporine withdrawal one month after infusion. When we quantified by Western blot circulating anti-SEMA3B antibodies, we observed that OBI appeared to reduce anti-SEMA3B antibodies more substantially than rituximab (figure d.). At 9 months, CD19+ B-cell reconstitution occurred but proteinuria did not reappear at 10 months follow-up. Figure e. shows clinical course of the patient: the amount of urinary protein/creatinine ratio (green line), CD19+ B cells (orange line) and anti-SEMA3B antibody (purple crosses and dashed line) relative to the first available serum sample (6 months after the first RTX infusion).

OBI is a second generation anti-CD20 humanized monoclonal antibody that can overcome primary rituximab failure or loss of effectiveness by skipping the B-cell internalization and the rise of human anti-chimeric antibodies induced by chimeric anti-CD20 monoclonal antibodies.

This first experience on pediatric use of OBI for MN, is an encouraging step to expand its use to other pediatric patients with primary MN, particularly if they present resistance to rituximab. OBI was safe and well tolerated, and may therefore represent an effective therapeutic alternative in children experiencing adverse reaction to rituximab.



Su-3MP 148

VACCINE RESPONSES IN CHILDREN WITH CONGENITAL NEPHROTIC SYNDROME IMMUNIZED DURING NEPHROSIS

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**Aims:** Immunizations in children with congenital nephrotic syndrome (CNS) are commonly postponed until bilateral nephrectomy or deterioration of kidney function. The rationale for this stems from a hypothetically inferior response to immunizations due to nephrosis. On the other hand, by starting immunizations before the nephrectomies, vaccine-related delays of transplantation are avoided. However, the response of vaccinations given during heavy proteinuria remains unclear.

**Methods:** Serological vaccine responses in six children with CNS who received immunizations during nephrosis were investigated. Antibody concentrations after MMR, DTaP-IPV-Hib, varicella, combined hepatitis A and B, and the pneumococcal conjugate vaccine (PCV) were analyzed using microneutralization assays and enzyme-, luminescence- and fluorescent-microsphere immunoassays. The results were interpreted using in-house reference values for a protective immune response, except for PCV, where WHO's antibody threshold of 0.35 µg/mL was applied. The serological vaccine responses were measured after transplantation in 4/6 children and before transplantation in the remaining two children.

**Results:** Immunizations were started at a median age of 8 months, with a concurrent median proteinuria of 36500 mg/L. Bilateral nephrectomy was performed at a median age of 21 months, and the children underwent renal transplantation 10–59 days after the nephrectomy. The median interval between immunization and measurement of respective antibody levels was 19 months. Protective antibody levels were detected in all children for hepatitis B and C, tetani, in 4/5 for varicella, in 4/6 for H. influenzae type B and C, diphtheriae, in 3/5 for poliovirus and vaccine-type pneumococcal serotypes, in 2/5 for hepatitis A, and in 1/2 for the MMR pathogens. None of the 6 children had protectable IgG-levels against B. pertussis. No significant differences were noted in serological responses according to the period between vaccination and measurement of antibody levels or the patient age at immunization, nephrectomy, or transplantation. However, the two children investigated before transplantation tended to show better serological responses.

**Conclusion:** Immunizations during severe congenital proteinuria result in reasonable serological responses, comparable to those seen in children after transplantation in general. Serological responses seemed to mostly depend on the interval between transplantation and serological assessment.

Su-3MP 149

LATE STEROID-RESISTANCE AND DEGREE OF PROTEINURIA PREDICT TREATMENT RESPONSE TO RITUXIMAB IN CHILDHOOD STEROID-RESISTANT NEPHROTIC SYNDROME: AN INTERNATIONAL, MULTI-CENTRE STUDY

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**Background:** It remains unclear whether rituximab induces remission in childhood steroid-resistant nephrotic syndrome (SRNS) and which patient subgroups benefit most from the therapy.

**Methods:** We conducted a retrospective cohort study at 28 paediatric nephrology centres from 19 countries in Asia, Australia, Europe and North America. Children with SRNS unresponsive to prednisolone and calcineurin inhibitors were included. Primary outcome was complete or partial remission (CR/PR), defined by IPNA/ KDIGO guidelines, at 3-, 6- and 12-month post-rituximab. Secondary outcomes included kidney survivals.

**Results:** 246 children (age,  $6.9 \pm 4.2$  years; 55% boys) were included, of which 112 and 134 patients presented with initial and late SR. The commonest histological diagnosis was focal segmental glomerulosclerosis (FSGS;  $n = 136$ , 57%), followed by minimal change disease ( $n = 79$ , 33%). Majority of patients received rituximab at 750mg/m<sup>2</sup> ( $n = 114$ , 46.3%) and 1500mg/m<sup>2</sup> ( $n = 100$ , 40.7%). 99.2% patients achieved B-cell depletion. Median follow-up from rituximab administration was 32.4 (IQR, 18.6–64.9) months. All patients were non-remission (serum albumin < 30g/L) prior to rituximab, and proteinuria were in nephrotic- and subnephrotic-range in 86% and 14% patients. The median eGFR was 93 ml/min/1.73m<sup>2</sup> (IQR, 66–126.3) and urine protein/creatinine ratio was 3.2mg/mg (IQR, 2.9–7.6). Overall, 32.5% patients attained CR/PR (19.9%/16.6%) at 3-month, which significantly increased to 42.3% at 6-month (CR/PR, 23.2%/19.1%;  $p < 0.001$ ) and remained similar at 12-month (43.3%; CR/PR, 24%/19.3%) (Table 1). More children attaining disease remission at 12-month had late SR (CR/PR, 28.9%/24.2% vs 18.1%/13.3%,  $p = 0.001$ ; ORadj 2.73, 95%CI 1.25–5.98,  $p = 0.01$ ) and subnephrotic-range proteinuria at baseline (CR/PR, 36.7%/30% vs 22.2%/17.7%,  $p = 0.01$ ; ORadj 9.91, 95%CI 1.83–53.72,  $p = 0.01$ ). In contrast, patients with advanced chronic kidney disease stage 3 or above were at risk of non-remission (ORadj 0.21, 95%CI 0.08–0.06,  $p = 0.003$ ). Rituximab dose, concurrent immunosuppression and additional rituximab did not impact on disease remission. Non-remission at 6- and 12-month were associated with poor kidney survival (Fig 1; log rank  $p < 0.001$ ). Upon cox regression, non-response to rituximab at 6-month (HRadj 6.95, 95%CI 2.22–21.76,  $p < 0.001$ ), pre-existing chronic kidney disease stage 2 or above (HRadj 2.4, 95%CI 1.04–5.57,  $p = 0.04$ ), and FSGS (HRadj 4.3, 95%CI 1.4–13.23,  $p = 0.01$ ) were significant predictors for kidney failure and/or death.

**Conclusions:** 40% patients with SRNS respond to rituximab, with late SR and subnephrotic-range proteinuria being favourable predictors. While treatment effect plateau by 6–12 months, non-remission predicts poor long-term outcome which warrants alternative therapy.

Su-3MP 150

EFFICACY AND SAFETY OF SINGLE-DOSE RITUXIMAB BIOSIMILAR IN INITIAL EPISODE OF PAEDIATRIC STEROID-SENSITIVE NEPHROTIC SYNDROME

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**Aims/Purpose:** The 12-month relapse-free survival rate is less than 30% in steroid-sensitive nephrotic syndrome (SSNS) children after the standard corticosteroid therapy, with approximately half becoming frequent relapsers or steroid dependent and necessitating the need for alternative immunosuppressive agents. The first relapse of SSNS most occurs within 6-12 months of onset and contemporary cohorts suggest up to 16-42% of children with SSNS continue to have relapses in adulthood. Rituximab and rituximab biosimilar appear effective to reduce the relapse in children with frequent relapse or steroid dependent nephrotic syndrome. Accordingly, we hypothesize in paediatric SSNS, rituximab added to guideline-recommended corticosteroid therapy is effective for maintaining remission for the first year of onset, expected to improve long-term outcome.

**Methods:** An open-label, single-arm, multicentre trial was performed at eight centers in China with 12-month follow-up (NCT04783675) [1]. The first episode of SSNS children treated with standard corticosteroid are eligible for inclusion. Eligible patients received a single dose of 375 mg/m<sup>2</sup> rituximab biosimilar within one week after achieving remission. The primary outcome is the 12-month relapse-free survival rate after rituximab added to corticosteroid therapy and is compared with historical controls treated without rituximab on NCT03878914. Safety endpoints were frequency and severity of adverse events.

**Results:** Totally, 44 children were treated with rituximab and all but 1 patient completed 1 year of follow-up (Table 1). Rituximab therapy was associated with a higher 12-month relapse-free survival rate than historical control (Fig 1). Treatment was well tolerated. Besides 2 patients with decreased neutrophil count, all the other adverse events were fully resolved.

**Conclusion:** In children with initial episode of SSNS, rituximab appears to be an effective and safe treatment in maintaining disease remission. It provides the evidence for the initial treatment strategy of SSNS in children to prevent the recurrence, which might improve the long-term outcome.

Table 1: Characteristics of the patients

Characteristic	N = 43
<b>Demographic</b>	
Male sex – no. (%)	33 (77%)
Median age at onset of NS (IQR, range) – years	4.3 (3.4 to 5.9, 1.6 to 12.2)
<b>Age group – no. (%)</b>	
< 4 years	17 (60%)
≥ 4 years	26 (40%)
<b>Anthropometry</b>	
Median height – m	1.1 ± 0.2
Body mass index – kg/m <sup>2</sup>	16.5 ± 2.8
<b>Medical history</b>	
Median days to remission (IQR)	8 (7 to 11)
Median days from remission to rituximab infusion (IQR)	5 (3 to 6)
<b>Laboratory values</b>	
Median CD19 at 1 month after rituximab infusion (IQR) – %	0.05 (0 to 0.10)
Abbreviations: IQR, interquartile range.	

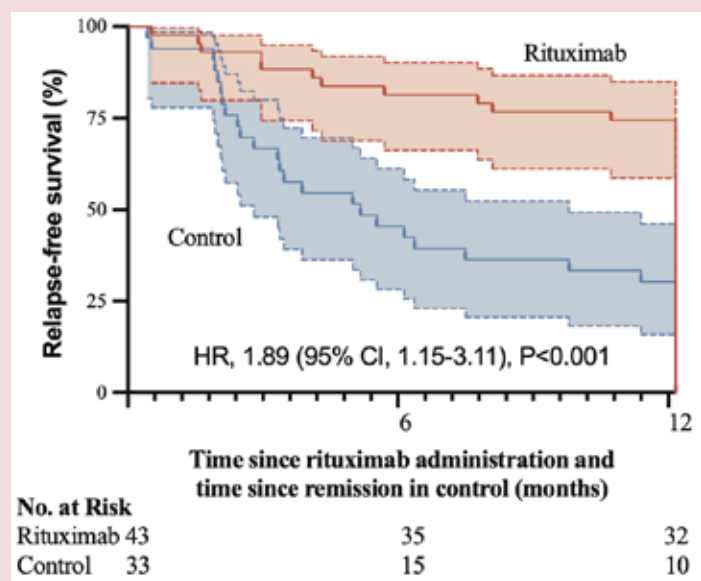


Figure 1: Kaplan-Meier curve of relapse-free survival in patients with rituximab and historical control. Kaplan-Meier curves indicating the percentage of patients who maintained remission at 6 months and 12 months after rituximab biosimilar (HANLIKANG) infusion and in control. Shading indicates 95% CIs.

Reference

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Su-3MP 151

RENAL RELAPSE IN CHILDREN AND ADOLESCENTS WITH CHILDHOOD-ONSET LUPUS NEPHRITIS: A 20-YEAR STUDY

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**Aims/Purpose:** Renal relapse adversely impacts kidney survival in patients with lupus nephritis, but there is little data in patients with childhood-onset lupus nephritis (cLN).

**Methods:** A retrospective review of all biopsy-proven cLN with age of onset < 18 years diagnosed in 2001-2021 was conducted to investigate the incidence and long-term outcomes related to renal relapse.

**Results:** 95 Chinese cLN patients (91% proliferative LN) were included. Induction immunosuppression was prednisolone and cyclophosphamide (n = 36, 38%) or mycophenolate mofetil (MMF, n = 33, 35%). Maintenance immunosuppression was low-dose prednisolone and MMF (n = 53, 54%) or azathioprine (AZA, n = 29, 31%). The rates of complete/partial remission at 12-month were 78.9%/7.4%. 70 episodes of renal relapses occurred in 39 patients over a follow-up of 10.2 ± 5.9 years (0.07 episode per patient-year), and 19 patients (20%) had repeated renal flares (> 1 episode during follow-up). Relapse-free survival was 94.7%, 86.0%, 80.1%, 71.2%, 68.3%, 50.3%, and 44.5% at 1-, 2-, 3-, 4-, 5-, 10-, and 20-year, respectively. Multivariate analysis showed that LN diagnosis before the age of 13.1 (HRadj 2.59, 95% CI 1.27-5.29, p = 0.01), AZA maintenance (HRadj 2.20, 95% CI 1.01-4.79, p = 0.05), partial remission (HRadj 3.9, 95% CI 1.03-9.19, p = 0.01) and non-remission (HRadj 3.08, 95% CI 1.35-11.3, p = 0.04) at 12-month following induction were predictive of renal relapse. Renal relapse was significantly associated with the development of advanced CKD (stage 3-5) and end-stage kidney disease during follow-up (17.9% vs 1.8%, p < 0.01). Furthermore, patients with renal relapse(s) also showed increased incidence of infections (30.8% vs 10.7%, p = 0.02), osteopenia (38.5% vs 17.9%, p = 0.04) and hypertension (30.8% vs 7.1%, p < 0.01), compared with non-relapsers.

**Conclusion:** Renal relapse adversely impacts long-term kidney outcome in cLN, and is associated with increased incidence of morbidity and mortality. Attaining complete remission and the use of MMF instead of AZA appear to have reduced the incidence of renal relapses.

Su-3MP 152

MEMBRANOUS NEPHROPATHY FOLLOWING TREATMENT WITH SEBELIPASE ALFA IN WOLMAN DISEASE

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**Aims/Purpose:** We describe a previously unreported finding of membranous nephropathy (MN) in Wolman disease (WD). WD is a rare genetic disorder caused by pathogenic variants in the LIPA gene. Lysosomal acid lipase deficiency (LAL-D) presents with, gastrointestinal symptoms, growth failure, hepatosplenomegaly, and often hyper-inflammatory features. Untreated, children develop liver failure and do not survive beyond six months of age [1]. Enzyme replacement therapy (ERT) sebelipase alfa2 was licenced in 2015 by the European Medicine Agency. Individuals have also received haematopoietic stem cell transplantation (HSCT) in conjunction with ERT. A male child was diagnosed with WD at 8 days of age. ERT given within 2 weeks. He developed sub-nephrotic proteinuria (48–150 mg/mmol) and hypertension at 6 months. He developed high titres of anti-sebelipase antibodies, associated with a suboptimal response to ERT, he underwent HSCT at 30 months. ERT dose was reduced by 40% at 34 months. At 36 months he developed features of nephrotic syndrome (NS): urine protein creatinine ratio (5770 mg/mmol) and serum albumin (8 g/l) [2]. A native kidney biopsy was performed.

**Methods:** Plasma autoantibodies for MN and testing for 70 NS genes were performed. In addition to histology and electron microscopy of the kidney biopsy, we performed additional immunofluorescence to detect LIPA in the glomerulus. Tissue sections were dewaxed to water using Leica ST5010 Autostainer. Heat induced antigen retrieval used and immunolocalization was performed for LIPA and the podocyte markers nephrin and podocalyxin. Images taken using a Zeis Axio Imager.

**Results:** Normal investigations included anti-PLA2R antibodies, glomerulonephritis screen, hepatitis screen, HIV and immune deficiency panel. Analysis of 70 genes detected no pathogenic variants. Immunofluorescence did not detect a signal for LIPA in normal human glomeruli. However, there was a diffuse signal for LIPA in the child's biopsy. The signal localised to the glomerular capillaries (Fig 1 yellow arrows). The LIPA signal also appeared in the lumen/brush border of proximal tubules (Fig. 1 white arrow).

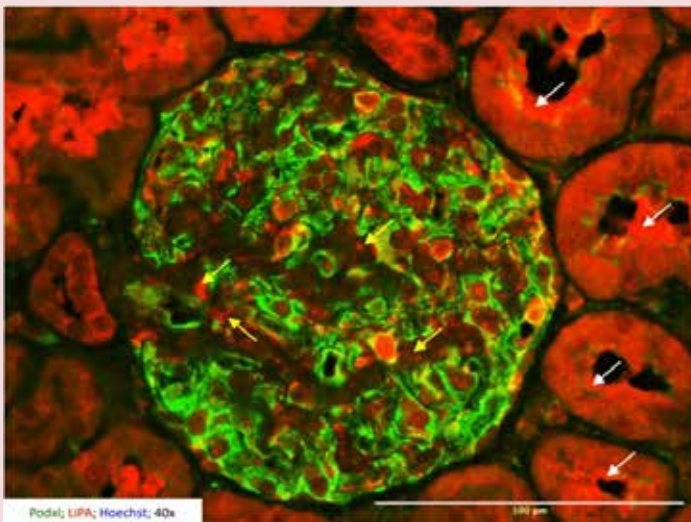


Figure 1. Biopsy 1819-18LIPA (red) and podocalyxin (green).

**Conclusion:** The biopsy shows features consistent with immune complex mediated MN and we propose allo-immunisation against sebelipase as the cause. Children with WD must be monitored for NS and anti-sebelipase antibodies, whilst receiving ERT. As advances in treatment and life expectancy in WD improve, we may see increasing cases of MN associated with ERT.

References

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Su-3MP 153

**RAVULIZUMAB LEADS TO RAPID AMELIORATION OF CLINICAL AND LABORATORY FINDINGS IN TREATMENT NAIVE PAEDIATRIC AHUS PATIENTS: SINGLE REFERRAL CENTRE REAL-LIFE EXPERIENCE**

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**Aims/Purpose:** Haemolytic uremic syndrome (HUS) represents a heterogenous group of diseases in terms of aetiology and management alike. While the mainstay of STEC and S pneumoniae associated HUS remains the supportive therapy, patients with no findings suggestive of these agents could be considered as having complement mediated atypical form of the disease (aHUS) and treated with C5 component inhibition. Beside Eculizumab being available for more than 10 years, a new long-acting inhibitor Ravulizumab (RAV) has recently been approved, with only scarce reports of its use in everyday clinical care of children with aHUS available.

**Methods:** Retrospective study of treatment naïve aHUS patients receiving  $\geq 3$  doses of Ravulizumab and followed up  $\geq 3$  months.

**Results:** The presenting symptoms were fever in 4, vomiting in 3, diarrhoea in 2 and nausea in 2 patients. All the patients had increased CRP (median (MD) 18.1 mg/L), LDH (MD 2241 U/L) and creatinine (MD 130  $\mu$ mol/L), with decreased Hb (MD 67 g/L), PLT (MD 19.5  $\times 10^9$ /L) and haptoglobin, schistocytes in peripheral blood, and signs of alternative pathway dysregulation. Moreover, 3 had proteinuria (2 nephrotic range). Extensive microbiology analysis revealed SARS-CoV-2 in 2 and influenza A in 1 patient. Plasmapheresis and CRRT were employed in 1 patient. The MD time to start RAV was 5 days after the disease onset, and to reach lower reference range after treatment initiation was 31, 6 and 37 days for Hb, PLT, and creatinine, respectively. The genetic analysis revealed pathogenic or likely pathogenic (PLP) variants in 2 and variant of unknown significance (VUS) in 3 patients, while 3 had risk factors for development of aHUS. The MD follow up was 4 months, during which 1 patient developed severe eosinophilia ( $= 3.7 \times 10^9$ /L) along with rise in PR3 and MPO ANCA antibodies.

Sex and age (months)	Microbiology findings	PLP variants	VUS	Risk factors
F, 116	/	CD46 (c.286+2T > G)	C3 (c.3687C > T, p.N1229N)	CD46 MCPggaac haplotype; CFH c.-331C > T polymorphism;
F, 92	Influenza A	/	MCP (p.Ser274Ile)	CFH H3 haplotype; CD46 MCPggaac haplotype;
F, 29	SARS-CoV-2	C3 (c.3478G > A)	DCKE (c.35C > T)	/
M, 20	SARS-CoV-2	/	/	CFH H3 haplotype;

**Conclusion:** While presented patients had different etiology, RAV has led to rapid amelioration in all, with no significant infectious complication amid standard prophylactic regimens. Observation of persistent eosinophilia could be partially attributed to atopic diathesis, but there is no clear explanation for rise in ANCA antibodies, implicating a possibility of RAV being a culprit drug. Although only one patient had a well-defined pathogenic mutation, C5 inhibition therapy has induced sustained remission off medication in other three patients with unambiguous infectious trigger and uncertain variants as well, emphasizing the efficacy of this treatment modality in wide(r) group of children with aHUS.



Su-3MP 154

10-YEAR OUTCOME OF CHILDREN WITH IDIOPATHIC NEPHROTIC SYNDROME IN FRANCE: THE NEPHROVIR POPULATION-BASED COHORT

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**Aims/Purpose:** Idiopathic Nephrotic Syndrome (INS) is often a chronic disease. Most patients experience relapses and are exposed to second-line treatments for years. Few studies have reported the long-term outcome in a population-based cohort. We report the 10-year outcome of children included from December 2007 to June 2010 in the prospective multiethnic and regionwide population-based NEPHROVIR study.

**Methods:** This was a cross-sectionnal study conducted in 2022. Data were collected from medical charts and/or by phone-call for patients with no follow-up visit after 2020. Primary outcome was the proportion of patients still under treatment 10 years after onset. Secondary outcomes included time to treatment discontinuation and frequency of relapse after 18 years of age.

**Results:** Hundred-and-thirty-nine patients were included, out of 188 of the NEPHROVIR study (74%). Median duration of follow-up was 13 years (IQ 9.8-13.8). Median age at last follow-up was 17 years (13.7-19.3). Among 130 patients with steroid-sensitive NS (SSNS), 111 (85%) were off-treatment and 91 (70%) off-treatment since > 3 years. When considering only frequent-relapsers, 29% were still under medication at 10 years. Seventy patients aged > 18 were contacted and 9 (13%) had experienced > 1 relapse at adulthood.

**Conclusion:** These results confirm in a population-based study that only 15% of patients with SSNS are still under medication for an active disease 10 years after onset and that 13% relapse in early adulthood. Such a study might help to inform families on long-term outcomes, and also discuss the definition of long-term remission in childhood INS.

Su-3MP 155

## BENEFITS OF EARLY INTERVENTION AT THE ONSET OF PROTEINURIA IN STEROID DEPENDENT NEPHROTIC SYNDROME

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**Aims/Purpose:** During the COVID-19 pandemic, travel between different cities in Sri Lanka was severely restricted for nearly 18 months. Children with steroid dependent nephrotic syndrome attending a tertiary centre from remote cities were advised to communicate through WhatsApp for advice. All parents were trained to test and record proteinuria on daily basis. Parents were requested to communicate if a child develops proteinuria 1+ or more for two consecutive days. Following a telephone consultation, if there is no contraindication, the parents were advised to administer prednisolone 1mg/ kg/ day for seven days. If proteinuria persisted or develops oedema, the full dose of prednisolone was commenced. This study was carried out to determine the outcome of this remote management strategy.

**Methods:** Patients who completed one year of remote management were studied, focusing on the relapse episodes, total steroid dose and any adverse events compared to the previous year. Continuous variables were visualized with density plots and summarized using mean and standard deviation (SD). The number of relapses were modeled using a Bayesian Poisson regression model, while the total steroid dose was analyzed using a hierarchical linear model with weakly-informative priors.

**Results:** The study included 34 children aged 6.2 to 16.8 years (mean age 10.5, SD 2.48). The mean cumulative steroid dose before and during the pandemic were 93 mg/kg (SD 64.2) and 76 mg/kg (SD 51.3), respectively. The Poisson regression model estimated an incidence rate ratio (IRR) of 0.40 (89% credible interval [CrI] 0.26 – 0.63), indicating a 60% reduction in the number of relapses with the remote-management strategy. The estimated reduction in cumulative steroid dose during the pandemic was 16.69 mg/kg (89% CrI 11.67 – 21.86). No significant adverse events were noted.

**Conclusion:** Early intervention at the onset of proteinuria reduces the number of nephrotic syndrome relapses as well as the cumulative steroid dose.

**Su-3MP 156**

**DETECTING, IDENTIFYING, “VISUALIZING” URINE ODORS WITH ELECTRONIC NOSE ARYBALLLE NEOSE ADVANCE**

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*Medical Center Mrcheveli, Tbilisi, Georgia*

**Aims/Purpose:** Urinalysis includes physical, chemical, microscopic, and microbiologic examination of urine. Physical examination involves determination of color, clarity, specific gravity, and odor. Most parameters are measured objectively qualitatively, semi quantitatively and quantitatively. In contrast to other parameters urine odor is assessed subjectively. In modern laboratories with medium or high numbers of urine samples per day urinalysis is performed on automated devices urine odor is not determined at all. As defined in the European urinalysis Guideline 2023: The normal urine is generally mild in odor. Infected urine may be ammoniacal or fetid. Some metabolic diseases have characteristic urine odors. In recent decades there were publications regarding Application and Uses of Electronic Noses for Clinical Diagnosis on Urine Samples with aim to measure odors objectively with high accuracy and precision. Aim of this study was to detect and “visualize” urine odors mentioned above (ex. phenylalanine, ketones/acetone et ctr.).

**Methods:** We analyzed the gaseous headspace of urine and lyophilized components using electronic nose NeoSe Advance Aryballe. Measuring and analyzing principal components and odor intensity.

**Results:** Device and software give possibility to identify, “visualize” and compare urine odors.

**Conclusion:** Electronic nose NeoSe Advance Aryballe can detect, visualize, and compare/recognize specific odors of urine. After standardization of procedure device can be integrated in automated urine analyzers.

Odour	Disease
Sweaty feet	Isovaleric acidemia and glutaric acidemia
Maple syrup	Maple syrup urine disease
Cabbage, hops	Methionine malabsorption
Mousy	Phenylketonuria
Rotting fish	Trimethylaminuria
Rancid	Tyrosemia

Su-3MP 157

FOXD2 DYSFUNCTION IS IMPLICATED IN SYNDROMIC CONGENITAL ANOMALIES OF THE KIDNEY AND URINARY TRACT (CAKUT)

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**Aims/Purpose:** In only about 16% of individuals with CAKUT, a monogenic cause can be identified so far. The aim of this study was to expand the genetic spectrum of monogenic CAKUT.

**Methods:** Six individuals with similar phenotypic features from 2 unrelated consanguineous families were identified. Exome sequencing (ES) was performed. CRISPR/Cas9-derived Foxd2 knock-out (KO) mice were generated and deep phenotyping was done. Transcriptomic analyses and genome wide association studies (GWAS) were performed. The  $\Delta\Delta G$  value between the wild type protein and results of altered amino acid substitution were calculated for the missense variant and 3D structures of the wild type and altered FOXD2 protein structures were generated with DynaMut2.

**Results:** Shared phenotypic features in affected individuals were facial dysmorphism, developmental delay, kidney hypoplasia, and glomerular proteinuria. Renal biopsy was compatible with focal segmental glomerulosclerosis in one individual. ES in the index individuals revealed two different rare homozygous variants in FOXD2 (NM\_004474.4), a transcription factor not previously implicated in CAKUT in humans: a frameshift (c.789dup, p.(Gly264Argfs\*228)) in family 1 and a missense (c.628A > G, p.(Met210Val)) variant in family 2 with segregation pattern consistent with autosomal recessive inheritance. Foxd2 KO mice recapitulated the phenotype of humans with FOXD2 dysfunction. Transcriptomic analyses showed enrichment of several genes important in renal/urogenital development including Pax2 and Wnt4 as well as gene expression changes indicating a cell identity shift towards a stromal cell identity compatible with histologic findings in KO kidneys.

**Conclusion:** We implicate FOXD2 dysfunction as a possible rare cause of autosomal recessive syndromic CAKUT. Disturbances of the PAX2-WNT4 cell signaling axis contribute to this phenotype. GWAS data further suggest that FOXD2 could play a role in maintenance of podocyte integrity during adulthood.

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# POSTER SESSION 1A

## Dyalisis

Fr-P 001

LONG-TERM KIDNEY FOLLOW-UP AFTER PEDIATRIC KIDNEY SUPPORT THERAPY FOR CHILDREN LESS THAN 15 KG

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**Aims:** In small children, acute dialysis (pediatric acute kidney support therapy (paKST)) is increasingly used in recent decades; however, it is challenging for many reasons. In this study, we aimed to compare the clinical characteristics, predictors of long-term outcomes of the patients who had peritoneal dialysis (PD), hemodialysis (HD), and continuous kidney replacement therapy (CKRT) when weighing less than 15 kg.

**Methods:** Patients with a history of pediatric acute kidney support therapy (CKRT, HD, PD) when weighing < 15 kg and ≥ 6 months of follow-up at Hacettepe University were included in the study. Surviving patients were evaluated at last visit.

**Results:** The study included 109 patients (57 females and 52 males). The median age at the time of paKST was 10.1 months (IQR: 2–27 months). In total, 43 (39.4%) patients received HD, 37 (34%) received PD, and 29 (26.6%) received CKRT. In total, 64 (58.7%) patients died a median 3 days (IQR: 2–9.5 days) after paKST. The percentage of patients that used vasopressor agents, had sepsis, and underwent mechanical ventilation was lower in the patients that survived than in those that died. After a mean follow-up period of 2.9 ± 2.1 years, 34 patients were evaluated at last follow-up visit. The mean age at last visit was 4.7 ± 2.4 years. The median spot urine protein/creatinine was 0.19 (IQR: 0.13–0.37). Besides, 12 patients (35.3%) had non-nephrotic proteinuria. Three patients had estimated glomerular filtration rate (eGFR) less than < 90 mL/min/1.73m<sup>2</sup> and 2 patients (6%) had hyperfiltration. At the time of the last follow-up visit 15 of the patients were aged > 5 years, of which 9 patients' parents consented to 24-hr ambulatory blood pressure monitoring (ABPM) and 4 of them optimum ABPM results, of which only 1 patient had hypertension who had normal office measurement. In total 22 patients (64.7%) had at least one risk factor (elevated BP/HT, hyperfiltration, GFR less than 90 ml/min/1.73m<sup>2</sup>, and/or proteinuria) at the last visit. In this cohort, 9 patients had 2 risk factors (41%). None of the patients had three or more risk factors. All of these 22 patients were less than 3 years of age at the time of paKST.

**Conclusion:** In acute period, patients on mechanical ventilation and vasopressor treatment should be followed-up more closely. After surviving the acute period, pediatric acute kidney support therapy patients need to be followed-up closely during the chronic stage.

Fr-P 002

**THERAPEUTIC PLASMA EXCHANGE FOR PEDIATRIC RENAL AND NONRENAL DISEASE INDICATIONS AND OUTCOMES: OVER 30-YEAR, SINGLE CENTER EXPERIENCE**

**Carlota Fernández Cambor, Diego Morante Martínez, Manuel Vaqueiro Graña, Alejandro Zarauza Santoveña, Juan Bravo Feito, Angel Alonso Melgar, Maria Paz González Pérez, Natalia Perea Dominguez, Maria Aparicio López**  
*Hospital Universitario “La Paz”, Pediatric Nephrology, Madrid, Spain*

**Aims/Purpose:** To retrospectively characterize clinical indications, efficacy and safety of therapeutic plasma exchange (TPE), in children with different renal and non-renal disorders

**Methods:** This analysis is a single-center, retrospective cohort study of pediatric patients with renal and non-renal diseases, including neurological, gastrointestinal or hemato-oncological diseases and sepsis/multiorgan failure all treated with TPE by membrane separation technique from 1990 to 2022 in our tertiary referral center.

**Results:** 175 patients (55 % male) with a median age of  $9 \pm 5.5$  years (= 1 month - 20.4 years) underwent a total of 1190 TPE sessions, with a mean number of TPE of  $5 \pm 6.6$  sessions per patient (1-58 sessions). The main indications for TPE in the renal disease group (67 patients) were: antibody-mediated rejection (n = 18); ABO or HLA desensitization (n = 15); hemolytic-uremic syndrome (n = 8); vasculitis (n = 9); rapidly progressive glomerulonephritis (n = 7) and steroid-resistant nephrotic syndrome/focal segmental glomerulosclerosis (n = 8). In the non-renal disease group (108 patients) main indications for TPE were: Sepsis/multiorgan-failure (n = 28); macrophage activation syndrome (n = 11); antibody-mediated rejection in solid graft other than kidney (n = 12); acute liver failure (n = 6); Guillen-Barré syndrome (n = 4) and myasthenia gravis (n = 4). American Society of Apheresis (ASFA) classifications were as follows: category I (36.6 %) category II (12 %); category III (51.4 %). TPE was given as adjunctive therapy along with primary treatment for the disease in most of our patients. 70% patients in the renal group and 56% in the non-renal group showed partial or total recovery with combined treatment. 53% of our patients experienced mild complications, the most frequent being asymptomatic hypocalcemia. No major procedural complications were seen. In all, 43 patients died, 40% of them in the context of multiorgan failure.

**Conclusion:** In our experience TPE is a safe and widely applicable adjuvant procedure for children of all ages resulting in improvement in partial or total recovery in 62% patients

Fr-P 003

THE CHANGING TRENDS IN PEDIATRIC RENAL REPLACEMENT THERAPY – A 40-YEAR FOLLOW-UP OF THE POLISH REGISTRY OF RENAL REPLACEMENT THERAPY IN CHILDREN

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**Background:** In recent decades, with environmental changes and advances in medical technology, a change in the aetiology of end-stage renal disease (ESRD), age of initiation of renal replacement therapy (RRT) and treatment modality in both adult and children has been observed.

**Objectives:** To assess the variability in the aetiology of ESRD, age of onset and treatment modality among children undergoing RRT in Poland between 1980 and 2022.

**Material and Methods:** Data of 1466 children treated in 13 paediatric dialysis centers reported to the Polish Registry of Renal Replacement Therapy in Children were analysed. The primary kidney disease was assessed according to the ESPN/ ERA-EDTA classification with division into 6 groups (urinary tract abnormalities, genetically related diseases, glomerulopathies, systemic diseases, malignant diseases and others). Age, gender, as well as methods of RRT at onset were analyzed. The evaluation was performed in 3 periods: 1980–1999, 2000–2009, 2010–2022; the size of each group was respectively: 321, 582, 563 children.

**Results:** In all 3 periods, urinary tract abnormalities were the most common cause of ESRD (38.9% vs 42.2% vs 40.4%). Glomerulopathies were reported significantly less frequently in subsequent periods: 16.5%, 9.9% and 8.8% ( $p < 0.016$ ), while genetically related diseases were respectively: 25.8%, 31.8%, 27.9%. In the last follow-up period, acute kidney injury as an aetiology of ESRD was diagnosed significantly more frequently than previously and unknown aetiology – significantly less frequently. Mean age at initiation of RRT differed between periods (10.06 vs 10.67 vs 9.05 years) and was significantly lower in the last decade ( $p < 0.001$ ). Age at onset was significantly different between diagnosis groups; the youngest children started RRT due to malignancy and genetically related diseases ( $p < 0.002$ ). Peritoneal dialysis was the most frequently chosen modality (55.9%) in all periods, followed by hemodialysis (32.2%) and pre-emptive transplantation (10.8%).

**Conclusions:** 1. Urinary tract abnormalities are consistently the leading cause of ESRD in children, while glomerulopathies are observed to be significantly less frequent in the 40 years of data collection. 2. Acute kidney injury is significantly more frequently reported in the last decade of follow-up. 3. The mean age at onset was significantly lower in the last decade of observation. 4. Peritoneal dialysis remained the most commonly chosen method of renal replacement therapy in children.



Fr-P 004

THE USE OF RENAL REPLACEMENT THERAPY WORSENS OUTCOME IN CHILDREN WITH ACUTE KIDNEY INJURY AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION

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**Aims/Purpose:** We retrospectively analyzed data on 12 patients undergoing renal replacement therapy (RRT) due to acute kidney injury (AKI) in a group of 211 patients treated with allogeneic hematopoietic stem cell transplantation (HSCT) at the Children's University Hospital in Krakow from 2006 till 2021.

**Methods:** We reviewed data such as: indications for HSCT, conditioning protocol, transplant specificity (donor type, HLA match, GVHD prophylaxis, number of HSCT procedures) and clinical data on RRT (method of RRT used, indications for initiation of RRT, procedure parameters, treatment outcome). The indication for HSCT included haemato-oncological disorders in all cases, in 5 patients - recurrence of the disease.

**Results:** 11/12 patients presented with normal eGFR before HSCT, one was previously diagnosed with chronic kidney disease stage (CKD) 3 and in this case CRRT was planned as a preparation for HSCT. RRT was performed in 5.4% of all recipients, peritoneal dialysis was chosen in one child, and CRRT (hemodiafiltration, HDF) in the remaining children. The indications for RRT were: hypervolemia (50%), biochemical indicators of AKI (33%), multiorgan failure (8.3%), in a patient with CKD - prophylaxis. In 10/12 - RRT was performed within 100 days from the date of HSCT. The mean duration of dialysis was: 15.6 days. Comorbidities (except AKI) were present in all patients and included: Graft-versus-Host Disease in various stages, sepsis (41.7%), Cytomegalovirus infection (33.3%) and other. 2/3 of children died up to 2 months after starting RRT, 1 patient later died of CKD. The only child with CKD at the time of HSCT maintained a stable CKD stage. In children without AKI and RRT, overall mortality was 18%.

**Conclusion:** Children with acute kidney injury after allogeneic HSCT require RRT relatively rarely, while the necessity of its use significantly increases the mortality of these patients.

Fr-P 005

EVALUATING CARDIOVASCULAR FINDINGS IN CHILDREN RECEIVING HAEMODIALYSIS USING ARTERIOVENOUS FISTULA FOR MANAGEMENT OF END STAGE KIDNEY DISEASE

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**Introduction:** Arteriovenous fistulae (AVF) are considered the gold standard vascular access modality for patients receiving long term haemodialysis (HD) for end stage kidney disease in both the adult and paediatric population. Adult studies have investigated both short and long term effects of arteriovenous fistula on cardiac haemodynamics and structure. One adult study identified possible associations between AVF creation, significant right ventricular dilatation and deterioration in RV function potentially as a result of increased cardiac flow from the AVF. Increased right heart stress is associated with increased risk of heart failure and risk of mortality. Another adult study assessed and identified no significant correlation of AVF formation and the development of pulmonary hypertension on patients receiving HD. The effects of AVFs on cardiac structure and haemodynamics in the paediatric population has previously been unreported. The aim of this study was to identify cardiovascular changes following arteriovenous fistula formation in paediatric patients with end stage kidney disease receiving haemodialysis.

**Methods:** A retrospective review was performed looking at echocardiography details on paediatric patients that had an AVF formed between 2015–2020 in a single tertiary paediatric nephrology centre in the United Kingdom. Information obtained included; sex, age at time of AVF procedure, site and type of AVF and pre and post AVF echocardiography data.

**Results:** Between 2015–2020, 23 patients had an AVF formed. 12 of these patients were male and the median age at time of AVF formation was 11 years. Of these, 14 AVFs were performed on the left arm. Radiocephalic was the most common type of AVF (52.2%), followed by Brachiocephalic (34.8%) and Brachiobasilic (13%). Echocardiography data pre and post AVF formation was available for 56% of the patient cohort. The average time post AVF formation for repeat echocardiogram was 8 months. Baseline echocardiography data identified normal biventricular (BV) size and function in 62%, concentric left ventricular (LV) hypertrophy in 30%, LV impairment in 8% and BV dysfunction in 8% of patients. Echocardiography findings in children with AVF included LV mass reduction in 46% and increased LV hypertrophy in 8% of patients. There were no observed right sided cardiac changes or findings suggestive of pulmonary hypertension in any patients.

**Conclusion:** Our preliminary findings suggest no early adverse effects on cardiac function following creation of AVF in children receiving haemodialysis. None of the patients showed deterioration in right-sided cardiac function. Further longitudinal follow up including larger, prospective studies are needed to help understand impact of AVF creation on cardiovascular haemodynamics in this population.

Fr-P 006

**A RETROSPECTIVE STUDY OF ACUTE AND CHRONIC PERITONEAL DIALYSIS: A SINGLE-CENTER EXPERIENCE**

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**Introduction:** Peritoneal dialysis is the preferred method of kidney replacement therapy for acute and chronic renal failure for most children of all ages. Since our country does not provide transplantation therapy in very small ages, peritoneal dialysis is our initial course of action.

**Method:** On this retrospective study we present our experience from 2005 until today. During this time, we managed children with acute and chronic renal disease. Furthermore, we review the epidemiology, etiology of chronic kidney diseases, principles of dialysis, the complications and outcome.

**Results:** We studied 39 patients from which 27 were boys and 12 girls, until the age of 15yo, with a mean age of 4.2yo. The patients were divided into two groups, as acute peritoneal dialysis (Group 1) and chronic peritoneal dialysis (Group 2). Group 1 consists of 12 children, while the rest 27 were in Group 2. The most common causes of acute renal disease in newborns of Group 1 were, 40% metabolic diseases, 30% congenital heart diseases and the rest birth asphyxia. The primary cause of chronic renal disease in Group 2 was corticosteroid resistant nephrotic syndrome (FSGS) 59% and the second most frequent being the congenital anomalies of the kidney and urinary tract 33%. For all the children, a straight single cuff Tenckhoff catheter was placed, through a surgical procedure. The mean value of creatinine initially was 4.1 mg/dl and eGFR was 8.2 mL/min/1.73. The PD was an extensive procedure with a mean duration of 3 years. Catheter revision was performed in 7,6%. From Group 2, an 11% did continuous ambulatory peritoneal dialysis (CAPD), to 51% was applied automatic peritoneal dialysis (APD) and 37% did APD and CAPD simultaneously. At the onset of the therapy, 70% of Group 2 maintained a normal diuresis, resulting, in the end of this procedure, in 52% maintaining their diuresis. Regarding the non-infectious complications of Group 2, were hydrocele and omphalocele. Concerning the infectious complications, 62% had peritonitis, with Staphylococcus being the major identified microbe, consisting mainly children that had done CAPD and APD. The cause of failure of this therapy in Group 1 was the leakage at the exit site of the catheter. Whereas, in Group 2, ultrafiltration insufficiency, outflow obstruction or migration of the catheter and relapses of peritonitis were responsible. Lastly, the mortality in Group 1 was estimated at 33.3%, while in Group 2 was 3.7%.

**Conclusions:** Although, peritoneal dialysis is a relatively safe option for a long-lasting renal substitution, peritonitis remains as one of the most recurrent complications. Overall, from the data collected we concluded that, APD application reduces the risk of peritonitis. We observed that the main complication in infants was leakage in the exit site. Despite the long period of therapy, the complications and the mortality rate are remaining low in children with chronic peritoneal dialysis.

Fr-P 008

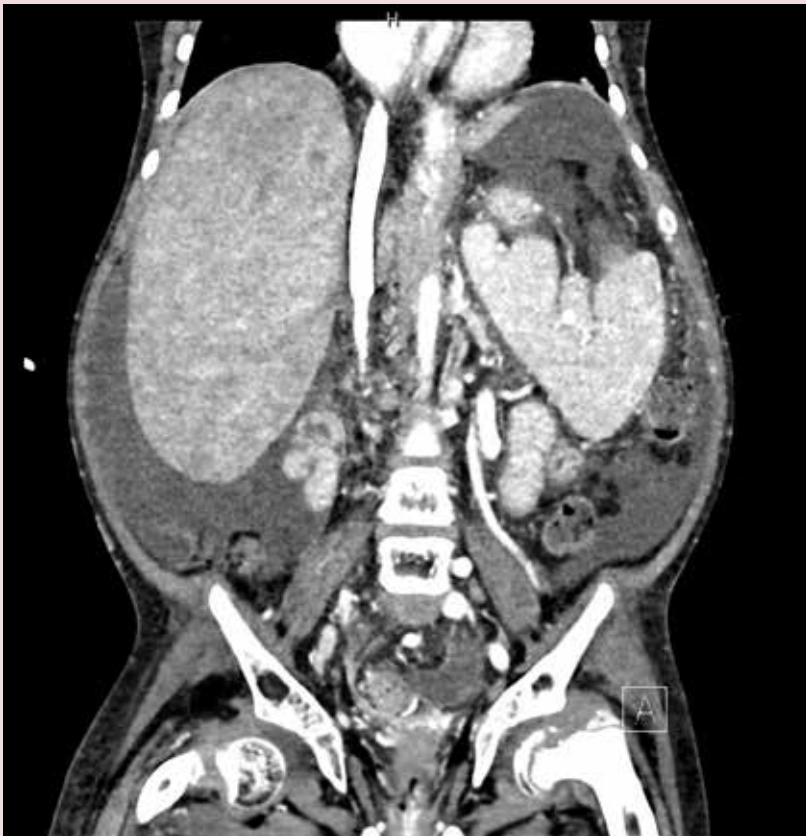
**BUDD CHIARI SYNDROME: A RARE COMPLICATION OF TUNNELED HEMODIALYSIS CATHETER**

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**Aims/Purpose:** The Budd-Chiari Syndrome is a rare condition. It is associated with hepatic venous outflow obstruction. This syndrome is rare in infants and children. Common causes include hypercoagulable states, malignancy, oral contraceptive use, pregnancy and rarely, idiopathic causes. We present a rare case of a child who developed Budd-Chiari syndrome and its subsequent complications as a result of a right-sided indwelling tunnelled-dialysis catheter in the right female vein.

**Case Report:** An 11-year-old female patient with congenital anomaly of the kidney and urinary tract (CAKUT) with solitary kidney and end stage renal disease (ESRD) on hemodialysis since 1 year old and living in a remote area. She was maintained on peritoneal dialysis initially but switched to hemodialysis due to recurrent peritonitis and catheter malfunctions. Her hemodialysis access was problematic and she required multiple catheter exchanges and replacements due to malfunctions (up to 17 exchanges) including right and left internal jugular veins, left hepatic vein and right femoral vein. Her neck veins were completely occluded. Her current hemodialysis access (#17) is inserted in the right femoral vein. She was admitted to the emergency room for complaints of malfunctioning right femoral vein requiring exchange. The procedure was difficult and required venoplasty of the common iliac vein and inferior vena cava. Post operatively, she developed worsened abdominal distention, fever, significant ascites and impaired liver function/transaminitis. The tunneled dialysis catheter placed in the right femoral vein with evidence of calcification of the inferior vena cava (IVC) and perihepatic segment. She was diagnosed with Budd Chiari Syndrome was established by abdominal tomography that showed hepatosplenomegaly, extensive intra-abdominal varices, ascites and features of hepatic venous outflow obstruction (see picture). Budd Chiari Syndrome was suspected due to the chronic indwelling HD catheter with calcified IVC and periphepatic segment. The calcification lead to obstruction of the hepatic vein. She was managed with angioplasty of the IVC and stenting. She is dependent on regular paracentesis.



**Conclusion:** This case raises awareness and importance of timely monitoring of hemodialysis catheter position after insertion is essential for early diagnosis and treatment of such a rare complication. In pediatric population it is very important to protect and preserve the vascular access and avoid complications such as infection, stenosis, thrombosis and hemorrhage. In our care, palliative care was considered due to poor vascular access.

Fr-P 009

QUALITY OF LIFE OF CHILDREN WITH END STAGE RENAL DISEASE UNDERGOING HEMODIALYSIS

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**Aim/Purpose:** To describe the quality of life (QoL) of children undergoing haemodialysis and to assess coping strategies to improve QoL.

**Methods:** We conduct a descriptive study of the quality of life of children with end stage renal disease (ESRD). All patients between 8 and 18 years undergoing hemodialysis in our pediatric nephrology department in Sousse, TUNISIA were included. All patients and their parents were asked to fill out the PedsQL™ score scale version 4.0 questionnaire.

**Results:** A total of 7 Children were recruited, Sex ratio was equal to 5/2, the age at diagnosis was between 2–14 years old. CAKUT was the most frequent etiology of renal failure and dialysis duration varied from 1 to 8 years. 5 patients were accompanied with their parents and QoL was assessed from parental reports 61.9 % and children's reports 70.9%. The school activities aspects were the lowest score parameters studied. The mean score scale of PedQL for young patients was 71.5% while their parents showed a lowest mean score 52%. Youth and adolescents between 13 and 18 years old mean's score scale was equal to 70.48% , that correlates with their parents scores 71.8%. Most influencing factor of QoL was length of diagnosis.

**Conclusion:** The measurement of the QoL score is not yet carried out in current practice. Attitude of practitioners following childrens with chronic kidney disease shouldn't be only to obtain remission but also to ensure an identical QoL to healthy children.

Fr-P 010

TYPICAL HEMOLYTIC UREMIC SYNDROME IN CHILDREN: CLINICAL PRESENTATIONS AND SHORT-TERM OUTCOMES

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**Aims/Purpose:** To analyse the frequency of clinical presentations and the need for renal replacement therapy (RRT) in children with the typical hemolytic uremic syndrome (tHUS) during the hospitalization and 6 months after the discharge.

**Methods:** 26 case histories of children with clinical diagnosis of tHUS who were treated in LSMU Hospital Kauno klinikos between 2007-2022 were analyzed in this retrospective study. Data of sex, age, hospitalisation period, RRT, mortality and clinical presentations of the patients at the time of arrival, discharge and 6 months after the discharge were evaluated.

**Results:** 26 patients formed the study group: n = 16 (61.5%) boys and 10 (38.5%) girls. The median age at the time of hospitalization was 22 (7-90) months. Median hospitalization period was 14.5 (4-66) days. 61.5% (n = 16) of the patients arrived for the follow-up visit 6 months after the discharge. 61.5% (n = 16) of the children developed arterial hypertension during the acute period of the disease, which remained in 62.5% (n = 10) from them at the time of discharge and in 37.5% (n = 6) 6 months after. 23.1% (n = 6) of the patients experienced temporal disturbances of consciousness during the hospitalization. Although proteinuria was found in all the patients at the time of arrival (median proteinuria 3 (0.5-6.0) g/l), in half of them (50%, n = 13) it disappeared during hospitalisation. Proteinuria remained in 37.5% (n = 6) of those who arrived for the follow-up visit. All the patients presented with hematuria (38.5% with macrohematuria) which remained in most of these cases (46.2%, n = 12) at the discharge. At the time of arrival, kidney dysfunction was found in 76.9% (n = 20) patients (median creatinine level of 196.5 (23-619)  $\mu\text{mol/l}$  and urea level of 26.85 (2.8-49.6) mmol/l). 26.9% (n = 7) of the children developed anuria. RRT was applied in 50% (n = 10) of the children with a median duration of 12 (4-48) days. Hemodialysis was a primary choice in most (80%, n = 8) of these patients. Remaining kidney function impairment at discharge was observed in 42.3% (n = 11) but only in 6.3% (n = 1) 6 months after. No deaths appeared in the study sample.

**Conclusion:** In most patients who developed proteinuria and arterial hypertension during the acute phase, it remained 6 months after the discharge. Even though RRT had to be performed in more than a third of the patients, remaining kidney function impairment 6 months after the discharge was only found in 1 patient.

Fr-P 011  
FIRST VASCULAR ACCESS IN CHILDREN PERFORMING HEMODIALYSIS

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**Aims/Purpose:** Hemodialysis (HD) is gaining popularity as a kidney replacement therapy (KRT) in the pediatric population with end-stage kidney disease (ESKD), especially before the patient achieves proper conditions for kidney transplantation (KT). Therefore, it is of utmost importance to describe and analyze the outcomes and variables in this population. We aim to describe the pediatric population under HD treatment in a tertiary pediatric hospital, and to analyze variables that correlate with first vascular access (VA) choice.

**Methods:** We conducted a retrospective study including all the pediatric HD patients in our center, between January 2005 and March 2023. We collected data on demographic variables, VA choice, and clinical outcomes. Statistical analysis was performed using SPSS software.

**Results:** Fifty-three pediatric patients were submitted to HD, mostly males (52.8%), with a median age at beginning of treatment of 12.4 years (IQR 6.9–14.8). The most frequent etiology of ESKD was congenital anomalies of kidney and urinary tract (CAKUT; 52.8%). Twenty-one patients (39.6%) were submitted to peritoneal dialysis (PD) before HD. Median follow-up time was 0.5 years (IQR 0.1–1.5), and the main cause of loss of follow-up was KT (62.2%); 9 patients (17.0%) were transferred to PD, and 2 patients (3.8%) reached > 18 years; mortality rate was 7.5% (n = 4). In what concerns to the first VA, most patients (77.4%) began HD through a central venous catheter (CVC). There was an inverse statistical correlation between age at beginning of treatment and the CVC use (p = 0.032), with younger patients more frequently exposed to CVC. There was also a significant correlation between CAKUT and the use of arteriovenous fistula (AVF; p = 0.016). No differences were found in what concerns to gender and transference from another KRT. Six of the patients starting with CVC (14.6%) were submitted to AVF creation during the follow-up period. There was a total of 135 hospitalizations, 33.3% of which related to VA complications.

**Conclusion:** We observed that younger age was associated with CVC usage, probably related to technical challenges in AVF performance in these patients. We also observed that patients with CAKUT were more probable to initiate HD through an AVF, which we think is related to the better predictability of this disease's course, when compared to patients with glomerular pathologies. One strong point of our study is the sample size; one caveat is the short follow-up period, but we highlight the high KT rate, which is known to provide better long-term outcomes.

Fr-P 012

LECLERCIA ADECARBOXYLATA IN PERITONEAL DIALYSIS PATIENTS: A SYSTEMATIC REVIEW

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**Aims/Purpose:** *Leclercia adecarboxylata* is a Gram-negative bacterium belonging to the family Enterobacteriaceae, which can rarely cause infections in humans, especially in immunocompromised individuals. Even rarer are the peritonitis cases due to *L. adecarboxylata* in peritoneal dialysis (PD) patients presented in the worldwide bibliography. We have recently encountered a case of peritonitis due to *L. adecarboxylata* in a PD young patient with favorable outcome and we systematically review the international literature for other such cases, with aim to enrich our knowledge about this noteworthy pathogen.

**Methods:** We searched PubMed and Scopus databases and we reviewed such cases reported, including our patient.

**Results:** Our case was a 14.5-year-old immunocompetent male started treatment with PD because of corticosteroid resistant nephrotic syndrome – focal segmental glomerulonephritis, 4 years ago. He developed signs and symptoms consistent with peritonitis, such as cloudy PD effluent, low-grade fever (38.4°C) for 8 hours, abdominal pain and vomit. Microbiologic investigation of the PD effluent revealed a white cell count of 3,700/μL, with a polymorphonuclear cell ratio of 82%. The PD effluent culture was reported as growing *L. adecarboxylata* established by a VITEK-II GN card and by conventional tests. Finally, the patient treated with intraperitoneal ceftazidime (125 mg/L) which was given for a total of 21 days. The review of the literature showed 13 (two children, 11 adults) PD cases due to *L. adecarboxylata* with a mean (± SE) age of 53.2 ± 22.5 years and a male to female ratio 1:1.6, approximately. Their mean vintage period on PD prior to *L. adecarboxylata* peritonitis was 37.5 ± 25.3 months. VITEK card was the identification diagnostic tool in most cases (63%). The antimicrobial agent that was most frequently used was ceftazidime in 50% of cases as initial therapy, either monotherapy or combination, while, in only two patients (15.3%) Tenkhoff catheter was removed. Median duration of treatment was 18 days (range of 10–21 days), while, all 13 patients that were reviewed in this study were healed.

**Conclusion:** Physicians should be aware that *L. adecarboxylata* noticed to cause rarely peritonitis to PD patients, however, this pathogen seem to be sensitive to most antimicrobial agents and can resulted to a favorable outcome with the selection of appropriate treatment.



Fr-P 013

SEVERE ACUTE KIDNEY INJURY CAUSED BY PAROXYSMAL COLD HAEMOGLOBINURIA: A CASE REPORT

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**Aims/Purpose:** Autoimmune haemolytic anaemia (AIHA) is uncommon in childhood. Paroxysmal cold haemoglobinuria (PCH) constitutes a peculiar type of cold-AIHA, characterized by the presence of a byphasic haemolysin binds to the surface of red blood cells at low temperatures (4°C), but can activate the complement cascade at 37°C, causing intravascular haemolysis. There are very limited data in the literature, regarding renal complications in PCH. Our purpose is to present a rare case of a child with severe acute kidney injury secondary to PCH-related haemoglobinuria.

**Methods:** Patient's medical record was reviewed and history with diagnostic and therapeutic data are presented.

**Results:** A 2-years old girl toddler admitted to our department due to severe acute kidney injury (eGFR: 20 ml/min/1.73m<sup>2</sup>) combined with AIHA. Diagnosis of AIHA was based on severe anemia, increased haemolysis markers and positive direct antiglobulin test. Diagnosis of PCH was confirmed by positive Donath-Landsteiner test which is specific for the certain disease. Regarding PCH, intravenous methylprednisolone and per os folic acid was administered, while the patient received twice red blood cells transfusions due to life-threatening anaemia. Acute kidney injury was initially treated with fluid restriction, correction of electrolytes and administration of diuretics. However, due to the rapidly progressive kidney failure (persistent metabolic acidosis, oligo-anuria) patient was placed on peritoneal dialysis (PD) through a Tenckhoff catheter for a total of 15 days. A kidney biopsy was performed to establish the diagnosis and its finding were indicative of acute renal tubular injury due to haemoglobinuria. Renal function was restored, eGFR and diuresis returned to normal two weeks following PD onset. Of note, the patient's hematological profile remained stable with no need for further blood products transfusions. Finally, patient dismissed after hospitalized for a total of 33 days, without any need of medication or other support.

**Conclusion:** PCH is a rare subtype of AIHA in childhood which usually has a mild clinical course. However, it can be complicated with life-threatening events, such as severe acute kidney injury. Patients with PCH should be monitored closely to avoid side effects. High clinical suspicion is required in order to have early diagnosis and appropriate treatment of severe complications which requires the cooperation of a team of experts.

Fr-P 014

## THE IMPACT OF COVID-19 IN CHILDREN UNDERGOING CHRONIC HEMODIALYSIS: A SINGLE-CENTER EXPERIENCE

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**Aims/Purpose:** COVID-19 is known to severely affect adults receiving chronic hemodialysis. The purpose of our study was to describe the prevalence and clinical characteristics of COVID-19 infection in children undergoing chronic hemodialysis in a single pediatric nephrology center.

**Methods:** We reviewed the medical records of 13 patients (10 males) who were undergoing hemodialysis in a 2.5-year period during the pandemic in our center. 5 patients had Focal Segmental Glomerulosclerosis (FGGS), 4 had Congenital Anomalies of the Kidney and Urinary Tract (CAKUT), 3 had cystic nephropathy and 1 patient had thrombotic microangiopathy (TMA). Average hemodialysis duration was 3.6 years.

**Results:** Out of the 13 children, 10 contracted COVID-19 infection (76.9%), and 3 patients had two episodes of infection. All episodes were of mild severity. Only 2 needed oxygen support, since they also suffered from portal hypertension and valvular heart disease, respectively and they were both unvaccinated. 3 children in total, required hospitalization, of an average 6 day duration and treatment with remdesivir. There was no need for mechanical ventilation. Out of 13 children, 7 had been vaccinated (53.8%). 5 out of 7 vaccinated children contracted COVID-19 (71.4%), as well as out of the 6 non-vaccinated (83.3%).

**Conclusion:** COVID-19 was frequent and mostly mild in children undergoing hemodialysis in our department. In two children who suffered from comorbidities and were unvaccinated the disease was more severe.

Fr-P 015

**SECOND HOME. ALMOST 40 YEARS OF DIALYSIS AT THE SAME DIALYSIS STATION**

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**Aims/Purpose:** We present long-term experience in renal replacement therapy from childhood to adulthood and numerous complications in the described patient. We also want to honor the Patient, whom each of our team knew well and took part in his treatment.

**Methods:** A case report of a patient undergoing dialysis at the Dialysis Station of University Children's Hospital in Krakow from 1986 till 2023.

**Results:** A 51-year-old patient with end-stage renal disease (ESRD) due to congenital bladder exstrophy, secondary cast urolithiasis and chronic obstructive and reflux nephropathy. In early childhood he underwent multiple surgeries to remove kidney cast stones and obtain closure of bladder mucosa, reconstruct the external genitalia. At the age of 13 (1986) severe clinical condition led to initiation of renal replacement therapy (peritoneal dialysis, then hemodialysis 3 times a week). In 1989 left kidney was removed due to recurrent deep subcutaneous tissue abscesses. In 2002 parathyroidectomy was performed because of advanced hyperparathyroidism. In 2007 the patient received a kidney transplant with formation of Bricker ileal conduit, complicated by hematoma, necrosis of the ureter and intestines, abscesses of the abdominal skin, and then need to remove the transplant, which resulted in disqualification from the potential next transplant. Complications of ESRD in the patient: chronic circulatory failure, growth deficiency, uremic osteodystrophy (2014 – hip arthroplasty), significant chronic ion disorders (hyperphosphatemia, hypercalcemia), HCV infection (asymptomatic). There was also a significant hearing loss (probably drug-induced), requiring a hearing aid. In 2021, after bleeding from an arteriovenous fistula (operating for over 25 years), a permanent catheter was inserted into the jugular vein. The patient had been on dialysis in our center for over 37 years. He did not require erythropoietin throughout the treatment period. Apart from diagnostic hospitalizations and the above-mentioned complications, he has never required acute admission for the last 25 years. Until the end, he remained independent, well-groomed, cheerful, grateful for help and close to the entire team. He died of a hip fracture, complicated by sepsis.

**Conclusion:** Managing a patient on dialysis for many years brings great challenge and satisfaction for the whole medical team.

Fr-P 016

PLEURAL EFFUSION COMPLICATING ACUTE PERITONEAL DIALYSIS IN SHIGA TOXIN PRODUCING E.COLI HEMOLITIC UREMIC-CHILDREN

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**Aims/Purpose:** We report three STEC-HUS-children admitted to our unit between September 2017 and October 2018, who developed pleural effusion after low-volume peritoneal dialysis.

**Methods:** The diagnosis of STEC-HUS was made by the presence of the triad of hemolytic anemia, thrombocytopenia, and acute kidney injury and the identification of Shiga toxin producing *E. coli* in faecal samples. The diagnosis of pleural effusion was made with clinical and radiological criteria.

**Results:** The patients' characteristics are summarized in the Table.

	Clinical data		
	Patient 1	Patient 2	Patient 3
Gender	Male	Female	Male
Age years	2	2	3
Hemorrhagic diarrhea	Yes	Yes	Yes
HUS	D+STEC No serotype isolation vtx2/eeae +	D+STEC O26:H11 Stx2a	D+STEC O26:H11 Stx2a
Comorbidities	No	No	Diaphragmatic hernia
Pleural effusion	4th day of PD	2nd day of PD	1st day of PD
Side	Right	Bilateral (Right more than left)	Right
Intervention	stop PD and start CVVH	stop PD and start CVVH	Continue PD till full recovery
Drainage	chest tube for 2 days	chest tube for 15 days	chest tube for 20 days
Complication	bowel perforation	bowel perforation, deep venous thrombosis, cerebral haemorrhage and posterior reversible encephalopathy syndrome, hepatic ischemia	bowel obstruction

All three patients developed acute renal failure requiring peritoneal dialysis, initiated at low fill volume (10 ml/kg). They all presented respiratory symptoms few days after the dialysis start and diagnosis of right-side pleural effusion was made. They all had gastrointestinal complications late on which required major surgery.

**Conclusion:** Hydrothorax results when dialysate passes from the peritoneal cavity into the pleural space. The mechanism is still not clear, though a high pressure gradient between the cavities and high dialysate volumes can predispose to hydrothorax. As our patients all developed pleural effusion at a low fill volume we do not believe that the high peritoneal pressure was the main cause of the fluid movement. STEC-HUS-patients have been described by Burtani et al. to be more likely to develop pleural effusion while receiving peritoneal dialysis compared with those who received peritoneal dialysis other causes. In these patients tissue edema and fluid collection in cavitory spaces is likely the consequence of microvascular leakage, mediated by Shiga toxin induced expression of SDF-1. Microvascular leakage may account for the high incidence of peritoneal-hydrothorax in STEC-HUS patients. We suggest that pleural effusion should be suspected in every child undergoing peritoneal dialysis who develops acute respiratory symptoms, especially in severe STEC-HUS.

References

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Fr-P 017

## ENCAPSULATING PERITONEAL SCLEROSIS: A PEDIATRIC CASE REPORT

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**Aims/Purpose:** Encapsulating peritoneal sclerosis (EPS) is a rare but fatal complication of long-term peritoneal dialysis. It is characterized by diffuse thickening and encapsulation of the bowel and peritoneum that may compromise digestive tract function. In this report, we describe a case of EPS in a 12-year-old boy

**Results:** Observation. A 12-year-old boy with a history of chronic renal failure due to bilateral high-grade vesicoureteral reflux has been on automated peritoneal dialysis since the age of 2 years. During his dialysis a 10 years period, he presented several episodes of bacterial peritonitis. He presented with chronic persistent epigastric pain, occasionally associated to vomiting. Gastric endoscopy showed signs of gastritis. As symptoms kept on aggravating with anorexia and weight loss MRI was performed. It showed aspects of encapsulating peritoneal sclerosis. The patient received steroids, enteral feeding. He was switched to haemodialysis. In spite of these measures, he was not improved and developed symptoms of acute intestinal obstruction with acute abdominal distension, fecaloid vomiting and septic shock. Abdominal computed tomography scan revealed small bowel distension with fluid levels, localized fluid collections, absence of pneumoperitoneum. The patient underwent laparotomy. At abdominal exploration small bowel was covered with a thick cocoon that could not be separated from the intestinal wall. 30 cm of ischemic small bowel were removed. There were multiple perforations of the mid ileum that were repaired with sutures. The patient died within two days after surgery due to refractory hemodynamic instability.

**Conclusion:** EPS is a long-term complication of peritoneal dialysis and typically seen in adults. Rare cases may be diagnosed in the paediatric population and require an appropriate surgical approach that is effective and lifesaving for these patients.

Fr-P 018

**EXTRAGONADAL YOLK SAC TUMOR OF THE PELVIC REGION IN A 9-MONTH-OLD BOY: A CASE REPORT AND TREATMENT CHALLENGES**

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**Aims/Purpose:** To summarize a case of yolk sac tumor manifestation, discuss its treatment difficulties, complications, and highlight the importance of multidisciplinary care management.

**Methods:** We present a case of a 9-month-old boy who presented with constipation, significantly decreased nutrient intake and pelvic mass. The diagnosis of yolk sac tumor stage IV was confirmed with percutaneous needle biopsy. Multiple metastases were also detected in lungs and liver. Chemotherapy with carboplatin, etoposide and bleomycin was initiated. Severe complications of chemotherapy in combination of sepsis manifested after the first course including gastrointestinal bleeding, bone marrow suppression, sepsis with multiple organ dysfunction syndrome and coagulation disorder. The patient was admitted to Pediatric Intensive Care Unit due to progressive failure of kidneys, liver and respiratory system. The patient underwent invasive mechanical ventilation, and a tracheostomy tube was placed later on. Continuous venovenous hemodiafiltration choice was made instead of peritoneal dialysis due to hepatomegaly, severe ascites and increased intra-abdominal pressure. As a result of critical state, severe multiple organ failure unresponsive to active treatment methods, the patient was transferred to the Palliative Care Unit. During one month of palliative care the patient's state has improved: invasive mechanical ventilation was discontinued, ascites abated, inflammatory markers reduced, and general developmental skills revived. Therefore, the patient was transferred to Pediatric Oncology and Hematology and chemotherapy course with carboplatin, etoposide and bleomycin was reintroduced, and well tolerated.

**Results:** Patient was discharged from the hospital in progressive recovery state – oral nutrition was tolerated, developmental skills were improved, respiratory function was sufficient without invasive methods nor tracheostomy tube. He tolerated the three subsequent chemotherapy courses and there were no complications as well as reduced metastases in the liver and lungs.

**Conclusion:** Extragonadal yolk sac tumors (grade IV) are extremely rare and raise diagnostic and treatment challenges as only a few cases are reported worldwide in English literature. The management requires a combined modality of chemotherapy with multidisciplinary care.

Fr-P 019

## IMPACT OF THERAPEUTIC PATIENT EDUCATION ON KNOWLEDGE'S AND ATTITUDES OF HEMODIALYSIS CHILDREN

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**Aim/Purpose:** We aimed to evaluate how attending therapeutic educational workshops improved a group of patients' short term knowledge's and attitudes.

**Methods:** We conduct a descriptive study of the short-term effect of Therapeutic patient education (TPE) of hemodialysis children in the pediatric department of Sahloul Sousse Tunisia. knowledge and attitudes were assessed via a questionnaire distributed to children and their parents before and after 3 educational sessions concerning the clinical manifestations, nutritional and therapeutic aspects with appropriate attitudes towards emergencies.

**Results:** 12 patients were included in our educational program, mean age was equal to 14 years old. Sex-ratio = 5/1. The average age of onset of chronic kidney disease was 7 years old and hemodialysis duration varied between 1-8 years. CAKUT was the most frequent cause of extra-renal therapy. Knowledge about the disease was assessed via first 7 questions, significant increase of correct answers (49% before TEP to 62.5% after) was noticed, nutritional knowledge was the most impacted aspect with an increase of 18% of correct answers. Treatment knowledge had also improved with a raise from 65.49% to 82.9%. Attitudes towards emergency situations of the disease was significantly improved after TPE (from 56.6% to 78.7%).

**Conclusion:** Chronic kidney disease requires complex care and therapeutic patient education is necessary in the development of a care pathway adapted to each stage.

Fr-P 020

TENCKOFF CATHETER DYSFUNCTION IN CHILDREN ON CHRONIC PERITONEAL DIALYSIS: A SINGLE CENTER EXPERIENCE

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**Aims/Purpose:** Chronic peritoneal dialysis is a frequently used dialysis modality in children with end-stage kidney disease. The most commonly used are Tenckhoff catheters, after surgical placement. This technique may be associated with several complications, particularly catheter dysfunctions. In this report, we discuss the frequency and factors related to peritoneal dialysis catheter's dysfunction in the paediatric nephrology department of Sahloul.

**Methods:** We retrospectively reviewed medical charts of children with end stage renal disease having chronic peritoneal dialysis between 2012 and 2022, in the department of paediatric nephrology at the university hospital Sahloul (Sousse).

**Results:** We included 35 patients, aged from 7 months to 16 years at dialysis initiation. The most common cause of renal failure was vesicoureteral reflux. Mean age at catheter insertion was 8.3 years. Catheters were inserted by a paediatric surgeon in all the cases. Mean delay of first catheter use was 14 days after placement. Peritonitis was the most common complication affecting 57% of peritoneal dialysis catheters. Migration and bleeding, which occurred in 22% (8 cases) and 8.5 % (3 cases) of cases, respectively. One patient developed pleural effusion requiring chest drainage and transfer to intensive care unit, another one had a pneumoperitoneum. One patient presented a chyloperitoneum, associate to a chylothorax leading to technique change. Hydrocele occurred in three cases. Inguinal hernia in two cases and umbilical hernia in 2 cases. Surgical repositioning as well as replacement of the catheter was required in 14% of the patients each. Three patients required a switch to haemodialysis. The most common cause of dysfunction was constipation.

**Conclusion:** Catheter dysfunction in peritoneal dialysis may be significant and lead to surgical management and or a change of dialysis modality, and must therefore, be prevented.



# POSTER SESSION 1B

## CKD

Fr-P 022

RESPONSE TO rhGH TREATMENT IN CHILDREN WITH AUTOSOMAL RECESSIVE POLYCYSTIC KIDNEY DISEASE

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**Purpose:** Approximately 40% of children with chronic kidney disease (CKD) achieve a height below the third percentile compared to their peers. Short stature has a negative impact on the quality of life, self-acceptance, and psychosocial relations. Autosomal Recessive Polycystic Kidney Disease (ARPKD) may affect growth independently of decreased kidney function, perhaps due to disturbances in the growth hormone/insulin-like growth factor (IGF)-1 axis or via decreased expression of growth hormone receptors in the liver. The objective of this study was to compare growth parameters in children with ARPKD to those with other congenital causes of CKD in a retrospective case-control study.

**Methods:** Height SD scores (z-scores) at the start of rhGH treatment and the annual change in height z-score were analyzed in children with ARPKD (n = 18) – group A compared with matched children with kidney hypodysplasia or obstructive uropathy – group B (n = 18). In each group, there were 13 boys and 5 girls with CKD stage II-IV, qualified for growth hormone (rhGH) treatment (height Z-score < -1.88). Glomerular filtration rate (eGFR) and IGF-1 levels were compared at the beginning and after 12 months of rhGH treatment in both groups. All patients received somatotropin at a dose of 0,05 mg/kg/day subcutaneously.

**Results:** Children in the study groups did not differ in, median age (group A – 7.3, IQR 5.5–12.3 years; group B – 7.9, IQR 5.6–12.5 years), or eGFR at the beginning of rhGH treatment (group A – 35 vs group B – 35.6 ml/min/1.73m<sup>2</sup>). Median height z-score in children with ARPKD was -2.95 IQR (-3.2;-2.3) vs group B -2.2 IQR (-2.8;-1.7) p = 0.021. After 12 months of rhGH treatment, the median height z-score in groups A and B were -2.05 IQR (-2.95;-1.62) and -1.15 IQR (-2.3;-1.0) respectively p = 0.024. The mean growth rate (delta height z-score) was higher in group B (0.83 vs 0.7 p < 0.05). Mean eGFR after 1 year of treatment did not differ between the groups (37.5 – group A vs 32.3 ml/min/1.73m<sup>2</sup> – group B, NS). The mean IGF-1 level was significantly higher in the control group at the beginning and after 12 months of treatment (p = 0.04 and p = 0.002 respectively).

**Conclusion:** 1. The growth rate of ARPKD patients treated with rhGH was lower compared to children with hypodysplasia/obstruction uropathy independent of the CKD stage. 2. Lower IGF-1 levels in children with ARPKD may be one of the reasons for the poorer response to rhGH treatment.

Key words: ARPKD, rhGH treatment, chronic kidney disease

Fr-P 023

**ROUTINE BLOOD PRESSURE MEASUREMENTS IN CHILDREN IN PRIMARY CARE SETTING: ARE WE DOING IT RIGHT? A PARENTAL SURVEY**

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**Introduction and Aims:** Increasing prevalence of arterial hypertension (AH) in children and adolescents represents a major global health problem. European Society of Hypertension (ESH) highlights routine measurements of blood pressure (BP) in children and adolescents as simple non-invasive tool that can help to timely identify children at risk at a minimal cost. However, strict adherence to recommended techniques of BP measurement are essential for reliable results. The aim of the study was to evaluate real-life BP measurement practices in Lithuanian children at the primary care setting and compliance with ESH guidelines.

**Methods:** Web-based cross-sectional survey was conducted in Lithuania from October 2022 to January 2023 for parents having children up to 18 years of age. The questionnaire consisted of 15 questions related to BP measurements practices in the primary care setting, including illustrations as references.

**Results:** 1504 parents answered the questionnaire. The mean age of children was  $5.1 \pm 3.9$  years, 47.3% were girls, 4.7% had chronic disease like diabetes, chronic kidney or heart disease; 12.9% were born premature or stayed in neonatal intensive care unit and 1% were already diagnosed with AH. 33.1% of the parents reported that their children had BP measured at least once in the primary care setting. Among the latter, BP was measured annually in majority (74.9%) of cases. BP was measured at rest in 81.5% of children and 62.7% parents reported the use of appropriately sized upper arm cuff (as indicated by illustration). Majority of parents (83.7%) reported that BP was measured only one time during the visit. 42.6% reported incorrect positioning of the child during measurements – child was not sitting straight, feet not resting on the floor, arm was not relaxed or upper arm cuff was not placed at the same level as the heart. Physician feedback on BP results to the parents was reported in 24.9% cases only.

**Conclusion:** Our study showed that primary care physicians in Lithuania do not follow the recommended practices on BP measurements with poor compliance with ESH guidelines.

Fr-P 024

URINARY BETA2MICROGLOBULIN AS BIOMARKER OF RENAL FUNCTION IN NEONATES ADMITTED TO NICU

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**Aims:** The optimal way to assess kidney damage in neonates remains debated. Several biomarkers have been studied and serum creatinine (sCr), the current gold standard, is a useful, but limited index. Purpose of this study was to investigate the values of urinary beta2microglobulin (uB2M) in first days of life in newborns admitted to Neonatal intensive care unit (NICU) and its trend in acute kidney injury (AKI).

**Methods:** We enrolled in this single center, prospective, observational trial all newborns admitted to NICU, regardless of gestational age (GA), birth weight and comorbidities. uB2M excretion was measured, expressed as uB2M/urinary creatinine (uCr) ratio ( $\mu\text{g}/\text{mg}$ ), from postnatal days 1 to 15, every time sCr was measured according to clinical indication. Urine output was monitored daily. All the patients with at least 2 sCr and 1 uB2M values were enrolled. We defined AKI as an increase in sCr of at least 0.3 mg/dL or urine output lower than 1 ml/kg/h, based on the modified neonatal Kidney Disease: Improving Global Outcomes (KDIGO) definition.

**Results:** 41 neonates were enrolled (20 females), with a median GA of 33.6 weeks (26–41) and median birth weight of 1750 g (680–3770). Nephrotoxic medication exposure was present in 31/41 patients (75.6%), surgery in 4/41 (9.8%), clinically significant ductus arteriosus in 3/41 (7.3%). 6 patients developed AKI (14.6%). uB2M/uCr was higher in patients with AKI than in those with normal kidney function (mean = 297.4 vs 69.7  $\mu\text{g}/\text{mg}$ , median = 181.3 vs 40.7, considering all 76 measurements, including repeated measures). We tried to evaluate the longitudinal behavior of uB2M/uCr in individual patients, even if with the limitation of a small number, using a mixed model with random intercept for patients. The only variables significantly associated with uB2M/uCr values in the model were the diagnosis of AKI (with higher uB2M/uCr values in AKI, coefficient = 204.6,  $p = 0.0006$ ) and GA (coefficient = -14.8 per week of GA,  $p = 0.005$ ). uB2M/uCr values in newborns seem to decrease with the increase of GA, with a mean reduction of about 15  $\mu\text{g}/\text{mg}$  per week of GA. Establishing a threshold of  $> 130 \mu\text{g}/\text{mg}$  (corresponding approximately to  $> 80$ th percentile), uB2MG/uCr was higher than this limit in at least one measurement in 4/6 patients with AKI (66.7%) and in 4/35 neonates without AKI (11.4%;  $p = 0.009$ ).

**Conclusion:** uB2MG is a promising biomarker of kidney damage in newborns admitted to NICU. Since uB2MG may reflect both physiological tubular immaturity and tubular damage, further work is needed to evaluate potential reference values for the diagnosis of AKI in this population.

Fr-P 025

**REAL-WORLD EVIDENCE OF LISINAPRIL IN PEDIATRIC HYPERTENSION AND NEPHROPROTECTIVE MANAGEMENT: A 10-YEAR COHORT STUDY**

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**Background:** Pediatric hypertension (pHTN) occurs in 2 to 4% of children and is expected to further increase due to the obesity epidemic. Currently, most children have hypertension due to renal dysfunction. A commonly used antihypertensive and nephroprotective agent in Europe is lisinopril, an angiotensin-converting enzyme inhibitor (ACE-I), currently prescribed off-label. A limited number of studies have been conducted that evaluate long-term safety and potential biomarkers relevant to achieve blood pressure- or proteinuria reduction.

**Methods:** A monocentric observational study was conducted at the Ghent University Hospital, Belgium between 2011–2021. A total of 91 participants between 1 and 18 years with hypertension and/or proteinuria were included with over 2200 standard-of-care outpatient visits. The data were stratified according to three groups: chronic kidney disease (CKD), pHTN without CKD and proteinuria without HTN and without CKD (PT) to correlate with clinical use. Treatment target was defined as blood pressure lower than the 95th percentile and proteinuria lower than 0.2 g/g creatinine. Exploratory data analysis, descriptive analysis, and a linear multiple regression model was built, using Prism (version 8.4.0, 2020), R Studio (version 2022.12.0+) and SPSS (version 28.0, 2021).

**Results:** The mean age of the participants was 7.5 years (SD = 4.5) with a mean eGFR of 130 ml/min/1.73m<sup>2</sup> (SD = 45) at baseline and a lisinopril starting dose of 0.07 mg/kg/day. An eGFR of less than 60 ml/min/1.73m<sup>2</sup> was present in 16% of patients and 7% developed an eGFR lower than 45 ml/min/1.73m<sup>2</sup> during follow-up. Blood pressure reduction was achieved in 47% and 45% of patients (n = 61) after 24 weeks for systolic and diastolic blood pressure, respectively. Proteinuria disappeared in only 16% of participants (n = 36) at 24 weeks. The covariates eGFR, gender, age, obesity and exploratory parameters renin, aldosterone, aldosterone-renin- as well as mineralocorticoid ratio were not independently significant for either treatment target at 24 weeks. Hyperkalemia (defined as higher than 5.5 mmol/L), occurred in 7 cases (3 cases with CKD) but resulted in dose reduction in only 4/7.

**Conclusion:** Pediatric use of lisinopril in monotherapy reaches blood pressure control in almost half of the cases after 6 months, but proteinuria control in less than a tenth of patients. Demographic and exploratory covariates do not affect results at 6 months.

Fr-P 026

**IDIOPATHIC NEPHROTIC SYNDROME IN CHILDREN BEFORE AND DURING COVID-19 PANDEMIC: A SINGLE-CENTER RETROSPECTIVE STUDY**

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**Aims/Purpose:** Pediatric patients with idiopathic nephrotic syndrome (NS) are at greater risk of infections regardless of whether they receive long-term immunosuppressive therapy. Infections may also lead to relapses of NS. We performed a single-center retrospective study to estimate the severity of all COVID-19 infections reported in children with idiopathic NS. We also evaluated the risk of new-onset idiopathic NS and relapses of those children with a known diagnosis of idiopathic NS during the COVID-19 pandemic compared to previous data.

**Methods:** We conducted a retrospective study comparing two periods, 2014–2016 to 2020–2022, regarding the cases of new-onset idiopathic NS and the number of relapses per subject per year. We also reported the severity of all COVID-19 infections in children with idiopathic NS.

**Results:** During the 2014–2016 period, 12 cases with new-onset idiopathic NS were identified, while only two new cases were noted during the 2020–2022 period. The paired rate ( $\pm$  SD) of relapse per subject per year was significantly lower ( $p = 0.01$ ) and less severe during the pandemic period (relapses per subject per year:  $0.5 \pm 1$ ) compared to the pre-pandemic period (relapses per subject per year:  $1.5 \pm 0.9$ ). A total of 25 cases of children with idiopathic NS and COVID-19 infection have been reported. The disease course was mild for all patients with idiopathic NS during the COVID-19 pandemic. There were no relapses due to COVID-19 infection.

**Conclusions:** The number of cases with new-onset idiopathic NS and disease relapses was lower during the COVID-19 pandemic, likely due to reduced exposure to other infectious triggers. Children with idiopathic NS, with or without immunosuppression, are not at higher risk of severe COVID-19 infection. COVID-19 infection did not trigger disease relapses.

Fr-P 027

EVALUATION OF SARS-COV-2 SEROPREVALENCE BEFORE AND AFTER THE COVID-19 VACCINE PERIOD IN CHILDREN WITH CHRONIC KIDNEY DISEASES

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**Aim:** During the COVID-19 pandemic, pediatric patients diagnosed with CKD were exposed to the SARS CoV-2 virus. We aimed to evaluate SARS-CoV-2 seropositivity in pediatric patients with CKD before and after the adult vaccination program, and to measure the effect of parental vaccination in the home environment on the child.

**Method:** Pediatric patients with chronic kidney disease (kidney transplant recipients, patients receiving HD/PD, and stage 2-5 CKD) followed up regularly were included in the study. Patients were divided into two groups: the pre-vaccination period from January 2021-2022 and the adult vaccination period after January 2022. Anti-SARS-CoV-2 antibodies against the S1 domain of the SARS-CoV-2 spike protein were investigated with a micro ELISA kit.

**Results:** A total of 182 patients with a mean age of  $11.0 \pm 4$  years and 55% male were included in the study. 54.4% of patients were kidney transplant recipients, 9.9% were HD/PD patients, and 35.7% were stage 2-5 CKD patients. Of all the patients, 57 (31.3%) were seropositive and 125 (68.7%) were seronegative. The mean age was similar between seronegative and seropositive. Seropositivity rate is 30.3% in kidney transplant recipients, 38.8% in HD/PD patients and 30.7% in stage 2-5 CKD patients, respectively. The rates of primary kidney disease and the presence of immunosuppressive therapy were similar between seronegative and seropositive patients ( $p = 0.865$ ). Anti-SARS CoV-2 antibody positivity was 24.1% in the pre-vaccination period and 43.9% in the post-vaccination period ( $p < 0.05$ ). The proportion of patients with symptoms were higher in the post-vaccine period compared to pre-vaccine (95% vs. 54%;  $p < 0.05$ ). Symptoms that may be associated with COVID-19 were fever (40%), cough (33%) and GI symptoms (25%) in order of frequency. The rates of compliance with the isolation rules (mask, social distance, hand washing) and stay-at-home consciousness were significantly higher in the pre-vaccination period ( $p < 0.05$ ). In total, 53.8% of patients underwent PCR testing; of these, 15.3% were PCR positive. 66.6% of PCR positive patients were seropositive.

**Conclusion:** Seropositivity rate and symptom frequency in patients with CKD increased after community immunization. This can be attributed to the decreased sensitivity to the preventive measures introduced by the vaccination program.

Fr-P 028

## THE IMPORTANCE OF DETECTING MASKED HYPERTENSION IN OBESE CHILDREN AND ADOLESCENTS

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**Aims/Purpose:** Masked hypertension (MH) is defined as an office and home normotension with ambulatory hypertension. It occurs in approximately 10% of children and adolescents and it is known that the prevalence is greater in obese patients. Both patients with MH and obesity have higher risk for adverse cardiovascular outcome later in life. The aim of our study was to establish the prevalence of MH in a group of obese, but otherwise healthy children and adolescence, to point out the differences in blood pressure (BP) values between normal weight and obese children and to determine are there some parameters in 24-hour ambulatory blood pressure monitoring (ABPM) that could predict MH.

**Methods:** In this study we included 161 children and adolescents of both genders, who underwent ABPM at the Department of Pediatrics, Sestre Milosrdnice University Hospital Center Zagreb, Croatia. Data were processed using a software SPSS version 20.0, with the values of  $p = 0.05$  as the minimum level of statistical significance.

**Results:** Among 161 participants, 119 (73.91%) were obese, and 42 (26.09%) were normal weight healthy children. 27.73% (33) of obese patients and 4.76% (2) of normal weight patients had MH. When we categorized obese patients according to BMI Z-score, 50% of those with Z-score above 3.55 had MH. Obese patients with MH had significantly higher systolic and diastolic office BP ( $p = 0.002$ ,  $p = 0.003$ , respectively) and ABPM daytime and nighttime systolic and diastolic BP values ( $p = 0.001$ ) compared to obese children without MH. Daytime systolic blood pressure variability was also significantly higher among obese patients with MH ( $p = 0.001$ ), as well as morning blood pressure surge (MBPS;  $p = 0.003$ ). Using logistic regression analysis to predict MH based on ABPM parameters showed that high daytime systolic BP load could predict MH ( $p = 0.017$ ).

**Conclusion:** In monitoring obese patients, high normal office BP and high BMI Z-score should arouse suspicion of MH while higher daytime systolic BPV, BP load and MBPS values in ABPM of those patients are red flags that could help us predict which patients are in greater risk of adverse outcomes.



Fr-P 029

EFFECT ON BLOOD PRESSURE AND CARDIOVASCULAR RISK (CVR) FACTORS IN PEDIATRIC PATIENTS DURING COVID-19 PANDEMIC CONFINEMENT (COBECOR STUDY)

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**Aims/Purpose:** Patients monitored in the CVR consultation usually present overweight/obesity, metabolic syndrome, hypertension (HT), unhealthy lifestyle with great resistance to change, influence of the environment and, frequently, psychosocial limitations. We asked whether home confinement for COVID-19 (March–May 2020) could have negative effects in relation to CVR in these patients.

**Methods:** Assess this hypothesis with respect to HT and the use of antihypertensive drugs in these patients. Secondary objective: assessed changes in other parameters (body mass index (BMI), level of physical activity and diet).

**Results:** Retrospective cohort study with review of 738 ambulatory blood pressure monitoring (ABPM) between 2019–2022 obtaining, after applying the exclusion criteria (no overweight/obesity, poor therapeutic compliance, underlying renal pathology or failure to perform two ABPM in the study period), a final cohort of 46 patients divided into two groups (23 each): one group exposed to home confinement (G1) with one ABPM before and after home confinement and another group not exposed to confinement (G2) with two ABPM in different periods between 2021–2022. Blood pressure (BP) percentile values, dipper pattern, variability and blood pressure load, as well as the rest of the CVR parameters were compared in both periods. The mean age was 13 years (13.8 G1/13.2 G2) with a mean time between the 1st and 2nd ABPM of 11 months (11.08 G1/10.95 G2) and a greater reduction in BMI in G2 than in G1 (1.05 G1/1.21 G2). Despite this, results were not statistically significant nor were the differences in HBP or worsening of the dipper pattern (30.4% in G1 and 21.7% in G2). We did observe differences ( $p < 0.022$ ) in the use of antihypertensive drugs, although contrary to our initial hypothesis, with greater use of drugs in G2.

**Conclusion:** Although the low sample size, the biases inherent in the design and the lack of previous studies make the interpretability and statistical significance of some results difficult, they reinforce that the measures during confinement did not contemplate all spheres of health and the need to implement specific CVR consultations. Obesity and its associated pathologies are an important public health problem that pediatricians have the responsibility to address.

Fr-P 030

**VEDOLIZUMAB INDUCED INTERSTITIAL NEPHRITIS IN A CHILD WITH VERY EARLY ONSET INFLAMMATORY BOWEL DISEASE: A CASE REPORT**

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**Aims:** Inflammatory bowel disease (IBD) may be complicated by renal involvement. The most common renal diseases are nephrolithiasis, interstitial nephritis, glomerulonephritis and amyloidosis. Presumed pathogenic mechanisms may be related to intestinal activity or are independent of the bowel disease. Also drug induced nephrotoxicity has been reported, mainly in immunosuppressants and monoclonal antibodies. Here, we present a case of a boy with very early onset (VEO)-IBD and severe chronic interstitial nephritis.

**Methods:** Here, we present a case of a boy with VEO-IBD and persistent increased level of renal parameters. Kidney biopsy revealed chronic tubulointerstitial nephritis.

**Results:** A seven-year-old boy manifested IBD at the age of 2 years. His disease was classified as VEO-IBD. He was initially treated with conventional therapy (corticosteroids, azathioprin). After several attempts to withdraw corticosteroids his bowel disease always relapsed. First line biological therapy infliximab was started at the age of 3 years. Infliximab was switched to adalimumab after 5 months due to poor control of the disease activity. The latter also did not prove effective, colonoscopy showed florid inflammatory changes in colon and terminal ileum. Therefore, vedolizumab (integrin receptors antibody) treatment was started at the age of 4 years. At the same time the therapy needed to be intensified because of the severe relapse with pancolitis. Later all the immunosuppressive medication was stopped except for vedolizumab. At the age of 7 his kidney parameters increased and urinalysis showed leucocyturia and tubular proteinuria. Renal biopsy revealed morphology of prolonged interstitial nephritis with extensive inflammatory destruction of tubules and interstitium, glomerular fibrosis (30% of glomeruli) and destruction of glomeruli (50% of glomeruli). Overall, the sample showed severe chronic changes. These histological findings were strongly suspicious of drug-induced toxicity. Therapy with corticosteroids and ACE inhibitor was started and vedolizumab treatment was discontinued. After wash-out period ustekinumab was initiated. The patient has been followed-up with stable kidney function (CKD, stage 3) and mild proteinuria.

**Conclusion:** Clinicians should be aware of the kidney involvement in IBD patients. Monitoring of kidney function and urine chemical examination should be included in regular follow-up tests of children with IBD.

Fr-P 031

FACTORS ASSOCIATED WITH FATIGUE IN CHILDREN WITH CHRONIC RENAL FAILURE

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**Aims/Purpose:** We aimed to detect factors, including dietary acid load, effective on PedsQL Multidimensional Fatigue Scale in children with chronic kidney disease (CKD).

**Methods:** A total of 31 children aged 10–18 years with the diagnosis of CKD stage III–V were included in the study. Anthropometric measurements and 3-day food consumption records were taken to evaluate the nutritional status. The net endogenous acid production (NEAP) score and potential renal acid load (PRAL) were calculated to determine dietary acid load. Laboratory findings and the “PedsQL Multidimensional Fatigue Scale” composed of three subscales were used to assess the fatigue score.

**Results:** The mean age of the cases (M/F = 20/11) was  $10.75 \pm 2.3$  years. Total fatigue score was significantly correlated with an erythrocyte sedimentation rate ( $p = 0.002$ ,  $r = 0.574$ ), urea ( $p = 0.001$ ,  $r = 0.629$ ), eGFR ( $p < 0.001$ ,  $r = -0.625$ ), PTH ( $p = 0.003$ ,  $r = 0.524$ ) and hemoglobin ( $p = 0.029$ ,  $r = -0.392$ ) levels. NEAP or PRAL had no effect on fatigue. Their levels were similar between the patients with CKD Stage III vs. Stages IV and V. When regression analysis was assessed, eGFR was the only independent factor effecting fatigue ( $p < 0.001$ ).

**Conclusion:** This study showed that decreasing eGFR is associated with increased fatigue, and dietary acid load determined by NEAP or PRAL had no effect on fatigue in children with CKD.

Fr-P 032

RETROSPECTIVE ANALYSIS OF A PEDIATRIC TUBEROUS SCLEROSIS POPULATION

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**Aims/Purpose:** The primary purpose of this study was to evaluate the incidence of angiomyolipomas and renal cysts in pediatric patients with tuberous sclerosis. The secondary objectives of the study were as follows: to assess the correlation between specific genetic alterations and the presence of angiomyolipomas and cysts, to evaluate renal outcome (renal function and blood pressure) and the size changes of angiomyolipomas in patients who started everolimus therapy due to neurological symptoms.

**Methods:** This was a retrospective multicenter observational study. All pediatric patients (under 18 years of age) with a diagnosis of tuberous sclerosis evaluated at 4 medical centers of the Italian region of Emilia Romagna between 01/01/2018 and 06/31/2021 were included in the study.

**Results:** 57 patients were identified, 23 females and 34 males. Thirty-six (63%) of the patients had cysts and 23 (40%) had angiomyolipomas. Seizures in postnatal diagnoses were the most common symptom at onset. Forty (70.1%) patients had renal involvement. Seven patients were prescribed everolimus therapy: the size of the angiomyolipomas of 2 patients remained unchanged, one patient's cysts decreased in size, one patient showed a reduction in size however embolization was required, and one patient was lost to follow-up.

**Conclusions:** Renal involvement, in terms of both cysts and the presence of angiomyolipomas, is frequent in pediatric patients. The number and size of the angiomyolipomas increase with age. Everolimus seems to be effective in slowing angiomyolipoma growth. A multidisciplinary approach including kidney ultrasound evaluation is important for pediatric patients with tuberous sclerosis and should be started at diagnosis.

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Fr-P 033

**THE ASSOCIATION OF SERUM NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN AND CYSTATIN-C WITH BLOOD PRESSURE IN EX-PRETERM CHILDREN AND ADOLESCENTS**

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**Aims/Purpose:** Preterm birth is a risk factor for the development of chronic diseases, such as hypertension, throughout life course. The aims of the study were to evaluate serum biomarkers in ex-preterm children and examine for associations with office and ambulatory blood pressure (BP) parameters.

**Methods:** This case-control study included children and adolescents born prematurely (ex-preterms) and at full term (controls) who underwent office and ambulatory BP monitoring and assessment of central systolic BP (cSBP). Neutrophil gelatinase-associated lipocalin (NGAL), matrix metalloproteinase-2, -9 (MMP-2, -9), and Cystatin C (CysC) were measured using enzyme-linked immunosorbent assay

**Results:** Serum biomarkers levels did not differ between groups. In univariate analysis, NGAL presented significant correlations with office and day SBP z-score and CysC with office DBP z-score and cSBP z-score in the ex-preterm group. 38% and 17% of the ex-preterm children presented office and ambulatory BP hypertension respectively. Half of the ex-preterm children had white-coat hypertension. ROC analysis showed that NGAL could predict hypertension in ex-preterm children (AUC:0.713,  $p = 0.010$ ), while CysC predicted high cSBP (AUC:0.687,  $p = 0.024$ ).

**Conclusion:** In ex-preterm children, serum NGAL was significantly associated with peripheral SBP, and serum CysC with cSBP suggesting the possible role of these biomarkers on early prediction of hypertension development in ex-preterm children.

Fr-P 034

**BURDEN, DISTRESS, QUALITY OF LIFE AND COPING STYLES IN CAREGIVERS OF CHILDREN WITH CHRONIC KIDNEY DISEASE IN DIFFERENT STAGES!**

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**Aims/Purpose:** Caregivers of children with chronic kidney disease (CKD) are exposed to several circumstances that may lead to adverse psychosocial consequences. As literature is scarce, we envisage that this study will help us know the extent of these problems, and whether such issues increase with advanced stages of CKD.

**Methods:** This is an observational study whereby 50 consecutive caregivers of children with CKD attending Pediatric Nephrology Unit, PGIMER, at Chandigarh between July 2020 and June 2021, were recruited. They were divided into two groups, one with caregivers of CKD Stage 1-2 and the other with caregivers of CKD Stages 3-5. Caregivers were assessed on WHO QOL Brief Scale for quality of life (QOL), Pediatric Renal Caregiver Burden Scale (PR-CBS) for burden, Depression anxiety stress scale (DASS) scale for distress and Coping Styles. Appropriate statistical tests were applied.

**Results:** Caregivers of children with advanced CKD stages (3-5) reported more depression, anxiety and stress; had poorer QOL and felt a significantly high burden compared to those with initial stages. However, these caregivers opted problem-focused coping strategies (planned problem-solving, positive reappraisal, accepting responsibility and self-controlling) as equally as their counterparts. Families with lower socio-economic status, poor maternal education and lower family income had more stress and poorer QOL. They opted distancing as their coping mechanism. Those who experienced a higher burden also reported a poorer QOL.

**Conclusion:** Severity of disease have a negative impact on QOL, coping strategies, distress and burden of caregivers. Poor socioeconomic status and poor education also worsen the psychosocial problems. These caregivers are at risk of psychosocial problems and may benefit from early psychological interventions.

Fr-P 035  
PSYCHOSOCIAL ASPECTS AMONG CHILDREN WITH CHRONIC KIDNEY DISEASE!

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**Aim:** Children with chronic kidney disease (CKD) encounter various situations due to underlying disease, its treatment and complications. These may lead to various psychosocial problems. We aimed to determine the magnitude of this problem among pediatric CKD patients, and compare the severity of those with early and advanced stages of CKD.

**Methods:** This was an observational study conducted between July 2020 and June 2021 among children with CKD aged 8 to 15 years. They were categorized into 2 groups based on stage of disease (Group I – CKD 1, 2; Group II – CKD 3-5). The primary outcome was to compare the psychosocial aspects among children of both groups using standard assessment scales [Paediatric Quality of life, Adolescent Coping Scale, Children Self Esteem Scale and Pre-Adolescent Adjustment Scales]. Secondary outcome was to compare the effect of various demographic factors, clinical variables and treatment modalities amongst the two groups. Appropriate Statistical tests were applied.

**Results:** We enrolled 50 consecutive children (24 in Group I and 26 in Group II) with Median (IQR) age of  $10.8 \pm 1.8$  years. Children in Group II had significantly lower Peds QOL ( $39.7 \pm 16.6$  Vs  $75.2 \pm 12.3$ ;  $p=0.000$ ), self-esteem ( $33.5 \pm 11$  Vs  $48.2 \pm 6.4$ ;  $p=0.0001$ ) and adjustment ( $11.9 \pm 8.5$  Vs  $21 \pm 5.3$ ;  $p=0.0001$ ) scores and had higher maladaptive coping strategies ( $6.4 \pm 2.5$  Vs  $3.8 \pm 1.5$ ;  $p=0.045$ ). Gaps in schooling and lower maternal education had significant negative impact on Peds QOL, self-esteem and adjustment. Children with higher parental education had increased anxiety levels. Those with underweight, anaemia, mineral bone disease and on haemodialysis [compared to those on continuous ambulatory peritoneal dialysis] had poorer scores.

**Conclusion:** A significant proportion of children with CKD suffer from poor psychosocial effects. Various factors associated with it include severity of disease, presence of complications, gaps in schooling, lower maternal education and haemodialysis (as compared to CAPD). Children with higher parental education had increased levels of anxiety. Early identification, providing comprehensive social support system, ensuring child's education and preventing complications may reduce these inevitable psychological challenges.

Keywords: CKD, QOL, Coping, Adjustment, self-esteem

Fr-P 036

**THE RELATIONSHIP BETWEEN SERUM COPEPTIN LEVELS AND PERITONEAL TRANSPORT PARAMETERS AND BIOIMPEDANCE MARKERS IN PEDIATRIC PATIENTS UNDER PERITONEAL DIALYSIS**

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**Aim/Purpose:** The pathophysiology of hypervolemia in chronic kidney disease (CKD) is based on multiple mechanisms and it is known that arginine vasopressin (AVP) also plays a role. Copeptin is a molecule located at the C-terminus of AVP and is often used instead of AVP in clinical studies. In our study, we first aimed to determine serum copeptin levels in pediatric end-stage renal disease (ESRD) patients undergoing peritoneal dialysis (PD). Depending on copeptin findings, we then aimed to evaluate a possible correlation between bioimpedance parameters (BIA) and peritoneal transport parameters obtained from the peritoneal equilibration test (PET).

**Methods:** The study included 37 PD patients who were followed up in Marmara University Faculty of Medicine, Department of Pediatric Nephrology. The control group consisted of 37 children of the same gender and similar age as the patient group, who did not have acute or chronic diseases. The serum copeptin levels of the patient and control group were evaluated. The patients' peritoneal dialysis fluid copeptin levels, PET and BIA parameters were also evaluated simultaneously and the possible relationship between them was examined.

**Results:** Serum copeptin levels in the patient group were found to be significantly higher than in the control group (7.31 ng/ml vs 2.55 ng/ml,  $p < 0.001$ ). A negative correlation was found between serum copeptin levels and age of the control group ( $r = -0.596$ ,  $p < 0.001$ ). There was no relationship between serum copeptin levels and age and gender in the patient group. No significant correlation was found between serum copeptin levels and PET parameters [ $KpT/V$  ( $r = -0.166$ ,  $p = 0.325$ ),  $KpT_{w}/V$  ( $r = -0.147$ ,  $p = 0.387$ )] in the patient group. No significant correlation was also found between serum copeptin levels and BIA parameters and overhydration (OH).

**Conclusion:** Blood copeptin levels are higher in PD patients with ESRD than in the healthy group. There was no significant relationship between serum copeptin level and BIA and PET parameters. It was thought that further studies should be done on this subject.



Fr-P 037

**FIBROBLAST GROWTH-FACTOR 23 – KLOTHO AXIS, MYOKINE PROFILE AND SYSTEMIC INFLAMMATION IN CHILDREN WITH CHRONIC KIDNEY DISEASE**

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**Aims/Purpose:** Inflammation is identified as a causative factor of bone mineral and muscle disorders in chronic kidney disease (CKD). Nevertheless, clinical data on this issue are limited in pediatric population. Moreover, although CKD is widely considered as a both bone and muscle weakening disease, the interaction between myokine and bone mineral profile has been scarcely explored. This cross-sectional study investigates the link between fibroblast growth-factor 23 (FGF23)/Klotho axis, myostatin/insulin-growth factor-1 (IGF-1) axis and systemic inflammation in pediatric chronic kidney disease (CKD).

**Methods:** Serum calcium, phosphorus, 25-hydroxyvitamin D (25(OH)D), parathormone (PTH), c-terminal FGF23,  $\alpha$ -Klotho, myostatin, IGF-1 and interleukin-6 (IL-6) were measured in 53 children and adolescents with CKD stage 3-5D. Myostatin adjusted to lean mass (LM) and myostatin to IGF-1 ratio were calculated.

**Results:**  $\ln$ IL-6 was correlated to  $\ln$ FGF23 ( $r_s = 0.397$ ,  $p = 0.004$ ),  $\ln$ Klotho ( $r_s = -0.297$ ,  $p = 0.078$ ), myostatin/LM ( $r_s = 0.385$ ,  $p = 0.005$ ) and myostatin/IGF-1 ( $r_s = 0.395$ ,  $p = 0.004$ ) after adjustment for CKD stage. High IL-6 was significantly associated with  $\ln$ FGF23 (OR 3.212, 95% CI 1.442-7.155),  $\ln$ Klotho (OR 0.261, 95% CI 0.083-0.821), myostatin/LM (OR 1.373 95% CI 1.001-1.024) and myostatin/IGF-1 (OR 1.097, 95% CI 1.021-1.180) after adjustment for CKD stage. In backward logistic regression analysis,  $\ln$ FGF23 and myostatin/IGF-1 remained significantly associated with high IL-6. Correlations were observed between myostatin/LM and  $\ln$ FGF23 ( $r_s = 0.423$ ,  $p = 0.002$ ), myostatin/IGF-1 and  $\ln$ Klotho ( $r_s = -0.367$ ,  $p = 0.007$ ), after adjustment for CKD stage, IL-6 and other mineral bone parameters.

**Conclusion:** In pediatric CKD, high FGF23 and myostatin/IGF-1 imbalance are linked with systemic inflammation. Moreover, myostatin/IGF-1 imbalance is correlated to FGF23/Klotho axis, indicating a muscle-bone interplay in this population.

Fr-P 038  
TUBULOINTERSTITIAL NEPHRITIS AND UVEITIS SYNDROME: CASE SERIES

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**Aims/Purpose:** Tubulointerstitial nephritis and uveitis syndrome (TINU) is the inflammation of renal interstitium and uveal tissue. TINU occurs more frequently in young females. Renal disease can be asymptomatic but may cause acute kidney injury and chronic kidney disease. Eye involvement is most commonly bilateral anterior uveitis.

**Methods:** We presented the initial presentation, clinical findings, laboratory results, renal histopathology findings, and prognosis of children with TINU syndrome.

**Results:** We included 15 children (6 female) with TINU syndrome. The mean age at the presentation was 14.3 (9–17) and the mean follow up period was 18.4 (6–37) months. Presenting symptoms were headache (n:1), fatigue (n:3), back pain (n:3), red eye (n:5), photophobia (n:2), fever (n:2), vomiting/nausea (n:3) and muscle weakness (n:1). Muscle weakness developed secondary to hypokalemia and improved after potassium treatment. Two patients had previous history of upper respiratory tract infection. Previous medicines were naproxen, clarithromycin, paracetamol, aspirin and vitamin C, amoxicilline-clavulonic acid, Hyocin-N-Butilbromur-sertraline, escitalopram and ibuprofen. All had non-nephrotic range proteinuria. Eight patients had undergone kidney biopsy. Figure 1 represents one of the patient's renal histopathological findings. All had acute kidney injury but none of them had undergone dialysis. Laboratory features were given in Table 1. Only one patient had permanent kidney impairment and others improved without sequela. Uveitis had occurred two months prior to kidney involvement in one patient. Eight patient had uveitis at the same time. Others had uveitis after TIN onset (1, 4 (n:2), 7, 9, and 11 months later). Eight patient had persistent eye findings at the last control.

**Conclusion:** Children with acute TINU syndrome had severe kidney involvement at the initial presentation. In long term follow up the renal findings improved however severe eye findings had persisted in most of the children. Children with tubulointerstitial nephritis must be checked for eye involvement and uveitis patients vice versa.

Table 1: Clinical and Laboratory Findings of Children with TINU

	Age	Sex	Presenting Symptoms	Previous History of Infection	Previous History of Medicine	Initial Serum Creatinine (mg/dl)	Maximum serum creatinine (mg/dl)	Initial Proteinuria (Dipstick/spot protein/creatinine [mg/mg] 24-hour urine protein [mg/m <sup>2</sup> /hr])	Dipstick Glucosuria	Last control creatinine (mg/dl)	Last control proteinuria (Dipstick/spot protein/creatinine) ([mg/mg])
Case 1	14	Girl	Headache	None	Naproxen	3.23	5.03	1+/0.65/15.4	1+	0.75	Negative /0.12
Case 2	12	Boy	Fever, vomiting	Upper Respiratory Tract Infection	Clarithromycin, paracetamol	1.37	2.2	1+/0.18/3.68	1+	0.81	Negative /0.1
Case 3	12	Girl	Fever, vomiting	Upper Respiratory Tract Infection	Amoxicillin-clavulanic as, paracetamol, ibuprofen	1.27	1.27	2+/0.2/4.85	Negative	0.5	Negative /0.06
Case 4	10	Boy	Fatigue	Balanitis	None	0.8	0.86	1+/0.53/7.93	1+	0.56	Negative/0.18
Case 5	12	Girl	Fatigue	None	None	1.24	1.36	2+/1/11.13	1+	0.74	Negative/0.17
Case 6	16	Boy	Muscle weakness	None	None	2.5	2.5	1+/0.59/25	3+	1.25	Negative /0.06
Case 7	15	Boy	Photophobia/polyuria	None	None	1.27	1.27	1+/0.25	1+	0.87	Negative/0.05
Case 8	13	Girl	Red eye, back pain	None	None	1.2	1.2	2+	Negative	0.87	Negative/0.11
Case 9	14	Boy	Red eye, photophobia	None	None	1.1	1.1	1+/0.3	1+	0.76	Negative/0.01
Case 10	15	Boy	None	None	None	1.23	1.23	1+	Negative	0.8	Negative/0.06
Case 11	16	Girl	Red eye, back pain	None	None	1.47	1.47	1+	Negative	0.6	Negative/0.07
Case 12	17	Girl	Vomiting, back pain, polyuria	None	Hyocin-N-Butilbromur-paracetamol	1.69	1.89	1+	1+	0.8	Negative
Case 13	16	Boy	Back pain, photophobia	None	None	1.4	1.8	1+/0.25	Negative	0.96	Negative/0.07
Case 14	16	Boy	Fatigue	None	Aspirin, Vitamin C	2.75	3.01	1+/0.71/17.6	3+	0.79	Negative/0.09

Case 15	14	Boy	Red eye, nausea, fatigue	None	Sertraline, escitalopram, protein	1	2.72	1+/0.13/5.9	1+	1.12	Negative/0.05
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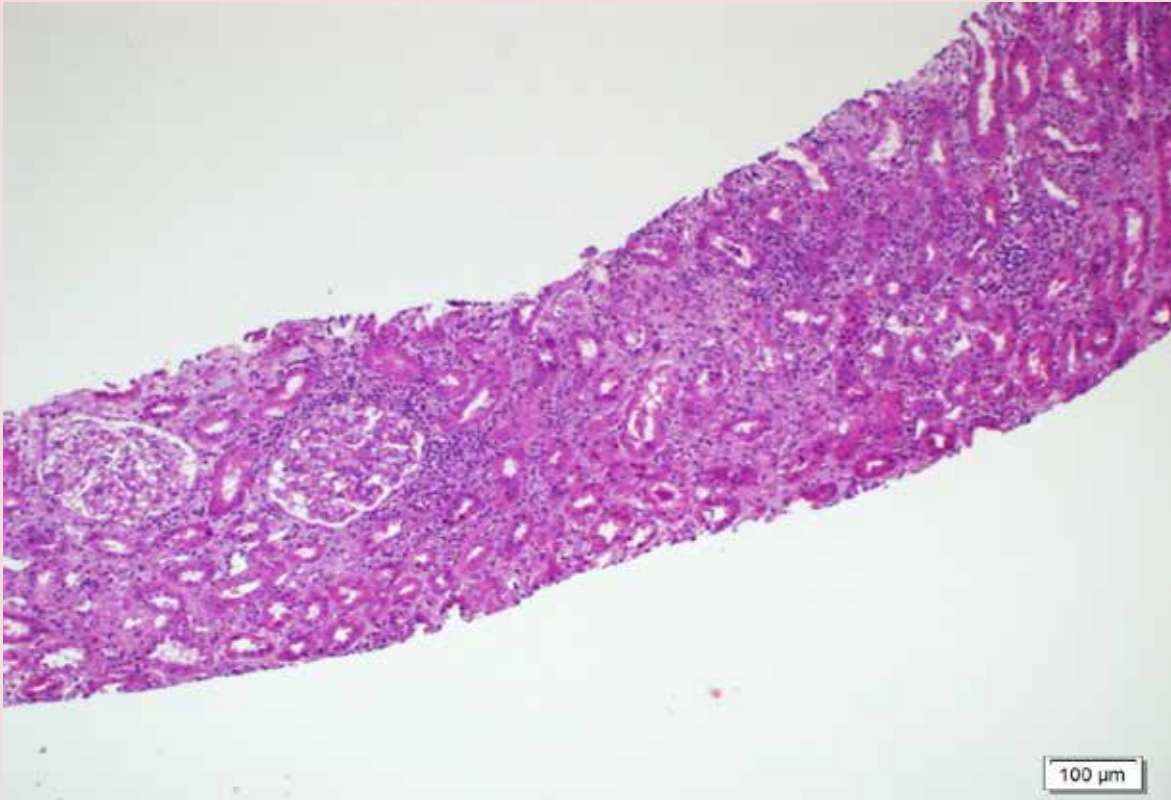


Figure 1: Glomerulus are normal, severe lymphoeosinophilic infiltration of the renal interstitium.

Fr-P 039

CHRONIC KIDNEY DISEASE AFTER PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION A SINGLE CENTER STUDY

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**Aims/Purpose:** Hematopoietic stem cell transplant (HCT) is an effective and sometimes the sole therapeutic alternative for various conditions including malignant and non-malignant conditions. Despite the significant advances of the years it entails many complications and is linked to high mortality rates. The kidney is commonly affected after HCT in children and adults and Acute kidney injury (AKI) commonly occurs. Chronic kidney disease (CKD) after HCT has been reported in limited studies especially among children. The objective of this study was to evaluate rates of CKD in pediatric HCT recipients in tertiary pediatric center in Israel over the course of 20 years and identify risk factors for CKD development.

**Methods:** A retrospective single center cohort chart review study of pediatric HCT recipients followed at Schneider Children's Medical Center of Israel (SCMCI) between the years 2000–2020. The study was approved by the Institutional Review Board at SCMCI. Demographic and clinical data was extracted from the Clalit HMO database; retrospectively analyzed. The primary outcome CKD was defined as GFR below 90 ml/min/1.73m<sup>2</sup> based on height and serum creatinine (CKID Formula) after 1, 3 and 5 years respectively. Multiple variable logistic regression models were used to identify risk factors for CKD development.

**Results:** Over the course of the study period during the years 2000–2020 389 transplants of 312 children were included in the analysis. The cohort included 312 children, 53% Males with a median age of 11.6 yrs. (IQR 6.3,15.7). The most common indication for HCT among the cohort was malignancy (66%) following Bone marrow failure (12%) Immunodeficiency (9%) Genetic/metabolic (8%) Benign hematological (5%). 40% were autologous transplants and 60% were allogeneic HCT. CKD rates after 1, 3, 5 years were 5%, 9%, 20% respectively. Risk factors for CKD development included type of transplant, donor type and medication exposure.

**Conclusion:** Rates of CKD after 5 years HCT are as high as 20% and over the years rates increase needing close surveillance of these patients specifically in high risk patients.

# POSTER SESSION 1C

## CAKUT

Fr-P 040

## CLINICAL AND RADIOLOGICAL PREDICTORS OF POSTERIOR URETHRAL VALVES IN BOYS AFTER THE NEONATAL PERIOD

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**Aims/Purpose:** To identify the diagnostic performance of clinical and radiological signs toward urethroscopy-confirmed posterior urethral valves (PUV) diagnosis.

**Methods:** 118 males (median age = 0.8 years, range = 1 month–14 years, 48 toilet-trained) consecutively undergoing voiding cystourethrography (VCUG) for any reason in a 2-year period were prospectively enrolled. We defined as direct PUV sign the presence of dilated posterior urethra and as indirect PUV signs the presence of hypertrophied bladder neck, musculus interuretericus hypertrophy, and trabeculated appearance of the bladder wall. Pathological uroflowmetry was defined by patterns suggesting infravesical obstruction.

**Results:** 22 patients with direct, 28 with indirect PUV signs on VCUG and one patient with normal VCUG and persisting micturition symptoms with pathological uroflowmetry underwent urethroscopy and in 43/51 (n = 22, 51.2%, with direct PUV signs) a final PUV diagnosis was made. In only 8 patients with indirect signs, PUV were not confirmed. Among non-toilet-trained patients none of the clinical signs/symptoms was associated to PUV while among toilet-trained patients only pathological uroflowmetry (Odds ratio, OR = 4.0 [95% confidence interval, CI:1.2–13.2; p = 0.02]) and pathological uroflowmetry with history of urinary tract infection (OR = infinity) were significantly associated with PUV. Examining radiological signs, significant association with PUV of VCUG direct and indirect signs was found both in toilet-trained and non-toilet trained patients. Direct PUV signs had 100% specificity and sensitivity while indirect PUV signs showed sensitivity = 58.1% and specificity = 89.3%. Evaluating any PUV sign (direct and/or indirect) the prognostic accuracy toward PUV reached sensitivity = 97.7%, specificity = 89.3% and negative predictive value = 98.5%

**Conclusion:** Only half of patients with endoscopy-confirmed PUV present with direct signs of PUV on VCUG. Accounting for indirect PUV signs on VCUG and pathological uroflowmetry could improve the PUV detection rate. The absence of any PUV sign on VCUG provides a very high negative predictive value excluding with reasonable certainty the presence of PUV.

Fr-P 041

DEVELOPMENT OF STEROID-RESISTANT NEPHROTIC SYNDROME IN A CHILD WITH RENAL HYPODYSPLASIA/APLASIA, TYPE 3

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**Introduction:** Pathogenic variants of GREBIL gene can lead to the development of renal hypodysplasia/aplasia type 3 (PHDA3), which may be characterized by incomplete penetrance. And pathogenic variant of UMOD gene caused chronic kidney disease (CKD) associate with the development of autosomal dominant tubulointerstitial kidney disease type 1 (TKD), familial hyperuricemic nephropathy, and cystic kidney disease. None listed gene's association with steroid-resistant nephrotic syndrome (SRNS) have previously showed.

**Purpose:** To report a rare case of SRNS with PHDA3 and TKD.

**Clinical case:** A girl from unrelated parents is observed in our department with PHDA3 since 1 yr. (ultrasound showed left-side renal agenesis, the parenchyma of the only right kidney with depleted of blood flow is poorly differentiated, has a subcapsular solitary cyst (30x40 mm), increase in  $\beta$ 2-MG (4290 mcg/day), CKD 2. Based on full-exome sequencing, heterozygous missense-variant of the GREBIL gene (p.Val347Leu) was detected which also found on proband's father according to Sanger's sequencing (trio). At 18 months, due to varicella, NS debuted (edema), BP (130/80 mmHg), oliguria (1.5 ml/kg/24h), proteinuria (6 g/l; 1.34 g/day), hematuria (19-65), hypoproteinemia (38.3 g/l), hypoalbuminemia (21 g/l), creatinine (86  $\mu$ mol/l), eGFR (41.8 ml/min/1.73m<sup>2</sup>), urea (26.3 mmol/l), non-permanent hyperuricemia (0.44-0.61 mmol/l), PTH (125.2pg/ml), alkaline phosphatase (53IU/l), hypocalcemia (1.97-2.21 mmol/l), anemia (Hb-81 g/l, reticulocytosis). After 6 weeks from the start of steroid therapy PZ (60 mg/m<sup>2</sup>), SRNS was diagnosed. MMF therapy was initiated at a dose of 900 mg/m<sup>2</sup>, however the drug was canceled due to frequent acute infectious diseases. After positive treatment by antiviral drugs, nephroprotective therapy (enalapril) was prescribed. Currently, isolated mixed proteinuria remains. Given the SRNS, on again whole-genome sequencing, besides the previously identified variant of GREBIL gene, an additional variant of UMOD gene (c.1332-16C = G) was revealed in splicing area.

**Methods:** The evaluation of clinical and anamnestic data and the results of molecular genetic studies in a child with PHDA3 was carried out. Post-infectious development of SRNS required a revision of the genetic screening.

**Results:** On the whole-genome sequencing were not found candidate genes for SRNS. Infectious etiology of the development of SRNS is assumed.

**Conclusion:** The showcased severe PHDA3 excels by the polymorphism of the clinical picture and the variability of genes variants not associated with the development of SRNS.

Fr-P 042

**GENOTYPE- PHENOTYPE ASSOCIATION AND OUTCOMES OF CHILDREN WITH WT1 VARIANTS: A SINGLE CENTER EXPERIENCE**

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**Aims/Purpose:** Pathogenic variants in WT1 gene are associated with severe renal and extrarenal manifestations. We aimed to describe genotypic and phenotypic associations, management, and outcome of children with these variants managed in our center.

**Methods:** Retrospective analysis of clinical and genetic characteristics of children with variants in WT1 gene.

**Results:** Eight patients with pathogenic WT1 variants have been managed in our center between 1994 to date. Median age at presentation was 10.3 months (range 0.1- 65.3). At presentation two patients had isolated nephrotic syndrome (NS) (both phenotypic female, 1 with 46XY and 1 with 46XX karyotype, respectively), 2 had nephrotic range proteinuria (NRP) and eGFR < 10ml/min/1.73m<sup>2</sup> (female phenotype and 46XX karyotype), 2 NRP and cryptorchidism-hypospadias (karyotype 46XY) and 2 had Wilm's tumor and cryptorchidism-hypospadias (karyotype 46XY). Seven patients had exonic missense and 1 had a truncating variant. Focal segmental glomerulosclerosis and diffuse mesangial sclerosis were revealed on kidney biopsy in 2 and 3 patients, respectively. Seven underwent nephrectomy and 2 bilateral gonadectomies. Two of three patients that received ciclosporin achieved partial remission of proteinuria for 6 and 8 years, respectively. After a median follow-up of 12.4 years (range 11.3- 18.7), 7 patients were on kidney replacement therapy. Median time to kidney failure was longer in those with Wilm's tumor at presentation or with response to ciclosporin versus non-responders or not treated with ciclosporin (8.4, 10.6 and 0.6 years, respectively; p = 0.02).

**Conclusion:** There is a wide phenotypic spectrum associated with WT1 variants. Primary manifestations such as Wilm's tumor or NS responding to ciclosporin are associated with a favorable kidney outcome.



Fr-P 043

PREVALENCE OF SYMPTOMS AND SIGNS OF KIDNEY DISEASES IN CHILDREN DURING THE COVID 19 PANDEMIC

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**Aims/Purpose:** The purpose of the study was to determine the prevalence of symptoms and signs of kidney diseases in Slovenian children at the primary care level during the COVID-19 pandemic.

**Methods:** The study methodology was cross-sectional. Data were obtained via an anonymous online questionnaire sent to all primary care paediatricians in Slovenia via e-mail. An exact binomial test was used for each symptom case in order to determine whether the proportion of symptoms and signs in the sample deviates from the “theoretical” prevalence reported in the literature.

**Results:** Data were obtained from 65 paediatricians and 9829 evaluated children were included in the study. The prevalence of symptoms and signs of kidney diseases, mostly found incidentally, such as haematuria, proteinuria and hypertension, were 0.67%, 0.68% and 0.71%, respectively, which is statistically significantly lower than described in the literature. The prevalence of symptoms and signs suggesting serious kidney diseases, such as oedema, persistent proteinuria and CAKUT with associated congenital abnormality of another organ system were 0.01 %, 0.13 % and 18.5 % respectively, which is not a statistically significant difference compared to literature (Table 1).

Table 1. Prevalence of symptoms and signs of kidney diseases in the sample compared with those in the peer-reviewed literature.

	Number of patients	Prevalence in the study (CI - confidence interval)	Prevalence reported in the literature	P-value
Children with any symptoms and signs of kidney diseases	548	5.57 % [95%CI 5.13-6.05%]	23.89 %	(p = 0.001)
Urinary tract infection	102	1.04 % [95% CI 0.85 - 1.26%]	6-8 %	(p = 0.001)
CAKUT	54	0.55 % [95% CI 0.41 - 0.72%]	3.26 %	(p = 0.01)
CAKUT and associated congenital abnormality of another organ system	10/54	18.5 % [95% CI 9.5 - 31%]	30 %	(p = 0.871)
Oedema due to kidney disease	1	0.01 % [95% CI 0.002 - 0.005%]	4.7/100 000 children	(p = 0.370)
Nocturnal enuresis	96	0.98 % [95% CI 0.78% - 1.19%]	5-10 %	(p = 0.001)
Haematuria	66	0.67 % [95% CI 0.52%-0.85%]	1.5-2 %	(p = 0.001)
Proteinuria	67	0.68 % [95% CI 0.53%-0.86%]	10 %	(p = 0.001)
Persistent proteinuria	13	0.13 % [95% CI 0.07%- 0.23%]	0,10 %	(p = 0.334)
Sport related proteinuria	17/67	25.4 % [95% CI 15,5%-37,5 %]	18-100 %	(p = 0.05)
Hypertension	70	0.71 % [95% CI 0.56-0.90%]	4 %	(p = 0.001)

**Conclusion:** Children with serious kidney diseases, mostly presenting as oedema, persistent proteinuria or CAKUT with associated congenital abnormality of another organ system, were identified as commonly as described in the literature, despite the COVID-19 pandemic. The latter influenced negatively the discovery rate of symptoms and signs of kidney diseases that are found incidentally, such as haematuria, proteinuria and hypertension, or that are not threatening, such as nocturnal enuresis.

Fr-P 044

UROPATHOGENS AND ANTIMICROBIAL RESISTANCE IN INFANTS HOSPITALIZED WITH A FIRST FEBRILE URINARY TRACT INFECTION

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**Introduction:** Urinary tract infection (UTI) is a common cause of fever in infants, and requires early diagnosis and treatment. In this study, we aimed to investigate the isolated agents and antibiotic susceptibility in the first febrile urinary tract infections (fUTIs) in infancy.

**Materials and Methods:** The medical records of patients aged 2–24 months which are hospitalized with the diagnosis of first fUTI ( $\geq 38^{\circ}\text{C}$ ) between January 2017 and December 2019 were reviewed retrospectively. All patients had a paired urinalysis and urine culture, and all urine specimens were obtained by bladder catheterization. UTI was diagnosed with significant bacteriuria (positive urine culture  $\geq 5 \times 10^4$  CFU/ml) and/or pyuria ( $\geq 10$  WBCs /mm<sup>3</sup> in uncentrifuged urine specimens by hemocytometer and positive leukocyte esterase test). Cases with contaminated cultures were excluded.

**Results:** A total of 67 patients were included (43 females and 24 males,  $p = 0.02$ ). Median age was 7 months in female, and 3 months in males at the time of diagnosis. Twenty-nine (43.2%) patients had only fever without any other symptoms on admission. 22 (92%) boys were uncircumcised. Nitrite and leukocyte esterase were positive in %21 and %80.6 of patients, respectively. The most common pathogen was *Escherichia coli* ( $n = 37$ , 55.3%), followed by *Klebsiella spp.* ( $n = 14$ , 21.5%), *Enterococcus faecalis* ( $n = 8$ , 12.3%), *Pseudomonas aeruginosa* ( $n = 3$ , 4.6%), *Enterobacter spp.* ( $n = 3$ , 4.6%), *Proteus mirabilis* ( $n = 1$ , 1.5%). The rates of resistance of *E. coli* to ampicillin, trimethoprim/sulfamethoxazole and sefixim was 80.5%, 44.4% and 38.8%, respectively. The antimicrobial resistance rate of the *E. coli* to ceftriaxone and gentamicin was 19.4% and 13.8%, respectively. Extended-spectrum beta-lactamases (ESBL) were noted in 26 (26/67, 38.8%) cases; 16 in *E. coli*, 7 in *Klebsiella spp.*, and 1 case in each *P. aeruginosa*, *Enterococcus faecalis*, *Enterobacter spp.* Male gender was significantly associated with ESBL positivity in multivariate analysis (OR; 1.686, 95% CI ; 0.499–5.699,  $p = 0.004$ ).

**Conclusion:** Appropriate use of antibiotics for UTI immediately after diagnosis is imperative. Therefore, the choice of empirical therapy should be determined according to common uropathogens and their local antibiotic susceptibility pattern.

Fr-P 045

## THE IMPACT OF URINARY TRACT MALFORMATION ON BACTERIAL FLORA AND ITS ANTIBIOTIC RESISTANCE IN CHILDREN WITH INPATIENT URINARY TRACT INFECTIONS

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**Objective:** The purpose of this study was to determine the relationship between the composition and drug susceptibility of the bacterial flora of urinary tract infections (UTI) and the presence of a congenital urinary tract malformation in children.

**Methods:** The study included analysis of 515 urine cultures obtained from patients hospitalized at a tertiary referral hospital over a 24-month period. Drug susceptibility of *Escherichia coli* strains, which are the leading uropathogen in UTI, to antibiotics of the group: penicillins, carbapenems, aminoglycosides, fluoroquinolones, and nitrofurantoin and trimethoprim-sulfamethoxazole were determined using the automated Vitek 2 Compact method, the plate-diffusion method and E-tests. The abundance of strains producing an ESBL (extended-spectrum beta-lactamases) type resistance mechanism was also analyzed.

**Results:** The distribution of cases for *Escherichia coli* (N = 228), was comparable (p = 0.134) for patients with (40.10%) and without urinary tract defects (46.86%). Comparing the numbers of etiological agents in this group of patients, statistically significant differences were found for infections caused by yeast-like fungi - *Candida spp.* (p = 0.011) and *Pseudomonas aeruginosa* (p = 0.002). In terms of *E.coli* antibiotic resistance, statistically significant differences in their effectiveness were observed for all cephalosporins analyzed, as well as for nitrofurantoin. No such effect was noted for other antibiotics. ESBL-type resistance mechanism was present in *Escherichia coli* strains isolated from patients with a urinary tract defect - 10.13% of cases, versus only 2.01% of cases for patients without a malformation (p = 0.016).

**Conclusions:** The study showed, the presence of a urinary tract defect in children predisposes to *Pseudomonas aeruginosa* infections, but does not affect the frequency of isolation of *Escherichia coli* or other strains of bacteria causing urinary tract infections. The presence of malformation significantly reduces sensitivity to the most commonly used first-line antibiotics (cephalosporins and nitrofurantoin). Moreover, it increases the risk of *E. coli* strains with beta-lactamase-producing extended substrate spectrum (ESBL+).

Key words: urinary tract infection, CAKUT, children, antibiotic susceptibility

Fr-P 046

## CONGENITAL KIDNEY DISEASES IN CHILDREN ARE THE MOST COMMON REASON OF CHRONIC KIDNEY DISEASES

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During intrauterine growth, kidneys develop on 9th gw. And further development is depend on factors motherhood, genetic, enviroiment. And the possbile anomalies are a lot. As many as 150 different genetic disorders are found to cause kidney abnormalities isolated, combinet with other organs or syndromic. Disorders functional or structural anatomic. Might be familiar genetic. Almos 30% of this anomalies are found during intrauterine life, by Obstretian. Kidney disorders are corrected sugically in adequat time and right correction in order to prevent kidney function maximally.and some might need surgical correction further in bigere age like cystic diseases. As earlied detected and corrected the better disease prognose. And treatment is not alwayes full recovery, some of them should be further followed with treatment. 10% of adult people and almos all children with inborn anomalies end up with CKD, RRT, transplant. And transition to adult fellow up and treatment is a big chalenge for patient.

Although with multidisciplinary aproach of team Obstretician, Pediatric Nephrologis, Peidatric Surgeon, Urologist, Neurosurgeon and Parent with carefull monitoring from birth to adulthood we can preserve and maintenin the maximal potential of the patients kidney.

Keywords: kidney abnormalities, children, chronic kidney disease, multidisciplinary

Fr-P 047

DACT1 AND TSHZ3 ARE MUTATED IN PATIENTS WITH CONGENITAL ANOMALIES OF THE KIDNEY AND URINARY TRACT

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**Aims/Purpose:** The diagnostic yield of genetic testing in patients with congenital anomalies of the kidney and urinary tract (CAKUT) is only 16% on average, underscoring the need for further gene identification. More than 180 genes, such as DACT1 and TSHZ3, have been associated with murine CAKUT, and represent promising novel candidate genes for human CAKUT. Since we found DACT1 and TSHZ3 to be mutated in one CAKUT family each, we aimed to investigate their role in human CAKUT pathogenesis.

**Methods:** Whole-exome or targeted DACT1 and TSHZ3 sequencing was performed on leukocyte DNA of 209 or 301 clinically well characterized CAKUT patients. Binding of mutant proteins was analyzed by immunoprecipitation. Dact1 and Tshz3 expression was determined by RNA in situ hybridization on sections of murine embryos or kidneys. Genotype-phenotype correlations were established.

**Results:** Very rare heterozygous non-silent DACT1 variants were detected in eight of 209 (3.8%) CAKUT families, significantly more frequently than in controls (1.7%). Five different rare heterozygous TSHZ3 variants predicted to be deleterious were identified in nine of 301 (3%) CAKUT families; a 5' hotspot region of TSHZ3 was affected significantly more frequently in CAKUT patients than in controls. DACT1 variants were located in the interaction region with DVL2, and showed reduced DVL2 binding. N-terminal TSHZ3 variants were located in the interaction region with SOX9 and myocardin, and showed altered SOX9 or myocardin binding. During murine development, Dact1 was expressed in organs affected by anomalies in patients with DACT1 variants, including the kidney, anal canal, vertebrae, and brain. Tshz3 was expressed in murine neural tissues and the mesenchymal compartments of the developing lung, bladder and ureter as well as in the medullary stroma of the developing kidney. Patients carrying DACT1 variants presented with kidney agenesis, duplex or (multi)cystic (hypo)dysplastic kidneys with hydronephrosis and features of Townes-Brocks syndrome 2. Patients carrying TSHZ3 variants were significantly more frequently affected by hydronephrosis, previously observed in Tshz3-null mutant mice, multicystic dysplastic kidneys, developmental delay and genital anomalies than patients without TSHZ3 variants.

**Conclusion:** Our results provide evidence that heterozygous DACT1 and TSHZ3 variants cause human CAKUT and specific extrarenal features.

Fr-P 048

**POSTERIOR URETHRAL VALVE FROM THE MALAYSIA'S PERSPECTIVE: A 24 YEARS EXPERIENCE IN MAJOR COMBINED NEPHROLOGY-UROLOGY REFERRAL CENTRE IN MALAYSIA**

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**Aims:** Posterior Urethral Valve is the commonest cause of bladder outlet obstruction among boys with an incidence rate of 1:2500-4000. Eventually 20-40% of these boys end up having end stage kidney disease (ESKD) [1,2,3,4]. Malaysia is a multi-ethnic country with an ethnicity breakdown of 69.6% Malay, 22.6% Chinese, 6.8% Indian and 1% others [5]. Despite being one of the minority ethnicities, we observed that boys of Indian ethnicity were more frequently diagnosed with Posterior Urethral Valve. We aim to establish the link between ethnicity and incidence of Posterior Urethral Valve.

**Method:** The records of a total of 105 boys who were under our combined Paediatric Nephrology and Urology clinic follow-up for Posterior Urethral Valve between the Year 1998 - 2022 were reviewed. Of these, 36 boys were excluded due to incomplete data.

**Results:** Among these 69 boys reviewed, 34 (49.3%) are of Indian ethnicity and 35 (50.7%) are of non-Indian ethnicity - 44.9% Malay ethnicity, 4.4% Chinese ethnicity and 1.4% others. When compared between boys of Indian and non-Indian ethnicity, 42% vs 23% had Chronic Kidney Disease (CKD) Stage I-II, 11% vs 12% had CKD Stage III-IV and 47% vs 65% had ESKD. There is no significant discrepancy between boys of Indian and non-Indian ethnicity in terms of timing of diagnosis, creatinine level at diagnosis (median 167 vs 132,  $p > 0.05$ ), post intervention nadir creatinine level (median 66 vs 37,  $p > 0.05$ ) and the time to development of ESKD (median 11.3 vs 12 years,  $p > 0.05$ ). The cohort of interest also did not demonstrate higher incidence of recurrent urinary tract infections (63% vs 84%), incontinence (33% vs 57%) and detrusor overactivity (25% vs 36%).

**Conclusion:** A significant number of boys of Indian ethnicity (49.3%) were diagnosed with Posterior Urethral Valve in a country where Indian ethnicity comprises just 6.6% of its total population. Despite the increased incidence, there is no change in terms of creatinine level at the time diagnosis, post intervention nadir creatinine level, proportion and progression time to CKD and ESKD as well as incidence of recurrent urinary tract infection, incontinence and detrusor overactivity in boys of Indian ethnicity.

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Fr-P 049

PREVALENCE OF URINARY TRACT INFECTION PATHOGENS IN CHILDREN AND ANTIMICROBIAL SUSCEPTIBILITY AND RESISTANCE PATTERNS

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**Aims/Purpose:** The study aimed to identify the main causative pathogens of urinary tract infections in children in 2022, their antibiotic susceptibility and resistance patterns and to evaluate dynamics comparing data of 2001 and 2022 years in the same hospital.

**Methods:** The study was carried out using a retrospective analysis of urine cultures in children below 18 years of age treated at Vilnius University Hospital Santaros Klinikos pediatric departments in 2022. All the positive urine culture reports with pure growth of  $> 10^5$  CFU/ml of a single organism were included in the analysis. Findings were compared with results of the 2001 in children departments published by P. Kaltenis in 2002. Changes in outcome were assessed using Chi-square test, where p value less than 0.05 was considered statistically significant.

**Results:** In 2022, a total of 807 urine cultures were analysed with a positive growth of microorganisms in 427 (52.91%) cultures and compared to 640 urine cultures with a positive growth of microorganisms in 2001. *Escherichia coli* (62.3%) was the most common isolate. The vast majority of *E. coli* strains (95% and more) were susceptible to cefadroxil (95%, n = 258), cefuroxime (95%, n = 264), gentamicin (97%, n = 264), nitrofurantoin (100%, n = 262), ciprofloxacin (95%, n = 265). Data analysis showed that, compared to year 2001, in year 2022 *E. coli* had an increased resistance to the following antibiotics: amoxicillin-clavulanate (5%, n = 439 compared to 12%, n = 250, p value = 0.00132) and ceftazidime (1%, n = 439 compared with 6%, n = 418, p value = 0.000195). The second most common causative agent was found to be *Enterococcus spp.* (11.7%), followed by *Klebsiella species* (8%). Since 2001 a statistically significant increase in the prevalence of *Enterococcus* and *Klebsiella species* (4.1% compared to 11.7% and 0.8% compared to 8% respectively) and a statistically significant decrease in the prevalence of *Enterobacter species* (7.7% compared to 0.9%) were observed (p < 0.001).

**Conclusion:** For 20 years, there has been a trend of increasing *E. coli* resistance, as well as an increase in *Enterococcus* and *Klebsiella species* in pediatric urinary tract infections. Antibiotic resistance rates should be continuously monitored and changes in the local antibiotic strategy should be attempted.

Fr-P 050

**MERCAPTOACETYLTRIGLYCINE-3 DIURETIC RENOGRAPHY IN THE DETECTION OF OBSTRUCTIVE NEPHROPATHY: HOW MUCH HAS OUR PRACTICE CHANGED DURING THE LAST DECADE?**

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**Aims/Purpose:** During the last decade, indications of mercaptoacetyltriglycine-3 diuretic renography (99mTc-MAG3) have remained broadly the same. The 99mTc-MAG3 scan is used to estimate differential kidney function and assess kidney drainage. The aim of our study is to compare two time periods (2014–2015 to 2021–2022) assessing the changes in 99mTc-MAG3 scan use and results to identify those patients who need further treatment.

**Methods:** We retrospectively reviewed the medical records of pediatric patients who underwent a 99mTc-MAG3 scan during two time periods (2014–2015 and 2021–2022) in the Nuclear Medicine Department of our hospital. We also included patients' history and ultrasonographic data before the 99mTc-MAG3 scan.

**Results:** All patients included in this retrospective study had undergone an ultrasound of the urinary tract system. Patients' history combined with their ultrasonographic findings led to the decision of urinary tract system evaluation with a 99mTc-MAG3 scan. In 2014–2015, 92 pediatric patients underwent a 99mTc-MAG3 scan to identify obstruction in the urinary tract system. Obstructive lesions were found in 17 patients (~18.5%) and eight of them underwent immediate surgery (~47.1%). During the 2021–2022 period, 81 pediatric patients underwent a 99mTc-MAG3 scan and 17 pediatric patients (~21%) with obstructive lesions were detected. Seven patients (~41.2%) with obstructive uropathy underwent immediate surgery. All patients (100%) who underwent immediate surgery in both time periods had an anteroposterior pelvis diameter > 20 mm and cortical thinning < 5 mm in ultrasound which are associated with obstructive lesions. Of 34 patients who were diagnosed with urinary tract obstruction, 21 patients were under the age of 12 months and 13 were over two years of age. The ratio between girls and boys with obstructive pattern in the 99mTc-MAG3 scan was ~1.4 accordingly.

**Conclusions:** It appears that the 99mTc-MAG3 scan provides additional significant information on the obstruction degree to assess the necessity of surgical intervention. Urinary tract obstruction is less common in females compared to male pediatric patients. Finally, it is noted that during the last decade, the rates of pediatric patients with urinary tract obstruction and those who need surgical treatment have remained unchanged.



Fr-P 051  
EVALUATION OF CHILDREN WITH A DIAGNOSIS OF BLADDER

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**Aims/Purpose:** Bladder diverticulum is the name given to the herniation of tissue epithelium through muscle fibers. They are usually detected incidentally. The relationship between infection and voiding dysfunction and diverticulum is not clearly explained in the literature and there is no optimal medical or surgical consensus. In this study, cases followed in our clinic due to bladder diverticulum were evaluated in terms of treatment and urinary tract infection (UTI).

**Methods:** The cases who applied to the Pediatric Nephrology Clinic of Health Sciences University Tepecik Training and Research Hospital between 2012 and 2022 and were diagnosed with bladder diverticulum were evaluated retrospectively. Demographic, clinical, and laboratory data were obtained from file records.

**Results:** A total of 37 (22 male) pediatric patients were evaluated. Evaluation of presentation symptoms revealed UTI in 11 patients, antenatal hydronephrosis in 10 patients, voiding dysfunction in 8 patients, meningomyelocele and voiding dysfunction in 6 patients, and bladder diverticula incidentally in 1 patient. In the follow-up of the cases, it was observed that all of the operated patients needed surgery due to UTI. The median number of UTIs, which was 3 (1-11) in the preoperative period, decreased to 0 (0-2) in the postoperative period. However, when the patient subgroups were examined, it was found that patients with a single diverticulum benefited from surgical treatment in terms of UTI ( $p = 0.018$ ), while patients with multiple diverticula did not benefit from surgical treatment ( $p = 0.180$ ). Similarly, it was found that patients with voiding dysfunction benefited from surgical treatment in terms of UTI ( $p = 0.026$ ), while patients without voiding dysfunction did not benefit ( $p = 0.109$ ).

**Conclusion:** In the case of surgical indication in patients with bladder diverticulum, voiding dysfunction should be investigated in detail. It should be kept in mind that patients with multiple diverticula may also have UTIs in the postoperative period.

Fr-P 052  
COMPLICATED URINARY TRACT INFECTION IN CHILDREN

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**Aims/Purpose:** To assess the significance of the difference among patients with acute pyelonephritis (APN) and complicated acute pyelonephritis according to: gender, age, duration of fever before hospitalization, laboratory analyses (leukocytes, neutrophils, C-reactive protein) and congenital anomaly of kidney and urinary tract (CAKUT). Analyze sensitivity and specificity of CRP in predicting complicated APN.

**Methods:** Retrospective study was performed in Institute for mother and child health care Belgrade between 1.1.2020. and 31.12.2021. We included 120 patients age 1 to 16 years. They were divided in two groups. The first group included 78 patients with APN, and the second group 42 patients with complicated APN. Patients with complicated APN had lobar nephronia or kidney abscess detected by ultrasound exam. We performed laboratory analyses (CRP, blood count, biochemistry, urine culture, blood culture, ultrasound) in all patients, and voiding cystourethrography according to indications. Acute lobar nephronia presents as focal lesions with hypoperfusion and poorly defined irregular margins disrupting corticomedullary differentiation and kidney abscess like well-defined hypoechoic area with the cortex or in corticomedullary parenchyma.

**Results:** Patients age was  $18.1 \pm 20$  months, with predominant males 77 (64.2%). In 42/120 (35%) the fever lasted more than 72 hours before hospitalization. In addition to elevated body temperature, 9 (7.5%) had abdominal pain, 4 (3.3%) vomiting and diarrhea, 2 (1.7%) dysuric complaints and 3 (2.5%) febrile seizure. The most common causative agents of urinary infections were *E. coli* (83.3%) and *Klebsiella pneumoniae* (6.7%). In 2/120 patients, *E. coli* was isolated in the blood culture. Among patients 65 (54.2%) had pathological ultrasound: 13 (10.8%) of them had enlarged and hyperechoic kidneys, 9 (7.5%) hydronephrosis, 38 (31.6%) lobar nephronia, 4 (3.3%) kidney abscess and 2 (1.7%) kidney hypodysplasia. Vesicoureteral reflux (VUR) was found in 19/60 (31.7%). In relation to the total number of our patients, 22/120 (18.3%) had CAKUT. Of these, 19/120 (15.8%) had VUR, two had kidney hypodysplasia, and one had unilateral megaureter. Patients with complicated APN are older, have a longer duration of temperature and higher inflammation parameters compared to patients with uncomplicated APN ( $p = 0,05$ ). No difference was found in the prevalence of CAKUT in patients with uncomplicated APN and complicated APN. Based on the ROC curve for CRP with an area under the curve of 0.67, a CRP value greater than 100 mg/L has a sensitivity of 71.4% and a specificity of 61.3% for the diagnosis of complicated APN.

**Conclusion:** Patients with complicated APN are older, have a longer duration of temperature and higher inflammation parameters compared to patients with uncomplicated APN. A CRP value over 100 mg/L may indicate complicated APN.

Fr-P 053

EVALUATION OF THE CLINICAL AND THE RISK FACTORS OF CONGENITAL ANOMALIES OF KIDNEY AND URINARY TRACT IN CHILDREN

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**Propose and Aims:** Congenital Anomalies of the Kidney and Urinary Tract (CAKUT) is the most frequent form of malformation at birth that occur in 1 in 500 live births and represent the cause of 30–60% of childhood-onset and 7% of adult end-stage renal disease worldwide and predispose patients to hypertension and cardiovascular disease throughout life. This study evaluated the prenatal and postnatal characteristics of CAKUT patients and aimed to examine the factors affecting the surgical indications of CAKUT patients.

**Material and Methods:** The current study retrospectively examined the information of patients registered with the diagnosis of CAKUT in a tertiary hospital database. This study analyzed data regarding the patient's antenatal diagnosis age, postnatal radiological findings, the mother and father's clinical characteristics, the mother and father's disease and drug status, and the course of CAKUT in the pediatric population.

**Results:** The study included six hundred fifty-eight children under 18 diagnosed with CAKUT and followed up in Ondokuz Mayıs University Faculty of Medicine Department of Pediatric Nephrology. 449 (68.23%) of these cases were interpreted antenatally, and the mean age of diagnosis was 22.14 (SD 3.77) pregnancy weeks. The most common feature was antenatal hydronephrosis (49.1%), and the most common abnormalities in the postnatal period were VUR (15%), agenesis (12%), and UP stenosis (5.9%). There was a decrease in hydronephrosis in 161 (24.5%) patients, complete healing in 96 (14.6%) patients, and no improvement in 200 (30.4%) CAKUT patients. 161 (24.5%) of the 658 CAKUT patients underwent surgery in the long-term follow-up period. The most common reasons for the surgery were UP stenosis (39 patients), VUR (28 patients), UV stenosis (4 patients), ureterocele excision (4 patients), and urethral diverticulum correction (2 patients). Follow-up of the indication for surgery and related conditions revealed that factors such as gender, prematurity, parental consanguinity, maternal gestational diabetes, gestational hypertension, maternal/paternal smoking, family history of renal disease, chronic drug use, hypertension did not significantly affect the decision to undergo surgery. The presence of hydronephrosis or any urinary tract and renal abnormality in antenatal, postnatal, and on the 1–2–6-month late follow-up ultrasonographic control are significantly related to surgery indication in CAKUT patients.

**Conclusion:** In our study, approximately 70% of the patients were diagnosed in the antenatal period, and hydronephrosis was the most common CAKUT. About 25% of the patients underwent surgical intervention; the most common cause was ureteropelvic obstruction. The effect of family history and environmental factors were not associated with the clinical course of CAKUT patients. Determination of prognostic factors and close multidisciplinary follow-up of CAKUT, one of the causes of end-stage renal disease, will guide its long-term approach.

**Keywords:** Congenital anomalies, CAKUT, fetal hydronephrosis, prenatal diagnosis, cystic renal disease, renal agenesis, urinary tract malformations.

Fr-P 054

ANTIBIOTICS SUSCEPTIBILITY TO THE CAUSATIVE MICROORGANISMS OF URINARY TRACT INFECTION IN CHILDHOOD; A FOLLOWING RESULTS AFTER 10 YEARS IN A SINGLE CENTER

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**Aims/Purpose:** Urinary tract infections (UTIs) is the most common bacterial disease and a common indication for antibiotic use in children. Because of the difficult in early diagnosis and rising resistance to antibiotics, the appropriate selection of antibiotics in treating bacterial UTIs is necessary to avoid the antibiotic overuse and misuse. The aim of this study was to compare the antibiotic susceptibility changes of UTIs with those before 10 years in Korea.

**Methods:** We performed urine culture tests and selected 571 samples in which urinary tract pathogens formed more than  $1.0 \times 10^5$  CFU/mL. We retrospectively identified the causative pathogens from these 571 samples and analyzed the change in antibiotics susceptibility according to the times compared to the previous our study (Korean J Pediatr, 2011;54:79-85) conducted at the same center.

**Results:** Among culture (+) 571 UTI patients, 561 (98.2%) samples were Gram-negative strains: *E. coli* (509 samples; 89.1%), *Klebsiella spp.* (21 samples; 3.7%), *Enterobacter spp.* (17 samples; 3.0%), *Proteus spp.* (8 samples; 1.4%), etc. Among 509 patients with *E. coli* cultured, the antibiotic susceptibilities were as follows: imipenem, 100%; amikacin, 100%; gentamicin, 58.2%; cefepime, 95.3%; piperacillin/tazobactam, 93.7%; ceftazidime, 90.2%; aztreonam, 87.4%; ciprofloxacin, 83.9%; cefotaxime, 64.2%; amoxicillin/clavulanate, 58.2%; trimethoprim/sulfamethoxazole, 51.7%; and ampicillin, 21.0%. Comparing the differences in antibiotics susceptibility between 2003-2008 and 2015-2020, all bacteria (2003-2008, n = 405; 2015-2020 n = 558); antibiotics susceptibility was significantly decreased in 2015-2020 compared to 2003-2008 in the following antibiotics.; aztreonam 96.2% → 87.1% (p < .001), cefazolin 81.15% → 58.8% (p < .001), ceftazidime 93.67% → 80.8% (p < .001), gentamicin 93.02% → 61.5% (p < .001), trimethoprim/sulfamethoxazole 71.8% → 55.2% (p < .001), 3rd generation cephalosporin (2003-2008 ceftriaxone, 2015-2020 cefotaxime) 95.61% → 66.1% (p < .001). Imipenem has the same sensitivity of 100% in 2003-2008 and 2015-2020. ESBL-positive rates were 116 (20.3%) among all bacteria (n = 571) and 112 (22.0%) among the *E. coli* (n = 509), which were much higher than that reported among 2003-2008 data. Among the 571 patients diagnosed with UTI, vesicoureteral reflux (VUR) was detected in 100 (21.6%) of 462 patients by VCUG. We found that the more severe grade of VUR, the higher antibiotics resistance (Standardized J-T statistic 2.032, p = 0.042).

**Conclusion:** In summary, we concluded that as the antibiotic resistance of bacteria causing UTIs increases in Korea as time goes by, the selection of antibiotics in treating bacterial UTIs in antibiotics-overused community would be considered very carefully.

Fr-P 055  
IS IT POSSIBLE TO PERFORM LESS VCUG?

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Our study analyzes the negative predictive value of renal ultrasonography (RUS) for vesicoureteral reflux (VUR) in patient who underwent that voiding cystourethrogram (VCUG) due to febrile urinary tract infection (UTI) and antenatal hydronephrosis (AH), in order to propose a more practical approach in the diagnosis of VUR.

**Material and Methods:** We performed a retrospective review of all children (median age:12 month) underwent VCUG who were followed up at the Pediatric Nephrology Department, Istanbul Medipol University Hospital, Turkey, between January 2018 and December 2022. 188 [90(47.9%) male] children with and without VUR were included in the study. We used VCUG indications according to the American Academy of pediatrics and NICE criteria. Among 188 children with febrile UTI and/or AH, VUR was detected in 50% (94 patients, 144 units): 46.8% (44) unilateral, 53.2% (50) bilateral, 27.7% (40) low Grade (I-II) and 72.3% (94) high Grade (III-V). We examined the variables and risk coefficients of patients who were diagnosed with VUR. We detected VUR in 78.1% of patients suffering from pyelonephritis ( $p < 0.001$ , odds ratio 7.5), 38.6% of patients with AH ( $p: 0.039$ , odds ratio 0.5) and 75% of patients with duplex system ( $p: 0.001$ , odds ratio 3.8) and found it statistically significant in predicting VUR. Fever ( $p < 0.001$ , risk ratio: 4.8), leukocytosis ( $p < 0.001$ , risk ratio: 6.7) and high CRP ( $p < 0.001$ , risk ratio: 6.2) were found to be statistically significant in predicting VUR. Ureteral dilatation alone ( $p: 0.37$ , risk ratio: 0.7) and SFU grade 3-4 hydronephrosis compared to grade 1-2 (43.2%,  $p: 0.35$ , risk ratio: 0.7) were not significant.

**Discussion:** We support RUS as a screening method for VUR in infants under 2 years of age after their febrile UTI. Given the high negative predictive value, if the RUS is abnormal in patients with febrile UTI, we propose performing VCUG. We do not recommend performing VCUG in cases with AH with ureteral dilatation alone, which is not considered an abnormality of the lower urinary system that does not suffering to febrile UTI.

Fr-P 056

ESTIMATING SOLITARY FUNCTIONING KIDNEY (SFK) LENGTH BY AGE OR HEIGHT: A COMPARATIVE STUDY

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**Aims/Purpose:** SFK length has been shown to correlate with estimated glomerular filtration rate (eGFR) and SFK compensatory hypertrophy (CH) was suggested to be a protective factor. We aimed to compare the effects SFK length standardization to age or height.

**Methods:** A single-center prospective cross-sectional study of children ( $\geq 2$  years) with SFK (congenital or acquired; excluding nephrectomies due to malignancy). SFK length was standardized to height and age specific z-scores (SFKz) according to recent Central European reference data. eGFR was calculated using updated Schwartz equation. Compensatory hypertrophy (CH) was defined as SFK length  $> 95$ th percentile and small SFK (SK) was defined as SFK length  $< 50$ th percentile.

**Results:** 52 children (8 [5.0–14.1] years; 50% boys) with a mean eGFR of  $92 \pm 21$  ml/min/1.73m<sup>2</sup> were enrolled. 11 (21%) patients had anomaly of SFK. Primary SFK cause was agenesis ( $n = 34$ ), multicystic dysplastic kidney ( $n = 10$ ), nephrectomy ( $n = 6$ ) or undetermined ( $n = 2$ ). 21 (38%) patients had eGFR  $< 90$ . There was a significant difference between SFKz by height and by age (SFKz  $1.7 \pm 1.7$  and  $1.6 \pm 1.7$ , respectively; mean difference  $0.13 \pm 0.43$ , 95% CI 0.01 to 0.25,  $p = 0.04$ ). 28 (54%) had CH and 8 (15%) had SK according to SFKz by age. When SFKz was calculated according to height, 38% patients with normal SFKz by age were reclassified (4 and 2 to CH and SK), while 1 patient with SK and 1 with CH were reclassified as normal size. SFKz difference (height – age) correlated negatively with height z-score ( $r = -0.71$ ,  $p < 0.001$ ) but not age ( $p = 0.74$ ). eGFR correlated significantly with SFKz by height and age ( $r = 0.60$  and  $0.55$ ; both  $p < 0.001$ ,  $R^2 = 0.34$ ) but higher  $R^2$  was observed with SFKz by height (0.34 and 0.29). The proportion of eGFR  $< 90$  was higher in those without CH according to height compared to age (57% vs 50%,  $p = 0.04$  and 0.19). Similarly, more children with SK presented with eGFR  $< 90$  according to SFKz by height compared to age (78% vs 63%,  $p = 0.01$  and 0.17).

**Conclusion:** Our study showed potentially clinically relevant disparities between SFKz standardization to height or age. SFKz standardized to height appears to be better related to SFK function and frequency of its impairment.

Fr-P 057

ACUTE KIDNEY INJURY IN THE FIRST 3 YEARS OF LIFE – A 10-YEAR RETROSPECTIVE STUDY

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**Aims/Purpose:** Acute kidney injury (AKI) is the abrupt loss of function resulting in a decline of the glomerular filtration rate (GFR). AKI has been associated with higher morbidity and mortality, both in critical and non-critical care. Furthermore, children who survive AKI may progress to chronic kidney disease (CKD). We aimed to characterize demographically and clinically patients diagnosed with AKI in the first 36 months (M) of life, and to identify clinical and laboratorial predictive factors, determine prognostic factors and differentiate patients with AKI, according to etiology and presence/absence of congenital anomalies of the kidney and urinary tract (CAKUT).

**Methods:** Data was retrospectively collected, from clinical records of patients aged between 0–36M, admitted to our pediatric tertiary center with the diagnosis of AKI, between 1/2010 and 12/2020. Demographical data was recorded, as well as clinical parameters of pregnancy, labor, clinical and laboratorial information regarding the hospitalization associated to AKI and posterior evolution. Patients were excluded if there was no follow-up in pediatric nephrology appointments.

**Results:** Forty patients were included, 31 (77.5%) males, with median age at presentation of 2M (IQR 0–11M). Among these, 21 (52.5%) had identified CAKUT. History of familiar renal disease was present in 3 (7.5%) patients. Thirteen (32.5%) patients were born premature, 10 (25.0%) were light for gestational age at birth, and 4 (10.0%) needed advanced life support after birth. Most frequent causes associated to AKI were infections (20.0%), post-surgery (12.5%) or use of nephrotoxic medications (7.5%), while in the other cases a single definite cause was not identified. At presentation, median urea values were 56 mg/dL (IQR 36.8–101.5), while median creatinine values were 1.0 mg/dL (IQR 0.7–2.2). Median maximum urea values during evolution of AKI were 100 mg/dL (IQR 58.5–154.5), while median maximum creatinine values were 2.0 mg/dL (IQR 1.0–4.3). Hyperkalemia was detected in 22 (25.0%) patients and hyponatremia in 11 (27.5%). During evolution of disease, 13 (32.5%) patients were hospitalized in intensive care units and 10 (25.0%) needed dialysis. Evolution to CKD occurred in 21 (52.5%) patients, 9 of them with stage 5 CKD. After surpassing AKI, seven (17.5%) patients did not survive at long term. When evaluating patients with CAKUT, these were more frequently male (90.5% vs 63.2%,  $p = 0.045$ ) and had a worse prognosis, with more evolution to CKD (76.2% vs 26.3%,  $p = 0.002$ ). There were no differences between groups in terms of age at presentation, urea/creatinine initial and maximum values, or survival rate.

**Conclusion:** Our study supports that AKI presentations in the first 3 years of life occur mostly in males, and in patients with CAKUT. Evolution to CKD is frequent, especially in patients with CAKUT, and death at long term occurs in a considerable percentage.

Fr-P 058

EVALUATION OF KIDNEY FUNCTIONS IN OPERATED MENINGOMYELOCELLA PATIENTS

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Spina bifida is a birth defect causing the protrusion of the nerves and meninges as a result of the improper closure of the neural tube during the early weeks of gestation. Myelomeningocele (MMC) is a severe form of spina bifida, where a layer of the spinal cord is herniated outwards from the midline defect as a sac. The nephrological and urological pathologies observed in such cases also vary. In patients with myelomeningocele, bladder noncompliance and retraction, urinary incontinence, urinary stones, urinary tract infections, neurogenic bladders, vesicoureteral reflux (VUR) and chronic renal failure (CRF) can be observed. In this study, it is aimed to evaluate the renal functions in operated patients with meningomyelocele.

This study was conducted in Firat University Hospital between February 2019 and June 2020. A total of 34 children, who were diagnosed with meningomyelocele and underwent surgery, and who presented to the departments of pediatric neurology and pediatric nephrology were included in the study. The control group was comprised of 34 healthy children aged between 4 and 17, who had applied to the department of pediatrics, had no acute or chronic diseases and used no medication, and whose demographic characteristics resembled those of the patient group. During the admission, patients' complete blood counts, complete urinary values, sodium, potassium, chlorine, calcium, phosphor, magnesium, uric acid, creatinine and urea levels in blood, sodium, potassium, creatinine, phosphor, chlorine, uric acid, magnesium, calcium, protein and urea levels in spot urine were examined. Moreover, nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF) and neutrophil gelatinase-associated lipocalin (NGAL) molecule values, which are the indicators of renal parenchymal damage, were checked in the blood and urine of all the patients.

The serum NGF levels of the patient group were found significantly higher than those of the control group ( $p = 0.003$ ). No significant difference was detected between the patient group and the control group in terms of serum BDNF and serum NGAL levels ( $p > 0.05$ ). No significant correlation was discovered between the patient group and the control group in terms of urine NGF, BDNF and NGAL levels ( $p > 0.05$ ).

Consequently, the serum NGF levels of the patient group were found to be significantly higher than those of the control group. We believe that more comprehensive studies are needed especially to research serum BDNF, NGAL and urine NGF, BDNF and NGAL levels in patients with myelomeningocele.



# POSTER SESSION 1D

## Transplantation

Fr-P 059

TOWARDS HOME-MONITORING WITH CAPILLARY MICROSAMPLING AND MHEALTH OF SOLID ORGAN TRANSPLANTED ADOLESCENTS AND YOUNG ADULTS – A PILOT STUDY

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**Background:** New, reliable methods to detect and improve medication non-adherence in solid organ transplanted adolescents and young adults are warranted to optimize clinical outcomes and avoid graft loss. In a pilot study we aimed to evaluate the impact on medication non-adherence, using a medication-manager application (TusenTac<sup>®</sup> -app) in combination with at-home blood sampling of tacrolimus (Tac).

**Material and Methods:** We included kidney and combined solid organ transplanted recipients between 14-25 years in the period Jan 2021 to Jun 2021, with follow-up data until Jun 2022. During an 8-week intervention period, the participants were instructed to use the transplant-specific, age-adapted TusenTac<sup>®</sup>-app daily and perform weekly Tac trough finger-prick microsampling at home using volumetric absorptive microsampling (VAMS<sup>™</sup>). At the start and end of the home monitoring period we compared Tac trough concentrations in standard venous blood samples to the microsamples. Medication implementation and persistence adherence were measured with BAASIS-questionnaires, TusenTac<sup>®</sup>-registrations, Tac trough concentration coefficient of variation (CV%) and self-reporting by interview. For comparison, Tac trough CV% were obtained from the year before and after the intervention.

**Results:** Twenty-two recipients were included, 2 withdrawals, leaving 20; median age 17.9 (14.5-24.8) years, twelve females (60%). At inclusion, 11 recipients (55%) were non-adherent assessed with BAASIS-questionnaire, four of these (36%) turned adherent during the intervention-period. During the intervention, the electronic monitored medication non-adherence rate was 27% ( $\pm$ 22%). At the end of the intervention, 70% reported improved timing-adherence at the interview. The relative mean difference between the venous and the microcapillary Tac concentration was 2.1% (95% confidence interval [CI], -2.3% to 6.6%), and 88% (n = 37) of the sample pairs had differences within  $\pm$  20%. There was no significant change in Tac CV% from the year before to the year after the intervention.

**Conclusion:** Home-monitoring, combining microsampling of Tac trough concentrations and daily use of a medication manager app is feasible. It improved medication adherence in four of 11 non-adherent adolescent and young adult solid organ transplanted recipients. Overall, 70% of the participants perceived improvement in dose-timing. There were no significant changes in Tac CV% confirming the need for individualized interventions.

Fr-P 060

EPSTEIN-BARR VIRUS ANTERIOR UVEITIS IN A PAEDIATRIC KIDNEY TRANSPLANT RECIPIENT

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**Introduction:** Epstein-Barr Virus (EBV) poses significant risks to immunosuppressed patients following kidney transplant, including post-transplant lymphoproliferative disorder (PTLD). This can be associated with renal allograft loss and increased mortality [1]. EBV is a potential, but uncommon, cause of virus induced anterior uveitis (AU) in immunosuppressed patients. Definitive diagnosis of EBV in the eye can be made by aqueous or vitreous humour PCR analysis [2].

**Methods:** A 7 year old girl with end stage kidney disease, secondary to bilateral renal dysplasia, underwent a pre-emptive living maternal donor kidney transplant (mismatch 0, 1, 1, EBV D+/R-, CMV D+/R-). The immediate post-transplant period was complicated by EBV and BK viraemia. One year post-transplant, evidence of worsening EBV viraemia (blood PCR DNA = 1.8 million IU/ml and generalised lymphadenopathy) was treated with intravenous rituximab. There was a temporary improvement in EBV levels followed by persistent EBV viraemia. Three years post-transplant the patient developed red, photophobic eyes with no history of trauma.

**Results:** Ophthalmological examination under anaesthesia (EUA) confirmed bilateral granulomatous uveitis with mixed anterior chamber hypopyon and hyphaema, vitritis and absence of retinitis. An anterior chamber fluid sample revealed positive EBV, Cycle Threshold (CT) value 26.7 and negative HSV, VZV and CMV, indicating a probable diagnosis of EBV AU. Blood EBV PCR DNA was = 1.8 million IU/ml. Following treatment with bilateral orbital floor injections of triamcinolone, significant improvement in intraocular inflammation was observed. Treatment with topical corticosteroid drops was continued in addition to oral prednisolone and tacrolimus. Six months post triamcinolone injections, the patient had persistent EBV viraemia (blood PCR DNA = 1.8 million IU/ml) and chronic AU. A further course of rituximab resulted in improvement in EBV viraemia (blood PCR DNA reduced to 33,600 increasing again to 300,478 IU/ml) and reduction in degree of intraocular inflammation. She underwent subsequent EUA with left lensectomy, anterior vitrectomy and intravitreal dexamethasone implant injection with eye samples sent for aqueous viral PCR, lens matter viral PCR and histopathology. Histopathology showed occasional scattered acellular lens matter. Molecular analysis revealed significant EBV presence with CT value 30.28.

**Conclusion:** This case describes the first report of probable EBV AU in a paediatric kidney transplant recipient. It highlights additional complications posed by post-transplant EBV viraemia and the complexities in the balance of immunosuppression and risks of viraemia while maintaining renal allograft function. The long term prognosis of EBV AU in this paediatric cohort remains unclear due to limited reports in literature. Close monitoring and early intervention are required to limit long term effects on vision.

References

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Fr-P 061

ARE HEMODYNAMIC VALUES RELATED TO RENAL-INJURY BIOMARKER EXCRETION IN PEDIATRIC KIDNEY TRANSPLANTATION?

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**Aims/Purpose:** Pediatric kidney transplantation with young acceptor and adult donor requires significant increases in the acceptors cardiac output (CO) and blood pressure to optimize donor kidney perfusion. Therefore, perioperative suprphysiological hemodynamic targets are recommended in most protocols. However, liberal fluid administration and vasopressor therapy to reach these targets risks fluid overload and limited graft perfusion. This study analyses kidney injury biomarker profiles in relation to hemodynamic variables to evaluate the effect of hemodynamic management on early postoperative donor kidney injury.

**Methods:** Observational, single centre study, including young children for living donor kidney transplantation between December 2017 and April 2021. Perioperative hemodynamic targets were cardiac index  $\geq 3.5$  L/min/m<sup>2</sup> and mean arterial pressure (MAP)  $\geq 65$  mmHg. Patient demographics, perioperative fluid administration, urine output and kidney function were collected. Cardiac output (CO), central venous pressure (CVP), MAP and norepinephrine infusion rates (Nor) were recorded at one and four hours postreperfusion (t1 and t4). Urine samples were collected from t4 until three days postoperative at 8 12 hour intervals. Urine concentrations of KIM-1, NGAL, LFABP, IGFBP and TIMP were analyzed with commercially available ELISA kits. Data analysis included correlation analyses of total splint urine biomarker excretion in the first three postoperative days with hemodynamic values at t1 and t4.

**Results:** Fifteen patients were included with mean [IQR] age 6 [5-8] years, weight 21 [16-25] kg and donor/acceptor BSA-mismatch of 2.4 [2.1-3.0]. All patients had diuresis within one hour after kidney reperfusion and good renal function at discharge. Relevant trends of negative correlation were found between CO and all biomarkers (Figure 1). Trends of positive correlation were found between CVP and Nor with both IGFBP and TIMP, and MAP with KIM-1. These trends were not unidirectional between biomarkers (Figure 1).

**Conclusion:** Our results support the hypothesis that a sufficiently high CO is needed to prevent post-reperfusion kidney injury. They also suggest that careful titration of fluids and vasopressors is important to limit kidney injury. The absence of statistically significant correlations might be due to the small sample size and the protocolized HD management.

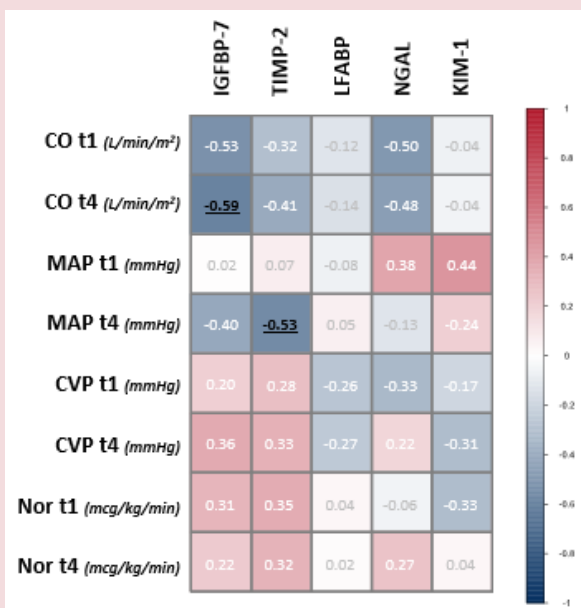


Figure 1: Correlogram of total splint-biomarker production and hemodynamic variables. Pearson correlations coefficients of log-transformed data are displayed. Positive correlations are displayed in red, negative correlations in blue. Significant correlations ( $p = 0.05$ ) are displayed in bold font. CO = cardiac output, MAP = mean arterial pressure, CVP = central venous pressure, Nor = Norepinephrine dosage.

Fr-P 062

**ASSOCIATION BETWEEN TACROLIMUS VARIABILITY AND DEVELOPMENT OF DONOR-SPECIFIC ANTIBODIES IN PEDIATRIC KIDNEY TRANSPLANTATION**

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**Aims/Purpose:** Donor-specific antibodies (DSA) is a well described predictor of antibody-mediated rejection and an important cause of graft loss in kidney transplantation. In adult population it has been demonstrated that high inpatient tacrolimus variability is associated with the development of de novo DSA. There are very scarce publications regarding this condition in pediatric kidney transplant recipients. The aims of present study were to analyze the inpatient variability of tacrolimus trough levels and their possible relationship with the appearance of de novo DSA in pediatric kidney transplant recipients.

**Methods:** A single-center retrospective study included pediatric kidney transplant recipients ( $\leq 18$  years), transplanted between 2015 and 2020. Inclusion criteria: patients on tacrolimus treatment, with more than 2 years follow-up and  $\geq 3$  measured tacrolimus trough levels. Patients with pre-transplant DSA were excluded. Inpatient tacrolimus variability was defined using the coefficient of variation for all trough levels obtained after 3 months post-transplant.

**Results:** From the 99 patients transplanted in our institution during the studied period, 61 patients were included in our final analyses. The median age at transplant was 11 (6.46–15.54) years. 14.75% of the patients developed de novo DSA. There was no significant difference in age and gender between those who developed DSA and those who did not. There was a significant association between de novo DSA development and thymoglobulin induction. A statistically significant association ( $p = 0.03$ ) was demonstrated between the increase in the variability of tacrolimus levels and the development of de novo DSA in the logistic regression model (Fig. 1).

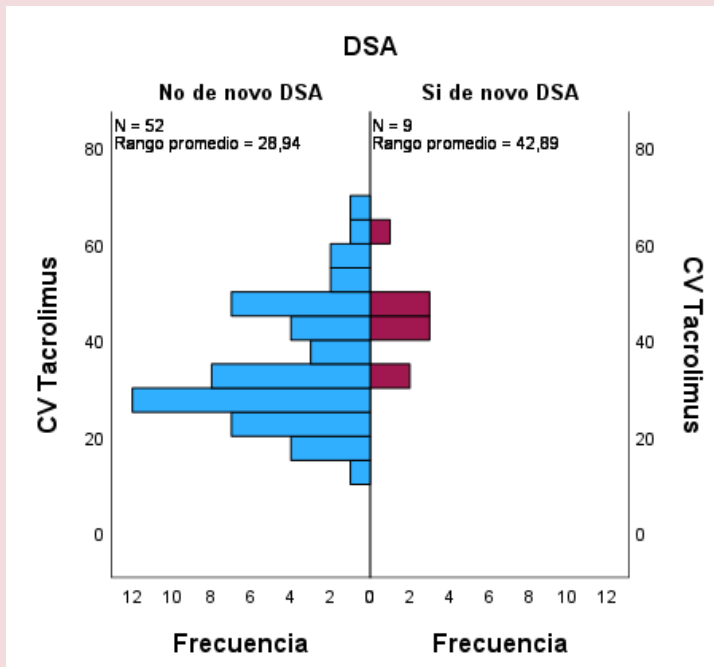


Figura 1: Frequency range of tacrolimus CV by de novo DSA development.

**Conclusion:** In the pediatric renal transplanted population studied, an association between variability in tacrolimus trough levels and the development of DSA was demonstrated. These results can help to early identify the population at risk of developing de novo DSA, to modify the dose of immunosuppression preemptively.

Fr-P 063

POST-TRANSPLANT RECURRENCE AND GRAFT LOSS IN GENETIC VS. NON GENETIC STEROID RESISTANT NEPHROTIC SYNDROME: THE CASE OF VARIANTS OF UNCERTAIN SIGNIFICANCE

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**Aims:** Multidrug-resistant nephrotic syndrome (NS) is characterized by high risk of recurrence after kidney transplantation (KT). Causative pathogenic variants (15–66% of children and young adults with NS) are considered at lower risk of recurrence than non-genetic forms. Genetic NS usually lead to fast progression to ESKD, but are less likely to recur after KT. Less clear is for NS cases with variants of uncertain significance (VUSs) in genes involved in NS. We compared the risk of NS recurrence and graft survival between genetic, non-genetic, and VUSs, for which there is insufficient information available to be considered as benign or pathogenic.

**Methods:** We analyzed the outcomes of patients with MRNS who received a KT at our pediatric center in last 30 years. All subjects were tested for monogenic causes of NS through NGS. Recipients were divided into positive (Genetic) and negative for pathological and likely pathological variants in autosomal or recessive dominant gene causing NS; then, negative group was split and VUSs were considered as a separated group.

**Results:** We identified 72 subjects who received a KT due to MRNS, with no differences among the three groups at baseline. Recurrence of NS was reported in 28/72 (40%) subjects (mean time of 15 days). Negative (including VUSs) had a relapse rate significantly higher ( $p = 0.003$ ) than genetics (Fig. 1A). When considered alone, VUSs had a relapse rate significantly higher than in the other groups. (Fig. 1B). NS recurrence was overall associated with a significantly shorter graft survival (Fig. 1C). When patients were stratified in genetic and negative, graft survival was higher in pathological variants ( $p = 0.002$ ). However, when patients were stratified in the three genetic risk cohorts, only VUSs had a significantly shorter graft survival ( $p = 0.002$ ) (Fig. 1E) Despite similar therapies, remission of recurrence was achieved in all genetics, in 75% of VUSs and 60% of non-genetic ( $p = 0.03$ ).

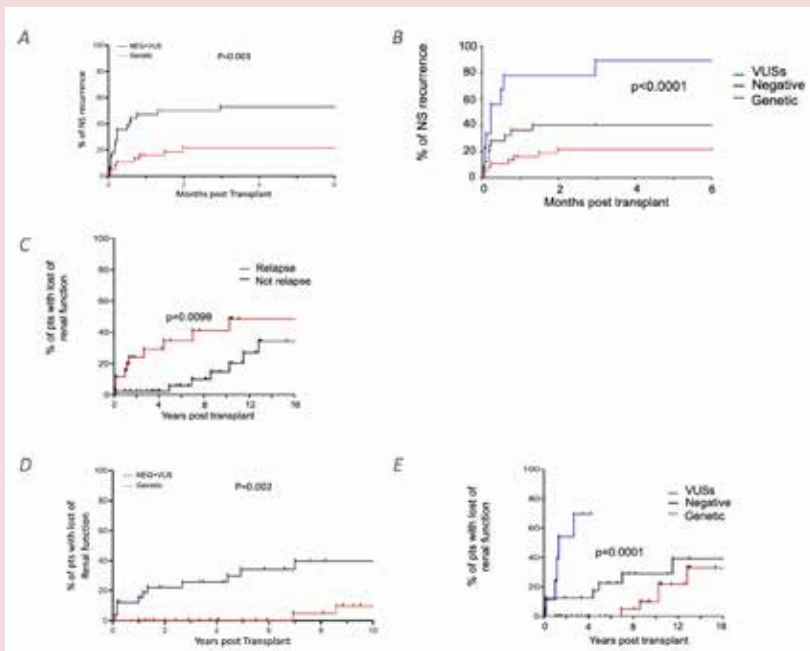


Figure 1: Kaplan-Meier curves for proteinuria recurrence in patients stratified in genetic and non-genetic. VUSs are considered in non-genetic ( $p = 0.003$ ) (a). Kaplan-Meier curves for proteinuria recurrence in patients stratified in genetic, VUSs, and non-genetic ( $p = 0.0001$ ) (b). Kaplan-Meier curves for graft survival in patients stratified in relapse and not of NS ( $p = 0.0099$ ) (c). Kaplan-Meier curves for graft survival in patients stratified in genetic, VUSs, and non-genetic ( $p = 0.001$ ) (e). p values represent significance levels across the groups.

**Conclusion:** Recurrence of NS in KT is used as evidence of the existence of a circulating permeability factor in negative forms. Based on this paradigm, no transplant recurrence of SRNS should be reported, however, the recurrence of genetic NS does not represent a novelty at all. In our cohort, we found a higher rate of recurrence of genetic forms (24%) compared to previous reports, mainly represented by mutations in NPHS2. Then, we considered VUSs as a separated group. We found that VUSs is an independent risk factor of NS recurrence and graft failure. Based on our results, the less favorable outcome usually attributed to non-genetic forms, may be worsened by considering as a single cohort VUSs and non-genetic NS. Given the rarity of the disease, a major strength of our study is the large cohort of subjects, all tested for monogenic causes of NS with a long follow-up. In sum, our study identifies the presence of VUS as a major risk factor for poor prognosis after KT in MRNS cases.

Fr-P 064

DENTAL STATUS AND TREATMENT OF DISORDERS IN CHILDREN ON DIALYSIS AND AFTER KIDNEY TRANSPLANTATION

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**Introduction:** End-stage chronic kidney disease (CKD5) and its associated drug therapy have adverse effects on both soft and hard oral tissues. The aim of this study to evaluate the dental status, as well as the effectiveness of treatment of the identified oral pathology in patients with CKD5.

**Materials and Methods:** The study included 55 patients on renal replacement therapy (RRT): 3 on dialysis and 55 after kidney transplantation; 37 children with a median age of 13.8 [10.9; 15.5] years and 21 young adults aged 23.3 [23.0; 23.7]. The dental examination included: an assessment of the prevalence and intensity of dental caries (indices DMFT, DMFT+dmft, dmft), developmental defects of enamel (MDDE), oral hygiene (PLI), periodontal status (GI), bleeding and the degree of gingival overgrowth. In 26 patients with permanent dentition therapeutic and prophylactic toothpastes were prescribed, as well as toothbrushes with soft bristles, and changes in dental status were assessed after 2 months of its use.

**Results:** The prevalence of caries was 48.3%, the intensity – in primary dentition of dmft = 0, in mixed – 1 [1; 5], in permanent – 4 [2; 7]. Enamel developmental defects were detected in 62.1% of the examined, the median number of teeth with defects was 12 [6; 18]: with code 1 – 3 [2; 4], with code 2 – 10 [4; 15], with code 3 – 4 [2; 7]. During initial examination, the median of oral hygiene index ranged from 1.40 [0.95; 1.85] in primary dentition, 1.50 [1.30; 1.90] in permanent to 1.80 [1.30; 1.90] in mixed. The median of the GI index was 1.35 [1.03; 1.60]. Gum bleeding was diagnosed in 55.2% of the examined patients, amlodipine-induced gum hyperplasia – in 53.4%. Re-examination of patients with permanent dentition two months after the use of moisturizing toothpaste and soft toothbrush revealed that the median PLI, GI and gingival bleeding decreased from 1.50 [1.30; 1.80] to 0.85 [0.30; 1.30] ( $p < 0.001$ ), from 1.30 [1.00; 1.50] to 0.5 [0.30; 1.10] ( $p < 0.001$ ) and from 56.0% to 31.6% ( $p = 0.042$ ) respectively. The proportion of patients with gingival hyperplasia decreased slightly from 57.7% to 50.0% ( $p = 0.78$ ), which confirms the leading role in the development of this condition of drug therapy.

**Conclusion:** There is a low intensity of caries, poor oral hygiene and inflammation of the gum tissues of moderate severity, the presence of defects in the development of enamel in patients undergoing RRT. Correction of individual oral hygiene contributes to the improvement of dental status.

Fr-P 065

## ADULT SELF-REPORTED QUALITY OF LIFE AFTER PEDIATRIC KIDNEY TRANSPLANTATION

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**Aims/Purpose:** It is widely accepted that kidney transplantation (KT) is the best renal replacement therapy for children with end of stage renal disease (ESKD). However scarce data is published regarding feelings, social development and perceptions of adult patients who have undergone a pediatric KT. The purpose of this study is to describe and analyse patient-reported outcomes (i.e. social, educational and subjective outcomes) of adult population who previously underwent a pediatric KT.

**Methods:** We performed a self report study in adult population (> 18 years old) who received a pediatric KT in our institution between 1979 and 2019, with > 1 year follow-up. Patients were contacted by e-mail or by phone and were invited to fulfill a self report survey with open ended questions about education/training, laboral life, social and familial status, physical and emotional development, healthy lifestyle and free topic comments.

**Results:** Of the 287 pediatric patients who received 345 KT in our institution, 17 were lost to follow-up, 45 died and 75 patients were < 18 years old. From the 150 remaining patients asked to fulfill the survey, 82 subjects (54.7%) accepted answering the survey. From the 82 participants only 32 (39%) cases had become independent, most of them (37.8%) living together. Ten patients (12.2%) had children. Regarding education, 28% completed upper secondary/post-secondary non tertiary education and 16% tertiary education level. An early education dropout was referred by 42% cases. Fifty three subjects (64.6 %) were unemployed. Only 26% cases reported a good quality of life (QOL), compared to healthy population of similar age. Nearly one third (30%) referred serious comorbidities (defined as conditions affecting an extrarenal organ). Only 9% patients practiced regular sports. Five patients (6%) admitted drug addiction. Concerning to self corporal image, 13 (15.9%) and 4 patients (4.8%) were deeply troubled for their short stature and obesity, respectively. Finally, most patients (97.6%) were grateful and had good memories from their stay in our pediatric nephrology unit.

**Conclusion:** The studied population presented worse patient-reported outcomes in their adult life compared to general population. Despite pediatric KT is the best treatment for children with ESKD, there are still many limitations and concerns that affect both their QOL and social and psychological development. These findings highlight the importance of a multidisciplinary approach in the follow-up and adult transition of pediatric kidney transplanted patients.



Fr-P 066

## PAEDIATRIC RENAL DIETETIC INPUT POST RENAL TRANSPLANT: A SURVEY OF UK PAEDIATRIC RENAL DIETITIANS

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**Aims/Purpose:** It is known that children with chronic kidney disease, including those who have received a renal transplant, are at increased risk of cardiovascular disease. Dyslipidaemia, overweight and obesity are prevalent in children who have received a renal transplant. Whilst continued assessment of growth and nutrient intake has been suggested by KDOQI in this patient group, there is a lack of published data on the current dietetic services for children post renal transplant in the UK.

**Methods:** We surveyed paediatric renal dietitians from the 13 tertiary paediatric nephrology centres in the UK using an electronic survey.

**Results:** An analysis of the responses received showed that there were no protocols in place for commencing early post-operative nutrition aimed at maintaining appropriate nutritional status. Whilst dietetic advice was provided initially post-transplant (e.g. healthy eating, food safety advice), apart from children requiring oral nutritional supplements or enteral feeds, 69% of dietitians did not regularly review these patients in the outpatient setting. The main reasons for lack of regular follow up included issues with staffing levels (67%), a review on request service was available (100%) and it was felt that diet advice, if required, could be managed by community paediatric dietitians (56%). The main dietetic concerns noted were large weight gain post-transplant (85%), difficulties weaning off enteral tube feeds (23%) and following 'healthy eating' advice (31%). The paediatric renal dietitians noted a need for improved resources (e.g. videos, nationally approved post-transplant diet sheet) (33%), a dedicated paediatric renal dietitian/more frequent reviews (91%) and community dietetic support/referral system for weight management advice (25%).

**Conclusions:** This survey identified a need to improve the current paediatric dietetic services to paediatric renal transplant patients in the UK. The main current barriers to this appear to be related to issues with staffing levels and funding for this type of service in the hospital and community settings.

Fr-P 067

**INVESTIGATING OUTCOMES IN THE USE OF INCREASED RISK DONOR ORGANS IN PAEDIATRIC SOLID-ORGAN TRANSPLANTATION: A SYSTEMATIC REVIEW**

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**Aims/Purpose:** Solid-organ transplantation (SOT) is the gold-standard treatment for end-stage organ failure. However, the insufficient supply of organs often results in high morbidity and mortality. Increasing the utilisation of organs from increased risk donors (IRD), which carry increased risk of HIV, Hepatitis B and/or C, is a potential method to better utilise organs already present within the donor pool. Therefore, this study aimed to assess the impact of IRD organ use in paediatric SOT recipients on patient outcomes, in comparison to 1. Non-IRD organ use, and 2. Remaining on the transplant waiting list.

**Methods:** Systematic review of online databases followed by fixed-effects meta-analyses per outcome where possible. Outcomes of interest were 5-year patient survival, 5-year allograft survival, time on the transplant waiting list, and blood-borne virus transmission.

**Results:** 1,753 results were initially retrieved, with six studies included in the final review. The use of IRD organs compared to non-IRD organs observed no difference in patient survival, allograft survival, or transplant waiting list time. The use of IRD organs observed significantly improved patient survival (HR: 0.52, CI: 0.37-0.73, two studies) and reduced transplant waiting list time, compared to remaining on the transplant waiting list. One incident of donor-to-recipient disease transmission was reported, however no information regarding organ risk-status or post-transmission outcomes were reported.

**Conclusion:** Results suggest that IRD organs may be a beneficial equivalent to non-IRD organs, in appropriate circumstances (i.e., when remaining on the transplant waiting list may be detrimental to potential recipients). This does not necessarily suggest that the routine and indiscriminate acceptance of all IRD organs would observe the same patient benefits. Instead, careful consideration of donor and recipient factors (i.e., age, antigen mismatch, imminent loss of dialysis access, risk of death) is required to objectively evaluate the risks and benefits of IRD organ use in the clinical context.

Fr-P 068

**INCREASED KIDNEY ALLOGRAFT FIBROSIS IN PATIENTS WITH METHYLMALONIC ACIDURIA: A CASE CONTROL STUDY**

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**Background and Aims:** Chronic kidney disease (CKD) is a complication of methylmalonic acidemia (MMA), a rare metabolic disease. About 14% of patients with MMA and CKD reach kidney failure or have frequent metabolic decompensation needing kidney (KTx) or liver/kidney transplantation (LKTx). Histopathology data after transplantation are scarce but showed an early and extended fibrosis, suggesting a worse prognosis. We investigated fibrosis progression in MMA compared to controls.

**Method:** Retrospective case-control study: clinical, biological and histological characteristics at 3 and 12 months of MMA patients having received KTx or LKTx were compared to matched controls of transplanted patients with congenital uropathies. We included all MMA patients followed in Necker Hospital(Paris) and Robert Debré Hospital(Paris) between November2001 and August2022. All kidney biopsies slides were blinded reviewed by 2 renal pathologists. Banff elementary lesions, signs of calcineurin inhibitors (CNIs) toxicity, and grade, percentage and tissue distribution of interstitial fibrosis and tubular atrophy (IF/TA) were evaluated. The results are expressed as median(IQR), mean(standard deviation) or percentages and were compared using Fisher or Mann-Whitney-Wilcoxon tests (significance level for p-value < 0.05).

**Results:** 20 MMA patients (6 KTx, 14 LKTx) and 20 controls (20 KTx) were included. Mean age at transplantation was 10years in both cohorts (3 to 30 years in MMA and 3 to 26 years in controls). A higher percentage of IF/TA (Fig.1) was observed in MMA at 3 and 12 months ( $11\% \pm 13$  vs  $0.5\% \pm 2$ , ( $p = 0.014$ ) and  $40\% \pm 31$  vs  $12\% \pm 18$ , ( $p = 0.004$ )), respectively; with more inflammatory at 12 months (i-IF/TA  $1.0\% \pm 0.9$  vs  $0.1\% \pm 0.3$ ,  $p = 0.001$ ). MMA patients had a higher incidence of clinical/subclinical rejection at one-year follow-up ( $8/18$  vs  $2/20$ ,  $p = 0.016$ ), more peri-operative complications such as hypovolemia ( $16/20$  vs  $9/20$ ,  $p = 0.02$ ), need for blood transfusions ( $18/20$  vs  $5/20$ ,  $p = 0.00001$ ), and sepsis within 3 months after transplantation ( $9/20$  vs  $1/20$ ,  $p = 0.003$ ). They also presented higher inpatient variability of tacrolimus through levels (mean coefficient of variation  $44\%$  vs  $33\%$ ,  $p = 0.026$ ). Graft function was comparable in both groups at 3 and 12 months (median eGFR at 12 months: MMA  $69$  ( $54-94$ ) mL/min/1.73m<sup>2</sup>, controls  $67$  ( $55-78$ ) mL/min/1.73m<sup>2</sup>,  $p = 0.73$ ). However, in a subset of patients, the GFR at 3 months post-transplantation was measured using iohexol clearance showed a significant difference between eGFR using serum creatinine and measured GFR with a median delta eGFR-mGFR of  $25$  ( $2-40$ ) mL/min/1.73m<sup>2</sup> ( $p = 0.047$ ) confirming that serum creatinine is not a reliable marker of kidney/graft function in MMA, at least in the early post-transplant period.

**Conclusion:** We observed an early increase in kidney fibrosis in MMA. At one-year follow-up, graft function was still comparable in both groups. The respective contribution of methylmalonic acid accumulation and CNIs to graft toxicity and subsequent fibrosis needs to be evaluated in further studies with longer follow-up.

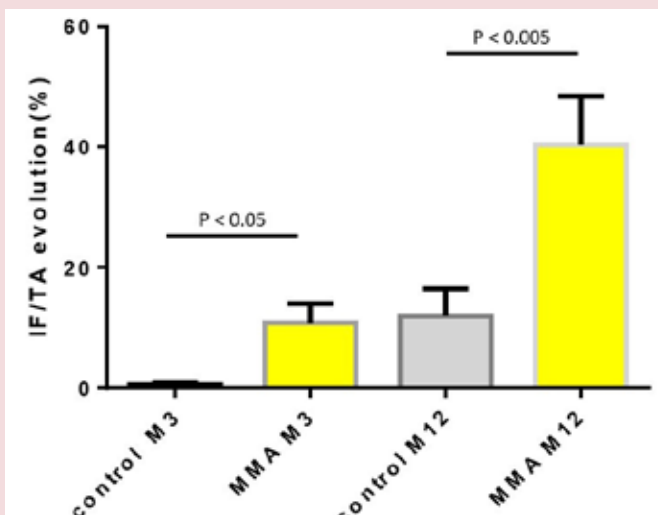


Figure 1: Interstitial fibrosis and tubular atrophy (IF/TA) on kidney biopsy at 3 months and 12 months after kidney transplantation.

Fr-P 069

**EFFICACY AND SAFETY OF CHRONIC ANTIBODY-MEDIATED KIDNEY ALLOGRAFT REJECTION TREATMENT: EXPERIENCE FROM A SINGLE CENTER IN NORTHERN ITALY**

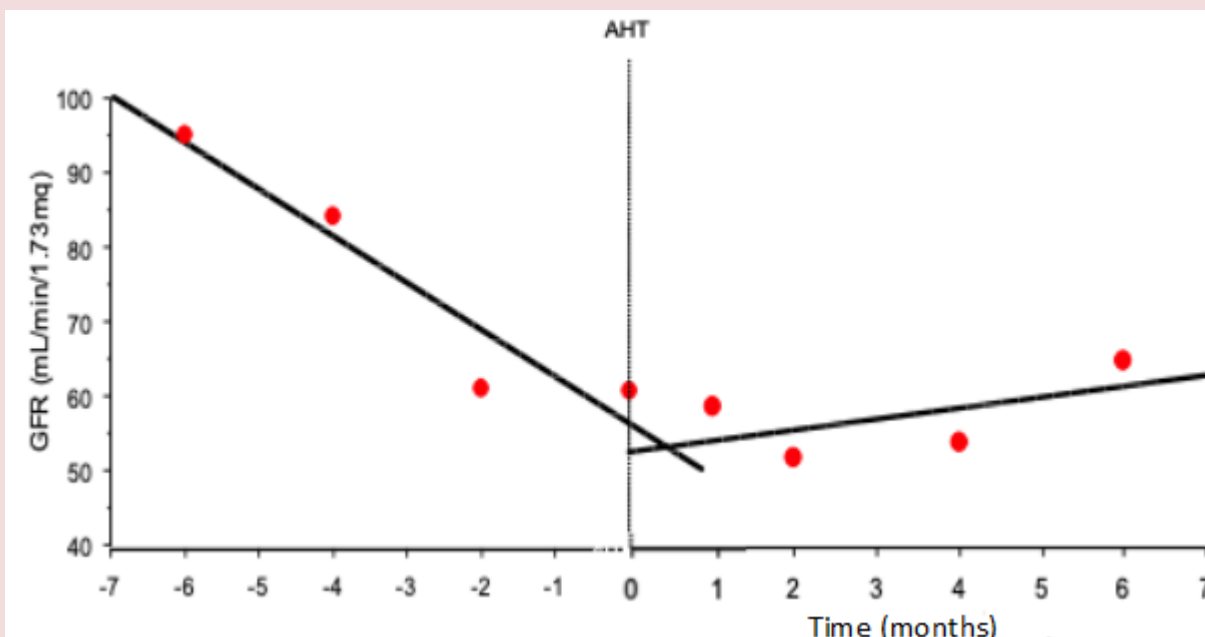
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**Aims/Purpose:** To investigate safety and response to anti-humoral treatment (AHT) in case of active chronic antibody-mediated rejection (CAMR) in a population of pediatric pts undergoing kidney transplantation (KT).

**Methods:** We retrospectively studied KT patients aged < 25 yrs, managed in our Center on maintenance IS therapy, that received a histological diagnosis of CAMR with detection of newly-onset specific anti-HLA donor antibodies (dnDSA). From 1st January 2014 to 31st December 2021 pts with diagnosis of CAMR underwent AHT with a combination of five sessions of plasmapheresis or immunoadsorption on alternate day if available suitable vascular access, followed by intravenous immunoglobulin (IVIg) 1 g/kg in four weekly doses and finally Rituximab (RTX) 375 mg/m<sup>2</sup>. Response to AHT was defined as: reduction of the rate of loss of GFR by at least 30% in the period of 6 mos after initiation of AHT compared with the period 6 mos prior to intervention; percentage decline of at least 50% of MFI of dnDSA; reduction of proteinuria if pathological.

**Results:** 107 pts were eligible; 15 (9M) pts were enrolled according to the inclusion criteria. Median age was 15.6 (IQR: 12.0–19.2) yrs, median time from KT was 67.5 (IQR: 25.2–96.1) mos. Pts undergoing plasmapheresis were 6/15 (40%). Pts who showed reduction of the rate of loss of GFR by at least 30% in the period of 6 mos after AHT were 10 (66.7%). The trend of GFR slope was significantly different in the two periods of 6 months pre and post-AHT: pre-AHT slope -6.29 Vs post-AHT slope +1.36 (p: 0.038) (Figure 1). Ten pts (66.7%) had a decline of at least 50% of MFI of dnDSA. None pts had pathological proteinuria. Plasmapheresis and initial level of MFI did not influence the response to AHT (p > 0.05). We analyzed data 24 mos after AHT: after the first 6-month period following AHT, GFR's decline resumed. Twenty-four mos after AHT the graft survival was 72%. There was no significant difference in 24-month graft survival between responder and non-responder pts. In pts with loss of graft function, median hemodialysis free time after AHT was 25.4 mos (IQR:12.7–32.4). No increase in infectious episodes have been detected in treated pts.



**Conclusion:** Our data show a stabilization or improvement of graft function 6 months after the end of the therapeutic protocol. AHT allowed a greater survival of the graft at 2 yrs compared to the natural course of CAMR. This combination of treatment can provide a safe and efficacious basis for the management of this post-transplant complication.

Fr-P 070

## RAVULIZUMAB “DE NOVO” IN PEDIATRIC PATIENTS WITH ATYPICAL HEMOLYTIC UREMIC SYNDROME (AHUS): FIRST WORLDWIDE CASES

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**Aims/Purpose:** Ravulizumab is a long-acting C5 inhibitor that has recently demonstrated its effectiveness for the control of hemolytic uremic syndrome compared to eculizumab, allowing average annual infusion times (up to 70% less). There's still no evidence in the literature of naïve treatment with this drug in pediatrics.

**Methods:** Present the first two pediatric cases worldwide using “de novo” Ravulizumab (in the onset of the disease and post-kidney transplant).

**Results:** 13-year-old girl with history of bloody stools, vomiting and compromise of consciousness with TMA, AKI III evolves to anuria and convulsive episode requiring corticosteroid boluses, 6 plasmapheresis sessions and 4 intermittent hemodialysis. Normal ADAMTS-13, negative direct Coombs and decreased complement. Due to persistent TMA and requirement of renal replacement therapy (RRT), ravulizumab was started with a loading dose (2400 mg) and a second one after 2 weeks. The need for RRT ceased with improvement of hemolysis and renal function. Genetic: CFHR3-CFHR1 deletion. Case 2: 7-year-old girl in chronic hemodialysis secondary to aHUS (CD46 mutation) was admitted for kidney transplant from a living donor. Low-intermediate immunological risk and high CMV infectious risk. Induction treatment: Basiliximab, tacrolimus, mycophenolate and steroids. First dose of Ravulizumab was infused the day before transplantation (900 mg), well tolerated. The patient has had a favorable evolution of renal function with normal creatinine value at discharge. Protein/Creatinine urine ratio increased to a maximum of 8 mg/mg (negative DSA levels). The option of renal biopsy was discarded due to a decrease in proteinuria. She received second dose after 2 weeks, remain stable with no data on recurrence of her underlying disease today.

**Conclusion:** Ravulizumab was satisfactory both in the acute phase of the disease and in the immediate post-transplantation. In the first case we observed a functional recovery from the first dose with no notable adverse effects up today, as in post-transplant patient, maintaining a good control of TMA despite more spaced dosing (8 weeks). The inclusion of this drug in the therapeutic arsenal opens a new safe treatment route in pediatric patients with aHUS.

Fr-P 071

CYTOPENIAS IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS: PRECEDING FACTORS AND CLINICAL CONSEQUENCES

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**Aims/Purpose:** Kidney transplantation is associated with secondary complications, including the risk of developing post-transplant cytopenias. This study aimed to evaluate the characteristics, identify predictors, and assess the management and consequences of cytopenias in the pediatric kidney transplant population.

**Methods:** This is a single-center retrospective analysis of 89 pediatric kidney transplant recipients. Possible factors preceding cytopenias were compared with the goal to recognize predictors for post-transplant cytopenias. Post-transplant neutropenias were analyzed for the total study period, and, separately for the period beyond 6-months post-transplant (late neutropenias), to rule-out the confounding influence of induction and initial intensive therapy.

**Results:** Sixty patients (67%) developed at least one episode of post-transplant cytopenia. All episodes of post-transplant thrombocytopenias were mild or moderate. Post-transplant infections and graft rejection were found to be significant predictors for thrombocytopenia (HR 6.06, 95% CI 1.6-22.9, and HR 5.82, 95% CI 1.27-26.6, respectively). 30% of post-transplant neutropenias were severe (ANC = 500). Pre-transplant dialysis and post-transplant infections were significant predictors for late neutropenias (HR 11.2, 95% CI 1.45-86.4, and HR 3.32, 95% CI 1.46-7.57, respectively). Graft rejection occurred in 10% of patients with cytopenia, all following neutropenia, within 3 months from cytopenia appearance. In all such cases, mycophenolate mofetil dosing had been held or reduced prior to the rejection.

**Conclusion:** Post-transplant infections are substantial contributors for developing post-transplant cytopenias. Pre-emptive transplantation appears to reduce risk for late neutropenia, the accompanying reduction in immunosuppressive therapy and the ensuing risk for graft rejection. An alternative response to neutropenia, possibly using granulocyte colony stimulating factor, may diminish graft rejection.

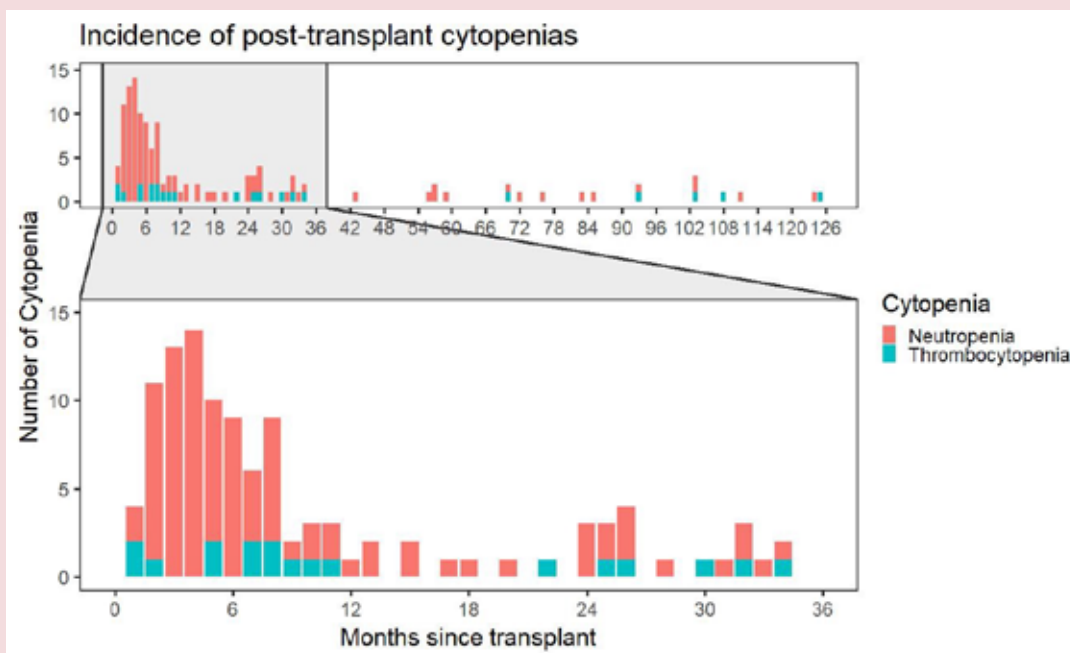


Figure: Cytopenia events over time since transplantation.

Fr-P 072

**SYSTEMATIC DIGITAL ASSESSMENT OF PATIENT-REPORTED OUTCOMES DURING FOLLOW-UP OF PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS: A PILOT STUDY**

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**Aims/Purpose:** Patient-Reported Outcomes (PROs) are defined as the measurement of a patient's perception of his/her disease and corresponding treatment without interpretation by a third person (i.e., healthcare personnel). In chronic kidney disease, especially regarding pediatric patients, PROs fill an important gap to achieve optimal disease control, treatment, and well-being. In addition, the digital and systematized collection of patient history has been shown to provide additional information in comparison to traditional methods. Currently, neither PROs nor digital patient history systems are frequently implemented in clinical routine. The aim of this study is the development, implementation, and analysis of a digital system for the collection of patient history and PROs for pediatric patients with kidney transplantation, in context of their kidney allograft function during follow-up.

**Methods:** Pediatric kidney transplantation patients at the Medical University of Vienna were regularly surveyed for their recent history (i.e., since the last visit) and several different PROs (e.g., adherence), at their regular outpatient clinic visits. The collected patient history elements and PROs were submitted to an unweighted, undirected network-based clustering analysis, and further associated with kidney allograft function and other clinical surrogate outcome parameters (e.g., creatinine).

**Results:** A total of 49 pediatric kidney transplant patients were included in this study, being 67%:33% male:female, with a median age of 14 years (IQR 11-16 years) and a median post-transplant follow-up time of 5.3 years (IQR 2.7-10 years). Of these, 45% were living donor recipients, and maintenance immunosuppression was mainly a triple regimen (tacrolimus, mycophenolate mofetil, steroids). The median graft function at baseline was 100 mL/min/1.72m<sup>2</sup> (IQR 70-124 mL/min/1.72m<sup>2</sup>). Patients were distributed to four distinct clusters, based on their collected history elements and PROs (e.g., defecation-related questionnaire elements), of which two clearly differentiated between patients with high and low kidney allograft function.

**Conclusion:** For the first time, we were able to demonstrate a clear differentiation between pediatric patients with high and low kidney allograft function based on different patient history elements and PROs. The longitudinal follow-up of pediatric kidney transplant patients with these systems could aid in the early identification of complications and facilitate early intervention during follow-up after transplantation.

Fr-P 073

## DARATUMUMAB IN POST-TRANSPLANT RECURRENCE OF SRNS

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**Aims/Purpose:** Post-transplant recurrence of steroid resistant nephrotic syndrome occurs in up to 50% of patients and is a major cause of graft loss. There is currently little consensus regarding the best management for SRNS recurrence. Plasma exchange (PE) or Immunoabsorption of immunoglobulins (IA), combined to rituximab are the most common strategies. However, complete remission or sustained remission are not always achieved. Long Lived Plasma Cells (LLPC) may be responsible of refractory forms of autoimmune diseases and targeting CD38 on plasma cells with Daratumumab (DARA) may be an additional option in the treatment of post-transplant recurrence.

**Methods:** This is a retrospective multicentre study in France. We identified all children with post-transplant recurrence of SRNS, unsuccessfully treated with PE and/or IA and B-cell depletion, that secondarily received 1 to 4 infusions of Daratumumab 1g/1.73m<sup>2</sup>.

**Results:** Five patients were included. Median age at INS onset was 5.9 years and median delay to End-Stage-Renal Disease was 1.4 years. One patient had experienced, under IA, a transient remission on native kidneys. Four patients underwent a first renal transplant and one patient a second graft. All patients experienced early recurrence. Four patients went into complete remission after PE and/or IA, combined to high dose steroids and calcineurin inhibitors, but relapsed when sessions were spaced, despite B-cell depletion with rituximab and/or Ofatumumab or Obinutuzumab. After reintensification, PE and/or IA were successfully stopped within 1 month following 1 to 4 weekly infusions of Daratumumab. The fifth patient was completely resistant to IA and B-cell depletion with Obinutuzumab. Proteinuria began to decrease one week after the 4th infusion of Daratumumab, at 3 months post transplantation. IA were discontinued at D147 and she remains in complete remission at 2 years of follow-up.

**Conclusion:** We report on five patients, resistant to standard-treatment of recurrent SRNS, who achieved complete and/or sustained remission after the addition of the anti CD38 antibody, daratumumab. Post-transplant recurrence of SRNS is a dramatically challenging situation. These results identify that targeting both CD20 positive B cells and plasma cells is a novel strategy for the treatment of post-transplant recurrence and suggest that the addition of daratumumab should be considered in refractory recurrent SRNS.



Fr-P 074  
HYPERPARATHYROIDISM AFTER KIDNEY TRANSPLANTATION IN CHILDREN

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**Objective:** Most patients with chronic kidney disease develop variable degree of secondary hyperparathyroidism (HPT) and it is considered to be resolved after kidney transplantation (KT). However, it is reported in adults that persistent HPT after KT occurs in up to 50% of KT recipients, with various risk factors including dialysis duration and pretransplant parathyroid hormone (PTH) level. We analyzed the prevalence of HPT after KT and its risk factors among children in a single referral hospital.

**Methods:** This retrospective observational study analyzed medical records of children who received KT between 2007 and 2020 in Seoul National University Children's Hospital. Persistent HPT was defined as median PTH level after KT of more than 55 pg/mL. Annual prevalence of persistent HPT with associated abnormalities, such as hypophosphatemia and hypercalcemia, was identified.

**Results:** Among 135 patients who received KT between 2007 and 2020, 56% of them were boys and their mean age was 10.5 years and. Prevalence of persistent HPT was about 40% after 1 years, which remained stable up to 4 years after KT. Occurrence of persistent PTH was associated with longer pretransplant dialysis duration and pretransplant hyperphosphatemia. 15 of them received cinacalcet therapy and 1 of them received parathyroidectomy. 49.6% of children were either on graft failure or last eGFR less than 60ml/min/1.732 after a median of 4.6 years post KT and hyperparathyroidism status was not associated with decreased kidney function.

**Conclusion:** Prevalence of persistent HPT after KT is common in children, with considerable portion of them being treated medically or surgically. Degree of secondary hyperparathyroidism before KT may be a risk factor of developing persistent hyperparathyroidism in children. However, adverse effect on graft function was not observed in our cohort. Further study is needed regarding precise bone metabolism among these population.

Fr-P 075

FIRST REPORT ON THE USE OF A HUMAN RECTUS SHEATH FASCIA TO AID ABDOMINAL CLOSURE FOLLOWING COMBINED LIVER AND KIDNEY TRANSPLANT IN A COMPLEX METABOLIC PATIENT

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**Aims/Purpose:** As medicine is advancing, more complex children are becoming multi-organ transplant candidates, bringing new challenges in all aspects of their care. We describe the first case of a small child receiving a combined liver and kidney transplant (CLKT) and an abdominal rectus sheath fascia transplant on a background of Williams Syndrome and Methylmalonic Acidaemia (MMA).

**Methods:** A 3 year old boy with MMA, Williams Syndrome and chronic kidney disease stage 5, and with a weight of 12.5kg, was listed for CLKT. There were many anaesthetic, medical, metabolic and surgical challenges to consider. Pre-operative planning included close collaboration between 9 specialties in 4 hospitals. A long general anaesthetic increased the risk of cardiac complications and metabolic decompensation given the patient's background. Gaining an in depth understanding of the metabolic state of the patient pre- and peri-operatively was crucial in avoiding metabolic decompensation. Hour by hour management protocol was drafted to facilitate transplant and included five domains: 1. Management at the time of organ offer, 2. Before the admission, 3. At admission and before theatre time, 4. Intra-operative management and 5. Post-operative management in the first 24 hours. Given the patient's small size, and the need for two intra-abdominal organ transplants without benefiting from an expanded abdominal cavity secondary to peritoneal dialysis or end stage liver failure associated ascites and/or hepatomegaly; abdominal closure posed an additional challenge to this case.

**Results:** The patient received left liver lobe and left kidney from a deceased donor. Abdominal closure was complicated due to the patient's small size and an organ size mis-match (donor was adult) with a graft recipient weight ratio of 3.7. Seven weeks after CLKT, patient received an abdominal rectus sheath fascia transplant from a second deceased donor, which to our knowledge, was the first use of human fascia for this indication. Requirement was for a blood group compatible donor with no additional immunosuppression needed as fascia is acellular and avascular structure. Through a multidisciplinary (MDT) approach and detailed pre-operative planning, a good outcome was achieved and 2 years post-transplant the child has good kidney and stable liver function, no transplant-related complications, improved growth and neurodevelopment, and an excellent quality of life as reported by the parents. Gastrostomy formed before transplant was preserved throughout. This peri-transplant protocol was used for all other patients with MMA we transplanted with excellent outcomes.

**Conclusion:** Rectus sheath fascia can be considered for abdominal closure following CLKT and can lead to good results. No additional immunosuppression is needed. MDT approach is essential for good clinical outcomes.

Fr-P 076

**SUCCESSFUL SEQUENTIAL HAPLOIDENTICAL MATERNAL HAEMATOPOIETIC STEM CELL AND KIDNEY TRANSPLANTATION FOR SCHIMKE IMMUNE-OSSEOUS DYSPLASIA**

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**Introduction:** Schimke Immuno-osseous Dysplasia (SIOD) is a rare autosomal recessive disease caused by homozygous SMARCAL1 gene mutation leading to FSGS, immunodeficiency and disproportionate short stature. The aim of improving quality and quantity of life relies on management of end-stage kidney disease (ESKD) and prevention of possibly fatal opportunistic infections caused by T-cell deficiency. We present a case of tolerance of the solid organ allograft with minimal immunosuppression, using haploidentical haematopoietic stem cell transplantation (HSCT) five months prior to living related kidney transplant (LRKT) from the same maternal donor.

**Case description:** A 5-year-old girl presented with steroid resistant nephrotic syndrome, dysmorphic features and short stature and had genetic confirmation of SIOD. In the year following her diagnosis, she reached ESKD and commenced haemodialysis (HD). The possibility of proceeding with maternal stem cell then kidney transplant from the same haploidentical donor, as per Stanford protocol, had been explored and accepted by both parents and our hospital's ethic committee. She underwent conditioning treatment with pharmacokinetic adjusted exposure to chemotherapy followed by successful engraftment of the  $\alpha\beta$  T-cell- and CD19 B-cell-depleted HSCT at 7 years of age. She was switched from HD to continuous veno-venous haemofiltration (CVVH) for 24 days in paediatric intensive care to sustain continuous and strict fluid control as chemotherapy and nutrition were given intravenously. Medications, including MESNA to protect her urothelium and bladder in view of future kidney transplant, were adjusted for CVVH. She developed mucositis and mild skin graft versus host disease which were resolved at discharge 40 days after conditioning had begun. The 175-day period between HSCT and LRKT was uneventful. She underwent LRKT now with no HLA mismatch, no induction or anti-proliferative agents and lower trough tacrolimus levels (5–7 ug/L). She recovered normal kidney function five days post transplant and remains stable with a plasma creatinine of 21 to 29  $\mu\text{mol/l}$  (eGFR of 112 to 155  $\text{ml/min/1.73m}^2$ ) with discontinuation of oral prednisolone and tacrolimus one month post-transplantation. Her infectious prophylaxis regimen included oral letermovir, aciclovir, co-trimoxazole, intravenous caspofungin and then conversion to oral itraconazole once stable trough tacrolimus levels were obtained.

**Discussion:** Haploidentical HSCT prior to LRKT is a high-risk intervention which could improve life expectancy in patients with SIOD. To our knowledge, we are the first team to demonstrate the success of the Stanford protocol in a paediatric recipient receiving CVVH and not HD during HSCT conditioning treatment. This intervention led to a successful LRKT with minimal immunosuppression, which was the first case performed in our centre.

Reference

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Fr-P 077

**PEDIATRIC KIDNEY TRANSPLANT AND ITS CARDIOMETABOLIC IMPACT – A 15-YEAR COHORT STUDY**

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**Aims/Purpose:** Kidney transplant (KT) is the treatment of choice for pediatric patients with end-stage kidney disease (ESKD). However, cardiovascular disease remains an important cause of morbidity/mortality in these patients. We aimed to evaluate KT impact on cardiometabolic risk factors, namely on overweight/obesity, hypertension (HTA), insulin resistance and dyslipidemia.

**Methods:** Retrospective analysis of patients who received a KT before 18 years-old, followed in our tertiary pediatric nephrology reference center, between 2008 and 2022. Pre-KT demographical and clinical data, namely regarding previous kidney replacement therapies were gathered. Body mass index (BMI), blood pressure (BP), and lipid profile (LP) were registered at baseline (BL) and compared with values at 6 and 12-months (M) post-KT. Glomerular filtration rate (GFR) was calculated using Schwartz bedside formula, at 6 and 12M post-KT. Patients with graft loss or follow-up for less than 12M were excluded.

**Results:** Sixty-six patients (60.6% males) were included, with a median (25th-75th percentile) age at KT of 12.2 (9.0-15.7) years-old. The most frequent ESKD etiologies were congenital abnormalities of the kidney and urinary tract (60.6%) and glomerular diseases (25.8%). In 8 patients (12.1%) KT was preemptive, while 26 (39.4%) undergone hemodialysis and 44 (66.6%) peritoneal dialysis. Median waiting time for KT was 0.9 years (0.6-2.7). Median estimated GFR values were similar at 6M and 12M post-KT (68.2 ml/min/1.73m<sup>2</sup>). Median BMI increased significantly from BL to both 6M and 12M post-KT (18.5 (16.2-20.7) vs 21.2 (16.5-24.7) vs 20.3 (16.7-23.5) kg/m<sup>2</sup>, respectively,  $p = 0.001$ ). Percentage of patients overweight/obese increased significantly when comparing patients at BL with 6M and 12M follow-up (20.0% vs 50.0% vs 42.4%, respectively,  $p = 0.001$ ). Considering BP, the rate of patients with HTA dropped significantly from BL to 6M post-KT (52.7% vs 46.9%,  $p = 0.001$ ), and from 6M to 12M post-KT (46.9% vs 40.0%,  $p = 0.001$ ). Post-KT, 6 patients (9.1%) developed diabetes mellitus. Regarding LP, total cholesterol, LDL and triglycerides levels diminished through follow-up, but only reaching significant differences at 12M post-KT ( $p = 0.002$ ,  $p = 0.003$ , and  $p < 0.001$ ). HDL levels raised when compared from BL to both 6M/12M post-KT, despite no significance ( $p = 0.053$  and  $p = 0.598$ , respectively). The proportion of patients with dyslipidemia diminished through follow-up period, but again only reaching significance when comparing BL to 12M post-KT (71.9% vs 51.9%,  $p = 0.007$ ).

**Conclusion:** Our study supports that BP and lipid profile significantly improved after KT. The increasing levels of BMI should be addressed, since obesity is also known to act as a risk factor for faster decline of allograft function. The importance of cardiovascular risk factors control is of utmost importance to lessen the global risk of death in this population.

Fr-P 078

TISSUE EXPRESSION OF ANGIOTENSIN TYPE 1 RECEPTOR, ENDOTHELIN TYPE A RECEPTOR AND TWO ADHESION MOLECULES OF THEIR DOWNSTREAM SIGNALING, IN PROTOCOL BIOPSIES OF PEDIATRIC KIDNEY TRANSPLANT PATIENTS

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**Aim:** Antibody-mediated rejection (AMR) is the major cause of premature kidney transplant failure. The role of alloantibodies against Human Leukocyte Antigens (HLA) in mediating AMR has been of primary interest in transplantation. However, there is evidence that non-HLA autoantibodies have a role in the involvement in AMR. Auto and allo antibodies (Abs) against angiotensin II receptor 1 (AT1R) and endothelin A receptor (ETAR) have been associated with poor allograft outcomes in renal transplantation. Nevertheless, evidence for routine tests remain insufficient, especially in the pediatric field.

This pilot study aims to evaluate the impact of circulating anti-AT1R and anti-ETAR Abs, investigating the tissue expression of these receptors and of two adhesion molecules downstream of their signalling, in protocol biopsies of pediatric kidney transplant patients.

**Methods:** In our pediatric renal transplant cohort was performed ELISA assay of anti-AT1R and anti-ETAR antibodies. From these patients, we selected 12 transplant recipients with at least protocol biopsies and antibodies dosage at 6 and 24 months after transplantation. Six patients had high levels of anti-AT1R and anti-ETAR antibodies ( $\geq 40$  U/mL) and six were negative ( $< 17$  U/mL). Immunohistochemistry was performed on patient's tissue biopsies to evaluate the expression of AT1R and ETAR receptors and adhesion molecules iCAM-1 and VCAM-1.

**Results:** Our analysis showed that there is no difference between AT1R and ETAR receptors expression in the presence or absence of circulating antibodies. In contrast, iCAM-1 and VCAM-1 expression was statistically significant in the presence of circulating antibodies at 24 months after transplant.

**Conclusions:** In our cohort, the presence of anti-AT1R and anti-ETAR antibodies does not seem to influence the expression of their receptors in the transplanted organ. However, anti-AT1R and anti-ETAR antibodies are associated with an increase of iCAM-1 and VCAM-1 expression in the graft. This preliminary study has some limitations, such as the low number of patients and a follow-up time which could be insufficient to observe the manifestation of a chronic change on biopsy. However, the increase in adhesion molecules could prove to be an event that anticipates the development of histological damage. Thus, increasing the cohort and extending long-term observation would help to better understand the impact of anti-AT1R and anti-ETAR antibodies after transplantation.

# POSTER SESSION 1E

## Glomerular Disorders

Fr-P 079

STEROID-RESISTANT NEPHROTIC SYNDROME WITH MUTATION IN TENSIN2 GENE

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**Aims/Purpose:** Idiopathic nephrotic syndrome (NS) is characterized by severe proteinuria, hypoalbuminemia and/or the presence of edema and hypercholesterolemia. Steroid-resistant NS (SRNS) occurs when complete remission of proteinuria is not achieved within 4–6 weeks therapy with steroids. In 10–30% of patients with non-familial steroid-resistant NS, mutations in podocyte-associated genes can be detected, while in the remaining cases an undefined circulating factor is presumed.

**Methods:** We present a 16-year-old girl with the first manifestation of NS with glomerular non-selective proteinuria, elevation of nitrogen catabolites, nephrogenic hypertension and findings of focal segmental glomerulosclerosis in renal biopsy. After the failure of steroids, cyclosporin A was added to NS therapy, at the same time severe hypertension was gradually treated with up to five combinations of antihypertensives, and repeated and long-term diuretic therapy was necessary for significant swelling, including ascites. The girl was discharged to home care after a two-month hospitalization without achieving NS remission. In the further course, the established treatment continued, three rehospitalizations with intensification and modification of the treatment were necessary due to the intermittent progression of swelling and deterioration of renal functions. Complications of corticosteroid therapy were the development of posterior subcapsular cataract, cushingoid habitus with large appetite, and steroid acne. After 6 months of therapy for the unsatisfactory condition described above, there was a late complete remission of NS with edema subsidence, renal function improvement and hypertension improvement.

**Results:** The results of the molecular-genetic examination, which were available shortly after the start of the treatment, did not show a mutation in the main 4 genes associated with NS, and subsequently also in other genes associated with NS. Subsequently, however, 2 heterozygous mutations in the tensin 2 gene (TNS2 gene) were demonstrated.

**Conclusion:** We present a case report of steroid-resistant nephrotic syndrome with a proven mutation in the tensin 2 gene and a delayed response to immunosuppressive therapy with the achievement and persistence of complete remission. Tensin 2 is an adhesion molecule that binds to actin, participates in various signaling pathways, and has a role in the regulation of cell migration. In the kidney, this protein is localized in the basolateral membrane of podocytes. Mutations in the gene for this protein can lead to the development of nephrotic syndrome, which can present as both steroid-sensitive and steroid-resistant.

Table 1: Remission status following rituximab therapy in children with steroid-resistance nephrotic syndrome unresponsive to corticosteroid and calcineurin inhibitors, stratified by timing of developing steroid-resistance and degree of proteinuria at the time of rituximab

	3 months				6 months				12 months				24 months			
	Total	Initial resistance	Late resistance	p value <sup>a</sup>	Total	Initial resistance	Late resistance	p value <sup>a</sup>	Total	Initial resistance	Late resistance	p value <sup>a</sup>	Total	Initial resistance	Late resistance	p value <sup>a</sup>
<b>All patients, n</b>	246	112	134		246	112	134		233	105	128		162	71	91	
Any remission n (%)	90 (32.5)	21 (18.8)	59 (44.0)	< 0.001	104 (42.2) <sup>b</sup>	27 (24.1)	77 (57.5) <sup>b</sup>	< 0.001	101 (43.3) <sup>b</sup>	33 (31.4) <sup>b,c</sup>	68 (53.1)	0.001	78 (48.1) <sup>b</sup>	25 (35.2)	53 (58.2)	0.004
Complete remission, n (%)	49 (19.9)	13 (11.6)	36 (26.9)		57 (23.2)	14 (12.5)	43 (32.1)		56 (24.0)	19 (18.1)	37 (28.9)		53 (32.7)	15 (21.1)	38 (41.8)	
Partial remission, n (%)	31 (12.6)	8 (7.1)	23 (17.2)		47 (19.1)	13 (11.6)	34 (25.4)		45 (19.3)	14 (13.3)	31 (24.2)		25 (15.4)	10 (14.1)	15 (16.5)	
<b>Nephrotic-range, n</b>	212	100	112		212	100	112		203	95	108		142	65	77	
Any remission n (%)	61 (28.8)	18 (18)	43 (38.4)	0.001	77 (36.3) <sup>b</sup>	20 (20)	57 (50.9) <sup>b</sup>	< 0.001	81 (39.9) <sup>b</sup>	26 (27.4) <sup>b</sup>	55 (50.9) <sup>b</sup>	< 0.001	63 (44.4) <sup>b</sup>	22 (33.8)	41 (53.2)	0.020
Complete remission, n (%)	34 (16.0)	11 (11)	23 (20.5)		41 (19.3)	13 (13)	28 (25)		45 (22.2)	16 (16.8)	29 (16.9)		44 (31.0)	15 (23.1)	29 (37.7)	
Partial remission, n (%)	27 (12.7)	7 (7)	20 (17.9)		36 (17.0)	7 (7)	29 (25.9)		36 (17.7)	10 (10.5)	26 (24.1)		19 (13.4)	7 (10.8)	12 (15.6)	
<b>Subnephrotic-range, n</b>	34	12	22		34	12	22		30	10	20		20	6	14	
Any remission n (%)	19 (55.9)	3 (25)	16 (72.7)	0.007	27 (79.4) <sup>b</sup>	7 (58.3)	20 (90.9) <sup>b</sup>	0.070	20 (66.7)	7 (70) <sup>b</sup>	13 (65) <sup>c</sup>	1.000	15 (75)	3 (50)	12 (86.7)	0.13
Complete remission, n (%)	15 (44.1)	2 (16.7)	13 (59.1)		16 (47.1)	1 (8.3)	15 (68.2)		11 (36.7)	3 (30)	8 (40)		9 (45)	0	9 (64.3)	
Partial remission, n (%)	4 (11.8)	1 (8.3)	3 (13.6)		11 (32.4)	6 (50)	5 (22.7)		9 (30)	4 (40)	5 (25)		6 (30)	3 (50)	3 (21.4)	

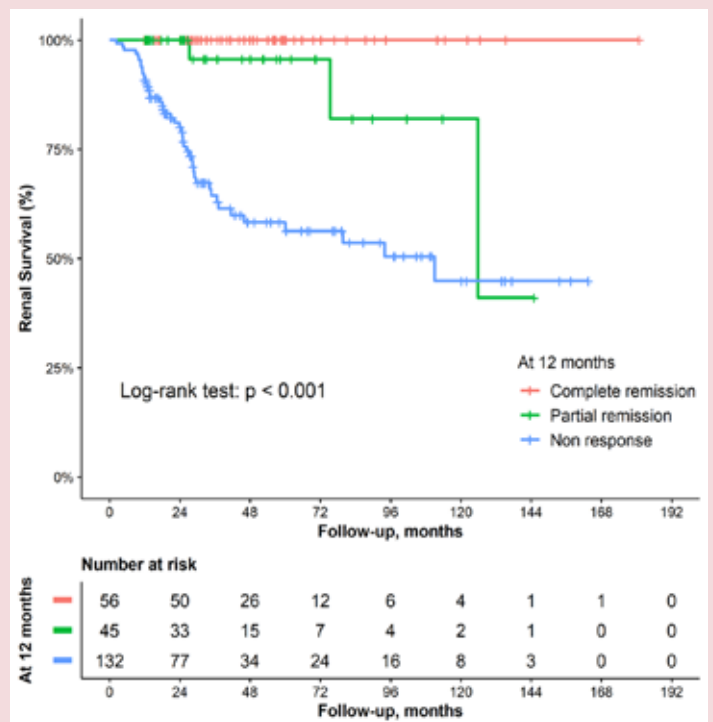
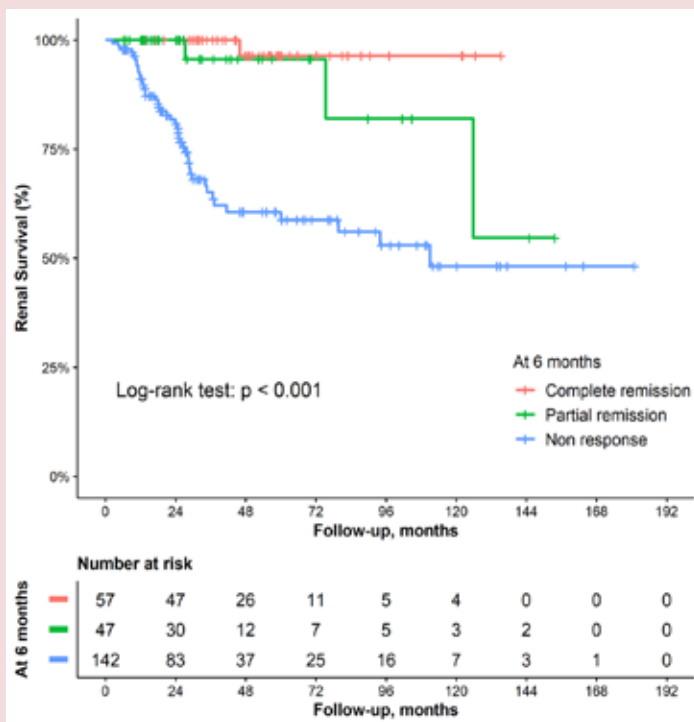


Figure 1: Renal survivals stratified by remission status at A) 6- and B) 12-month following rituximab therapy.



Fr-P 080

COMPARISON OF THREE PROTEINURIA MEASUREMENTS FOR NEPHROTIC SYNDROME IN CHILDREN: BASED ON INTERNATIONAL PEDIATRIC NEPHROLOGY ASSOCIATION GUIDELINE 2022

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**Aims/Purpose:** Our study aimed to review the roles of spot urinary protein creatinine ratio (UPCR) and automated and manual dipstick tests in pediatric nephrotic syndrome (NS) based on the International Pediatric Nephrology Association (IPNA) Guideline 2022.

**Method:** 96 children with NS diagnoses (initial, primary steroid-sensitive, steroid-dependent, and steroid-resistant NS) based on IPNA Guideline 2022 were included. 24-hour and random urine samples were collected. These were analysed using the ARCHITECT c8000 automated analyzer machine (Abbott USA) for 24-h UP (by the colorimetric method) and UPCR (by the Jaffe enzymatic method). Automated dipstick analysis was performed by Siemens CLINITEK Advantus<sup>®</sup> urine chemistry analyzer. A medical doctor who was blinded from the SN diagnoses interpreted the same sample using a manual dipstick.

**Results:** UPCR had the strongest correlation with 24-h UP ( $r = 0.838$ ), followed by automated urine dipstick ( $r = 0.801$ ) and manual urine dipstick ( $r = 0.796$ ). UPCR had the highest sensitivity (91.67%) and specificity (91.67%) for no remission/relapse, and high sensitivity (95.16%) but low specificity (44.12%) for complete remission. The optimal UPCR cut-off for complete remission in our study was 0.6 g/g (AUC value = 0.83, sensitivity = 69.35%, and specificity = 97.06%) compared to the recommended 0.2 g/g (AUC value = 0.70, sensitivity = 95.16%, and specificity = 44.12%). The optimal UPCR cut-off to identify no remission/relapse was 2.0 g/g (AUC value = 0.92, sensitivity = 91.67%, and specificity = 91.67%). Automated and manual dipstick tests showed equal performance in sensitivity (69.35% and 66.13%, respectively), specificity (91.18% and 94.12%, respectively), and AUC value (0.84 and 0.86, respectively) for complete remission. For no remission/relapse, automated and manual dipstick tests also showed equally limited performance in sensitivity (58.33% and 41.67%, respectively), but relatively accurate specificity (88.89% and 98.61%, respectively) and AUC value (0.89 and 0.94, respectively). Furthermore, manual and automated dipstick test readings had a moderate agreement (Kappa = 0.55,  $p = 0.001$ ).

**Conclusion:** In pediatric NS cases, UPCR was sensitive and specific to diagnose no remission/relapse, and sensitive but not specific to detect complete remission. The manual urine dipstick was comparable to the automated urine dipstick and can be used interchangeably to detect remission or relapse. Our study supported the IPNA Guideline 2022 that 2.0 g/g is the UPCR cut-off point for no remission/relapse. However, rather than the value of 0.2 g/g, 0.6 g/g is the optimal cut-off for complete remission diagnosis.

Keywords: creatinine, relapse, steroid-resistant, steroid-sensitive, steroid-dependent, urine

Fr-P 081  
ANNEXIN-5 LEVEL IN CHILDREN WITH CHRONIC KIDNEY DISEASES

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**Aims/Purpose:** The aim of the study is to evaluate the possibility of using annexin-5 as a marker of progression of chronic kidney diseases in children.

**Methods:** We examined 111 patients with chronic kidney diseases, who were observed in Belarusian Center of pediatric nephrology and renal replacement therapy 2nd Children's hospital Minsk: primary immune glomerular diseases (GD, n = 20), secondary immune GD (n = 33), nonimmune GD (n = 26). The comparison group included patients with non-glomerular nephropathies (n = 19). Healthy children without renal pathology (n = 13) were examined as a control group. The concentration of Annexin-5 in the blood serum and urine of patients was determined by the ELISA method using a test system Elabscience and Cloud-Clone Corp (China).

**Results:** The median (Me) concentration of annexin-5 in the blood serum of patients from the control group was 0 (0 – 6.25) ng/ml, in the urine – 0 (0 – 3.125) ng/ml. Excessive level of annexin-5 in blood serum was observed in patients of all study groups: primary immune GD – 0.45 (0 – 2.04),  $p < 0.05$ , secondary immune GD – 1.7 (0 – 4.87),  $p < 0.05$ , nonimmune GD – 1.48 (0 – 2.6),  $p < 0.05$ . The highest concentration of annexin-5 in blood serum was noted in children with non-glomerular nephropathies Me 2.4 (0 – 2.98),  $p < 0.05$  versus (vs) control. When comparing the level of annexin-5 in the urine of patients of the studied groups with the control group, the highest was observed in children with primary and secondary immune GD – 3.125 (0.6 – 6.25),  $p < 0.05$  vs control. In the group of nonimmune GD, an excess of the content of the studied molecule in the urine of Me 1.88 (0.19 – 8.94),  $p < 0.05$ , was also recorded. In the group of patients with non-glomerular nephropathies, the concentration of annexin-5 in urine showed the smallest difference with the control group – Me 0.79 (0 – 4.36),  $p < 0.05$ .

**Conclusion:** Thus, it can be concluded that further studies to determine annexin-5 in blood serum and urine as a marker of chronic kidney diseases progression may be of interest in patients with immune, nonimmune GD and non-glomerular nephropathies.

Fr-P 082

## NPHS1 AND NPHS2 MUTATIONS IN CHILDREN WITH NEPHROTIC SYNDROME

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**Aims/Purpose:** To investigate the mutational variability of NPHS1 and NPHS2 genes in distinct morphological forms of nephrotic syndrome (NS) in patients with different response to glucocorticosteroid (GCS) therapy.

**Methods:** 24 patients (m:f 17:7 (70.8:29.2%)) with NS were included in the study. Median age at the time of the study was 5 (4-12.5) years, duration of disease was 3 (1.3-8.5) years. Nephrobiopsy was performed in 19/24 (79.2%) patients. Light and immunohistochemical microscopy revealed the following morphological variants: focal segmental glomerulosclerosis (FSGS) in 8/19 (42.1%) cases, minimal change disease (MCD) in 7/19 (36.8%) and diffuse mesangioproliferative glomerulonephritis (DMPGN) in 4/19 (21.1%). According to the response to GCS therapy, all patients were divided into 3 groups: steroid-sensitive NS (SSNS), n = 5 (20.8%), steroid-dependent NS (SDNS), n = 9 (37.5%) and steroid-resistant NS (SRNS), n = 10 (41.7%). Gene fragments 5-8 kb in length were amplified using long-range PCR. Library preparation was performed according to Illumina DNA Prep protocol. Target fragments were sequenced on the Illumina MiSeq System. VCF files were generated using the tools available on the Galaxy platform. Variants were annotated using the ANNOVAR software and classified according to ACMG guidelines.

**Results:** After exclusion of intronic and synonymous variants of the genes studied heterozygous exon mutations were found in 4/24 (16.7%) patients. NPHS1 mutations were detected in two cases: the girl with FSGS and SRNS – NM\_004646: exon22: c.G3047A: p.S1016N with frequency 0.00006967 and the boy with FSGS and SDNS – NM\_004646: exon12: c.A1564G: p.N522D with frequency 0.0000147. Both were classified as variants of uncertain significance (VUS). NPHS2 mutations were found in two female patients: NM\_001297575: exon1: c.C59T: p.P20L with a frequency of 0.001969 (likely benign) in MCD and SDNS and NM\_014625: exon5: c.G724A: p.A242T with a frequency of 0.00001768 (VUS) in SSNS without morphological confirmation.

**Conclusion:** Analysis of the presented group of patients with NS revealed NPHS1 and NPHS2 gene mutations in 4/24 (16.7%) children with different morphological changes, more often with FSGS (in 2/4 patients). These results were obtained in a small cohort of patients and require further investigation.

Fr-P 083

A CASE PRESENTATION OF A CHILD WITH NEPHROTIC SYNDROME AND COMMON VARIABLE IMMUNODEFICIENCY

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We report a patient with genetically confirmed common variable immunodeficiency (CVID) and nephrotic syndrome (NS), one of the most common glomerulopathies in children. Idiopathic NS affects 1 to 3 per 100 000 children, < 16 years of age. Whereas most of them respond well to corticosteroid treatment, but as many as 20% experience a complicated course with steroid resistance.

**Aim:** Was to review the case of a child with NS and CVID followed in paediatric department of Vinnytsya Regional Children's Hospital.

**Methods:** We have a follow up of the patient with NS and CVID, determined clinically, laboratory, genetically in a Vinnytsya Regional Children's Hospital and Kyiv Children's Hospital №1.

**Results:** A 9-year-old boy presented with severe generalized oedema, weight gain. The results of laboratory tests revealed normal creatinine, hypoproteinemia, hypoalbuminaemia, and nephrotic range proteinuria (10 g/day). A diagnosis of idiopathic NS was made, and steroid treatment (prednisolone 60 mg/day) was started. After 4 weeks of therapy proteinuria decreased but it did not become negative. Resistant oedema also was present for a long time. He was treated with 3 high-pulse doses of methylprednisolone followed by steroid therapy. During conformation period he didn't show steroid sensitivity and steroid-resistant NS was confirmed. We couldn't perform nephrobiopsy or genetic testing, so therapy with cyclophosphamide was started. He achieved partial remission and even 1 year after finishing immunosuppressive therapy he presents with mild isolated proteinuria, and using of enalapril continues. In his past medical history there were recurrent infections, pneumonias, fungal infection of skin, episode of herpes zoster and signs of physical retardation. During treatment of NS, we also met frequent sinopulmonary infections and the consultation with immunologist was performed. Immunological tests showed reduction in serum concentrations of immunoglobulin (Ig)G, in combination with low levels of IgA and IgM, poor response to immunizations (Tetanus anatoxin) and heterozygous mutation TNFRSF13B gene. With the history of recurrent infections and low Ig levels, he was diagnosed as having CVID. Replacement therapy with IVIG (600 mg/kg every 3 weeks) was initiated.

**Conclusions:** CVID can be observed in NS in children. NS in children with CVID appears to be complicated and difficult to treat with corticosteroids alone. Further research is needed to understand whether CVID has a prognostic value in children with NS.

Fr-P 084

EPIDEMIOLOGY, MORPHOLOGY AND OUTCOMES OF NEPHROTIC SYNDROME IN CHILDREN

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**Introduction:** Idiopathic nephrotic syndrome (NS) is defined in the presence of severe proteinuria, hypoalbuminemia and/or edema, and occurs in 1,15 to 16,9 per 100 000 children per year. Approximately 85% of cases show a complete remission of proteinuria after daily oral administration of glucocorticoids (GC) in standard doses. The aim of our study was to determine the incidence of NS in children in Belarus in 2022, as well as morphological variants, the effectiveness of therapy and outcomes of NS over the last 5 years of follow-up.

**Material and Methods:** The first part of study included all 29 children with the first episode of NS in 2022: median age 5,0 (IQR 3.9; 7.5) years, 66% of boys. The second part was a retrospective analysis of medical records of 123 children with NS for period 2018–2022 years. Median age of NS onset 3.3 (2.2; 5.8) years, follow-up 9.9 (6.4; 14.9) years, 61% boys. Cases of secondary (SLE, IgA-vasculitis, etc.) and congenital NS were excluded from the study.

**Results:** The incidence of NS in children in Belarus was 1,6 cases per 100 000 children per 2022 year. 27 (93%) patients responded to GC therapy, and 2 patients were diagnosed with steroid-resistant NS (SRNS), morphologically: focal segmental glomerulosclerosis (FSGS). The most common clinical manifestation of NS in the retrospective analysis group was “pure” NS – 85 (69%), less often NS with hematuria and arterial hypertension (AH) – 24 (20%), with hematuria – 9 (7%) or with AH – 5 (4%). SRNS was diagnosed in 37 children (30%), steroid-dependent and/or frequently relapsing NS in 86 (70%). According to the results of kidney biopsy (carried out in 96% of patients): in 37 (30%) – minimal change disease (MCD), in 13 (11%) – MCD with initial signs of FSGS, in 31 (25%) – FSGS. Treatment of these morphological variants included: corticosteroid monotherapy in 10 (8%) patients, GC + cyclosporine A (CsA) in 30 (24%) patients, GC/CsA/other immunosuppressants in 10 (8%) patients. Complete remission was achieved in 94 (77%) children, partial – in 15 (12%), no effect was obtained in 14 (11%). FSGS was more often (in 65% of cases) associated with failure to achieve a remission of NS.

**Conclusion:** The incidence of NS in children in Belarus does not differ from the general European data. Steroid-sensitive variants predominate in the structure of NS morbidity. Lack or insufficient effect of immunosuppressive therapy is associated with FSGS.

Fr-P 085

NEED FOR NEXT-GENERATION SEQUENCING RATHER THAN SANGER SEQUENCING FOR SRNS IN A SETTING WITH CONSTRAINED RESOURCES

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**Aims:** Nephrotic syndrome, a common childhood glomerulopathy usually responds to steroid therapy. However, 10–15% of them are steroid-resistant, with a difficult course and higher chances of progression to chronic kidney disease (CKD). The etiology in such patients is multifactorial, though a monogenic cause is identified in up to 30%. In this study, we aimed to identify the frequency of ADCK4 gene mutation in our cohort of pediatric Steroid Resistant Nephrotic Syndrome (SRNS) by Sanger sequencing.

**Methods:** 2977 files of patients from a nephrotic clinic in a tertiary care center in northwest India were screened. 357 had SRNS. We included patients  $\leq$  12 years of age, with FSGS on biopsy and not responding to calcineurin inhibitors. While there were 54 patients who fulfilled this criterion, 20 of these patients, consented. These were screened for ADCK4 mutations by Sanger sequencing. Their clinicopathological profiles were recorded in a predesigned proforma. Appropriate statistical tests were applied.

**Results:** Twenty children were enrolled. It was a male predominant study with a sex ratio of 2.33:1. FSGS-NOS was the most common variant studied (75%), followed by collapsing variant (25%). The median age of onset of disease was 2.95 years (IQR: 2–5 yrs). 50% had initial resistance and 50% showed late resistance to steroid. Most of the children developed steroid toxicity, with 80% having cushingoid features and 30% having cataracts. 40% of the children progressed to CKD. About 60% children required more than two immunosuppressant. We used Sanger sequencing to look for mutations in the ADCK4 gene (exons 2, 7, 8, 10, 11, 13, and 15). No disease causing mutations were observed. However, few variations were observed, like the deletion of 4 bp in exon 10 in 4 patients and a missense variation in exon 11, which is homozygous in 3 patients and heterozygous in 4 patients, all of which were not pathogenic.

**Conclusions:** ADCK4 gene mutations were not observed in our cohort. However, it does not rule out other genetic causes of SRNS. Almost 40% of our cohort progressed to CKD, yet many continued to receive immunosuppressant therapy. This study highlights the importance of Next Generation Sequencing as a screening tool for identifying the monogenic causes of SRNS even in setting with limited resources.

Fr-P 086

AN UNUSUAL CAUSE OF DIARRHEA IN A CHILD WITH NEPHROTIC SYNDROME

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**Introduction:** Idiopathic nephrotic syndrome (NS) is an autoimmune kidney disease. Although steroids are the first-line treatment, at least 50% of patients develop multiple relapses and need alternative treatments. Rituximab (RTX) is a chimeric anti-CD20 monoclonal antibody which is a salvage treatment for refractory NS. It is generally well tolerated, but serious side effects may rarely occur. Here we report a 10-year-old boy who developed inflammatory bowel disease (IBD) after RTX therapy.

**Material and Methods:** Case report.

**Results:** A ten-year-old steroid-dependent and frequently relapsing NS patient came to clinical attention with diarrhea. He was first diagnosed with NS at the age of two years. Although remission was achieved with steroid therapy, multiple relapses were observed while on steroid weaning, and calcineurin inhibitory (CNI) therapy was initiated. Nevertheless, the patient experienced recurrent relapses on CNI treatment. Renal biopsy revealed mild segmental matrix and cell increase in the glomeruli. RTX was initiated with a 4-week course at a dose of 375 mg/m<sup>2</sup> per week. Two more doses were given in the following year and remission was sustained; prednisolone treatment was tapered and discontinued. Twenty months after the first RTX dose, the patient developed abdominal pain, foul-smelling bloody diarrhea, and tenesmus. No obvious infectious cause was detected and ileocolonoscopy and esophagogastroduodenoscopy were performed. Based on clinical and endoscopic findings, he was diagnosed with ulcerative colitis and treated using prednisolone and azathioprine. Immunohistochemical analyses showed complete depletion of CD19 or CD20+ lymphocytes in the intestinal mucosa. His symptoms rapidly resolved. A repeat colonoscopy after six months revealed complete resolution. Prednisolone was weaned and discontinued. No relapse of IBD or NS was experienced during the 2-year follow-up at the end of which azathioprine treatment was ceased.

**Conclusions:** RTX-associated IBD is a rare but serious side effect. In cases with abdominal symptoms and accompanying weight loss after RTX therapy, IBD should be kept in mind. Although the pathogenesis of RTX-related IBD is not fully understood, it is thought to develop secondary to immune dysregulation and T cell activation resulting from B cell depletion. Treatment directed against IBD and avoidance of RTX is the main management strategy.

Fr-P 087  
CARDIOVASCULAR EVALUATION OF FMF PATIENTS

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**Aim:** Chronic inflammatory era may result in cardiovascular changes. We aimed to evaluate children with familial Mediterranean fever (FMF) with respect to blood pressure (BP), arterial stiffness (AS) and left ventricular mass index (LVMI).

**Patients and Methods:** Patients with FMF who have homozygous/compound heterozygous mutations in the exon 10 of the MEFV gene and being followed up between April 2020 and February 2023 were included in the study. Ambulatory blood pressure monitoring (ABPM), central BP (cBP), pulse wave velocity (PWV), and augmentation index (AIx@75) values recorded with the same device, and LVMI were evaluated in an attack free period. The same tests were performed for a sex and age-matched control group.

**Results:** Finally, 50 cases with FMF and 50 healthy cases were included. Both systolic and diastolic MAP SDS values, 24-hour, daytime and nighttime systolic and diastolic BPs and 24-hour mean arterial pressure (MAP) SDS and nighttime mean MAP SDS levels were similar between the groups ( $p > 0.05$ ). Daytime diastolic BP z-score and daytime systolic load were significantly higher in FMF patients ( $p = 0.013$ ,  $p = 0.046$ ). Daytime diastolic load, nighttime systolic and diastolic loads and systolic and diastolic dips were similar between the groups. 24-hour, daytime and nighttime AIx@75 and PWV levels, and systolic and diastolic central BP levels were similar between FMF patients and the control group ( $p > 0.05$ ). All the parameters were similar between homozygous and compound heterozygous cases, either.

**Conclusion:** Well controlled inflammation may provide BP, arterial stiffness or left ventricular mass index values even in FMF cases with mutations suggesting the highest exposure to chronic inflammation similar to healthy age and sex-matched peers.

Keywords: Familial Mediterranean fever, arterial stiffness, blood pressure



Fr-P 088

POPULATION-LEVEL LONG-TERM OUTCOME ANALYSIS OF CHILDHOOD-ONSET IDIOPATHIC NEPHROTIC SYNDROME: FINDINGS FROM A HEALTH INSURANCE DATABASE

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**Aims/Purpose:** Unbiased evidence about the long-term (adult) outcomes of childhood-onset idiopathic nephrotic syndrome (INS) is lacking due to disproportionate losses follow-up patients. In a population-based research approach, we accessed longitudinal data collected by the largest German health insurance fund covering 33% of the general population.

**Methods:** The AOK Research Institute provided aggregated longitudinal data from all patients born between 1998 and 2002 who were diagnosed with childhood INS in 2007/2008 and still insured by AOK at young adult age in 2019–2021. INS relapses were estimated from the prednisone prescription patterns.

**Results:** Out of 413 INS patients diagnosed in 2007/2008, 232 patients were continuously insured throughout the 13-year observation period and had good data quality. 124/232 patients (54%) were still treated for INS at age 20–24 years. 24% received at least one prescription for prednisone or other immunosuppressive drugs in the past two years, 2% were on dialysis and 7% had undergone kidney transplantation. Patients were clustered according to whether or not they were still affected by INS and divided into three groups correlated to initial histopathological findings (no biopsy, MCD/MesPGN, and FSGS) to compare the number of relapses during the observation period. The fraction of patients who had lost the diagnosis of INS at last follow-up (assumptive remission) was 60.2% in the no-biopsy, 42.5% in the MCD/MesPGN and 17.6% in the FSGS group respectively. Among these patients, relapses had ceased within 5 (no biopsy), 7 (MCD/MesPGN) and 8 years (FSGS). In the patients with persistent INS, the mean biannual relapse rate decreased from 2.0 in 2007–2008 to 1.4 in 2020–2021 in the no-biopsy group, from 2.3 to 2.1 in MCD/MedPGN patients, and from 2.3 to 1.3 in the FSGS group. To explore potential long-term effects of medications used to treat INS, the spectrum of other diagnoses and specialist visits were studied. No major differences between young adults with childhood-onset INS and the age-matched general population were noted.

**Conclusion:** Approximately 50% of patients with childhood-onset INS still present the disease diagnosis at young adult age. Patients in whom disease relapses cease after 5–7 years from disease onset are unlikely to exhibit active disease in adulthood. Data obtained from health insurances are a promising source of unbiased natural history information for chronic diseases such as INS.

Fr-P 089

**ANCA ASSOCIATED VASCULITIS ACCOMPANIED BY ANTERIOR MEDIASTINAL MASS: IN INSIGHTFUL CASE REPORT OF A 15-YEAR-OLD GIRL**

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**Aims/Purpose:** ANCA-associated vasculitis (AAV) is a group of systemic immune mediated disorders characterised by the inflammation of small vessels, commonly in kidney where it can cause rapidly progressive glomerulonephritis (RPGN). The inflammatory process can affect almost all body systems producing variety of symptoms, therefore demanding a systemic examination and early initiation of immunomodulatory treatment.

**Methods:** We present a case of a 15-year-old girl with AAV/RPGN and an anterior mediastinal mass.

**Results:** She was transferred to our centre due to fatigue and vomiting lasting for two weeks, generalised oedema and laboratory signs suggestive of renal failure. She was previously healthy, with family history negative for both kidney and immune-mediated diseases. Six months earlier, she gave birth to a healthy term newborn. Kidney biopsy revealed chronic parenchymal changes consistent with diffuse proliferative glomerulonephritis. Immunological screening showed positive p-ANCA and anti-GBM, with increased inflammatory markers. To exclude alveolar haemorrhage chest CT scan was performed, revealing a large mass in the anterior mediastinum with pleural effusion. To further characterize the mass, PET CT was performed, showing increased metabolic activity, which necessitated extirpation. Brain MRI excluded vasculitis of the central nervous system. While no pathognomonic findings were observed after the histopathological examination, several differential diagnoses were considered, including Wegener's granulomatosis (WG), thymolipoma and thymoma, with the most likely being fibrosing mediastinitis (FM). Treatment with high doses of steroids was commenced, along with five plasmaphereses, followed by four weekly infusions of rituximab. Although the treatment led to amelioration of systemic symptoms and decrease of inflammatory markers, she remains dependent on chronic haemodialysis.

**Conclusion:** To our knowledge, this is the first case describing a child with AAV accompanied by anterior mediastinal mass. While the list of plausible diagnosis is wide, the most appropriate in our case is FM, a rare disease with possible connection to the *H. capsulatum* infection. The idiopathic form of the disease is also recognised and is often associated with AAV. Moreover, WG was also considered as ANCA are present in 80–90% patients, in addition to renal involvement, but in our case other specific signs and symptoms were absent. Even though a lymphoproliferative disorder was excluded, it is worth mentioning that the triad of symptoms consisting of an anterior mediastinal mass, pleural effusion and progressive renal failure is often indicative of a lymphoma. Finally, despite the diagnostic dilemmas, we believe that this case emphasizes the importance of timely administration of immunomodulatory treatment to prevent the spread of systemic inflammation beyond the kidneys.

Fr-P 090

**ANALYSIS AND STUDY ON FEATURES AND PROGNOSIS OF NEPHROTIC SYNDROME IN CHILDREN'S NEW CLINIC (TBILISI, GEORGIA)**

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**Aims/Purpose:** The purpose of the abstract is to present analysis and study on features and prognosis of nephrotic syndrome in Children's New Clinic in Tbilisi, Georgia as our clinic serves the largest part of nephrology patients of pediatric age across the country.

**Methods:** We reviewed medical records of patients who were diagnosed with Nephrotic Syndrome (NS) in children's new clinic in Georgia, Tbilisi from 2021 to 2023 were selected. It should be noted that during the Covid-19 pandemic, the clinic was transformed into a Covid clinic, which significantly reduced the number of nephrology patients. We should also mention that some of these patients were diagnosed by us before 2021, and some came to us at the time of disease recurrence. NS was defined as: nephrotic range proteinuria – urinary protein excretion greater than 50 mg/kg per day, hypoalbuminemia – serum albumin concentration less than 3 g/dL (30 g/L), edema, hyperlipidemia. Clinical data of patients were collected: sex, age, age of onset of disease, type of NS-Drug, frequency of disease recurrence, type of NS- morphology, type of treatment, presence of viral/other infections right before NS occurrence. Therapeutic Schedules: On the basis of consensus, prednisone therapy should be initiated at doses of 60 mg/m<sup>2</sup> per day (2mg/kg per day) administered for 4 to 6 weeks, followed by 40 mg/m<sup>2</sup> per dose (1.5 mg/kg) every other day for at least 6 to 8 weeks. Evaluation Criteria for Remission and Prognosis of Patients after Treatment : Complete remission: Urine protein creatinine ratio (uPCR) < 200 mg/g or < 1+ protein on a urine dipstick measurement for three consecutive days. Partial remission: Fifty percent or more decrease in proteinuria and uPCR between 200 and 2000 mg/g. No remission: Failure to reduce urine protein excretion by 50% from baseline or persistent excretion uPCR > 2000 mg/g.

**Results:** A total of 23 children (3-14 years) were included in the study. Age of onset of disease was from 1.5 -14 years (mean age-3.8). 2 of them (8.7%) were with steroid-resistant nephrotic syndrome, 1 (4.35%) with frequently relapsing nephrotic syndrome, 3 (13%) rarely relapsing NS and 6 (26%) were with steroid-dependent nephrotic syndrome, 6 (26%) – unknown, 5 (22%) steroid sensitive. The mean frequency of disease recurrence-3. Biopsy was completed in 5 patients, 40% of them -Minimal change disease, 40 % FSGS, 20%- C1Q Nephropathy. Prednisone was admitted in 100% of patients, endoxan (22%) , tacrolimus (4.35%) , Mycophenolate mofetil (8.7%) were used as steroid-sparing agents in some patients. Almost 90% of cases were preceded by an upper respiratory tract infection.

**Conclusion:** Almost 90% of patients with nephrotic syndrome admitted to our clinic had an upper respiratory tract infection before the onset of illness. Unfortunately, the identification of the virus was usually not possible due to the limited budget.

Fr-P 091  
NEPHROPATHY IN A CHILD WITH A FRAMESHIFT MUTATION ON THE COL7A1 GENE: A CASE REPORT

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**Aims/Purpose:** COL7A1 is expressed in the skin and other epithelial and mesenchymal tissues. Therefore, patients with COL7A1 mutations, such as recessive dystrophic epidermolysis bullosa (RDEB), may exhibit extracutaneous manifestations, including kidney disorders. Prolonged inflammation and recurrent skin infections in RDEB can lead to synthesising and depositing immunoglobulin A (IgA)-containing immune complexes in the glomerulus. Because most RDEB patients with IgA nephropathy (IgAN) progress to kidney failure within 5 years of IgAN diagnosis, early detection and appropriate treatment of IgAN are vital for RDEB patients. We describe a diagnosis and treatment scheme for nephropathy in an 11-year-old boy with RDEB.

**Results:** Our case was diagnosed with RDEB at the age of seven and received regular wound care for skin ulcers. He experienced recurrent skin infections that coincided with worsening hematuria. At 11 years old, he was referred to our center due to progressing proteinuria with a spot morning urine protein to creatinine ratio (uPCR) of 6252.8 mg/g. Genetic analysis with whole-exome sequencing revealed a frameshift mutation on the COL7A1 gene (exon51:c.4889\_4890insTTGCCCCCG), predicted to cause absent type VII collagen within the anchoring fibrils between the epidermis and dermis (p.R1630fs). Due to the parents' refusal of kidney biopsy, a presumptive diagnosis of IgAN was determined based on his clinical and immunological features. Our patient had increased IgA levels, normal serum complement, normal anti-streptolysin O titer, negative antinuclear antibodies, and normal anti-double-stranded DNA antibody. Despite initial treatment with an optimum dose of steroids and lisinopril, his nephrotic-range proteinuria persisted. Subsequent treatment with monthly intravenous cyclophosphamide (IV CPA; 500 mg/m<sup>2</sup>) for seven doses resulted in proteinuria remission and kidney function preservation for two years after CPA therapy completion.

**Conclusion:** Patients with RDEB may exhibit extracutaneous manifestations, including kidney disorders such as IgAN. IV CPA might be beneficial to improve proteinuria and kidney function deterioration in non-rapidly progressing IgAN in children with RDEB.

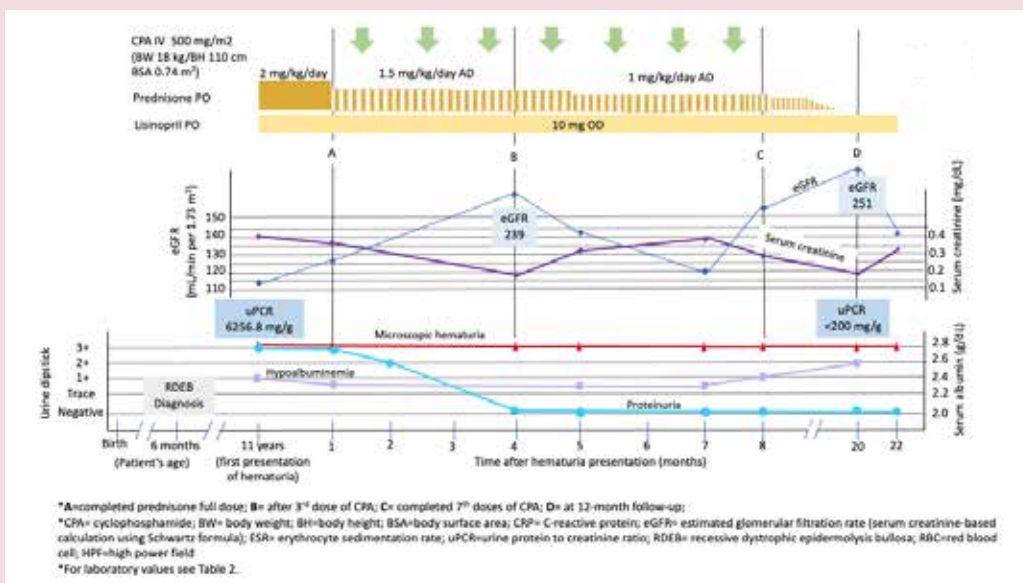


Figure 1: Clinical course of the case (A = completed prednisone full dose; B = after 3<sup>rd</sup> dose of CPA; C = completed 7<sup>th</sup> doses of CPA; D = at 12-month follow-up).

Fr-P 092

GENETIC SPECTRUM OF CHILDHOOD ONSET STEROID RESISTANT NEPHROTIC SYNDROME IN KAZAKHSTAN

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**Aims/Purpose:** Childhood-onset steroid-resistant nephrotic syndrome (SRNS) has not been studied in Kazakhstan. We aimed to investigate genetic variations of local pediatric patients with SRNS.

**Methods:** 47 unrelated children from birth to 18 years of age with SRNS who underwent comprehensive screening using next generation sequencing panels for genes associated with SRNS were selected for the study. Clinical, biochemical, genetic, and histopathologic data were collected both retrospectively and prospectively during the study period. Descriptive data analysis was performed using SPSS.

**Results:** Boys accounted for 71% (n = 33), 87% (n = 40) were Kazakhs, 13% were Russians. 83% of the cohort had first disease manifestation before 5 years of age with the median age at disease onset of 1.3 years (IQR 0.67 – 3.92). Congenital nephrotic syndrome was accounted for 11% of all cases. Kidney biopsy was performed in 23 (48.9%) patients. The most common histopathologic findings were focal-segmental nephrotic syndrome (65.2%) and mesangial-proliferative nephrotic syndrome (17.4%). 41 genetic mutations in 13 genes were detected in 87% of patients. Genetic detection rate was inversely proportional with the age at first disease manifestation (Figure 1).

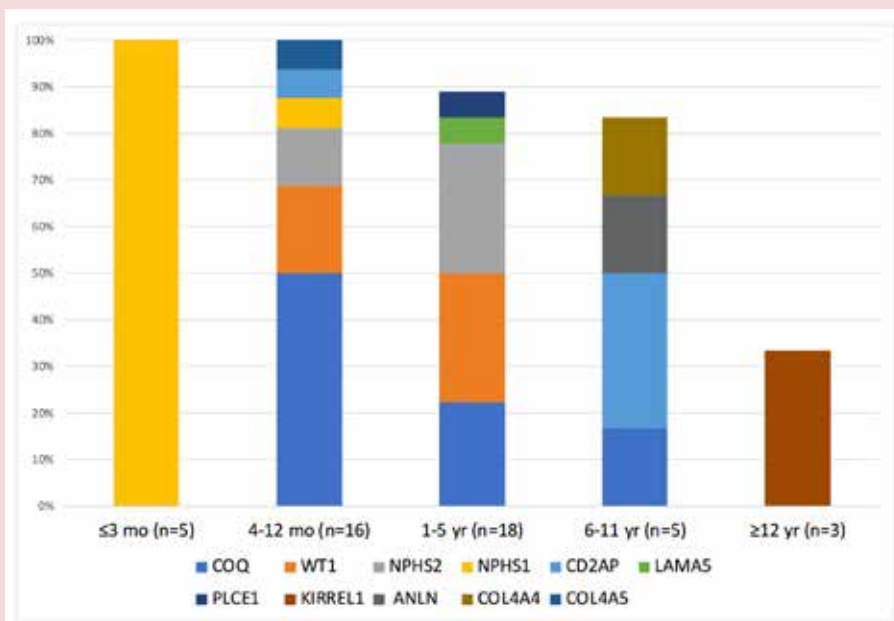


Figure 1: Distribution of causative genes by age at onset.

Table 1: Distribution of causative genes

Causative	N (%)	Kazakhs (N)	Russian (N)
COQ6	9 (21.9%)	9	-
WT1	8 (19.5%)	8	-
NPHS1	7 (17.1%)	7	-
NPHS2	7 (17.1%)	4	3
CD2AP	2 (4.87%)	2	-
ADCK4	1 (2.4%)	1	-
LAMA5	1 (2.4%)	1	-
PLCE1	1 (2.4%)	-	1
KIRREL1	1 (2.4%)	1	-
ANLN	1 (2.4%)	-	1
COL4A4	1 (2.4%)	1	-
COL4A5	1 (2.4%)	1	-
SMARCAL1	1 (2.4%)	1	-
Total	41 (100%)	36	5

The most common mutations were associated with COQ6 (n = 9, 21.9%), WT1 (n = 8, 19.5%), NPHS2 (n = 7, 17.1%), NPHS1 (n = 7, 17.1%) genes. All children with COQ6 mutation were not related Kazakhs and carried c.1058C > A (p.Ala353Asp) variant, while majority of not related Russians had mutation in NPHS2 (Table 1). 83% of children with untreated COQ6 mutation reached end-stage kidney disease over the median time of 5.8 months (IQR 0.5–20.8), lethality was 25% (n = 3).

**Conclusion:** Potentially treatable COQ6 mutation had a higher frequency in Kazakh population comparing with other countries' reports and could be attributed to the founder effect. Over 90% of tested children with SRNS under 5 years of age had monogenic cause with 80% of them due to mutations in COQ6, WT1, NPHS1 and NPHS2. Further comprehensive genetic screening of a larger cohort of children is warranted to confirm the genetic variation of pediatric SRNS.

Fr-P 093

**MIRAGE SYNDROME WITH ISOLATED NEPHROTIC-RANGE PROTEINURIA AND MINIMAL CHANGE DISEASE: DESCRIPTION OF THE FIRST CASE**

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**Aims/Purpose:** MIRAGE syndrome is a rare genetic disease discovered in 2016, caused by a gain-of-function mutation in the SAMD9 gene. Patients present growth restriction, myelodysplasia, recurrent infections, hypoadrenalism, genital phenotypes and enteropathy. To date, 44 affected individuals have been reported. Renal dysfunction with proteinuria, tubular acidosis, nephrotic syndrome was described in 8 of the 17 individuals who survived  $\geq 3$  years. Kidney biopsy was performed in 5, revealing focal-segmental glomerulosclerosis, interstitial nephritis and a clq nephropathy developed after bone marrow transplantation.

**Methods:** We describe a new case of MIRAGE syndrome with isolated nephrotic-range proteinuria.

**Results:** An 8-years-old girl with MIRAGE syndrome, presenting in the first months of life with failure to thrive, recurrent pulmonary infections, esophageal achalasia, chronic diarrhea, was referred to our clinic in June 2022. She had persistent isolated nephrotic-range proteinuria (uPr/uCr 3.5 mg/mg), accidentally detected during a concurrent infection (pneumonia). Oedema was not present and the body weight was stable. Blood tests were unremarkable except for mild hypoalbuminemia (3.3 g/dl). Renal function, cholesterol, immunoglobulins, complement, autoimmunity and kidney ultrasonography were normal. Deepening her medical history, isolated proteinuria was already present in February 2022 (2.19 mg/mg) but not further investigated. Considering the atypical presentation and her syndromic condition, a kidney biopsy was performed. Optical microscopy was consistent with minimal change disease (MCD), immunofluorescence was negative, while the ultrastructural evaluation excluded autoimmune deposits and podocyte effacement. Two months after the biopsy, the clinical picture was stable (uPr/uCr 5.01 mg/mg) without oedema nor hypoalbuminemia. Treatment with ramipril was started at a reduced dosage (3mg/m<sup>2</sup>/day) because of chronic diarrhea. During the follow-up, a 50% reduction of proteinuria was obtained (uPr/uCr 2.52 mg/mg) with an almost normalized albuminemia (3.7 g/dL). Therapy was well-tolerated and discontinued only during acute worsening of diarrhea.

**Conclusion:** Kidney involvement in patients affected with MIRAGE syndrome has been reported with different presentations. To date, this is the first case of MIRAGE disease presenting with isolated nephrotic-range proteinuria associated with MCD. ACE-inhibitors are effective and manageable even in MIRAGE patients with chronic diarrhea.

Fr-P 094

**CRB2 – ASSOCIATED FSGS AND CONGENITAL CEREBRAL VENTRICULOMEGALY**

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**Background:** Steroid-resistant nephrotic syndrome (SRNS) is a genetically heterogeneous disorder for which more than 25 single-gene hereditary causes have been identified. We will demonstrate a rare variant of a monogenic effect on the formation of FSGS in SRNS with congenital ventriculomegaly and macular dystrophia in this clinical case.

**Methods:** A girl from an unrelated marriage was diagnosed a cerebral ventriculomegaly in utero, a medium-high pressure ventriculoperitoneal shunt (Codman) was installed at birth. The onset of nephrotic syndrome was at the 3 years old: edema, proteinuria 2g/24h (= 1000 mg/m<sup>2</sup>), hypoalbuminemia 21 g/l, creatinine 35 µmol/l. The girl was treated by prednisone at a dose of 60 mg/1.73m<sup>2</sup>/24h for 6 weeks. The edema was stopped, but proteinuria and a low level of blood albumin (25 g/l) were stay. Due to the development of steroid resistance, the patient received cyclosporine for 24 months at a dose of 6 mg/kg/24 h (CO 109–132 ng/ml) with a partial response to therapy (proteinuria 1400 mg/ m<sup>2</sup>, blood albumin 41 g/l, creatinine 38 µmol/l).

**Results:** During the examination of girl in 5 years was diagnosed macular degeneration, pathology of the heart and genital organs were excluded. Kidney biopsy revealed FSGS and signs of cyclosporine nephrotoxicity. Then the patient was treated by MMF and rituximab, but the activity of the nephrotic syndrome persisted (proteinuria more than 3 g/24h, blood albumin 15 g/l, creatinine 38 µmol/l). Exome sequencing testing revealed a pathogenic homozygous variant in the CRB2 gene c.1813C > T (p. R605C). The parents of the girl have the same pathogenic variant CRB2 gene in a heterozygous state. The child was canceled immunosuppressive therapy. Currently, the duration of the nephrotic syndrome is 5 years, the girl has been receiving symptomatic therapy for 2 years (diuretics, ACE inhibitors, anticoagulants, 20% albumin) and has no edema, the filtration function is preserved (eGFR 91 ml/mine/1.73m<sup>2</sup>)

**Conclusions:** Our case highlights the importance of genetic testing in children with SRNS for prognosis and therapeutic strategy, which is very important in children with a progressive disease such as steroid-resistant nephrotic syndrome.

Fr-P 095

## COMPARISON OF URINARY TRANSFERRIN LEVELS AND RESULTANT IRON DEFICIENCY ANEMIA IN STEROID RESISTANT NEPHROTIC SYNDROME AND STEROID SENSITIVE NEPHROTIC SYNDROME

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**Aims/Purpose:** The aim of this study is to find out the prevalence of iron deficiency due to urinary transferrin loss and resultant development of anaemia in patients having Steroid Resistant Nephrotic Syndrome. Nephrotic syndrome is a common glomerular disease seen in children. Complications such as edema, infections, thrombosis and hypothyroidism are well studied. They have been shown to be due to the loss of various plasma proteins in urine, like albumin, immunoglobulins, hormone-binding proteins and coagulation factors. However, iron, transferrin, EPO, micronutrients and trace minerals are also lost in the process. Excessive urinary losses of transferrin may lead to iron deficiency development of anaemia. This loss would be more in those patients who are not responding to steroids, the first line of treatment. Such children may therefore need additional supplements to improve care. This study was focussed to understand the chances of development of iron deficiency and iron deficiency anaemia in SRNS, the correlation of loss of urinary transferrin and iron deficiency and thus, guidance to manage them more comprehensively.

**Methods:** Ethical clearance was sought from institutional ethical committee. Children less than 12 years of age with the diagnosis Nephrotic Syndrome were included in the study. Details including age of onset of disease condition, atypical features of hematuria and hypertension at onset of disease, dosage and duration of initial steroid therapy, response to steroids, need of alternative medications and complications if any due to either disease condition or medications were recorded. The response to steroids in terms of reduction of proteinuria or in other words, remission was noted. Patients were then classified as SSNS or SRNS. Other supportive medications given were also noted. In those patients who are Steroid Sensitive and where there is a follow up of 12 months or more, the number of relapses were questioned and thereafter the patient were classified as Infrequent Relapse Nephrotic Syndrome, Frequent Relapse Nephrotic Syndrome, Steroid Dependent Nephrotic Syndrome or Late Steroid Resistant Nephrotic Syndrome. Use of alternative drugs in case of steroid dependence, resistance or frequent relapse (Levamisole, CYP, MMF, Cyclosporin A, tacrolimus) were recorded. Serum iron, ferritin, TIBC and percentage of hypochromic RBC's and reticulocyte hemoglobin content was performed on the same EDTA blood sample taken for complete blood count (CBC). This analysis was done on Sysmex SN-1000 (Japan) automated hematology analyzer. Additionally, urinary transferrin levels were measured by using Nephrometry .

**Results:** 70 patients were included in the study. Average age of occurrence of symptoms was found to be 3.5 years. Out of 70 cases, 34 cases were diagnosed as SRNS. Prevalence of anaemia seen among SRNS group was 50% as compared to SSNS having 33.3%. Iron deficiency as a contributing factor for development of anaemia among SRNS group was found to be in 50 % as compared to 47.2% in SSNS. Urinary transferrin losses were compared in SRNS group with SSNS group and was found to be significant with SRNS group showing 55.9% having elevated urine transferrin in comparison to SSNS group in which 19.4% showed elevated urine transferrin.

**Conclusion:** Prevalence of iron deficiency was comparable in SRNS group versus SSNS group. Urinary transferrin losses were higher in SRNS group which can be attributed to increased and prolonged urinary protein losses. However the relation between increased levels of urinary transferrin losses in SRNS leading to increased risk of iron deficiency anaemia could not be curated. The study hence concludes that urinary transferrin loss is higher in SRNS patients but not a factor resulting in development of anaemia, suggesting the cause of anaemia to be reduced nutritional intake.



Fr-P 096

**GELSOLINE, ADIPSIN AND TAURINE LEVELS IN PLASMA AND URINE AS AN EARLY INDICATOR OF DIABETIC NEPHROPATHY IN CHILDREN WITH TYPE 1 DIABETES MELLITUS**

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Diabetes mellitus (DM) is a metabolic disease characterized by hyperglycemia caused by insulin secretion or the effect of insulin on tissues, or both. Urine microalbumin is currently the most valuable parameter for the diagnosis of DN. In this study, we aimed to investigate the usability of NGAL, Taurine, Gelsolin and Adipsin levels in the early diagnosis of diabetic nephropathy by measuring these parameters in the plasma and urine of healthy controls and type 1 diabetic patients with and without microalbuminuria.

In this study, 50 pediatric patients with type 1 diabetes mellitus (HbA1C = 6.5%, fasting blood glucose  $\geq$  126 mg / dl, postprandial blood glucose  $\geq$  200 mg / dl) who were followed up at the Pediatric Endocrine Outpatient Clinic of Firat University Hospital between the ages of 5 and 18 years were evaluated. 30 healthy children without diabetes who applied to the general pediatric outpatient clinic of Firat University Hospital for routine follow-up were selected as the control group. Biochemical parameters of these groups were obtained from hospital records. In addition, 5 ml blood and 10 ml urine samples were taken simultaneously. Gelsolin, adipsin, taurine and NGAL levels were studied in biological samples.

Consistent with the literature, urinary and plasma NGAL levels were significantly higher in children with Type 1 DM than in the control group. In children with type 1 DM, taurine and gelsolin levels were significantly lower in plasma and urine compared to the control group. Adipsin was lower in the plasma of children with Type 1 DM compared to the control group, whereas there was no significant difference in urine adipsin levels between the two groups.

According to the results, increasing NGAL, decreasing taurine and gelsolin are important markers in the diagnosis of DN, and since these parameters show a parallel with urine; we think that urine is going to be an important biological fluid (urine) in the diagnosis and follow-up of DN for patient comfort (not invasive).

# POSTER SESSION 1F

# Glomerular Disorders

Fr-P 097

VITAMIN C DEFICIENCY IS ASSOCIATED WITH INCREASED NEUTROPHIL EXTRACELLULAR TRAP FORMATION IN JUVENILE LUPUS NEPHRITIS

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**Aims/Purpose:** Vitamin C (vit C) regulates the formation of neutrophil extracellular traps (NETs), which are a major source of autoantigens. NETs are detected in the glomeruli of patients with lupus and contribute to the pathogenesis of lupus nephritis (LN). Our objective was to determine the correlation between vit C levels and NET formation in juvenile LN.

**Methods:** Serum vit C levels were evaluated in 46 children with LN and levels  $\leq 0.3$  mg/dL were considered deficiency. The patients were divided into 2 groups according to vit C status: normal and low ( $\leq 0.3$  mg/dL). NET formation was evaluated using the expression of Peptidyl Arginine Deiminase 4 (PAD4) relative to  $\beta$ -actin. The activity (AI) and chronicity (CI) indices of kidney pathology were determined.

**Results:** The mean serum vit C level was  $0.82 \pm 0.48$  mg/dL. Nine patients (19.6%) had vit C deficiency. There were no significant differences in age, sex, body mass index, hemoglobin, iron saturation, glomerular filtration rate, proteinuria, erythrocyte sedimentation rate, SLE disease activity index, and treatment between groups. The low vit C group had higher urine red blood cells, serum ferritin and PAD4 expression than the normal group (Table). Kidney pathology AI was significantly higher in the low vit C group, while CI was similar between both groups. PAD4 expression was negatively correlated with vit C levels (Figure).

Table: Characteristics of children with lupus nephritis by vitamin C status.

	Total (N = 46)	Normal (N = 37)	Low (N = 9)	p
Age (years)	14.5 $\pm$ 1.8	14.7 $\pm$ 1.8	13.6 $\pm$ 1.9	0.10
Female	38 (82.6)	32 (86.5)	6 (66.7)	0.18
Body mass index (kg/m <sup>2</sup> )	23.7 $\pm$ 5.3	24.2 $\pm$ 5.3	21.5 $\pm$ 5.3	0.18
Hemoglobin (g/dL)	12.2 $\pm$ 1.5	12.0 $\pm$ 1.4	13.0 $\pm$ 1.9	0.07
Iron saturation (%)	27.7 $\pm$ 14.4	26.8 $\pm$ 11.8	31.5 $\pm$ 23.0	0.39
Ferritin ( $\mu$ g/L)	417 $\pm$ 1320	226 $\pm$ 218	1201 $\pm$ 985	0.045
GFR (mL/min/1.73m <sup>2</sup> )	111 $\pm$ 34	114 $\pm$ 33	101 $\pm$ 39	0.34
Urine red blood cells (cells/high power field)	7.5 $\pm$ 17.8	3.9 $\pm$ 8.7	22.2 $\pm$ 33.7	0.004
Urine protein to creatinine ratio (mg/mg)	1.0 $\pm$ 1.8	0.8 $\pm$ 1.3	1.7 $\pm$ 3.2	0.19
ESR (mm/h)	25.8 $\pm$ 24.2	25.6 $\pm$ 20.0	26.7 $\pm$ 41.4	0.92
SLE disease activity index	6.2 $\pm$ 6.5	5.7 $\pm$ 6.0	8.6 $\pm$ 8.2	0.24
<b>Kidney pathology</b>				
Proliferative LN	27 (58.7)	21 (56.8)	6 (66.7)	0.72
Activity index	4.2 $\pm$ 4.0	3.2 $\pm$ 4.1	7.3 $\pm$ 1.0	0.02
Chronicity index	1.0 $\pm$ 1.5	1.1 $\pm$ 1.7	0.7 $\pm$ 0.5	0.59
<b>Treatment</b>				
Daily prednisolone dose (mg)	16.0 $\pm$ 17.0	15.0 $\pm$ 16.2	20.6 $\pm$ 20.8	0.40
Daily hydroxychloroquine dose (mg)	198 $\pm$ 46	197 $\pm$ 51	200 $\pm$ 0	0.88
Cyclophosphamide	19 (41.3)	14 (37.8)	5 (55.6)	0.46
Mycophenolate mofetil	14 (30.4)	13 (35.1)	1 (11.1)	0.24
PAD4 expression	1.48 $\pm$ 1.26	1.22 $\pm$ 1.08	2.64 $\pm$ 1.49	0.04

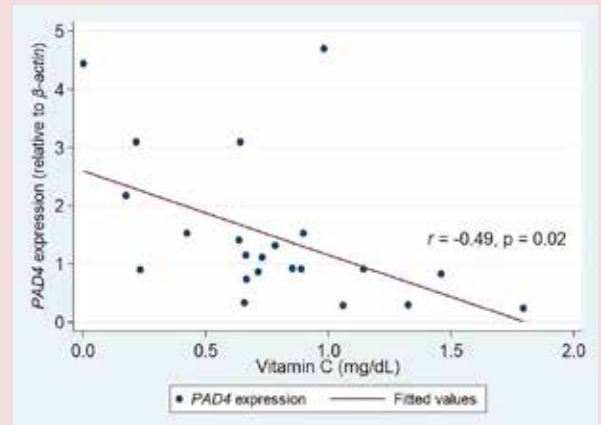


Figure: Correlation between serum vitamin C level and PAD4 expression in juvenile lupus nephritis.

**Conclusion:** Children with LN and vit C deficiency had increased NET formation, and kidney and systemic inflammation. Maintaining vit C levels within the normal range should be recommended in children with LN.

Fr-P 098  
INFLAMMATORY AND IMMUNOLOGICAL BIOMARKERS IN LUPUS NEPHRITIS

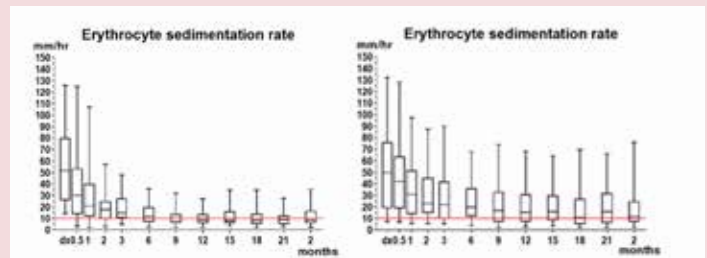
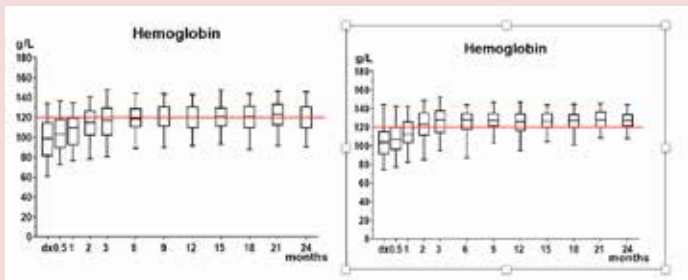
Chiara de Mutiis<sup>1</sup>, Kjell Tullus<sup>2</sup>, International Study Group in Lupus Nephritis

<sup>1</sup>Hospital Maggiore, Paediatrics, Bologna, Italy, <sup>2</sup>Great Ormond Street Hospital for Children, London, United Kingdom

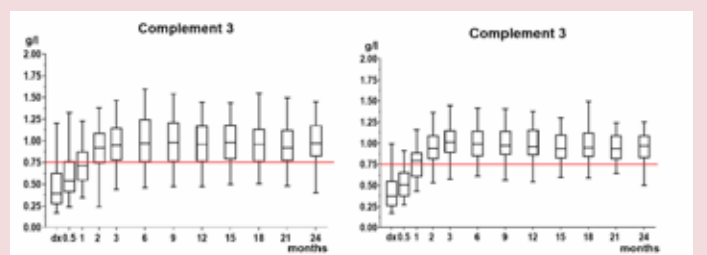
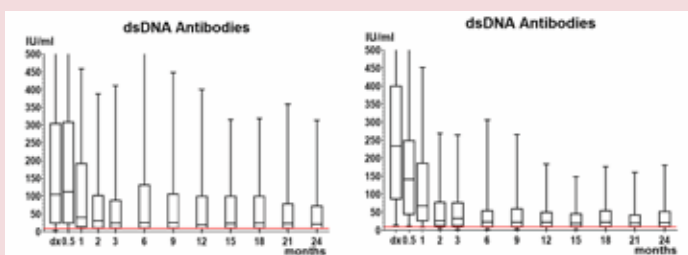
**Aims/Purpose:** We here define the levels of some inflammatory biomarkers, haemoglobin and ESR, and immunological biomarkers, double stranded DNA antibodies and complement C3, at onset and after treatment in a large international cohort of children with lupus nephritis (LN).

**Methods:** Retrospective data were collected from 428 children ( $\leq 18$  years old) with biopsy proven LN class  $\geq$  III diagnosed and treated in the last 10 years in 25 international centers from 11 countries in 3 continents. Participating centers were in USA, India, China, Thailand, Singapore, Japan, Brazil, France, Italy, Turkey, Hong Kong and UK. Complete renal remission was defined as urine-protein-creatinine ratio (UPCR)  $\leq 0.2$  mg/mg ( $\leq 23$  mg/mmol) and eGFR  $\geq 90$  ml/min/1.73m<sup>2</sup>. Data are presented in two groups: 1. Children with full renal remission from 6 to 24 month and 2. Children with signs of kidney involvement at least at one time point during that time.

**Results:** One hundred and seven patients (25%) maintained stable remission between 6th and 24th months of follow-up. A vast majority of the children showed anaemia at onset and this persisted in 50 and 25% of the patients in each group at 24 month follow-up.



ESR was similarly increased at both groups at onset but improved more by 24 months in the group that achieved long-term remission; 62% and 36% respectively had normal values, ( $p < 0.0007$ ). Patients who achieved stable kidney remission had, at diagnosis, higher dsDNA antibodies (234; 86–401 IU/ml) compared to the other group (104.2; 23–301 IU/ml) ( $P 0.0002$ ). At 24th month 34% and 35% of patients had normal dsDNA Ab in the two groups. At diagnosis complement 3 was similarly reduced in both groups, 0.39 (0.28–0.63) g/l and 0.37 (0.26–0.54) g/l. And no statistically significant difference was found also at 24 month where still a significant number showed low values.



**Conclusion:** The value at diagnosis of dsDNA but not C3 predicted outcome of LN. A high number of the children with long term full remission did still have abnormal values of these parameters at 24 month post treatment. Anemia and raised ESR was very common at onset and persisted to 24 month in a significant group of the children.

Fr-P 099  
TWO YEAR OUTCOME OF RENAL LUPUS

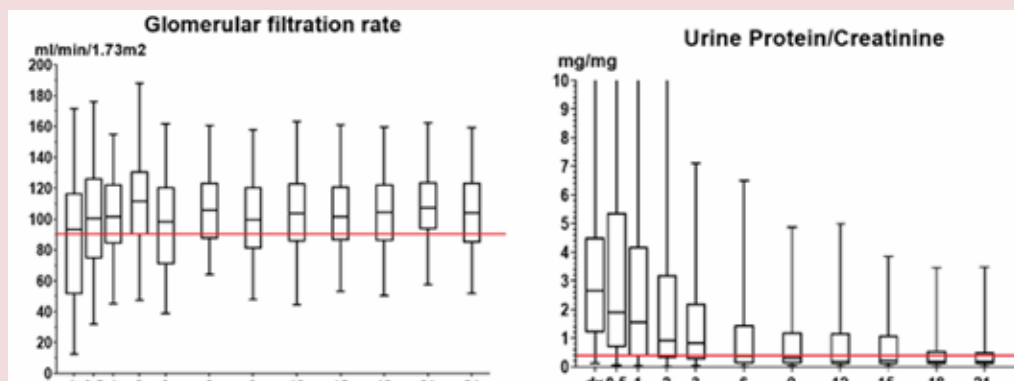
Chiara de Mutiis<sup>1</sup>, Kjell Tullus<sup>2</sup>, International Study Group for Lupus Nephritis

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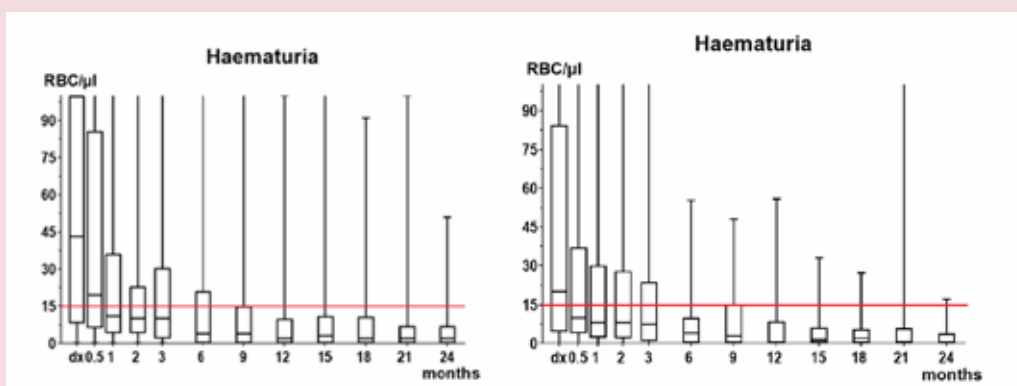
**Aims/Purpose:** The aim of our study was to describe 2 year renal outcome with focus on eGFR, proteinuria and haematuria in a large international cohort of children with lupus nephritis.

**Methods:** Retrospective data were collected from 428 children ( $\leq 18$  years old) with biopsy proven LN class  $\geq$  III diagnosed and treated in the last 10 years in 25 international centers from 11 countries in 3 continents. Participating centers were in USA, India, China, Thailand, Singapore, Japan, Brazil, France, Italy, Turkey, Hong Kong and UK. Complete renal remission was defined as urine-protein-creatinine ratio (UPCR)  $\leq 0.2$  mg/mg ( $\leq 23$ mg/mmol) and eGFR  $\geq 90$  ml/min/1.73m<sup>2</sup>. Data are presented in two groups: 1. Children with full renal remission from 6 to 24 month and 2. Children with signs of kidney involvement at least at one time point during that time.

**Results:** One hundred and seven patients (25%) maintained stable remission between 6th and 24th months of follow-up. The eGFR in the group without stable remission is shown in Figure 1. Thirty-one percent of these children showed impaired kidney function 24 month. Proteinuria was at that time point found in 41% of the patients, Figure 2.



Haematuria was a finding without major diagnostic relevance persisting in both groups of children for many month. Data from both groups of children are presented in Figure 3.



**Conclusion:** As many as 75% of the children with lupus nephritis did not achieve long term renal remission with 31 and 41 percent still having low eGFR or significant proteinuria at 24 month follow-up. This group children will have a high chance to over time develop worsening of their kidney function. Better treatments for lupus nephritis are thus needed.

Fr-P 100

CLINICAL COURSE AND OUTCOME OF THREE ANCA AND ANTI-GBM POSITIVE TEENAGE PATIENTS

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**Aims/Purpose:** Double positivity for both ANCA and anti-GBM antibodies are reported in 10–15 % of adult patients with ANCA vasculitis. In childhood, only few case reports are published about this rare and specific patient group.

**Methods:** Retrospective analysis of patients treated for the last ten years at our tertiary hospital.

**Results:** Three patients with double positivity for both ANCA and anti-GBM antibodies at presentation were included. Patient characteristics and outcome are presented in Table 1.

Sex	Age (years)	ANCA-antibodies (U/ml)	Anti-GBM antibodies (U/ml)	Max. creatinine ( $\mu\text{mol/l}$ )	Kidney biopsy	GFR at follow-up (ml/min/1.73m <sup>2</sup> BSA)
Female	13	MPO 113	24	1500	Global sclerosis in 14/19 glomeruli	< 15, transplanted
Female	16	MPO 51	6.9	260	Fibro-cellular crescents in 11/36 and global sclerosis in 22/36 glomeruli	68
Male	16	MPO 15, PR3 37	20	62	No crescents, segmental scleroses in 2/47 glomeruli	85

1. The first patient presented with acute kidney injury and required continuous kidney replacement therapy. She had decreased urine output (oligo/anuria) and high blood pressure. Despite aggressive treatment the patient developed kidney failure and received a kidney transplant eight months after the onset of disease. 2. The second patient presented with nonspecific symptoms, primarily fatigue. She had no edema, was normotensive, and had normal urine production. The patient partially responded to immunosuppressive therapy with moderately impaired kidney function as an outcome. 3. The third patient presented with hemoptysis, arthralgia, myalgia, skin rash as well as mild kidney involvement with microscopic hematuria, and no albuminuria. The creatinine value was normal. The patient responded well to induction treatment. Kidney biopsy confirmed features of both ANCA-associated vasculitis and anti-GBM glomerulonephritis in all three cases. The grade of inflammation on kidney biopsy differed significantly with global sclerosis in the first patient, partial sclerosis, and fibro-cellular crescents in the second patient, and low inflammation with no crescents in the third patient. All three patients were started on induction therapy with plasma exchange, cyclophosphamide and steroids followed by azathioprine or rituximab as a maintenance. None of the patients had a relapse.

**Conclusions:** Despite similar titers of antibodies in serum, our three patients had very different clinical picture, degree of kidney involvement, and outcome. Recent recommendations in adults are to initially treat these patients as anti-GBM disease with aggressive induction including plasma exchange, followed by long maintenance treatment as in ANCA vasculitis. Our experience suggests that this patient group is heterogenous, and individually tailored treatment may be more appropriate, but more data are needed.

Fr-P 101  
USE OF RITUXIMAB IN GLOMERULAR PATHOLOGY IN CHILDREN

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**Purpose:** To evaluate the effectiveness and safety of the use of rituximab in children with glomerular pathology on the example of 16 clinical cases.

**Methods:** 16 children aged 5–18 years with glomerular pathology were treated with rituximab according to established diagnoses. The study was a multicenter, randomized, open retrospective study with a Patient-Oriented Evidence that Matters (POEM) design.

Articles with information about rituximab on the resources of PubMed, Sage journal, BMC, NIH were analyzed and the experience of using rituximab in children with glomerular pathology in Ukraine was presented.

**Results:** After analyzing 16 case histories of children aged 5 to 18 who underwent intravenous administration of rituximab in connection with the progressive course of nephrological pathology. Distribution by gender – 5 boys (31.3%), 11 girls (68.8%). 12 children (75%) received administration of rituximab for frequently relapsing/steroid-dependent nephrotic syndrome (NS) and 4 (25%) children for lupus nephritis (Table 1).

Table 1. Characteristics of children who received rituximab

Patient	Sex	Age	Clinical/morphological diagnosis	initial/final level of proteinuria
M	boy	18	NS	5/1,7
D	girl	16	lupus nephritis	7/0,1
T	girl	12	lupus nephritis	8/2,5
K	girl	12	NS	3/0
A	boy	13	NS	3/0
P	girl	12	lupus nephritis	1/0
V	boy	9	NS	6/2,5
W	girl	18	lupus nephritis	4/0
S	girl	15	NS	3/0
B	girl	9	NS	6/0
W	girl	5	NS	3/0
K	girl	5	NS	3/0
P	girl	16	NS	4,5/1,5
L	boy	8	NS	3/0
W	boy	6	NS	2/0
W	girl	6	NS	3/0

In some cases, rituximab was prescribed against the background of per os glucocorticoids. Rituximab was administered according to a protocol in which methylprednisolone was pre-administered at a dose of 1 mg/kg, followed by rituximab at a dose of 15 mg/kg at a rate of approximately 50 ml/hour via an infusomate pre-diluted with 1 mg/ml saline. , with longer continuous monitoring of the child's condition [1]. Infusion of rituximab was carried out at least twice with an interval of two weeks. If necessary, after monitoring the level of CD20 in the blood serum, in the presence of any number of cells or the preservation of an active process, rituximab was re-administered 6 months after the last administration [2]. On the days of rituximab treatment, children who received per os steroids did not receive them, but on the next day after the infusions, per os glucocorticoids continued in the same dose. Some children received concomitant therapy per os with an angiotensin-converting enzyme inhibitor at a renoprotective dose that was not canceled on the days of rituximab administration. Adverse infusion reactions to rituximab administration were noted in two children in the form of a decrease in blood pressure and tachycardia, which mostly occurred against the background of increasing the rate of rituximab administration and against the background of stopping the infusion, with a subsequent decrease in the rate of rituximab administration helped to eliminate this side effect [1,3]. All other children tolerated rituximab infusion well. The effectiveness of rituximab therapy was assessed by the level of proteinuria, which at the beginning of treatment averaged 4.0 g/l, and after rituximab

infusion averaged 0.5 g/l (Table 1).

**Conclusion:** Rituximab is a chimeric (mouse/human) monoclonal antibody with the ability to deplete B-cell populations by targeting the CD20 antigen expressed on the cell surface. It was first approved for medical use in oncology, initially for the treatment of B-cell lymphoma and post-transplant lymphoproliferative disorders, but today it is used in various fields of medicine, where it has become one of the safest and most effective antibody-based therapies. Nowadays, rituximab is more often used in children with various kidney diseases, including lupus nephritis, vasculitis associated with antineutrophil cytoplasmic antibodies, nephrotic syndrome and in various scenarios before and after kidney transplantation [4,5,6]. An important practical aspect is the use of rituximab in children with nephrotic syndrome and lupus nephritis in the conditions of limited resources of the military state in Ukraine. The introduction of rituximab is actually an alternative to long-term glucocorticoid administration. Thus, the treatment is simplified, the number of side effects is reduced, and the effectiveness of the therapy is increased, ensuring a recurrence-free course, and the doctor can confidently monitor the implementation of his appointments given that the infusion is administered under the supervision of a pediatric nephrologist and lasts for 6–8 months.

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THE STUDY OF THE COURSE AND OUTCOME OF LUPUS NEPHRITIS IN CHILDREN

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**Aims/Purpose:** Lupus nephritis is a rare autoimmune disease that has a high morbidity rate and such intense symptoms that lead to death if not treated right. The aim of the study is to evaluate the course and factors influencing on short-term and long-term outcomes of the disease.

**Methods:** Observational and descriptive studies based on the data obtained from medical records of patients in the 2nd Children's hospital in Minsk Belarus from the nephrology department. The inclusion criterion was for patients less than 18 years old that have biopsy proved lupus nephritis.

**Results:** All 42 patients were eligible to the study, 5 of them were males (11.9%). Ages vary between 7 till 17 with the median being 15. The main cardiovascular disease was hypertrophy of the myocardium with a percentage of 31.5% and left ventricular hypertrophy in all cases with a median of left ventricular mass index (LVMI) 0.35 with a max of 0.54 in a 15-year-old patient and a min of 0.24 in a 16-year-old. Arterial hypertension observed in 86% of patients. 28/42 suffered from arthritis with 10% of them being males. Furthermore, all patients suffered some sort of a blood anomaly as an example 36% had increased cholesterol levels in blood and about 10% of them were males while 15% of the overall patients had low levels of HDL (high density lipoproteins) which promotes heart diseases (coronary heart disease, cerebrovascular disease etc.), about 8.5% had increased levels of uric acid in the blood 25% of them being males and 14% of all patients had diabetes mellitus males being 25% of all the overall patients. 35% of the patients suffered from relapsing herpes infection. About 21% of the patients had Antiphospholipid Syndrome. All patients received standard protocol of immunosuppression induction (puls therapy with intravenous methylprednisolone and/or cyclophosphamide) and maintains oral steroids and cytostatic therapy, 5-year renal survival was 89% (6%). 3/42 (7.14%) underwent a kidney transplant due to end stage renal disease, one of the patients died after transplantation (33.33%) due to infection. 3 patients from 42 died due to infections during first year after manifestation of the disease.

**Conclusion:** Short-term prognosis associated with infectious process due to aggressive course of lupus and high-dose immunosuppression, long term outcome with progression of chronic kidney disease and cardiovascular complications.

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WHEN NEPHROTIC SYNDROME IS NOT WHAT IT SEEMS

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**Aims/Purpose:** The initial diagnosis when we face a patient with nephrotic proteinuria with associated oedema and hypoalbuminemia is usually a nephrotic syndrome (NS), initiating treatment with oral corticotherapy (CT). Special attention should be paid to conditions, which are not typically associated, and to the absence of response to CT, which should make us reconsider the diagnosis and immunosuppressive treatment as well as further studies. Although guidelines recommend start of calcineurin inhibitors if SRNS while waiting for complementary studies, looking at the results of our two cases, the decision should be taken with caution because of their toxicity.

**Methods:** Retrospective review of two cases who were presented in our outpatient clinic, initially with proteinuria and with a possible NS with a final diagnosis that was not suspected at the onset of the disease.

**Results:** Case report 1. 11-year-old girl diagnosed of cortico-dependent NS at the age of 3 in Morocco, with microhematuria and no hypertension. Treated with CT with initial remission. At the age of 7 she began with frequent relapses and was treated with CT exclusively until her arrival in Spain four years later. In Spain, CT was tapered. Afterwards, she presented recurrent episodes of macroscopic hematuria (MH). Renal biopsy was then performed, showing 20 glomeruli, one globally sclerosed, the others with minimal mesangial expansion with pedicle fusion in 80% of the capillary surface. During follow up there was a new relapse of the NS and a new episode of MH. A review of the biopsy was then requested, noting a basement membrane slightly thinned. Heterozygous pathogenic variant in the COL4A4 gene was isolated, being diagnosed as autosomal dominant Alport Syndrome. Case report 2. 8-year-old girl from Dominican Republic, referred to outpatient clinic for oedemas with polyuria and polydipsia. Nephrotic range proteinuria and glucosuria, hypoalbuminemia, low IgG and IgA, IgM positive for *M. pneumoniae*, positive streptococcus serology and anti-DNA native antibodies with antichromatin positivity were found in the test performed. NS was initially diagnosed and CT was started. In the follow up, she continued with nephrotic proteinuria, diagnosing at that time a steroid-resistant NS. A renal biopsy was then carried out with a result suggestive of focal segmental glomerulosclerosis (FSGE). Treatment with ciclosporin was started. Later, in immunofluorescence, a “full house pattern” was described, initiating treatment with MMF and prednisone without response, switching afterwards to tacrolimus. Homozygous mutation G1/G1 was identified in the APOL1 gene.

**Conclusion:** Patients with atypical features of NS or with no response to CT should lead us to suspect that we are not dealing with an idiopathic NS, being necessary in these cases both genetic studies and biopsy to reach an etiological diagnosis to decide treatment and follow up.

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USE OF RENAL BIOPSY IN THE DIAGNOSIS AND MANAGEMENT OF PAEDIATRIC LUPUS NEPHRITIS WITH ANALYSIS OF OUTCOMES AT 6 AND 12 MONTHS IN A UK TERTIARY CENTRE

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**Aims/Purpose:** Lupus Nephritis (LN) occurs in 50-60% of children with Systemic Lupus Erythematosus [1]. European guidance on the management of LN was updated in 2019 [2]. Renal biopsy is the gold standard investigation in Lupus Nephritis, indicated by Urine Protein: Creatinine Ratio (UPCR)  $> 50$  mg/mmol and/or fall in Glomerular Filtration Rate. Histological classification guides immunomodulatory management [3]. We aimed to audit use of kidney biopsies and management of LN in a UK tertiary paediatric nephrology centre against the recommendations set out in EULAR 2020 [2].

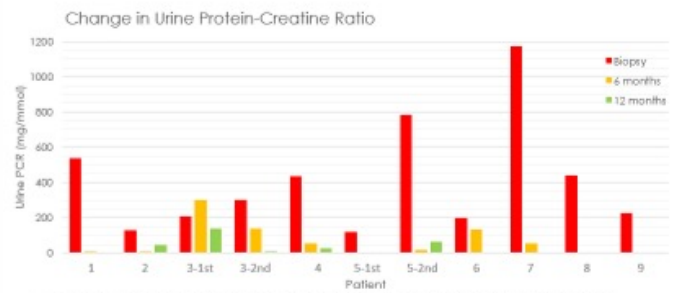
**Methods:** Consecutive data were collected over a 7-year period (September 2015 – October 2022) from the local Systemic Lupus Erythematosus patient database at Leeds Children's Hospital. Analysis was performed using Microsoft Excel.

**Results:** Nine cases were identified (Female = 5) with mean age twelve (IQR, 3, 11-14yo). At time of biopsy, mean eGFR was 119 and mean UPCR was 380 mg/mmol. Modal severity Class IV (n = 6), then II+V (n = 2), and II/III/V (n = 1 each). All patients received pulsed intravenous Methylprednisolone followed by weaning oral Prednisolone, four additionally received MMF, two received CP, and one patient received Rituximab. UPCR at 6- and 12-months reduced by 68% and 80%, respectively. At 6 months at least partial clinical response was achieved in 7 of 9 (78%) cases. At 12 months, 4 of 6 (66%) met complete remission criteria.

**Conclusion:** EULAR guidelines recommend management to achieve partial clinical response ( $> 50\%$  reduction in UPCR) at 6 months and complete clinical response (UPCR  $< 50$ mg/mmol) at 12 months. In our cohort, at least partial clinical response was achieved in 78% at 6 months; complete remission was even seen in 55%. Provisional 12 months data shows a further two achieved complete remission. These results are encouraging but more longitudinal data is required to assess long-term outcome and complications related to immunosuppressive therapies.

Patient	Sex	Age (y)	Ethnicity	Initial presentation	Class	Class	Creatinine	UPCR@0	UPCR@6m	UPCR@12m	6-Month Res	12-Month Res
1	M	11	Other	Haematuria	5	5	40	337	5	5	100	100
2	M	7	SA	Stomatitis, rash	4	5	34	133	20	44	70	100
3-1st	F	14	SA	Rash, lymphadenopathy	2	5	53	200	40	107	100	100
3-2nd	NA	14	NA	NA	5	5	53	300	207	30	50	100
4	F	14	SA	Investigation following Systemic Erythematosus	4	5	124	400	50	21	100	100
5-1st	F	10	AC	IT/ITs, Systemic, Rash/RA	3	5	32	100	-	-	-	-
5-2nd	NA	10	NA	NA	4	5	34	700	20	24	100	100
6	F	10	SA	Abnormal pulmonary function, weight loss	4	5	40	200	100	-	100	-
7	M	10	SA	Proteinuria, arthritis	4	5	34	117	17	-	100	-
8	F	10	SA	Allergy investigations	3	5	53	442	8	-	100	-
9	M	10	Other	Abnormal pulmonary function	4	5	50	220	-	-	-	-

Table 1: Summary of pertinent data points including Urinary Protein:Creatinine Ratio at time of biopsy, six months, and twelve months  
Sex: Male/Female; Age: years; Ethnicity: Caucasian, South Asian, Afro-Caribbean; Creatinine: micromol/L; UPCR, Urine Protein:Creatinine Ratio, mg/mmol



Graph 1: Representation of Urine Protein:Creatinine Ratio trends following biopsy and subsequent medical management.

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NEWLY DIAGNOSED NEPHRITIS IN CHILDREN FOLLOWING COVID-19 VACCINATION

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**Aims/Purpose:** Vaccination is one of the most effective strategies in ensuring effective control of COVID-19 infection spread. In Singapore, vaccination with the Pfizer-BioNTech messenger RNA vaccine was started in children aged 12–15 years old since June 2021, after authorisation by the Food and Drug Administration (FDA) since 10th May 2021. Intrinsic kidney pathologies following COVID-19 vaccination, particularly minimal change disease have been reported in adults. Although more recent reports have arose in children, information regarding adverse reactions in them is still limited. We report a case series of children who developed new-onset nephritis post-vaccination.

**Methods:** This was a retrospective cohort study of patients  $\leq$  18 years old who were newly diagnosed in KK Women's and Children's Hospital with biopsy-proven kidney diseases after their COVID-19 vaccination from June 2021 to December 2022. Data was collected by a combination of data extraction from electronic medical records and manual chart review. Data on the incidence of nephritis, patients' vaccination details, clinical characteristics and outcomes were collected.

**Results:** Eleven patients aged between 9 to 17 years old developed new-onset nephritis post-vaccination. Seven were females. Amongst them, 5 had IgA nephropathy (IgAN), 2 had tubulointerstitial nephritis (TIN), 2 had lupus nephritis, 1 had minimal change disease and 1 had ANCA-associated glomerulonephritis (ANCA-GN). Most patients (7) presented after the 2nd vaccine, with time of onset ranging between 0 days to 4 months post-vaccination. Two patients with IgAN had previous episodes of gross haematuria prior to vaccination. Two patients had crescents on kidney biopsy (1 IgAN and 1 ANCA-GN). All 11 patients received immunosuppression and the patient with ANCA-GN required plasma exchange in addition. At the time of their last follow-up, all patients had a normal serum creatinine and 9 had a normal eGFR. 1 patient with TIN and 1 with ANCA-GN had a mildly reduced eGFR of 85 and 83 ml/min/1.73m<sup>2</sup> respectively. None required any renal replacement therapy.

**Conclusion:** Benefits strongly outweigh risks in COVID-19 vaccination based on current evidence. New cases of nephritis may occur post-vaccination. Vigilance about such occurrences is needed. The most common new-onset nephritis in our institution is IgAN, with vaccination potentially unmasking existing disease. Prognosis is favourable as all cases responded well to immunosuppressive treatment.

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## RITUXIMAB AND MYCOPHENOLATE MOFETIL FOR TREATMENT OF GOODPASTURE SYNDROME: A BICENTRIC RETROSPECTIVE STUDY

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**Aims/Purpose:** Goodpasture syndrome (GS) is a rare small vessel vasculitis caused by pathogenic antibodies against the  $\alpha 3$ -subunit of collagen IV characterized by rapid progressive glomerulonephritis and a potentially lethal pulmonary hemorrhage. If left untreated, GS rapidly leads to end-stage kidney disease (ESKD). KDIGO recommends plasma exchanges (PEX) for antibody elimination and steroids in combination with cyclophosphamide (CTX) to suppress antibody production in adult GS patients. However, CTX is associated with serious side effects such as infertility and myelosuppression. Rituximab (RTX) and mycophenolate mofetil (MMF) were found to be equally effective as CTX in adult GS patients, but data in children are lacking.

**Methods:** A query was conducted among 8 pediatric nephrology centers in Germany. The clinical data of patients diagnosed between 2014 and 2023 were collected retrospectively.

**Results:** Five patients with Goodpasture syndrome without CTX therapy were identified at 2 centers. The mean age of the patients was 16 years (3 female and 2 male). The delay until diagnosis was 47 days on average. All patients had hematuria and glomerular proteinuria (mean: 2118 mg albumin/g creatinine). Anti-GBM antibodies were detectable in all patients (mean: 222 IU/ml). All patients had hemoptysis and an abnormal chest CT. Antibody clearance was achieved after a median of 13 PEX cycles (range 6-31). Four out of 5 patients received methylprednisolone pulses. All patients received oral prednisolone and MMF (5/5). Four patients received 2 to up-to 4 doses of RTX (375 mg/m<sup>2</sup>). Two patients showed an allergic reaction during RTX infusion, 2 patients had transient leukopenia, and 2 patients had an infection. After a mean follow-up of 27 month four out of five patients showed normalization of eGFR ( $\geq 90$  ml/min/1.73m<sup>2</sup>). One patient developed a recurrence of the disease resulting in ESKD. No pulmonary recurrences were observed.

**Conclusion:** In this small series of adolescent GS patients, treatment with RTX and MMF in combination with PEX showed good initial outcomes and was associated with an acceptable side effect profile. Those promising results demand adequately powered studies in adolescent GS patients.

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**AUTOIMMUNE LYMPHOPROLIFERATIVE SYNDROME UNDER THE MASK OF GRANULOMATOSIS WITH POLYANGIITIS**

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**Aims/Purpose:** The nephrologists usually do not consider primary immunodeficiency syndromes in patients with systemic vasculitis or autoimmune diseases, and diagnosis and appropriated treatment are often delayed.

**Methods:** The aim was to present a case of autoimmune lymphoproliferative syndrome (ALPS) with a clinical manifestation similar to granulomatosis with polyangiitis (GP).

**Results:** A patient with a history of hemolytic anemia (from 1 y), necrotizing rhinitis, stomatitis, pharyngitis with deforming stenosis of the pharyngeal ring, lymphadenopathy (from 2y), relapsing ulcerative necrotic skin rash, arthralgia, abdominal syndrome, thrombocytopenia (from 3y), splenectomy (at 8y) was seen for GP and received immunosuppression (Medrol, Cyclophosphamide, Methotrexate) for a long time without a satisfactory effect. He developed pneumonitis, hematuria, proteinuria (ANCA 1:40, ANF 1:160) at age of 12y. Despite treatment (induction with Solumedrol 30 mg/kg/d N<sup>o</sup>3, Cyclophosphamide 1000 mg/mo N<sup>o</sup>6; maintenance therapy with Medrol 1 mg/kg/d, cyclophosphamide 1 mg/kg/d p.o. for 1 year) gross hematuria, proteinuria persisted. Kidney biopsy (at 14y) did not demonstrate signs of glomerular diseases; ulcerative necrotic cystitis was diagnosed (switched to Mycophenolate Mofetil 750 mg/m<sup>2</sup>/day). Immunological evaluation (at 15y) revealed high ratio of double negative T cells (DNT, TCRabCD3+CD4-CD8-, 24%, N = 2%) and vitamin B12 level (1650 ng/l, N = 214-864) specific for ALPS, that has been confirmed by genetic analysis (FAS: c.941T > A, p.(Ile314Asn)). Treatment with Sirolimus (1.25 mg/m<sup>2</sup>, Co 7-9 ng/ml), VIG, azithromycin was started with a good control of vasculitis, arthritis, bicytopenia, normalization of DNT (2.1%), vitamin B12 (848 ng/l) levels.

**Conclusion:** The case indicates that ALPS may mimic GP and should be considered in the differential diagnosis in children with early-onset cytopenia, vasculitis, lymphadenopathy. Immunological evaluation may promote early diagnosis and leads to appropriated patient treatment and management.

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## RELAPSE OF NEPHROTIC SYNDROME FOLLOWING COVID-19 VACCINATION

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**Aims/Purpose:** Nephrotic Syndrome(NS) is the commonest glomerular disease in childhood. It results from immunological disturbances and is characterized by a relapsing course. Relapses are usually triggered by T-cell activation and release of cytokines. From 2021, Pfizer-BioNTech vaccine was offered to children with active renal disease between 12 and 18 years in Sri Lanka. As this vaccine recruits T-cells with release of cytokines, it is possible that a relapse could be triggered following COVID-19 vaccination. This study investigate the relapse rate in children with NS before and after receiving the COVID-19 vaccine.

**Methods:** The study was carried out at the Paediatric Nephrology Clinic at Teaching Hospital Peradeniya. All children with steroid sensitive disease between ages 12 and 18 years who received COVID-19 vaccination were considered for recruitment. All patients/parents are trained to test and record urine protein excretion. Urinary protein excretion 3+ or more for 3 consecutive days were considered as a relapse. Vaccination date was confirmed with the vaccination card and the relapse frequency one year before and after vaccination was noted. The number of relapses were analyzed using a Bayesian statistical Poisson regression model. Analysis was done using R language version 4.2.1

**Results:** Seventy-one children were analyzed (39 males and 32 females) with a mean age of 14.72 years (SD 1.67). The incidence rate ratio (IRR) for relapse within one year from vaccination was 1.53 (89% credible interval:1.23 – 1.91), indicating a 53% higher relapse rate than the pre-vaccination period. The IRR for relapse within 6 months and 3 months after vaccination was even higher, with values of 3.09(89% credible interval:2.20 – 4.34) and 4.57(89% credible interval:2.97–7.38), respectively.

**Conclusion:** The results suggest a significant association between COVID-19 vaccination and increased risk of relapse, particularly within the first few months after vaccination.

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### CLINICAL PROGRESS AND PROGNOSIS IN C3 GLOMERULOPATHY

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**Background:** C3 glomerulopathy, is a disease with heterogeneous clinical presentation and outcome, resulting from disorders in the control mechanism of the alternative complement system and characterized by predominant C3 accumulation in glomeruli without significant IgG.

**Material and Methods:** The clinical course, treatments and outcomes of 21 pediatric patients with biopsy-proven C3 glomerulopathy were reviewed retrospectively.

**Results:** Of 21 patients, 9 (43%) were girls and 12 (57%) were boys. The mean age at diagnosis was  $10.1 \pm 4.8$  years and the mean follow-up period was  $5.4 \pm 4.8$  years. On admission, five patients had  $eGFR < 50$  ml/min/1.73m<sup>2</sup>, the mean 24-hour proteinuria was  $78.4 \pm 65$  mg/m<sup>2</sup>/h and serum albumin  $3.1 \pm 0.8$  gr/dl. All patients had low serum C3 levels except two. Genetic testing was performed in 15 patients, 8 patients had mutations in factor H. At last visit only two patients had  $eGFR < 50$  ml/min/1.73m<sup>2</sup>, both of whom had ESKD and the mean 24-hour proteinuria was  $22.8 \pm 32$  mg/m<sup>2</sup>/h. Corticosteroid treatment was given to all patients, cyclophosphamide to 4 patients, cyclosporine to 4 patients, MMF to 9 patients, and rituximab to 2 patient. Three patients were treated with eculizumab.

**Conclusion:** C3 glomerulopathy is a disease with heterogeneous clinical presentation and outcome. In these patients, investigation of mutations in the alternative complement pathway is important and initiation of treatment with the C5a inhibitor eculizumab may be considered in treatment-resistant patients.



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SARS-COV-2 INFECTION AND ANTI-GLOMERULAR BASEMENT DISEASE: A CASE REPORT

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**Background:** Anti-GBM disease is an autoimmune disease leading to rapidly progressive glomerulonephritis and is extremely rare in children.

**Case Report:** A 8.5-year-old boy was admitted to the emergency department with macroscopic hematuria and oliguria. His previous medical history was unremarkable except pyelonephritis and COVID-PCR positivity five weeks ago. Systemic physical examination was unremarkable except pretibial and periorbital edema, and his blood pressure was BP 117/77 mmHg (95th centile). His COVID-PCR was still positive. All other viral markers were negative. There was no hypocomplementemia, and all autoantibodies were negative except anti-glomerular basement membrane (anti-GBM). Urinalysis revealed 2+ proteinuria and 3+ hematuria. During 2 days follow-up, serum creatinine steadily increased from 0.63 mg/dL to 6.4 mg/dL. Renal biopsy was consistent with crescentic glomerulonephritis associated with anti-GBM disease (Figure 1). He was treated successfully with methylprednisolone, cyclophosphamide pulse therapy, and plasmapheresis followed by intravenous immune globulin.

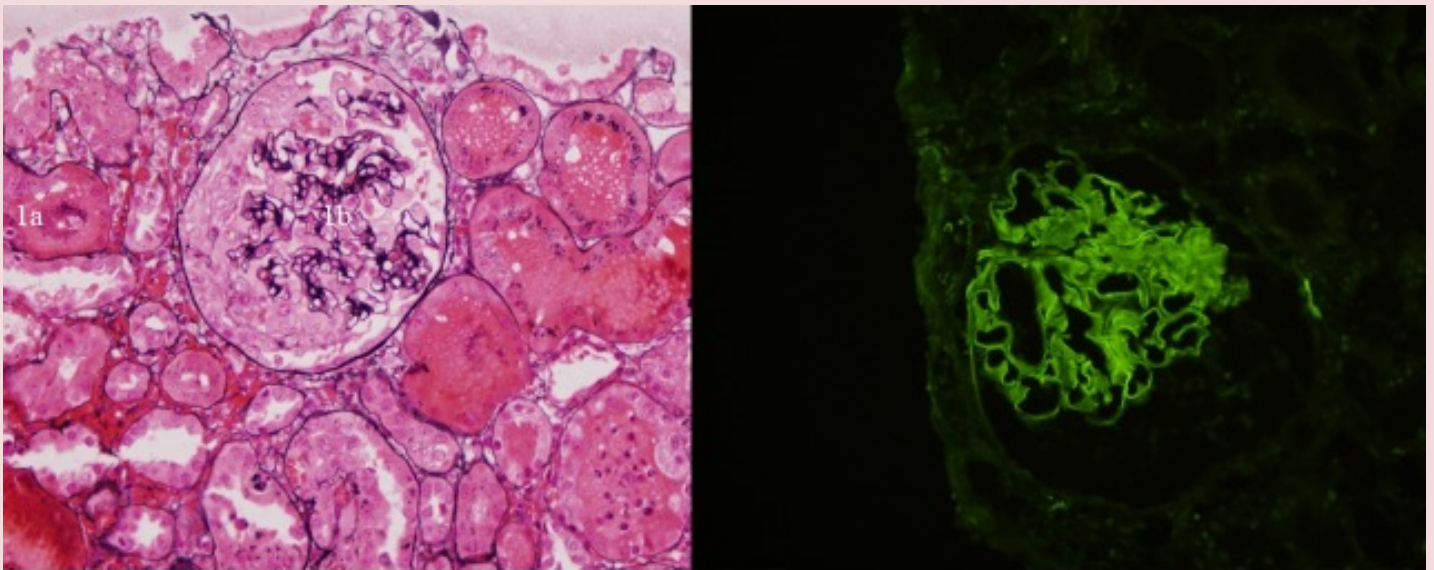


Figure 1a: Fibrocellular crescent in a glomerular (methenamine silver-periodic acid-Schiff stain, x400). 1b: diffuse and linear IgG deposition in the glomerular basement membranes (anti-IgG antibody, direct immunofluorescence, x400).

**Conclusion:** Our pediatric case report suggested a possible pathogenic association of COVID-19 infection triggering an autoimmune response leading to anti-GBM causing a rapidly progressive form of crescentic glomerulonephritis in children.

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## IGM NEPHROPATHY: CLINICAL MANIFESTATIONS AND PATHOLOGICAL FINDINGS

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**Introduction:** IgM nephropathy (IgM-N) is a very controversial clinical and pathological condition characterized by diffuse deposits of IgM in the mesangium on immunohistochemical staining, while light microscopy reveals minimal glomerular changes, focal segmental mesangial hypercellularity, less often focal -segmental glomerulosclerosis (FSGS). The aim of the study to determine the clinical and morphological features of IgM nephropathy in children, as well as to evaluate the effectiveness of the therapy and outcomes.

**Material and Methods:** The study included 18 children with a morphologically confirmed diagnosis of IgM-N and treated in the 2nd Children's Hospital in Minsk from 2019 to 2022. The median age of IgM-N onset was 3.7 (IQR 2.5; 5.7) years, follow-up 3.6 (1.0; 6.9) years, 72% of boys. IgM-N was diagnosed by detecting dominant IgM expression in the mesangial matrix.

**Results:** The most common clinical manifestation of IgM-N was nephrotic syndrome (NS) (17/18): "pure" – 13 (72%), with hematuria and arterial hypertension (AH) – 3 (17%), only with AH – 1 (6%), steroid resistance was observed in 5 children (29%): in 3 with "pure" NS and in 2 with NS with hematuria and AH. In all cases NS recurred. One patient with IgM-N had only isolated hematuria and did not require treatment. According to a NS histomorphology: only minimal changes disease (MCD) were in 2 patients, in combination with the initial signs of FSGS – in 4, with glomerulosclerosis – in 1; only mesangial proliferation – in 4, in combination with extracapillary proliferation – in 2, with FSGS – in 2, with glomerulosclerosis – in 1; only FSGS – in 1. Treatment of NS included monotherapy with corticosteroids (CS) in 3 patients (18%), in combination with cyclosporine A (CsA) – in 9 (53%), with chlorambucil – in 1, with pulse therapy with cyclophosphamide (CF) – in 1, different sequences of CS/CsA/CF – in 1, CS/levamisole/CsA/CS – in 1, CS/levamisole/CsA/chlorambucil – in 1. Complete remission of NS was achieved in 15 (88%) of 17 patients. Of the 3 children with NS with hematuria and hypertension, 1 had a partial remission (morphologically mesangial and extracapillary proliferation) and 1 therapy was ineffective (morphologically mesangial proliferation).

**Conclusion:** IgM nephropathy in children often is manifested by "pure" NS, less often NS in combination with hematuria and/or hypertension and rare isolated hematuria. Pathomorphological changes of IgM-N are more often presented by MCD with initial signs of FSGS and mesangial proliferation. In the vast majority of cases it is possible to achieve remission while taking CS with or without cyclosporine A, despite the recurrence of the disease. Insufficient effect of the therapy is noted in patients with NS with hematuria and hypertension.

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HUMORAL AND CELLULAR IMMUNE RESPONSE TO SARS-COV-2 VACCINE (BTN162B2) IN CHILDREN WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND DIFFULT-TO-TREAT NEPHROTIC SYNDROME

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**Aims/Purpose:** Immune response to SARS-CoV-2 vaccination is lower in patients receiving immunosuppression for systemic lupus erythematosus (SLE) and difficult-to-treat nephrotic syndrome (NS) compared with healthy individuals. However, limited data are available for the pediatric population. The aim of this study was to evaluate both humoral and cellular immune responses to SARS-CoV-2 vaccination in these two groups of the pediatric population.

**Methods:** In this cross-sectional, single-center study, 27 patients (16 with SLE, 11 with difficult-to-treat NS) and 19 healthy controls were evaluated for SARS-CoV-2-specific humoral (anti-spike IgG and neutralizing antibodies) and cellular (T-cell interferon  $\gamma$  release assay; IGRA) immune responses at least one month after two doses of SARS-CoV-2 mRNA vaccine (BNT162b2). None of the patients received rituximab or cyclophosphamide except one SLE patient six months before vaccination.

**Results:** There were no differences in sex, age, or duration after vaccination between the patient and the control groups (Table). None of the immune parameters differed between the difficult-to-treat NS and control groups (Table). Anti-SARS-CoV-2 IgG and neutralizing antibody positivity did not differ between the SLE and control groups, but IGRA positivity was significantly lower in the SLE group ( $p = 0.05$ ) (Table). There were no differences between IGRA-negative and IGRA-positive SLE patients in terms of disease duration, SLEDAI score, use of MMF-AZA, or dose of MMF-AZA, but lymphocyte count was significantly lower in the IGRA-negative SLE patients [ $1.6 (0.9;2) \times 10^3/\mu\text{l}$  vs.  $2.5 (2;3) \times 10^3/\mu\text{l}$ ,  $p = 0.011$ ].

**Conclusion:** Patients with difficult-to-treat NS have comparable humoral and cellular immune response to healthy controls, but pediatric SLE patients have lower cellular immune response to SARS-CoV-2 vaccine.

Table: Demographic characteristics and immune responses in the study group

	Difficult-to-treat NS	SLE n = 16	Control n = 19
Age, years (mean $\pm$ SDS)	n = 11	17.7 $\pm$ 1.8	15.9 $\pm$ 2.27
Sex, female, n (%)	17.6 $\pm$ 1.2	12/16 (75%)	10/19 (52.6%)
Duration after vaccination, weeks (median, IQR)	5/15 (45.5%)	28 (13-31)	18 (5-28)
Anti-SARS-CoV-2 IgG positivity, n (%)	17.6 (11-36)	16/16 (100%)	19/19 (100%)
Neutralizing antibody positivity, n (%)	10/11 (91%)	16/16 (100%)	18/19 (95%)
IGRA positivity, n (%)	11/11 (100%)	9/16 (56%)	17/19 (89.5%)

NS: Nephrotic syndrome, SLE: Systemic lupus erythematosus

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**COPA SYNDROME – A POTENTIAL UNDERDIAGNOSED DIFFERENTIAL DIAGNOSIS OF MPO ANCA POSITIVE VASCULITIS IN CHILDREN – A CASE REPORT WITH SUCCESSFUL MAINTENANCE TREATMENT WITH MYCOPHENOLATE MOFETIL**

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**Aim:** Presentation of a case with COPA syndrome as an important differential diagnosis of MPO positive ANCA associated Vasculitis (AAV) and discussion of the potential utility of mycophenolate mofetil (MMF) as maintenance treatment.

**Methods:** Case report.

**Results:** A now 13 year old girl presented initially at age 2–4 years, and again at 8 years with recurrent pulmonary hemorrhage. She was diagnosed with idiopathic pulmonary hemosiderosis and was treated intermittently with steroids, hydroxychloroquine and blood transfusions. At age 11 years she presented with fever, skin lesions with erythematous nodules and purpuric lesions, arthralgia, hematuria (1202 erythrocytes/mcl), minimal proteinuria (Protein/creatinine ratio 25 mg/mmol) and radiologic evidence of pulmonary haemorrhage without upper airway symptoms. Kidney function was normal. ANCA was positive at 1:80 (= 1:40) with Anti MPO of 20 U/ml ( $\leq 7$ ). Skin biopsy showed focal leucocytoclastic vasculitis. Kidney biopsy showed minimal focal necrotizing extracapillary proliferative pauci-immune Glomerulonephritis (GN) with one crescent. A diagnosis of AAV was made and iv pulse steroids, followed by oral steroids and MMF (570 mg/m<sup>2</sup>) was initiated. Hydroxychloroquine was continued. Clinical remission occurred rapidly. Maintenance therapy was continued with MMF and 5 mg prednisolone daily (child 70 Kg). After 13 months, despite persistent clinical remission, Anti MPO titers began to rise (max 26U/ml), with subsequent intermittent microscopic hematuria (92/ul). Rituximab was considered. Repeat kidney biopsy showed unchanged minimal pauci-immune GN without active lesions. No recurrent lung, skin or joint symptoms occurred since initiation of MMF. After 20 months of treatment a heterozygous mutation in the COPA gene was detected as a plausible unifying diagnosis for the very early onset interstitial lung pathology, and the autoimmune joint, skin and kidney findings following years later. Given the clinical stability, maintenance treatment with MMF was continued and steroids have slowly been tapered and stopped. Close follow up continues.

**Conclusion:** MPO ANCA vasculitis may have a less favorable prognosis in children. COPA syndrome may be an important underdiagnosed differential diagnosis contributing to this. Suggested maintenance therapy for COPA includes methotrexate, azathioprine, steroids, and recently JAK inhibitors. This case shows a stable pulmonary and renal course with MMF as induction and maintenance therapy after almost 2 years.

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**PEDIATRIC DOUBLE POSITIVE ANTI-GLOMERULAR BASEMENT MEMBRANE ANTIBODY AND ANT-NEUTROPHIL CYTOPLASMIC ANTIBODY GLOMERULONEPHRITIS: A CASE REPORT**

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**Aims/Purpose:** We report the case of a 9-year-old boy with doubly seropositive anti-GBM disease with complete remission on rituximab

**Methods and Results:** A 9-year-old boy was admitted with double-positive Goodpasture's disease revealed by rapidly progressive renal failure, proteinuria and macroscopic hematuria, without pulmonary involvement. Circulating anti-GBM antibodies were strongly positive as well as ANCAs. The diagnosis was confirmed by a kidney biopsy. He received 3 pulses of methylprednisolone followed by prolonged oral prednisone (2 mg/kg per day) and a pulse of cyclophosphamide. He underwent 11 plasma exchange sessions initially daily then alternately. The evolution was unfavorable at the beginning with worsening renal function and proteinuria. He benefited from two hemodialysis sessions, two other boluses of methylprednisolone and Rituximab was started. After two weeks, the evolution was favorable with a gradual improvement in renal function which then normalized and the anti-GBM and ANCA antibodies became undetectable. He received corticosteroids for 1 year, enalapril for 6 months and rituximab after normalization of CD 19. Last follow-up, 2 years after onset. The boy showed no clinical signs of disease activity and undetectable anti-GBM levels. kidney function remained stable.

**Conclusion:** The knowledge of anti-glomerular basement membrane disease leads to early diagnosis that allows prompt treatment and improves survival. An early aggressive and prolonged therapy is mandatory in order to control the disease. The literature on pediatric anti-GBM and double antibody positive disease is limited. Additional research is needed to assess the efficacy and safety of Rituximab especially in children.

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## HUMORAL RESPONSE AFTER SARS-COV2 VACCINATION IN CHILDREN WITH IDIOPATHIC NEPHROTIC SYNDROME

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**Aims/Purpose:** Vaccination against SARS-CoV-2 has drastically reduced COVID-19 morbidity and mortality. Nevertheless, patients with idiopathic nephrotic syndrome (INS) may display an impaired immune response. We aimed at investigating the humoral response after SARS-CoV-2 vaccination in children with INS.

**Methods:** We performed a prospective monocentric study enrolling children affected with INS, vaccinated with full SARS-CoV-2 schedule. The spike-receptor-binding-domain total Ig (S-RBD Ig) and the nucleocapsid protein antibody (anti-N Ig) were assessed 2-4 weeks after the second dose of SARS-CoV-2 vaccination. S-RBD Ig results were stratified according to the ongoing immunosuppressive therapy and the presence of anti-N Ig, documenting a previous SARS-CoV-2 infection.

**Results:** Ninety-one vaccinated INS children were identified. A total of 44 vaccinated patients who accepted to participate were enrolled (18 females, median age 12.0 years). 35/44 (79.5%) were on immunosuppressive therapy, 30 with a single drug and 5 with a combined therapy. According to the presence of anti-N Ig, 16 patients had a previous SARS-CoV-2 infection, while 28 were naïve. The overall seroconversion rate was 36/44 (81.8%). The seroconversion rate was significantly higher in previously infected children compared to naïve (16/16 vs 20/28;  $p = 0.018$ ). In naïve patients only, the rate of seroconversion was significantly different according to the ongoing immunosuppressive therapy (no drugs 100%, one drug 76.1%, > 2 drugs 0%;  $p = 0.09$ ). The overall median anti-S-RBD titre was 293.0 U/ml. Patients with a previous infection had a significantly higher median S-RBD Ig titre compared to SARS-CoV-2 naïve (4388 U/ml vs 130.5 U/ml;  $p = 0.014$ ). In SARS-CoV-2 naïve patients, immunosuppression with mono or combined therapies was associated with lower S-RBD levels ( $p = 0.008$ ). Conversely, in previously infected patients, ongoing immunosuppressive therapy had no impact on both anti-N Ig and S-RBD Ig titres ( $p = 0.46$ ). In the multivariate analysis on the total population, the presence of anti-N Ig and the number of immunosuppressive drugs were significantly associated with S-RBD Ig titre ( $p = 0.01$ ).

**Conclusion:** SARS-CoV-2 vaccination elicits seroconversion in most INS children. A previous SARS-CoV-2 infection and ongoing immunosuppression are associated with the humoral response.

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**A CASE OF PROGRESSING TO END-STAGE KIDNEY DISEASE WITH EXACERBATION OF IGA NEPHROPATHY AFTER COVID-19 INFECTION**

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**Aims/Purpose:** IgA nephropathy (IgAN) is the most common form of primary glomerulonephritis (GN) and is usually triggered by infections. Relapses or new-onset IgAN have been documented in most patients after vaccination against SARS-CoV-2. Although the development of new-onset or relapses of IgAN has been reported after COVID-19 vaccination, only one adult patient has been reported to have experienced an exacerbation of pre-existing IgAN during COVID-19 infection.

**Methods:** We present a first pediatric case diagnosed with IgAN and Alport syndrome who progressed to end-stage kidney disease (ESKD) after an exacerbation of IgAN associated with COVID-19 infection.

**Results:** A 16-year-old boy with biopsy-proven IgAN and genetically confirmed Alport syndrome was hospitalized with complaints of an increase in serum creatinine. His basal serum creatinine was 0.7–0.9 mg/dL, and his urine protein was 1.5 g/day. He had not been vaccinated against COVID-19. Three months before admission, he had a history of COVID-19 and had been hospitalized in another hospital with fever and elevated serum creatinine (1.9 mg/dL). During this hospitalization for COVID-19, ACEi had been discontinued, no additional treatment had been given, and no biopsy had been performed. On admission to our hospital, physical examination revealed edema and hypertension. Laboratory examination revealed a serum urea of 142 mg/dL, a creatinine of 4.7 mg/dL, albumin of 2.9 g/dL, and a 24-hour urinary protein excretion of 6 g. A kidney biopsy was performed, which revealed IgAN (2+ granular mesangial staining for IgA) with 50% fibrocellular crescents, with sclerosed glomeruli, tubular atrophy, and interstitial fibrosis. Five doses of pulse methylprednisolone were administered for crescentic GN; however, his serum creatinine did not decrease, hemodialysis was initiated, and immunosuppressive treatment was not continued because of the chronic findings in the biopsy specimen.

**Conclusion:** COVID-19 may pose a high risk for exacerbation of pre-existing glomerular disease. Therefore, kidney functions in patients with underlying GN should be closely monitored during and after COVID-19 infection, treatments should be given as soon as possible, and early biopsy should be considered if serum creatinine does not return to baseline, especially in cases with primary GN.

# POSTER SESSION 1G

## Inherited Kidney Disorders



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## RENAL INVOLVEMENT IN PATIENTS WITH CHARCOT-MARIE-TOOTH DISEASE

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**Aims/Purpose:** Variants in the *INF2* gene are associated with focal segmental glomerulosclerosis (FSGS) and Charcot-Marie-Tooth type hereditary neuropathy (CMT). The objective is to describe the clinical phenotype and evolution of three patients with renal disease secondary to *INF2* variants and to increase the knowledge of this entity.

**Methods:** Review of clinical history and genetic outcome of three patients with the diagnosis of FSGS and CMT.

**Results:** Patient one (woman, 34 years old) and patient two (boy, 13 years old) are children of the same father but different mother. Both patients debuted with orthopedic involvement (patient 1 with CMT) with subsequent detection of proteinuria. In less than 2 years, they have received a kidney transplant. Patient 2 also has a peculiar phenotype with multiorgan involvement: hydrocephalus, short height, bilateral cryptorchidism, congenital heart disease and hypermetropia, among others. There is no consanguinity in the family. In both the same variant was detected in *INF2*: c.230T > A(p.Leu77Gln) in heterozygosis considered probably pathogenic. The parents are asymptomatic and are not carriers of the mutation so it is assumed that the mutation is a germline mosaicism inherited from the father. Patient three (girl, ten years old) is an only child in a family with no family history of consanguinity. She is affected by CMT as a result of which proteinuria was determined to be non-nephrotic 4 months after diagnosis. She also has moderate psychomotor retardation and mild bilateral sensory-motor hearing loss. The patient carries the pathogenic variant in *INF2*: c.310T > C(p.Cys104Arg). The mother is healthy and the father has an asymptomatic axonal polyneuropathy with pes cavus. The father shows the same variant in *INF2* in mosaic (7% of the reads) which could explain the transmission and different severity of the phenotype of father and daughter.

**Conclusion:** The appearance of CMT and proteinuria should raise suspicion of a mutation in this gene. As in the literature these patients have glomerular renal involvement and CMT. To emphasize that in addition they present a more extensive clinical phenotype than previously described and at the same time, different between the siblings of the first family who have the same mutation. Therefore, studying these patients and making them known can increase the knowledge of this rare disease. A good initial approach, such as the detection of proteinuria during the follow-up of patients with CMT, could have provided an early diagnosis and consequently a slowing of the progression of renal disease. A multidisciplinary approach is important in rare diseases to provide adequate treatment and genetic counseling.

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CHARACTERISTICS, OUTCOME AND FOLLOW UP OF CHILDREN WITH RENAL CYSTS: RESULTS FROM A SINGLE TERTIARY REFERRAL CENTRE IN CROATIA

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**Aims/Purpose:** Renal cysts are common finding in a variety of diseases in children and adults alike, with heterogeneous aetiology and underlying mechanisms leading to diverse presentation and outcome. Despite a multitude of basic, clinical and translational studies aiming to provide valuable information regarding the detailed characteristics, adequate management and possible outcomes, there is still room for comprehensive characterization of cohorts from various centres throughout the globe, which could further inform everyday clinical practice.

**Methods:** Retrospective study of 112 patients followed for cystic kidney disease in the referral centre for paediatric nephrology of the Republic of Croatia from July 2011 to March 2023.

**Results:** Out of 112 patients (54 female), 54 were diagnosed antenatally, 14 in the first 28 days and 44 later in life (median age 6.00 ± 8.50). The final diagnosis was autosomal dominant polycystic kidney disease (ADPKD) in 19, autosomal recessive polycystic kidney disease (ARPKD) in 16, multicystic dysplastic kidney (MCDK) in 52, isolated renal cyst in 15, Joubert syndrome (JS) in 2, Tuberous sclerosis (TS) in 3, Bardet-Biedl syndrome (BBS) in 2, nephronophthisis complex in 2 and trisomy 13 in 1 patient. Positive family history was observed in 29 and genetic testing revealed disease causing mutation in 15 out of 20 tested patients. At the time of diagnosis, 51 patients had symptoms attributable to cysts, 7 developed symptoms later in life and 54 had none throughout the follow up. The most common presenting symptoms were abdominal distension (21%) and abdominal pain (15%). Apart from those who had posterior urethral valve (PUV) and hydronephrosis (MCKD excluded), 17 patients progressed to chronic kidney failure, with 13 (4 ARPKD, 4 MCDK, 2 JS, 1 BBS, 1 NPH, 1 TS) having end stage renal disease (ESRD). Coordinated transition to adult care occurred in 8 patients (median age 18 ± 0.50).

Time in months to ESRD in patients without PUV and hydronephrosis (MCKD excluded)

	ARPKD	BBS	JS	MCDK	NPH	TS
Valid	4	1	2	4	1	1
Median	116.50	141.00	34.50	64.00	162.00	241.00
SD	76.14		2.12	66.75		
Min	4.00	141.00	33.00	76.66	162.00	241.00
Max	183.00	141.00	36.00	139.00	162.00	241.00

**Conclusion:** The greatest unmet need in cystic kidney disease is to accurately predict, possibly prevent and safely delay progression into the end stage renal disease. In our cohort, all 13 of patients developing ESRD had symptoms at the time of diagnosis, indicating the importance of detailed initial examination of children with cystic kidney disease. While our cohort is heterogeneous and scarce, often lacking genetic information, it is the first of its kind collected in the Republic of Croatia and could therefore inform new comprehensive strategies for children with these intricating finding.

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TWO NEW FAMILIES WITH RRAGD GENE TUBULOPATHY, CHARACTERIZED BY SEVERE HYPOMAGNESEMIA AND DILATED CARDIOMIOPATHY

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**Aims/Purpose:** Introduction: RRAGD gene encodes a small Rag guanosine triphosphatase D expressed in heart and kidney, specifically in the thick ascending limb and distal convoluted tubule. Variants in this gene lead to a recently described tubulopathy called Autosomal Dominant Kidney Hypomagnesemia. Patients have a severe hypomagnesemia and/or dilated cardiomyopathy with early heart failure resulting in heart transplantation in a substantial subset of patients. The aim of the study is to describe the clinical phenotype of four patients (two families) affected with this new tubulopathy.

**Methods:** medical records review, molecular diagnosis by Whole Exome Sequencing and later sequencing by Sanger.

**Results:** Clinical data is detailed in Table 1. Patients A-II-1 and A-II-2 are monozygotic twins. A-III-1 is the daughter of A-II-1. Both were diagnosed of Gitelman syndrome during infancy. Their father died with diabetes mellitus and ischemic cardiomyopathy but no structural cardiomyopathy was found. Their mother is healthy and has no variants in RRAGD gene. Both parents of B-II-1 patient are healthy and no variants in RRAGD gene were found. Therefore we consider that the variants in RRAGD gene was de novo in our patient.

Table 1: Clinical data of patients

	Family A			Family B
	A-II-1	A-II-2	A-III-1	B-II-1
Polyhydramnios	No	No	Yes	-
Gestational age (weeks)	ND	ND	33	35
Age at renal manifestation/last-follow-up	3,5/47	3,5/47	6/8	11/15
Polyuria and hypomagnesemia or hypocalcemia symptoms at diagnosis	Yes	Yes	Yes	Yes
Length last follow up, SD	Normal	Normal	-1,4	-0,8
Dilated cardiomyopathy (age diagnosis, years)	Yes (32)	Yes (32)	No **	Yes (5)
Heart transplantation (age, years)	No*	Yes (42)	No	No
Initial laboratory findings (plasma)				
Na <sup>+</sup> , 135-145 meq/l	136	135	137	139
K <sup>+</sup> , 3,5-4,5 meq/l	2,8	2,8	3,3	3,5
Cl <sup>-</sup> , 95-105 meq/l	92	92	97	104
Mg <sup>2+</sup> , 1,7-2,5 mg/dl	1,1	1,3	0,9	1,2
Ca <sup>2+</sup> , 9-10,8mg/dl	6,7	Low	-	9,7
Metabolic alkalosis	Yes	Yes	Yes	Yes
Renal function last follow-up	Normal	Normal	Normal	Normal
Nephrocalcinosis (age first finding, years)	Yes	Yes	Yes (6)	Yes (11)
Therapy				
Mg/Ca/K supplementation	Yes/yes/yes	Yes/yes/yes	Yes/No/yes	Yes/No/yes
Heart failure medication	Yes	Yes	No	No
Other	No	Myfortic	Citrate	No
Variant RRAGD gene				

\* she is on the waiting list - \*\* Cardiac apical trabeculations

**Conclusion:** In the Autosomal Dominant Kidney Hypomagnesemia the cardiomyopathy has poor prognosis, whereas the renal prognosis appears to be good. However, further long-term studies of this new entity are needed.

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COMPARATIVE ANALYSIS OF RENAL INVOLVEMENT IN CHILDREN WITH OCULOCEREBRORENAL SYNDROME OF LOWE AND DENT DISEASE TYPE 2

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**Aims/Purpose:** The oculocerebrorenal syndrome of Lowe (LS; MIM #309000) and Dent disease, type 2 (DD2; MIM #300555) are ultrarare X-linked disorders caused by pathogenic variants in the OCRL1 gene. Patients with LS and DD2 show variable phenotype with renal and extrarenal manifestations. Renal phenotype in OCRL-related disorders is highly heterogeneous and characterized by decreased of proximal tubular reabsorption with progression to kidney failure. The aim of the study was to compare of renal phenotype and kidney function of LS and DD2 in Russian children.

**Methods:** We conducted retrospective longitudinal study of 24 boys with LS (n = 17) and DD2 (n = 7). The median age at the first examination of children with LS and DD2 were comparable: 32.2 (IQR: 15.5; 78.5) vs 63.0 (IQR: 25; 78) months (p = 0.31). eGFR was calculated using Bedside Schwartz Formula in boys with DD2 and revised k-value of 26 for patients with LS. Molecular genetic analysis was performed in all boys using NGS.

**Results:** There was no significant differences between boys with LS and DD2 at the first follow up in frequency of low molecular weight (LMW) proteinuria: 17/17 (100%) vs 7/7 (100%) (p = 0.999), nephrotic range of proteinuria: 8/16 (50%) vs 4/7 (57.1%) (p = 0.752), hypercalciuria: 14/17 (82.4%) vs 6/7 (85.7%) (p = 0.752), hypophosphatemia: 5/17 (29.4%) vs in 2/7 (28.6%) (p = 0.967), decreased TmP/GFR: 10/17 (58.8%) vs 3/7 (42.9%) (p = 0.476), hypouricemia: 4/17 (23.5%) vs 1/7 (14.3%) (p = 0.612), hypokalemia: 1/17 (5.9%) vs 0/7 (0%) (p = 0.512), glucosuria: 1/17 (5.9%) vs 0/7 (0%) (p = 0.512), nephrolithiasis: 3/17 (17.6%) vs 0/7 (0%) (p = 0.235). We found that boys with LS compared with DD2 had significant higher frequency in hyperuricosuria: 13/16 (81.2%) vs 1/7 (14.3%) (p = 0.003), metabolic acidosis: 13/17 (76.5%) vs 2/7 (28.6%) (p = 0.028), medullary nephrocalcinosis (NC) grade 2: 11/12 (91.7%) vs 0/7 (0%) (p = 0.0006), and CKD 3: 10/17 (58.8%) vs 1/7 (14.3%) (p = 0.047).

**Conclusion:** LMW proteinuria and hypercalciuria were the most common signs in children with LS and DD2. Half of patients with OCRL-related disorders have nephrotic proteinuria. Hyperuricosuria, metabolic acidosis and NC grade 2 are more common in patients with LS compared with DD2. Patients with DD2 did not demonstrated hypokalemia, glucosuria and nephrolithiasis. Children with LS showed a significantly lower eGFR compared with DD2 patients.

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## EXTRARENAL INVOLVEMENT IN CHILDREN WITH OCULOCEREBRORENAL SYNDROME OF LOWE AND DENT DISEASE TYPE 2

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**Introduction:** The oculocerebrorenal syndrome of Lowe (LS; MIM #309000) and Dent disease, type 2 (DD2; MIM #300555) are X-linked disorders caused by pathogenic variants in the OCRL1 gene. LS is characterized by congenital cataracts, intellectual disability, and severe degree of proximal renal tubular dysfunction. Patients with DD2 may present with mild extrarenal features of LS. The aim of the study was to compare of extrarenal phenotype of boys with LS and DD2 at the first follow up in Russian children.

**Methods:** We conducted retrospective longitudinal study of 24 boys with LS (n = 17) and DD2 (n = 7). The median age at the first examination of children with LS and DD2 were comparable: 32.2 (IQR: 15.5; 78.5) vs 63.0 (IQR: 25; 78) months (p = 0.31). Molecular genetic analysis was confirmed in all boys using NGS.

**Results:** We found that patients with LS in contrast to boys with DD2 had significant higher frequency in eye disorders, including congenital bilateral cataract: 17/17 (100%) vs 1/7 (14.3%) (p = 0.0001), strabismus: 9/17 (52.9%) vs 0/7 (0%) (p = 0.022), and nystagmus: 13/17 (76.5%) vs 0/7 (0%) (p = 0.001); intellectual disability: 17/17 (100%) vs 0/5 (p = 0.0001); failure to thrive 12/15 (80.0%) vs 2/7 (28.6%) (p = 0.004); bone disorders (rickets and osteoporosis): 16/17 (94.1%) vs 4/7 (57.1%) (p = 0.027). There were no significant differences between boys with LS and DD2 in frequency of growth retardation: 9/17 (52.9%) vs 5/7 (71.4%) (p = 0.276), elevated and reduced (without vitamin D therapy) serum level of PTH: 4/17 (23.5%) vs 0/5 (0%) (p = 0.535) and 8/17 (47%) vs 2/5 (40%) (p = 0.560), respectively; failure to thrive: 10/17 (58.8%) vs 1/7 (14.3%) (p = 0.178); muscle involvement as indicated by above-normal serum levels of creatinine kinase: 11/12 (91.7%) vs 5/7 (71.4%) (p = 0.243) and lactate dehydrogenase: 15/17 (88.2%) vs 5/6 (83.3%) (p = 0.759); congenital glaucoma: 3/17 (17.6%) vs 0/7 (0%) (p = 0.533); cryptorchidism: 6/17 (35.3%) vs 0/7 (0%) (p = 0.124); hypospadias: 3/17 (17.6%) vs 0/7 (0%) (p = 0.530); seizures: 2/17 (11.8%) vs 0/7 (0%) (p = 0.999).

**Conclusion:** Ocular abnormalities, intellectual disability, bone disorders and failure to thrive were the most common extrarenal features in boys with LS as compared to children with DD2. Growth retardation, muscle involvement, elevated or reduced serum PTH level were revealed with equal frequency in boys with LS and DD2. These findings suggest that extrarenal symptoms may overlapping in patients with LS and DD2.

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EFFICACY OF ANGIOTENSIN-CONVERTING ENZYME INHIBITORS IN CHILDREN WITH OCULOCEREBRORENAL SYNDROME OF LOWE

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The oculocerebrorenal syndrome of Lowe (LS) (OMIM #309000) is a rare X-linked recessive multisystemic disorder characterized by the triad of congenital cataracts, intellectual impairment, and proximal renal tubular dysfunction with progression to end-stage kidney disease in the second or third decade of life. Reports regarding the efficacy of RAAS inhibition on proteinuria and kidney function in LS are scarce. The aim of the study was to investigate the efficacy of angiotensin-converting enzyme (ACE) inhibitors in boys with LS in a single center.

**Methods:** We conducted retrospective analyses of clinical data of 8 boys aged 4.5 (IQR: 3.0; 8.5) years with genetically confirmed LS. Molecular genetic analysis was performed in all children by direct Sanger sequencing (n = 5) and NGS (n = 3). The median age of starting ACE inhibitors was 1.5 (IQR: 1.0; 4.5) years. The initial ACE inhibitors dosage was 0.19 (IQR: 0.16; 0.23) mg/kg/day. The median time of treatment with ACE inhibitors was 29.5 (IQR: 22.0; 32.5) months. eGFR was calculated using the original Schwartz method with a revised k-value of 26. Daily protein excretion assessed in 24-h urine collection (g/m<sup>2</sup>/d) were used.

**Results:** Treatment with ACE inhibitors did not lead to reduction of proteinuria in children with LS: 0.89 (IQR: 0.66; 1.21) vs. 1.19 (IQR: 0.88; 1.36) g/m<sup>2</sup>/day (p = 0.28). In 6/8 (75%) of boys proteinuria increased by 44.5% (IQR: 32%; 93%), in 2/8 (25%) - proteinuria decreased by 21% and 31% in each of cases, respectively. Increased eGFR at the last follow-up was found in 4/8 (50%) children. The median rate of increasing eGFR from baseline level on the treatment with ACE inhibitors was 20.2% (IQR: 12.8%; 24.5%). 3/8 (37.5%) boys with LS had declined eGFR at the last follow up by 6% (IQR: -11.2%; -5.9%). One patient had stable eGFR.

**Conclusions:** Treatment with ACE inhibitors lead to decreasing of proteinuria in 25% of boys and increasing of eGFR in 62.5% of children with LS. Further studies of efficacy of ACE inhibitors in children with LS are needed.

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**HNF4A MUTATION: NEONATAL HYPERINSULINISM AND/OR LATE-ONSET DIABETES ASSOCIATED WITH RARE AUTOSOMAL DOMINANT FANCONI SYNDROME**

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**Aims/Purpose:** Mutations in the HNF4A gene are associated with neonatal hyperinsulinism (HI) and maturity-onset diabetes of the young (MODY). Recently p.R63W mutation specifically linked to a rare autosomal dominant Fanconi syndrome (FS) and liver dysfunction has been described.

**Methods:** We present three patients with FS and HI caused by HNF4A mutations in the absence of a family history.

**Results:** Patient 1: A full-term large-for-gestational age boy developed hypoglycemia due neonatal HI. He was treated with diazoxide until the age of three months. At six months of age, failure to thrive, hepatomegaly and elevated transaminases were detected. At 18 months of age, physical exam and X-ray findings were typical of rickets. Complementary tests revealed: normal eGFR, nongap metabolic acidosis with acidified urine, glycosuria, generalised aminoaciduria and tubular proteinuria in addition to hypophosphatemia of renal origin (TRP 72%), hypercalciuria and carnitine deficiency. 25OHD was normal with supplementation, PTH and alkaline phosphatase were elevated. Patient 2: A 3-year-old girl with a history of benign myoclonus of infancy and genu varum presented with afebrile tonic-clonic seizures, prompting a metabolic study. Hypoglycemia secondary to HI was found, requiring diazoxide to the present day, as well as generalized hyperaminoaciduria. Further tests revealed chronic kidney disease (CKD) (eGFR 70 ml/min/1.73m<sup>2</sup>), nephrocalcinosis and FS features. X-rays also demonstrated rickets. No liver abnormalities were observed. Patient 3: A 11-year-old boy with very severe rickets preventing ambulation, malnutrition (height -8.3 SD, weight -4.1 SD), and CKD (eGFR 70 ml/min/1.73m<sup>2</sup>) was referred our center. FS was diagnosed at 3 years old following the detection of genu varum and fractures. No nephrocalcinosis or liver abnormalities were observed, and there was no history of hypoglycemia. In all cases, genetic testing detected the pathogenic variant p.R63W (c187C = T) in HNF4A. After proper metabolic and Fanconi treatment, all children showed catch-up growth and rickets healing. patient 1 progressed to CKD (8 years-old, eGFR 35 ml/min/1.73m<sup>2</sup>), whereas in patient 2 (5 years-old) and patient 3 (12 years-old) remained stable.

**Conclusion:** The novel HNF4A mutation should be considered in the genetic testing for FS diagnosis. Early identification of HNF4A mutations can lead to earlier and more proper management of both FS and HI. Close long-term follow-up is needed to monitor CKD progression and potential MODY onset. Family counselling is also required.

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**ADVANTAGES OF GENETIC TESTING IN PATIENTS WITH A CHRONIC SUBNEPHROTIC PROTEINURIA – PREVENTING UNNECESSARY DIAGNOSTIC AND THERAPEUTIC INTERVENTIONS. NOVEL IDENTIFICATION OF A MUTATION IN CUBN GENES**

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**Aims:** Chronic proteinuria commonly is a predictor of negative clinical outcomes including chronic kidney disease. However, proteinuria caused by biallelic cubilin (CUBN) mutations known as Imerslund-Grasbeck syndrome (IGS) might be benign, as in most of described cases - did not affect kidney function [1,2]. IGS is an autosomal recessive disorder characterized by intestinal cobalamin and renal tubular protein malabsorption resulting with megaloblastic anemia. Here we present a novel variant in C-terminal CUBN gene mutation.

**Methods:** Gene panel analysis (The Nephrotic Syndrome) using Next-Generation-Sequencing was performed on a patient with isolated subnephrotic proteinuria. A clinical, laboratory, pathological and molecular genetic data were fully evaluated and correlated.

**Results:** A 4-year-old boy was diagnosed with chronic proteinuria (protein to creatinine ratio ranging from 1.03 to 2.03 mg/mg, albumin to creatinine ratio 731 mg/g), hemoglobin concentration, MCV, cobalamin and homocysteine values were within normal ranges, eGFR value maintained around 135 ml/min/1.73m<sup>2</sup>, in physical examination the patient presented without oedema, hypertension or oliguria. There was no response to angiotensin-converting enzyme inhibitor (ACEI) which was then been modified to angiotensin receptor blocker (ARB) treatment, kidney biopsy did not reveal any abnormalities. Genetic analysis identified a heterozygous missense, likely pathogenic variant CUBN c.9053A > C, p.(Tyr3018Ser) which was previously detected, and a heterozygous, likely pathogenic frameshift variant CUBN c.9598del, p.(thr3200Profs\*21) – which, to best of our knowledge, has not yet been reported in the medical literature or databases, but bioinformatical analysis indicate variant as likely pathogenic, leading to premature protein termination.

**Conclusions:** Genetic testing of patients with chronic isolated proteinuria may indicate the optimal treatment modalities as well as avoidance of unnecessary invasive procedures.

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**INTRAFAMILIAL HETEROGENEITY AND IMPACT OF FAMILY SCREENING IN PRIMARY HYPEROXALURIA TYPE 1**

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**Aims/Purpose:** Primary Hyperoxaluria type 1 (PH1) is known for its extremely heterogeneous disease course, even within families. This raises questions which differences in the disease course between affected family members can be attributed to environmental factors and which to early diagnosis or therapy. The limited research on this subject results into prognostic challenges and leads to difficult decision-making concerning the timing of transplantation and therapy. The objective of this study was to determine whether and to what extent intra-familial heterogeneity is present, based on a clear definition of intra-familial heterogeneity in PH1 and to analyse the impact of therapeutic intervention and early diagnosis via family screening on the prognosis of siblings.

**Methods:** A retrospective registry study was performed using data from the OxalEurope registry. All families with PH1 were identified and analyzed. A six-point PH1 scoring system was developed to calculate the heterogeneity score within a family, based on the clinical outcome of siblings (e.g. symptoms including nephrolithiasis, nephrocalcinosis and kidney failure). A score  $\geq 2$  was considered as significant intra-familial heterogeneity. Assessment of the impact of family screening was conducted by stratification of the patients based on family screening and symptoms. The Fisher-Freeman-Halton exact test, Mann-Whitney U test, Kruskal Wallis test and Kaplan Meier analysis were used for statistical testing.

**Results:** A total of 88 families (193 patients) were included in this study. Family screening was conducted in most families (77%), although not all. Intra-familial heterogeneity was found in 38 (43%) families. A (partly) B6-responsive mutation did not lead to a significant difference in intra-familial heterogeneity score. In more than half of the families (54%), affected siblings had a better outcome than the index case and in 67% of families one or more cases of kidney failure occurred. Asymptomatic siblings had a significant better clinical outcome compared to symptomatic siblings and index cases based on clinical outcome score ( $p < 0.001$ ). Kaplan-Meier analyses (Figure 1) revealed that index cases reached kidney failure at an earlier age and earlier in follow-up compared to siblings (Log-rank,  $p < 0.0001$ ).

**Conclusion:** Intra-familial heterogeneity is found in nearly half of families with PH1. This confirms that intra-familial heterogeneity is present in PH1, in line with previous reports. Asymptomatic siblings found by family screening had a significant better outcome based on clinical outcome score and kidney survival, substantiating the benefit of family screening. Although the exact cause of heterogeneity in PH1 could not be identified, family screening is strongly recommended since it may improve kidney survival in siblings.

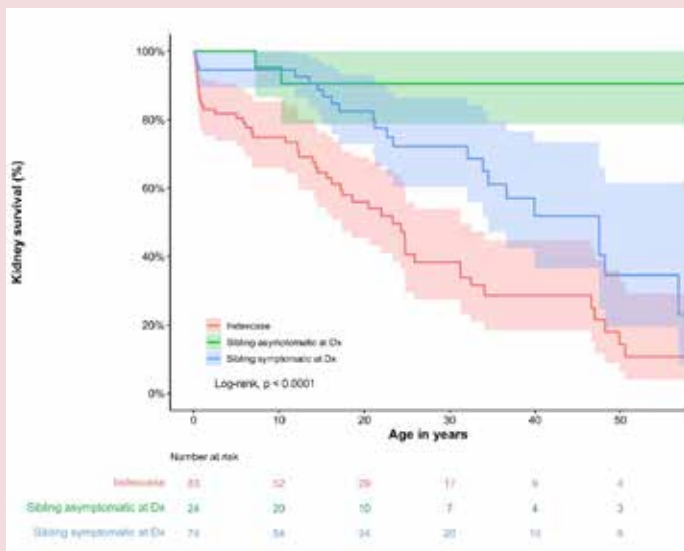


Figure 1: Kaplan-Meier analysis of death-censored kidney survival by age.

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LONG-TERM OUTCOMES IN DENYS DRASH SYNDROME : A NATIONAL COHORT STUDY

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**Aims/Purpose:** Denys Drash syndrome (DDS) is caused by WT1 mutations and is associated with a high risk of Wilms tumour (WT) and diffuse mesangial sclerosis leading to end-stage renal disease (ESRD). Onset of disease is variable and there is a wide clinical spectrum with a genotype to phenotype correlation. The aim of the study was to describe a national cohort of children with DDS and to assess the impact of WT on the outcomes.

**Methods:** Multicentric retrospective analysis of children diagnosed with a mutation of WT1 in exon 8 or 9 in all the pediatric nephrological centres in France between 2000 and 2022.

**Results:** Sixty patients were identified, 17 with a WT (WT+ group), and 43 without (WT- group). Median age at WT diagnosis was 0.6 years (IQR 0.12–1.36). Median follow up was 8 years (IQR 3.0–13.0). We found a higher proportion of exon 9 in the WT+ group compared to the WT- group (88% versus 47%,  $p = 0.004$ ). Patients in the WT+ group developed later ESRD at a median age of 1.73 years (IQR 1.2–4.2) versus 0.55 years (IQR 0.2–1.5) ( $p = 0.0004$ ). Overall survival was better in the WT+ group (Log-rank:  $p = 0.04$ ). The last nephrectomy was performed at the same age in the two groups (1.6 years versus 1.1 years;  $p = 0.14$ ). Children in the WT+ group were transplanted later than children in the WT- group (4.73 years versus 2.94 years;  $p = 0.003$ ).

**Conclusion:** Patients with DDS and WT have a later progression to ESRD and a better overall survival. In the WT- group, early ESRD leads to a poor prognosis with excess mortality, which may relate to the morbidity of neonatal dialysis and complications linked to the nephrotic syndrome.

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**PRIMARY COENZYME Q10 DEFICIENCY: A CASE SERIES REPORT**

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**Aims/Purpose:** Coenzyme Q10 (CoQ10) is involved in the mitochondrial energy production process. Primary coenzyme Q10 deficiency (PCQD) is caused by autosomal recessive mutations in genes involved in its synthesis. Symptoms can affect several organs including kidney. Our aim is to focus on PCQD as a rare cause of nephrotic syndrome and end-stage renal disease (ESRD) by presenting a case series report.

**Methods:** Review of electronic medical records of 3 patients with PCQD and kidney involvement.

**Results:** Case 1: 7-year-old boy from China. Incidental finding of nephrotic range proteinuria and hypertriglyceridemia with normal glomerular filtration rate (GFR). Ultrasound showed nephrocalcinosis. Biopsy, performed because of treatment resistance, showed focal and segmental glomerulosclerosis (FSGS) and genetic testing confirmed 2 heterozygous mutations in COQ8B. Proteinuria improved with ACE inhibitors but only dropped below nephrotic range after replacement therapy. 5 years after the diagnosis he stays asymptomatic, proteinuria is controlled and has normal GFR. Case 2: 15-year-old boy from Morocco with intellectual disability of unknown etiology. Incidental finding of ESRD with severe proteinuria. Biopsy showed terminal nephrosclerosis. After 2 years of hemodialysis, he received deceased kidney transplant and has normal graft function 1 year after. Genetic testing recently confirmed a homozygous mutation in COQ8B. Case 3: 12-year-old girl from Morocco with dilated cardiomyopathy of unknown etiology. Incidental finding of ESRD with nephrotic range proteinuria. No biopsy was performed, and genetic testing confirmed a homozygous mutation in COQ8B. After 3 months of hemodialysis, she received deceased kidney transplant. She is on CoQ10 replacement therapy with no signs of recurrence 1-year post-transplant.

**Conclusion:**

- PCQD should be considered as a possible cause of resistant nephrotic syndrome.
- COQ8B is the most frequently affected gene.
- FSGS is the most prevalent pathological finding.
- CoQ10 replacement therapy should be started before irreversible organ damage occurs and may change prognosis and prevent or delay progression to ESRD.

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## MAY THE TUBULE HAVE PROPELLERS?

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**Aims/Purpose:** HELIX syndrome is a new tubulopathy of genetic cause (claudin-10 deletion) characterized by salt-losing nephropathy and dyselectrolythemia (hypokalemia, hypermagnesemia, hypercalcemia and hypocalciuria) together with alterations in the homeostasis of ectodermal glands and skin integrity (lacrimal dysfunction, xerostomia, ichthyosis and heat intolerance)

**Methods:** Illustrate with a clinical case, a novel salt-losing tubulopathy

**Results:** 3-year-old boy with history of polyhydramnios and need for sodium intake (up to 1.5 mEq/kg/day) from birth due to persistent hyponatremia together with low-limit potassium with a high transtubular potassium gradient (GTK) and hyperreninemia. Subsequent controls with hypochloremic metabolic alkalosis with persistence of borderline potassium. Preserved renal function and tubular study with increased fractional excretions of sodium, potassium, chloride and hypocalciuria. Renal ultrasound without nephrocalcinosis. Given these findings, a genetic study was performed, which was negative for classic and antenatal Bartter syndromes, including MAGED-2, Gitelman syndrome, CaSR gain mutations, and pseudohypoaldosteronisms. As an important finding, clinically he presented xerostomia, so it was decided to expand the genetic study due to suspicion of an alteration in Claudin-10, which detected a deletion in the CLDN-10B gene. He maintained normal calcium levels, as well as magnesium levels at the upper limit of normal along with hypomagnesiuria. During his follow-up, he has required potassium and sodium contributions, markedly increasing his requirements in the event of decompensation due to intercurrent processes

**Conclusion:** Salt-wasting tubulopathies are underdiagnosed at any age, especially when dealing with infrequent or studied entities and in the face of high phenotype-genotype variabilities and phenotypes not yet clearly described. That is why the progressive knowledge of the pathophysiological processes of the renal tubule and the integral proteins of the tight junction, expressed not only in the kidney, but also in the skin and salivary glands (claudin-10b) will allow an early diagnosis and better management of these patients, allowing adequate genetic counseling and possible prevention of kidney disease progression

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**A RARE CASE OF HYPERURICEMIA, PULMONARY HYPERTENSION, RENAL FAILURE AND ALKALOSIS (HUPRA) SYNDROME**

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**Aims/Purpose:** To describe the clinical phenotype of a young child diagnosed with a novel homozygous mutation in the SARS-2 gene causing HUPRA syndrome. HUPRA syndrome is a rare autosomal recessive mitochondrial disease that presents in infancy with progressive renal failure, electrolyte imbalances, metabolic alkalosis, pulmonary hypertension, hypotonia and delayed development. Only few cases are reported in the literature and all patients died at early age.

**Methods:** Case report.

**Results:** A 1 year and 5 months child was referred to our tertiary hospital because of pancytopenia and acute kidney failure with hyperuricemia and metabolic hypochloreaemia. Physical examination was normal except for pallor, and the child had normal weight and length. Laboratory work-up revealed microcytic normochromic anaemia 86 g/l (reference (ref) 107–134), WBC 1,6x10<sup>9</sup>/L (ref 3.5–14), thrombocytes 40x10<sup>9</sup>/L (ref 210–590). Renal function parameters showed disproportionately higher urea 42 mmol/L (ref 3.1–7.8) than creatinine 97 µmol/l (ref 19–46), uric acid 958 µmol/L (ref 160–350). Urinalysis was normal. Abdominal ultrasound showed bilateral normal kidneys, except a minimal pelvic nephrolithiasis. Echocardiography was normal. Renal histology showed tubular damage with nephrocalcinosis. Electron microscopic examination of tubule epithelial cells showed a high degree of variation in mitochondrial size as well as single mitochondria containing aberrant circular cristae, as seen in congenital mitochondrial diseases. A muscle biopsy was without pathological changes and ATP synthesis in mitochondria isolated from muscle biopsies was within the normal range. Bone marrow aspiration showed hypocellularity where the three hematopoietic cell lines are hypoplastic but maturing without dysplastic features. Genetics analysis of the gene associated with HUPRA syndrome (SARS-2) showed 2 new homozygous variants (SARS-2 c.211G > C and SARS-2 c.256C > A) of unclear clinical significance. The child was treated, apart from conventional chronic renal disease treatment, with Allopurinol to decrease urate acid and Coenzymen Q10 and Serin to support mitochondrial function. At 27 months the child has no uremic symptoms and normal psycho-motor development. Urea is very high urea (40–35 µmol/L), and frequent erythrocytes transfusion. We did not yet started dialysis.

**Conclusion:** We have identified a novel mutation leading to the diagnosis of HUPRA syndrome in a young child. Our case has been clinically stable with supportive medication and might suffers a milder variant of HUPRA syndrome.

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## PRESENCE OF DICER1 MUTATION IN CHILDREN WITH MULTICYSTIC KIDNEY LESION IS A PREDICTOR OF ANAPLASTIC SARCOMA DEVELOPMENT

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**Introduction:** Pathogenic variations in DICER1 predispose to a variety of benign and malignant lesions in various tissues including the kidney like cystic nephroma, anaplastic sarcoma, or structural anomalies of the kidney or collecting system. Here, we report two patients with DICER1 mutation and multicystic renal lesions developing into anaplastic sarcoma in one of them.

**Case 1:** A 4-year-old boy was admitted with macroscopic hematuria. He described a similar attack four months ago. Family history was nonrevealing. Physical examination and laboratory work-up were normal. Abdominal ultrasonography and magnetic resonance imaging revealed septated cystic lesions in the left (7 cm) and in the right (12 cm) kidneys. Scanning of other organs for potential DICER1 syndrome revealed thyroid nodules and lung cysts. However, germline DICER1 mutation could not be shown. He experienced recurrent gross hematuria attacks. At the age of 8 years, he presented with acute right flank pain and severe hematuria leading to anemia. Imaging revealed solid components in the previous 12 cm lesion. Right nephrectomy was performed and pathological examination was consistent with anaplastic sarcoma having somatic DICER1 mutation. He was closely monitored for other DICER1-related tumors. Papillary thyroid carcinoma developed at the age of 9 years.

**Case 2:** A 3-year-old boy presented with a cystic lesion of the left kidney detected by ultrasonography performed for sterile pyuria. Past and family history were normal. Abdominal ultrasonography and magnetic resonance imaging revealed a 9 cm multicystic septated lesion in the left kidney. Scanning of other organs for potential DICER1 syndrome showed a solitary lung cyst. Therefore, the child underwent DICER1 genetic testing and a heterozygous germline DICER1 mutation was found (c.3805C > T). Left renal nephrectomy was performed.

**Conclusion:** DICER1 mutations should be screened in all patients with tumors such as pleuropulmonary blastoma, thyroid neoplasms, ovarian tumors, anaplastic sarcoma of kidney, cystic nephroma, and pulmonary and/or renal cysts. A prompt identification of this syndrome is necessary to plan a correct follow-up and screening during lifetime. It has been stated that large cystic nephromas and even asymptomatic renal cysts should be removed given the possibility of progression to anaplastic sarcoma in children with DICER1 mutations, although the data to support this are not currently available. In accordance with this, our first case developed anaplastic sarcoma after 4 years of follow-up, prompting us to perform a pre-emptive nephrectomy in the second case.

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**SURVIVAL BEYOND THREE YEARS OF AGE WITH MILD CHRONIC RENAL DISEASE IN A CHILD WITH RENAL TUBULAR DYSGENESIS DUE TO ACE MUTATION**

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**Background:** Renal tubular dysgenesis (RTD) is characterized by loss of proximal tubular differentiation due to hypoperfusion of kidney in utero. Autosomal recessive RTD is a disease of renin-angiotensin system, and two thirds of the cases are due to ACE mutations. Originally, the disease was considered always severe as most reported patients died in utero or soon after birth from respiratory distress, persistent anuria, and severe hypotension not responsive to usual treatments. However, there are few reports on long term survivors in the literature. We present a 3-year-old girl with RTD due to homozygous missense ACE mutation who survived by peritoneal dialysis in the neonatal period and whose kidney functions were partially recovered afterwards.

**Case Report:** The patient was born at 30th gestational week with wide sagittal cranial sutures, limb contractures and respiratory distress due to anhydramnios which was detected at 21st week. Kidneys were described as normal in antenatal ultrasonography. Her parents were relatives. There was a history of previous abortus at 17th week of gestation due to anhydramnios and pulmonary hypoplasia. Peritoneal dialysis was started as she was anuric. Laboratory test results were as follows: plasma renin activity > 1000 ng/mL/sec, aldosterone 143 pg/mL (range: 10-1600), ACE < 9 U/L. Fludrocortisone was added to treatment. Genetic analysis showed a class 2 missense homozygous, splice region ACE variant (c.3136G > A). After neonatal period, her urine output increased to polyuric levels. At the age of 3 years, she has mild proteinuria (urine protein/creatinine 0.52 mg/mg) and grade 2 chronic renal disease (creatinine clearance 65 ml/min/1.73m<sup>2</sup>).

**Conclusion:** As the number of surviving cases increases, it should be emphasized that RTD may not be universally fatal as previously reported. The type of mutation may have a prognostic significance. Peritoneal dialysis and fludrocortisone therapy in the early period may ensure the survival of the infants with missense ACE mutations.

Fr-P 132  
RARE CASE OF COQ8B NEPHROPATHY

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**Aims/Purpose:** COQ8B nephropathy is a rare autosomal recessive kidney disease characterized by proteinuria and progressive deterioration of kidney function with the development of steroid-resistant nephrotic syndrome. This disease occurs due to various mutations in the genes COQ2, COQ6, COQ8B, which leads to a deficiency of primary coenzyme Q10, mitochondrial dysfunction and disruption of cellular energy metabolism.

**Materials and Methods:** The boy is observed in the nephrology department of the Veltischev Institute, where he underwent a complete clinical laboratory and genetic examination.

**Results:** For the first time, clinical signs of the disease were detected at the age of 2 years in the form of a single episode of proteinuria up to 0.14 g/l, calciuria (Ca/Cr 1.5), signs of medullary nephrocalcinosis and moderate osteoporosis. In addition, the child has progressive myopia of a weak degree, impaired posture, flat-valgus deformity of the feet, calcifications in the liver and spleen. Hearing loss was not detected. Heredity is burdened by the presence of nephrocalcinosis, urolithiasis, angiomyolipoma of the right kidney, increased creatinine levels in the boy's father; my paternal grandmother has fatal kidney cancer. During the complete genome sequencing, a variant of rs1461368345, not previously described in the literature, was found in a heterozygous state in exon 3 of 15 of the COQ8B gene, leading to the amino acid substitution of p.Arg66His. In the same COQ8B gene, a variant of rs778827969, not previously described in the literature, was found in a heterozygous state in intron 1 of 14, leading to a possible disruption of splicing and a change in intron c.-3-460G > T. Pathogenic biallelic variants in the COQ8B gene lead to the development of autosomal recessive nephrotic syndrome, type 9 (OMIM 615573). Mutations were validated by direct Sanger sequencing. At the moment, the child has no clinical manifestations of nephrotic syndrome, but there are signs of nephrocalcinosis, which according to the literature is one of the clinical manifestations of COQ8B nephropathy.

**Conclusion:** The presented observation confirms the variety of clinical manifestations of kidney damage in violation of Coenzyme Q10 biosynthesis. The peculiarity of this clinical case is the absence of nephrotic syndrome in the patient, which does not exclude its manifestation in the second decade of life. It is difficult to assess the prognosis of the course of the disease due to the detection of a previously undescribed pathogenic variant, however, according to the literature, therapy is most effective with early diagnosis and preserved kidney function at the beginning of treatment.



Fr-P 133

PAEDIATRIC METASTATIC PHAEOCHROMOCYTOMA AND PARAGANGLIOMA: A CASE SERIES

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**Aims/Purpose:** Paragangliomas (PGL) and pheochromocytomas (PCC) are rare neuroendocrine tumours in children. Metastatic disease is associated with a genetic mutation, including NF1, VHL, SDH and RET mutations.

**Methods:** Database search with two paediatric cases of metastatic PGL/PCC.

**Results:** Case 1: A 9-year-old girl presented with headache, generalised tonic-clonic seizures and hypertension at 168/112 mmHg. Abdominal ultrasound, CT and MRI revealed lesion between left lower renal pole and aorta with compression of left renal vein and right-sided subpleural nodule. A diagnosis of PGL was made with elevated plasma and urinary metanephrines / catecholamines and positive 68Ga-DOTATATE PET/CT scan (after negligible uptake on MIBG). Following successful catecholamine blockade with phenoxybenzamine then propranolol, she underwent resection of the primary tumour including nephro-ureterectomy. Thoracoscopic resection of the right-sided subpleural nodule was performed two months later with histology confirming a completely resected metastatic PGL. Genetic testing revealed succinate dehydrogenase flavoprotein subunit (SDHA) mutation (also detected in father and brother). She had annual follow-up with urinary and plasma metanephrines / catecholamines and abdominal ultrasounds and remained disease-free for four years when biochemical surveillance and 68Ga-DOTATATE PET/CT scan detected multiple metastatic relapse with widespread bony and retroperitoneal disease and she commenced 177Lu-DOTATATE molecular radioisotope therapy. Case 2: An 11-year-old girl presented with one year history of dizziness, headache and vomiting and was hypertensive with a systolic blood pressure of 190 mmHg on initial assessment. Abdominal MRI revealed a heterogenous aorto-caval mass extending from the right kidney inferiorly to below her renal veins, also detected on SPECT-CT with 131I-MIBG. Plasma normetadrenaline levels were elevated. Subtotal resection of the primary tumour and right nephrectomy was performed with histology confirming paraganglioma; no genetic cause was identified. Follow-up 68Ga-DOTATATE PET/CT scans four months later identified two metastatic lesions in the skull. On retrospective imaging review, the right frontal bone lesion had been present at diagnosis. The patient received four courses of treatment with 177Lu-DOTATATE and at four years post-initial presentation is clinically stable with no evidence of disease progression.

**Conclusion:** Metastatic disease can occur in up to 12% of children and up to 70% with SDHB mutations. While isolated disease is usually treated with surgical resection, metastatic disease requires additional treatment modalities. 177Lu-DOTATATE molecular radioisotope therapy targets 68Ga-DOTATATE-avid lesions, providing a promising treatment option for challenging disease with early studies suggestive of favourable outcomes.

Fr-P 134

## CLINICAL MANIFESTATION OF FEMALES WITH FABRY DISEASE IN LITHUANIAN COHORT

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**Aims/Purpose:** Fabry disease (FD) is one of the X-linked lysosomal storage disorders [1]. Because of the X-chromosome inactivation (XCI), females are mosaic in the expression of some X-linked genes [2]. While males with classic FD form are usually severely affected, clinical presentation in females may be more variable ranging from asymptomatic or mild to symptoms which are as severe and multisystemic as those experienced by males with FD [1]. The aim of this study was to assess manifestations in females with FD in Lithuanian cohort.

**Methods:** Ten heterozygous carriers for GLA gene were recruited at Lysosomal storage diseases competence center of the Vilnius University Hospital Santaros Clinics for further evaluation and monitoring. Clinical, histological, genetic, and biochemical data, including activity of alpha-Galactosidase A (alpha-Gal A) and serum level of lyso-globotriaosylceramide (lyso-Gb3), were collected and analyzed. The manifestation of FD in females were classified into five categories: asymptomatic, classic, cardiac, renal or neurological.

**Results:** Ten females (three index cases) from 6 unrelated families were involved in the study. The mean age at diagnosis was 39.8 (16–59) years. Six different mutations of the GLA gene were found. Six out of the ten (60%) females were asymptomatic. Nine of the patients (90%) had disease causing variants associated with classic FD form, while one female had late onset cardiac variant. The average of Lyso-Gb3 was  $5.7 \pm 1.8$  ng/ml (reference:  $\leq 1.8$  ng/ml), whereas alpha-Gal A activity in women was in the lower normal range. Renal involvement with normal renal function at the time of FD diagnosis was found in 4 patients (40%), cardiac in 3 (30%), peripheral neuropathy in 3 (30%), angiokeratomas in 4 (40%), cornea verticillate in 5 (50%), tinnitus in 1 (1%), hypohidrosis in 1 (1%) of ten women. Fifty percent of females were on enzyme replacement therapy (youngest 16, oldest 58 years old).

**Conclusion:** Female patients of Fabry disease can display great variability in disease onset, severity and progression. The variability of Lyso-Gb3 cannot be associated with severity of the symptoms in females. The analysis of XCI would be useful tool for better evaluation of the correlation between skewed XCI and the severity of symptoms.

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Fr-P 135

## CLINICAL AND GENETIC ANALYSES OF 16 CHILDREN WITH NEPHRONOPHTHISIS-RELATED CILIOPATHY

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**Introduction:** Nephronophthisis is an autosomal recessive cystic kidney disease and one of the most common genetic disorders causing end-stage renal disease in children. Nephronophthisis is a genetically heterogeneous disorder with more than 20 identified genes that may cause isolated nephronophthisis. Additionally, more than 90 causative genes within the group of nephronophthisis is related ciliopathies. In 10%–20% of cases, there are additional features of a ciliopathy syndrome, such as retinal defects, liver fibrosis, skeletal abnormalities and brain developmental disorders. Here, we aimed to evaluate the clinical features and related gene mutations of children with nephronophthisis and related ciliopathies.

**Methods:** We retrospectively analyzed the medical records of the 16 biopsy or genetic-proven nephronophthisis patients. Comprehensive clinical and genotypic data were recorded.

**Results:** The 16 patients with nephronophthisis related ciliopathies included 11 (68.8%) girls and 5 (31.2%) boys. Mean age at presentation was  $7.7 \pm 4.6$  (0.1–15.5) year. Common presenting symptoms were abdominal pain (25%), polydipsia/polyuria (12.5%), growth retardation (6.3%), nausea (12.5%), weakness (6.3%) and hypertension (6.3%). Two patients were determined as coincidental (12.5%). Two siblings (12.5%) who have liver failure, they applied because of abnormal kidney function tests. The most common renal ultrasonographic finding was renal cyst (43%). Monogenetic defects were identified in 8 (50%) of 16 patients. The most frequent genetic defect was a homozygous NPHP1 gene deletion ( $n = 3$ ). The other gene mutations are DCDC2 ( $n = 2$ ), NEK8 ( $n = 1$ ), NPHP3 ( $n = 1$ ), BBS9 ( $n = 1$ ) gene mutation. Of 16 patients, 6 (37.5%) had isolated nephronophthisis, 7 (62.5%) nephronophthisis with extrarenal features. Two patients with mutations NPHP3 and DCDC2 have liver involvement. Six patients have congenital heart defects. One patient had Joubert syndrome and 3 patients had findings of Bardet-Biedl syndrome. All patients had impaired renal function. Renal transplantation was performed in half of the patients due to end-stage renal disease. Mean age at end-stage renal disease was  $9.2 \pm 4.8$  (2.5–16.5) year.

**Conclusions:** Nephronophthisis is genetically and phenotypically heterogeneous a disease. It should be considered in children with unexplained chronic kidney disease. All patients with nephronophthisis should be investigated for extrarenal anomalies.

Fr-P 136

IS HETEROZYGOTY IS A BYSTANDER OR A CULPRIT IN 24-HYDROXYLASE-RELATED DISEASES

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**Background:** Loss of function variations of 24-hydroxylase encoded by CYP24A1 induces autosomal recessive infantile hypercalcemia (ORPHA300547). It remains debatable whether heterozygosity in CYP24A1 may induce a milder phenotype because of haplo-insufficiency.

**Methods:** In our tertiary center of pediatric nephrology, 16 pediatric patients were found to have either homozygous (N = 1) or compound heterozygous (N = 6) either heterozygous (N = 9) variants in CYP24A1, with clinical symptoms beginning at the pediatric age. CYP24A1 exons 1-12 and intron/exon boundaries were sequenced (reference sequence NM\_000782.5). We retrospectively reviewed medical charts, mainly biological profile at the first manifestation. Descriptive results are presented as median(min-max); non parametric Mann-Whitney tests were performed.

**Results:** At first evaluation, 7 patients with homozygous/compound heterozygous variants were referred for severe symptomatic hypercalcemia (N = 4, from 3.71 to 4.88 mmol/L, among them 3 received bisphosphonates), nephrocalcinosis (N = 1) and family screening (N = 2). The 9 heterozygous individuals were referred for severe symptomatic hypercalcemia (N = 2; 3.9-4 mmol/L, 1 received bisphosphonates), nephrocalcinosis (N = 1), nephrolithiasis (N = 2), and family screening (N = 4). First symptoms occurred at 1.7 (0.32-15.0) and 3.5 (0.1-13.0) years, respectively (p = NS). At the time of diagnosis, in the two groups (homo/compound heterozygous vs heterozygous), calcium levels were 2.64 (2.40-4.88) and 2.49 (2.31-4.00) mmol/L (p = NS), phosphate levels 1.41 (1.06-1.70) and 1.44 (1.13-2.00) mmol/L (p = NS), normalized phosphate levels -1.9 (-3.0;-0.6) and -1.3 (-7.0;0.6) SDS (p = NS), PTH levels 10 (4-29) and 30 (11-67) ng/mL (normal 15-65, p = 0.01), 25 (OH) levels 126 (14-595) and 74 (14-131) nmol/L (p = NS), 1-25-(OH)<sub>2</sub> levels 127 (86-186) and 176 (62-288) pmol/L (normal 69-200, p = NS), eGFR 96 (71-137) and 108 (37-137) mL/min/1.73m<sup>2</sup> (p = NS), total ALP 141 (98-368) and 259 (97-401) UI/L (p = NS), urinary calcium 2.5 (0.5-7.5) and 1.4 (0.7-6.6) mmol/L (p = NS), and urinary Ca/creatinine ratios 0.76 (0.22-8.69) and 0.42 (0.05-2.33) mmol/mmol (p = NS), respectively. In total, 6/7 homozygous/ compound heterozygous patients displayed nephrocalcinosis without lithiasis, whilst 3/9 heterozygous had nephrocalcinosis and 3/9 nephrolithiasis. None had displayed fractures at the time of referral, but two of them had dental symptoms (numerous caries, fragile enamel).

**Conclusion:** Children carrying heterozygous variants in CYP24A1 may present a renal phenotype, with rather nephrolithiasis than nephrocalcinosis. The causality between such renal phenotype and the underlying genotype remains however to be proved, heterozygosity in CYP24A1 possibly being a risk factor for nephrolithiasis.

# POSTER SESSION 1H

## Inherited Kidney Disorders

Fr-P 137

SPECTRUM OF RENAL TUBULAR DISORDERS AMONG OMANI CHILDREN EVALUATED IN SULTAN QABOOS UNIVERSITY HOSPITAL

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**Aim:** Renal tubular disorders (RTD) are a group of heterogeneous disorders resulting from dysfunctions in variable renal tubular transporters. Most are hereditary and present in early age. The spectrum of RTD among Omani children attending Sultan Qaboos University Hospital (SQUH) in Muscat, Oman is described here.

**Methods:** Retrospective observational study conducted on Omani children aged 0 – 12 years old with RTD seen in the child health department at SQUH over 10 years. Non Omanis and patients with secondary and transient tubular dysfunction were excluded. The patients' specific tubular disorders and the associated clinical features were obtained. Creatinine, GFR, renal ultrasound were used to describe the renal outcome. The world health organisation (WHO) growth charts were used to calculate the Z score at diagnosis and follow-up to reflect the growth outcome.

**Results:** 1. Demographics.

Table 1: Description of study group

	Male	Female	Total
Number (%)	21 (51.22%)	20 (48.78%)	41 (100%)
Mean of age in months ± SD	28.17 ± 38.04	32.95 ± 31.74	30.50 ± 34.76
(range)	(1-116)	(1-110)	(1-116)
Mean serum creatinine in $\mu\text{mol/L}$ ± SD	22.76 ± 9.03	21.40 ± 5.50	21.40 ± 5.50
(range)	(13-42)	(12-95)	(12-95)

## 2. RTD types

Table 2: Spectrum of RTD among Omani children attending SQUH

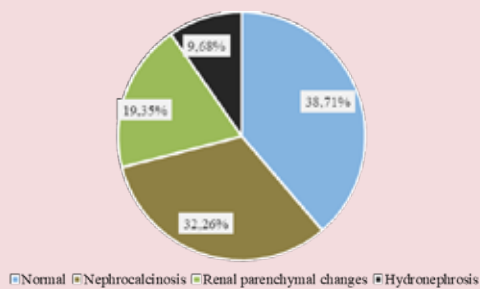
Renal tubular Disorders	Total children (n = 41)	Male/ Female ratio
d-RTAI	10	5/5
Bartter's syndrome	10	4/6
NDI2	4	3/1
Idiopathic hypercalcaemia	4	3/1
Nephrogenic cystinosis	3	0/3
AME3	2	0/2
Familial hypophosphatemia	2	1/1
Gitelman syndrome	2	1/1
Nephrocalcinosis	1	1/0
Hypomagnesemia	1	1/0
Isolated glycosuria	1	1/0
Cystinuria	1	1/0

### 3. Clinical Presentations

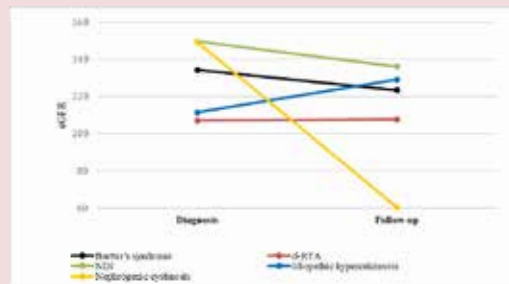
Table 3: Most encountered clinical features

The symptom	Number of patients
Failure to thrive	31
Polyuria	9
Ophthalmological findings	4
Limb deformities	3
Polydipsia	2
Nocturia/ nocturnal enuresis	2
Dysuria	2
Chronic diarrhea	2
Seizures	1
Hematuria	1
Passing stone	1
Persistent vomiting	1

### 4. Renal ultrasound findings



### 5. Renal outcome



### 6. Growth Outcomes

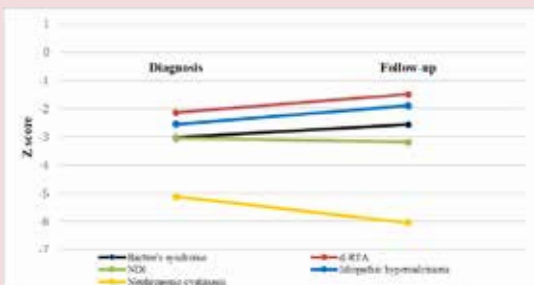


Figure 3. Height for age – mean Z score

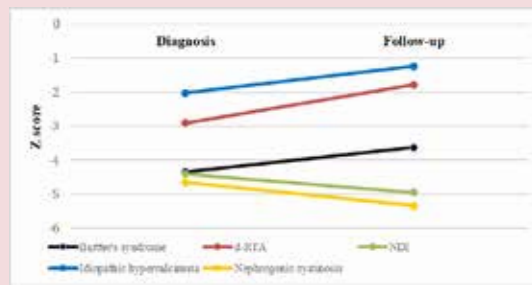


Figure 4. Weight for age – mean Z score

**Conclusion:** Bartter's syndrome and d-RTA were the most common RTD with FTT and polyuria being the most common clinical features. Except for the 2 patients with nephrogenic cystinosis, renal functions were preserved in all patients. As expected nephrocalcinosis was the most common renal abnormality on ultrasound. A trend of growth catch was seen in all but in NDI and nephrogenic cystinosis.

Fr-P 138  
ATYPICAL CLINICAL CASE OF SHIMKE'S SYNDROME

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Schimke syndrome (immunoosseous dysplasia, SIOD) is a rare genetic disease, with an autosomal recessive type of inheritance, which is usually characterized by spondyloepiphyseal dysplasia, proteinuria, growth retardation, primary immunodeficiency, impaired renal function up to end-stage renal disease and cerebrovascular disorders (more often the development of strokes).

In the Department of Nephrology Veltishchev` Institute , we observed a 2-year-old girl with an atypical course of the syndrome. From birth, the child has been observed for low growth rates (now her development is harmonious: weight - 7.5 kg, height -65 cm), multiple defects in the bones of the skull (defects of the parietal and occipital bones, non-closure of cranial sutures), primary immunodeficiency (leukopenia up to  $1.91 \times 10^9$ , decrease in T-lymphocytes - CD3 - 0.26, CD3-4 - 0.13, CD19 - 0.33, decrease in IgG - 4.85 g/l) and isolated glomerular proteinuria (urine protein 0.5 g/l, daily loss - 0.28 g / s = 37 mg / kg) without biochemical signs of nephrotic syndrome (total protein 66.3 g / l, albumin 36.3 g / l). Full exome sequencing revealed a compound heterozygous mutation in the SMARCAL 1 gene (variant c.2542G = T.p.Glu848Ter and variant c.1736 = T.p.Ser 579Leu), confirmed by Sanger (trio). A feature of the course was the development of malignant arterial hypertension and several episodes of tonic-clonic seizures. According to MRI of the brain, focal and diffuse changes were not detected, according to nighttime EEG video monitoring, no epileptic activity was obtained.

**Conclusion:** Thus, the child has an atypical course of Schimke's syndrome, unlike other previously described cases, the severity of which is due to malignant arterial hypertension in the absence of nephrotic syndrome and minimal changes in the immune system, the development of several episodes of tonic-clonic convulsions, which requires more detailed study and constant monitoring.



Fr-P 139

GENOMIC ANALYSIS IN UNEXPLAINED PEDIATRIC NEPHROPATHY: AN UNUSUAL DIAGNOSIS OF PRIMARY HYPEROXALURIA

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**Aim:** Primary hyperoxaluria type 1 (PH1) is a rare recessive disease caused by hepatic overproduction of oxalate leading to nephrocalcinosis, kidney stones, kidney failure and systemic oxalosis. Diagnosis should be discussed as soon as possible to start at least standard of care specific management (hyperhydration, urine alkalization, vitamin B6) and in the most severe cases RNA interference (RNAi) therapies, so as to prevent renal degradation.

**Methods:** We report on an infant with unusual tubular presentation and PH1 diagnosis after genomic analysis.

**Results:** A Caucasian eutrophic patient was born at 32 WG and diagnosed with proximal tubulopathy due to poor weight gain at 2 weeks of life: he displayed severe hyponatremia, metabolic acidosis, hypophosphatemia, hypomagnesemia, transient hypokalemia and acute renal failure. Renal ultrasounds showed two enlarged and hyperechogenic kidneys. Urinary beta2microglobulinuria was increased without hypercalciuria. Urinary oxalate excretion was not included in the initial tubular exploration. He received electrolytes supplementations until 2 months of age with potassium chloride and sodium bicarbonate. A persistent severe hypomagnesemia was observed, between 0.5-0.6 mmol/L despite supplementation with magnesium sulfate and oxide. Renal ultrasounds confirmed two enlarged hyperechogenic kidneys with poor corticomedullary differentiation evolving towards nephrocalcinosis. Targeted genetic analysis excluded our first hypothesis, namely HNF1 $\beta$  mutation. A tubular panel focused on hypomagnesemia was then performed, with negative results. Further genomic analysis was performed, finding double heterozygous mutation in the AGXT gene (c.508G > A (p.Gly170Arg), c.847-3C > G) and thus confirmed PH1 at the age of 3.5 years. Adequate treatment with RNAi therapy was then initiated, because of severe nephrocalcinosis but strictly normal kidney function.

**Conclusion:** PH1 diagnosis is not always easy, even in infants. Unusual presentations may lead to exhaustive genetic analysis including genomic analysis, especially since new targeted therapies are available.

Fr-P 140  
DIAGNOSTIC DELAY FOR PRIMARY HYPEROXALURIA REMAINS CONSIDERABLE

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**Aims/Purpose:** Primary hyperoxaluria (PH) is a rare genetic disease with a heterogeneous phenotype that can lead to kidney failure. Affected patients are often confronted with a diagnostic delay that has adverse consequences on the evolution, while RNA interference is opening a new era in the treatment of PH. The aim of this study is to describe the phenotype of currently diagnosed PH, as well as the evolution of these patients before diagnosis.

**Methods:** This is a national, observational, retrospective study. Patients with a genetic diagnosis of PH type 1, 2 and 3 between 01/01/2015 and 31/12/2019 were included, after looking for non-opposition. In collaboration with the nephrologists and pediatric nephrologists in charge of patients, data were collected from medical records. Diagnostic delay was defined as the time between symptoms at onset and the time of genetic diagnosis.

**Results:** A total of 52 patients, 34 children (= 18 years) and 18 adults, were included. There were 40 patients PH type 1 (77%), 3 patients PH type 2 (6%) and 9 patients PH type 3 (17%). Twelve patients (23%) required hemodialysis at diagnosis. Symptoms at onset were homogeneous in adults (renal colic in 69% of cases); and more diverse in children: renal colic (25%), nephrocalcinosis (16%), macroscopic hematuria (13%), acute pyelonephritis (13%), stones in diapers (9%) (Figure 1). Eight patients (15%) never had urolithiasis. The diagnostic delay was 1.2 (IQR 0.2–2.9) years in children, and 25 (IQR 17–35) years in adults (Figure 2). Urology was the main specialty involved before diagnosis. The assessment for systemic involvement of PH was rarely reported in the medical records. RNA interference was used in 23 patients (44%). Five patients (10%) underwent a liver–kidney transplantation, and 5 (10%) an isolated kidney transplantation.

**Conclusion:** This large and recent cohort highlights the significant delay in the diagnosis of PH, especially in adults, due to lack of diagnosis rather than diagnostic errors. It confirms the need for awareness of relevant specialties in the evaluation of calcium urolithiasis, especially in young subjects.

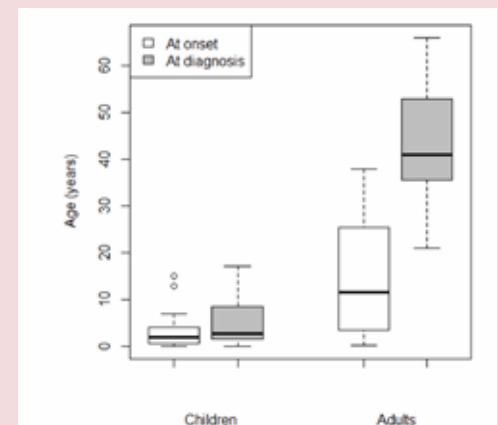
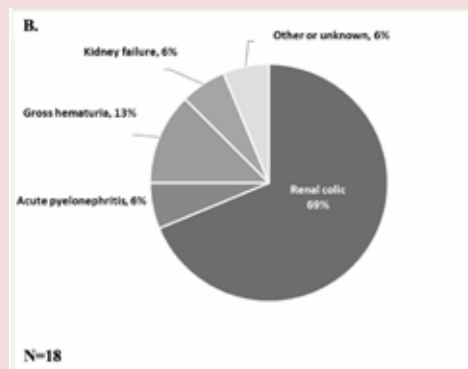
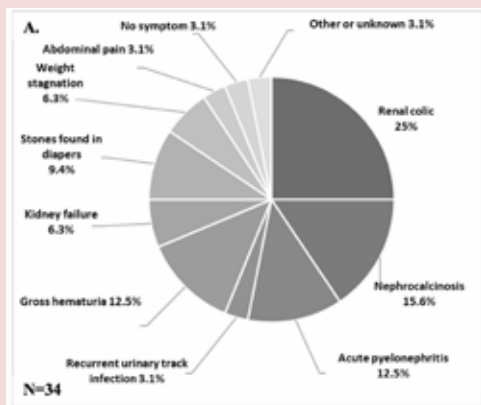


Figure 1: Distribution of symptoms at onset of primary hyperoxaluria in children (A) and in adults (B). Two missing data in adults.

Figure 2: Age at onset (white boxes) and age at genetic diagnosis (grey boxes) of primary hyperoxaluria in children (N = 33) and adults (N = 14).

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THE EFFECT OF LUMASIRAN THERAPY FOR PRIMARY HYPEROXALURIA TYPE I IN A PRE-SCHOOL AGE CHILD

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**Aim/Purpose:** To present the case of a 5.5-year-old male who was admitted to our Pediatric Department because of gross hematuria and dysuria. The patient was a refugee from Afghanistan. From his personal history, severe urolithiasis with onset at the age of 2 months was reported.

**Methods:** Urinary tract X-ray and urinary tract ultrasound showed multiple stones bilaterally. The biggest stone was 2.6 cm on the left kidney. Dilatation of calyces bilaterally, significant dilatation of the left pelvis (anterior-posterior pelvic diameter 3 cm) and thinning of renal parenchymal of the left kidney were also depicted. Urinalysis showed: urine specific gravity 1025, pH 5.5, albuminuria++, many RBCs, Hb +++, leukocytes 1-3/hpf, crystals of calcium oxalate. A 24h urinary collection showed no hypercalciuria or hyperuricosuria, excretion of TPR: 9.4-16 mg/m<sup>2</sup>/hr (normal < 4 mg/m<sup>2</sup>/h) and significant elevated excretion of oxalate: 96-184 mg/1.73m<sup>2</sup>/24h (normal range 12-45 mg/1.73m<sup>2</sup>/24h).

**Results:** Next generation sequencing of the AGXT, GRHPR and HOGA1 genes showed homozygous frameshift (nonsense mutation) in the AGXT gene (p.Lys12Glnfs\*156), confirming the diagnosis of primary hypercalciuria (PH) type 1. Lumasiran, an RNA interference (RNAi) therapeutic agent, which serves in reducing hepatic oxalate production by targeting glycolate oxidase, was initiated. Urinary excretion of oxalate after the first 3 doses was dramatically reduced reaching the normal range (19 & 22 mg/1.73m<sup>2</sup>/24h), without side effects.

**Conclusion:** Although the diagnosis of PH type 1 in our patient was quite delayed, lumasiran therapy was effective in reducing urinary oxalate excretion into normal levels, highlighting the necessity of early diagnosis of this condition, in the light of novel therapeutics.

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**PRIMARY HYPEROXALURIA IN ALGIERS; CHALLENGES IN DIAGNOSIS AND MANAGEMENT**

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**Introduction:** Primary hyperoxaluria is a hereditary disease with autosomal recessive transmission, it affects the metabolism of oxalates and is expressed by recurrent lithiasis and nephrocalcinosis, which leads to end-stage renal failure.

**Materials and Methods:** A retrospective analytical cohort study, on 35 children followed in pediatric nephrology consultation of the pediatric department "A", over a period of 7 years; from June 2015 to September 2022. All our patients had renal ultrasound with or without abdominal radiography. The diagnosis of hyperoxaluria was retained on set of arguments: anamnestic (consanguinity and similar cases in the family), radiological (recurrent lithiasis and nephrocalcinosis) and biological (renal insufficiency, stone study and 24H oxaluria determination).

**Results:** 35 cases were collected, 9 girls and 26 boys with a sex ratio of 2.8, the age ranged from 1 month to 14 years, the average age at diagnosis was 39 months, consanguinity was reported in 43% with a similar case in the family in 40% of cases. Ultrasound showed bilateral lithiasis in 48% of cases and nephrocalcinosis in 37%, 24-hour oxaluria determination was contributory in 40% of patients. 20% of the children underwent surgery, either endoscopic or open, and about 45% progressed to end-stage renal failure, half of them on dialysis. Eight patients died.

**Conclusion:** Hyperoxaluria is a dreadful disease, it is necessary to know how to recognize it early, since the spontaneous evolution is towards end-stage renal failure in more than 50% of cases. The current treatments are promising, and should be available in Algeria considering the important number of patients.

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**SUCCESSFUL KIDNEY TRANSPLANTATION IN PRIMARY HYPEROXALURIA TYPE 1 AFTER COMBINING RNA-INTERFERENCE THERAPEUTICS: A CASE REPORT**

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**Aims/Purpose:** Primary Hyperoxaluria type 1 (PH1) is an inherited disorder of glyoxylate metabolism. Increased oxalate production may cause kidney stones, nephrocalcinosis and kidney failure. Recently, two oxalate reducing RNA-interference therapeutics, lumasiran and nedosiran, have been developed. Theoretically, combining these therapies results in a synergetic effect, but this has not yet been described. Here, we report a 5-year old girl with PH1 who presented with kidney failure.

**Methods:** The diagnosis was established by mutation analysis of the AGXT-gene. Plasma oxalate concentrations were measured on a monthly basis and determined with gas chromatography mass spectrometry. The upper reference limit of normal for individuals with normal kidney function was 6.8  $\mu\text{mol/L}$ . The dialysis regimen consisted of hemodialysis (six days a week) and daily automated peritoneal dialysis. This schedule remained unchanged from initiation. The patient was enrolled in the Alnylam Early Access Program, during which she received four monthly loading doses followed by quarterly subcutaneous lumasiran injections (all 6 mg/kg). Novo Nordisk provided monthly doses of 3.5 mg/kg of subcutaneous nedosiran, as compassionate use product. In a process of shared decision making, the treating physician involved the parents in all steps. The parents also gave written informed consent for the publication of the details in this case.

**Results:** Monotherapy with lumasiran resulted in a decrease in plasma oxalate from 218 micromol/L to a plateau of 100 micromol/L after one year. As the risk of recurrent oxalate nephropathy was considered too high to perform a kidney transplantation, we started co-administration with nedosiran. After five months, plasma oxalate was 55 micromol/L and the patient underwent living-donor kidney transplantation. There was immediate graft function. Urinary oxalate excretion ranged between 0.67 and 1.35 mmol/24 hours/1.73m<sup>2</sup> in the first month post-transplantation. At ten weeks post-transplantation, plasma creatinine was 69  $\mu\text{mol/L}$ , corresponding to an estimated glomerular filtration rate of 59 mL/min/1.73m<sup>2</sup>.

**Conclusion:** Thus, co-administration of lumasiran and nedosiran resulted in an additional decrease in plasma oxalate, allowing the performance of successful kidney transplantation without liver transplantation.

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EFFICACY AND TOLERANCE OF STIRIPENTOL IN PATIENTS WITH PRIMARY HYPEROXALURIA

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**Aims/Purpose:** Stiripentol, an approved antiseizure drug, was shown to decrease in a dose-dependent manner the synthesis of oxalate by hepatocytes *in vitro* and to significantly reduce urine oxalate excretion *in vivo* after oral administration.

**Methods:** We reviewed the efficacy and tolerance of Stiripentol in patients treated for primary hyperoxaluria (PH) in our center within an open-label, prospective trial or for compassionate use. Stiripentol was initiated at 30mg/kg/day in patients over 12 years and 50mg/kg/day in younger patients and increased to 50 mg/kg/day ( $\geq 12$ ) or 75 mg/kg/day ( $< 12$ ) if well tolerated. Efficacy was assessed based on uOx/creat ratio (median of 3 consecutive measures for each time point).

**Results:** 7 patients were included, 2 patients with PH type II and 3 patients with PH type III were included within the clinical trial and 2 PH type I were included after screening failure for iRNA trials (reason for failure were low eGFR in one and uOx/creat ratio below threshold in the other). Age at treatment initiation ranged from 2 to 19 year old. Figure 1 displays the evolution of uOx/creat under treatment. Median change uOx/creat ratio was +4.8% in type III, -41% in type II and -67% in type I, respectively. In one type I patient (patient 7), stiripentol was initiated under stable regimen of pyridoxine and Lumasiran. Overall, the treatment was well tolerated and treatment duration ranged from 3 months (duration of the trial) to 36 months and only one patient discontinued the treatment because of abdominal pain and loss of appetite.

**Conclusion:** We observed a decrease in urinary oxalate excretion in patients with PH type I and II. Stiripentol may be effective in reducing oxalate excretion either alone or in association with iRNA treatment in patients with insufficient response. No change in oxalate excretion was found in type III with low baseline ratio.

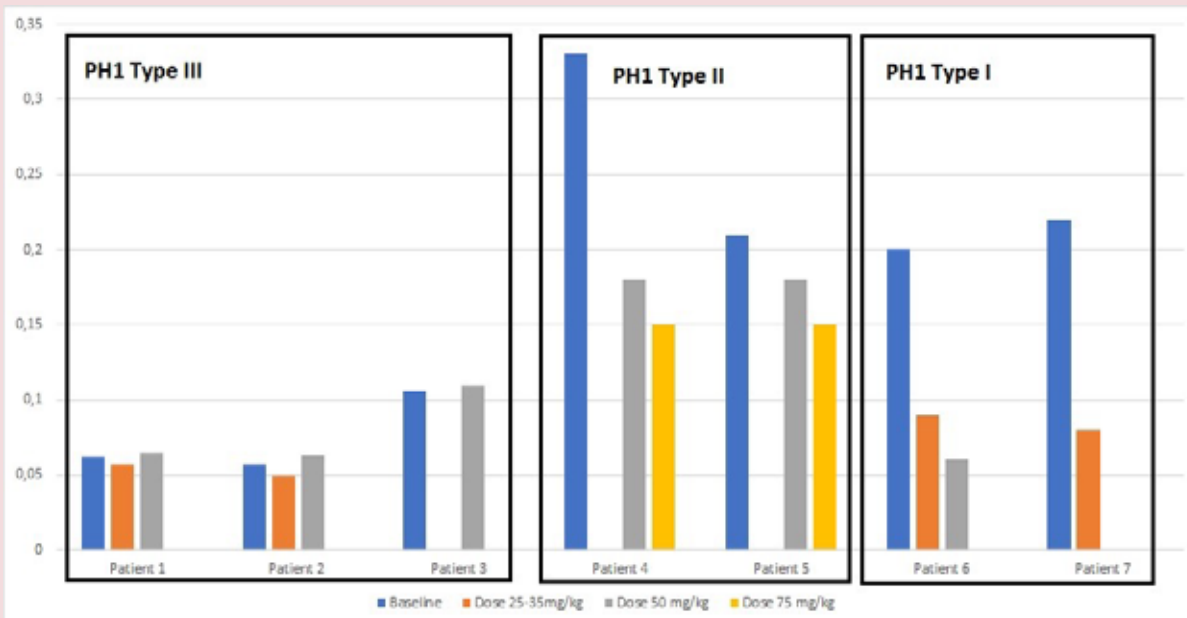


Figure 1: uOx/creat evolution under Stiripentol (in mmol/mmol)

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TUBULOINTERSTITIAL NEPHRITIS (TIN): DIFFERENT SIDES OF THE SAME COIN

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**Aims/Purpose:** TIN in pediatrics represents 7% of the causes of acute kidney injury (AKI). It has a variety of manifestations, even oligosymptomatic, with the classic triad (fever, eosinophilia and exanthema) being observed in only 10%. The causes are multiple (pharmacological 70%) and can be associated with clinical syndromes. The diagnosis is defined by histology, but renal biopsy is not always performed due to the rapid and good evolution of some patients. The pathogenic mechanism is immune-mediated, self-limited and reversible, could evolve to tubulointerstitial fibrosis and CKD. The aim of our study is to describe the clinical characteristics of patients with TIN.

**Methods:** 9 years (2013–2022) retrospective descriptive study of a series of cases with TIN (with/without biopsy) evaluating demographic, etiological, clinical-analytical, evolution and treatment parameters. Exclusion criteria: previous renal disease/renal transplantation. KDIGO 2012 criteria were used to evaluate AKI. eGFR was estimated using Schwartz 2009 equation in <math>> 1</math> year, by CKD-EPI in <math>> 12</math> years and by Filler equation in Cystatin C. Proteinuria was expressed as iPr/Cr (mg/mg) and Alb/Cr (mg/mmol). Fractional excretion of solutes were analyzed using urinary Beta-2-microglobulin (ug/ml) as a marker of tubular injury.

**Results:** Eighteen cases were identified, median age of 14 years (2–7 years). 11 renal biopsies were performed (61.1%). More frequently indication: Persistent AKI of non-filial etiology despite supportive treatment. 11 pharmacological cases were identified (61.1%), 3 infectious (2 *M. Pneumoniae*), 2 TINU and 2 idiopathic. Most common symptoms and signs were abdominal pain (94%) and fever (94%). The classic triad was detected in two cases (11.1%). On admission, all patients had normal BP, with only one patient oliguric on debut. The delay from clinical onset to diagnosis was a median of 8.5 days (IQR 20.5). Renal ultrasound showed renal hyperechogenicity (25%) and nephromegaly (12.5%). Median eGFR (1 month) was 79.72 mL/min/1.73m<sup>2</sup>, with only 1 case of recurrence and 2 of chronicity. 7 cases received treatment with corticosteroids and 2 with immunosuppressants

**Conclusion:** In AKI, TIN is one of the causes that we must always keep in mind in our differential diagnosis. In the series we confirm the wide forms of presentation of the disease and its various etiologies. Likewise, the evolution and prognosis will depend on the cause and the early diagnosis, conditioning the treatment.

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**SCHIMKE IMMUNOOSSEOUS DYSPLASIA. A 20-YEAR CASE SERIES FROM THE TERTIARY CENTER IN THE CZECH REPUBLIC**

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**Aims/Purpose:** Schimke immunosseous dysplasia (SIOD) is an ultra-rare inherited disease affecting many organ systems. Spondyloepiphyseal dysplasia, T-cell immunodeficiency and steroid resistant nephrotic syndrome are the main symptoms of this disease.

**Methods:** We aimed to characterize the clinical, pathological and genetic features of SIOD patients received at tertiary Pediatric Nephrology Center, University Hospital Motol, Prague, Czech Republic during the period 2001-2021.

**Results:** Five children with this ultra-rare disease were identified. The mean age at diagnosis was 21 months (range 18-48 months). All patients presented with growth failure, nephropathy and immunodeficiency. Infections and neurologic complications were present in most of the affected children during the course of the disease.

**Conclusion:** Although SIOD is a disease characterized by specific features, the individual phenotype may differ. Neurologic signs can severely affect the quality of life; the view on the management of SIOD is not uniform. Currently, new therapeutic methods are required.



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**DIFFICULT TO CONTROL ARTERIAL HYPERTENSION. TUMOR AS MAIN ACTOR**

**Marta Jiménez Moreno, Pedro Arango Sancho, Raquel Jiménez García, Ana Cristina Aguilar Rodríguez, Bernat Gomez Herrera, Yolanda Calzada Baños, Elena Codina Sampera, Álvaro Madrid Aris**

*Hospital Sant Joan de Deu, Pediatric Nephrology, Esplugues de Llobregat, Spain*

**Aims/Purpose:** Arterial hypertension (HT) is one of the main causes of morbidity and mortality worldwide. Its prevalence has increased mainly due to the epidemic of childhood obesity. Nevertheless, it continues to pose a diagnostic challenge due to the different clinical forms of presentation and the higher incidence of secondary hypertension in this population compared to adults.

**Methods:** Present a case of HT secondary to a tumor process.

**Results:** 14-year-old patient under follow-up by Neurology due to a flare-up of left optic neuritis (suspected relapsing-remitting multiple sclerosis). History of deceased father due to laryngeal cancer. She presented with acute headache and left fascio-brachio-cubital hemiparesis with HT (194/127 mmHg). Cranial scan showed posterior bulbar hematoma. She was admitted to the ICU where perfusion urapidil was started, followed by nifedipine and oral labetalol. As etiological diagnosis: urine with mild proteinuria (iPr/Cr 0.56 mg/mg); renal function, renal doppler ultrasound, echocardiography, thyroid, basal cortisol and ACTH were normal. Renin 63.6 IUU/ml, aldosterone 0.27 nmol/L. Catecholamines and metanephrines elevated in blood and urine. In view of these findings, the study was extended with MIBG scintigraphy, PET-CT dota, CT and abdominal MRI, showing a right retroperitoneal mass and another left one, as well as bone uptake at the atlas level. In view of the suspicion of metastatic paraganglioma, nifedipine was suspended and fenoxibenzamine was started. After achieving good blood pressure control, surgical excision was performed, confirming the diagnosis. Genetic study: Mutation in SDHD gene. Currently presents a good blood pressure control without drugs and a stable bone lesion.

**Conclusion:** Paragangliomas are endocrine tumors derived from chromaffin cells of the autonomic nervous system. Given their low incidence in childhood, a high degree of suspicion is required and they should be considered in the differential diagnosis of difficult-to-control AHT. Metastases are present in > 10% and cloud the prognosis. Prior to surgery, sequential blockade of alpha/beta adrenergic receptors is required, as well as good volume expansion to avoid intraoperative instability and fluctuation of blood pressure with tumor manipulation. 30-50% are part of hereditary syndromes (especially multiple/bilateral forms), genetic testing should be considered in patients with a confirmed tumor.

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## NEPHROPATHIC CYSTINOSIS—A SINGLE CENTER EXPERIENCE

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**Aims/Purpose:** Nephropathic cystinosis (NC) is an autosomal recessive disease caused by mutations in CTNS gene, which progresses to end stage renal failure in the first decade of life unless treated with cysteamine. This study aimed to describe the clinical course of two patients with NC.

**Methods:** Clinical presentation, investigations and management were reviewed from patient health records.

**Results:** The first case is a 21-year-old male, who presented at the age of 3 months with Fanconi syndrome and developed chronic renal failure at the age of 14 months. Nevertheless he was diagnosed with NC, only after corneal cystine crystals were found when he was 5 years old and subsequently high free cystine levels were measured in white blood cells (WBC) [12 nmol ½ cystine/mg protein, normal value < 0.2]. The patient was administered oral immediate-release cysteamine (IR-CYS) immediately after diagnosis. At the age of 10 years old he started dialysis treatment and he received a cadaveric transplant four years later. At the last follow up he has a functioning transplant, height z score -3.36 (despite treatment with growth hormone), well controlled hypothyroidism, osteopenia without history of fractures, mild pulmonary valve insufficiency, mild photophobia and halitosis. He remains on treatment with cysteamine immediate release. Latest levels of cystine are 1 nmol ½ cystine/mg protein. The second case is a 7-year-old girl presented at the age of 2 years with failure to thrive (height z score -1.88, weight z score -2), proteinuria, hypercalciuria, hypocitruuria, mild aminoaciduria, nephrocalcinosis grade III and osteoporosis. 6 months later, a slit lamp examination revealed crystals in the cornea. Notably molecular testing of CTNS gene was negative. There are reports that some patients with NC require transcript analysis to find DNA sequencing-undetectable mutations. Despite negative genetic testing, cystine measurement in WBC was done in a specialized center abroad, which confirmed diagnosis (11.34 nmol ½ cystine/mg protein). She was immediately treated with IR-CYS, with poor adherence due to gastrointestinal side effects and frequent administration every 6 hours. After two years, she switched to delayed release formulation of cysteamine (DR-CYS), given every 12 hours. Although she continues to complain for nausea and halitosis, she is more compliant. At the age of 7 years old, she has normal renal and thyroid function, her growth has been improved (height z score -0.67). Latest cystine levels are 0.8 nmol ½ cystine/mg protein.

**Conclusion:** Diagnosis of NC remains difficult since measurement of cystine in WBC, the gold standard diagnostic tool, is not available in every country. A negative traditional genetic testing is not sufficient to exclude NC. Prognosis of NC patients, mostly depends on the early diagnosis and adherence to the regimen. The DR-CYS might improve patient compliance.

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## EVALUATION OF CLINICAL AND LABORATORY FINDINGS AND THE OUTCOME OF RENAL TUBULAR DISORDERS IN CHILDREN

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**Aims/Purpose:** Hereditary renal tubular disorders (HRTDs) encompass various clinical syndromes and represent a group of genetic diseases characterized by fluid, electrolyte, and acid-base disorders. In this study, we aimed to evaluate the clinical spectrum of a series of primary tubulopathies diagnosed in a Pediatric Nephrology Unit and define the spectrum of clinical presentation and outcome.

**Methods:** This study included children with HRTD from one month to under 18 years old and followed up at the Pediatric Nephrology Unit of Ondokuz Mayıs University Hospital over ten years. Data were collected on patients' demographics, clinical features, growth profiles, and laboratory characteristics.

**Results:** We reviewed the medical records of sixty-four children (32 males) diagnosed with HRTD. Consanguinity rate was 34.4%. The median age at diagnosis was nine months. The most seen was Bartter syndrome (28 patients); the others were as follows: nephrogenic diabetes insipidus (10 cases), cystinosis (6 cases), distal renal tubular acidosis (9 patients), Lowe (1 patient), Gitelman syndrome (3 cases), Fanconi-Bickel (3 cases), FHHNC (1 case), the other case is MYH-9 related renal disease. The common presentation features were the failure to thrive, polyuria-polydipsia, and abnormal laboratory results. Weight SDS median was -1.43 (IQR 2.55), Height SDS -1.13 (IQR 3) at diagnosis, and weight median was -1.33 (1.98), height median was -1.87 (2.32) after a follow-up. Most metabolic decompensations are associated with short stature (38%). Three patients diagnosed with cystinosis underwent renal transplantation. Six of 9 patients with distal renal tubular acidosis developed sensorineural deafness.

**Conclusions:** In our center, Bartter syndrome is the most common tubulopathy that causes growth impairment. Renal function is preserved except for nephropathic cystinosis. Patients must be followed up for prolonged periods for adequacy of growth and renal functions.

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**HYPOPHOSPHATEMIC X-LINKED RICKETS (XLHR): WHEN CLINICAL AND BIOCHEMICAL SIGNS PREDOMINATE OVER MOLECULAR TESTS**

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Hypophosphatemic X-linked rickets (XLH) is a genetic disorder characterized by the deficiency of circulating inorganic phosphate levels, leading to a wide range of clinical symptoms, including skeletal deformities, growth retardation, and muscle weakness. While next-generation sequencing (NGS) genetic tests have greatly improved the diagnostic process, there are still instances where the results may not contribute to the timely diagnosis of XLH. We describe two girls in whom the clinical and biochemical signs play a crucial role in the early diagnosis and in the timely and appropriate treatment.

**Case 1:** 25-month-old girl, referred to the hospital due to her short stature, bow legs, and waddling gait. Height 82 cm (-1.09 DS), weight 12.700 kg (+0.36 Z-Score). Biochemical data at presentation are depicted in table 1. Treatment with phosphate and vitamin D was initiated. An ultrasound of the kidney and X-rays of the lower limbs showed normal kidney findings but widening of the proximal tibial on X-rays. Treatment with burosumab was started and the phosphate treatment was stopped. Molecular studies were conducted: no mutations were identified using NGS, but a heterozygous deletion of exons 21-22 of the PHEX gene was found through the MLPA assay. The treatment with burosumab resulted in significant increases in serum phosphorus levels, decreases in serum ALP levels (Tab. 2) and improvements in the radiographic appearance of rickets. Additionally, the girl reported reduced levels of pain and improved mobility, that led to a decrease in the waddling gait and tiredness associated.

**Case 2:** 2-year-old girl, referred to hospital because of short stature, bowed legs, and a waddling gait. Height 79 cm (standard deviation [SD] of -2.21) and weight 13.5 kg (z-score of +0.92). Biochemical data at presentation are depicted in table 1. The ultrasound showed normal kidney findings, but the X-rays revealed widening of the proximal tibia. Treatment with 0.5-1.5 g/day of phosphate was initiated plus Vit.D. Treatment with burosumab was started and phosphate treatment was discontinued. To confirm the diagnosis, molecular studies were conducted. The studies did not reveal any mutations using NGS. However, a heterozygous deletion of exon 15-22 of the PHEX gene was identified. Treatment with burosumab showed several beneficial effects on the biochemical signs (table 2) and clinical symptoms: relieve of bone pain and tiredness, correction of bone deformities with improvement of waddling gait. **Conclusion:** This paper aims to emphasize the importance of taking into consideration the clinical and metabolic manifestations of XLH when NGS genetic tests are not contributing to accurate early diagnosis and timely treatment. The paper will also provide insight into the importance to expand the molecular diagnostic testing to include alternative methods, such as MLPA assay.

Table 1: Biochemical data at presentation

Case	eGFR (mL/min)	VIT D (25 OH) (ng/mL)	ALP (IU/L)	P (mg/dL)	Ca (mg/dL)	PTH (pg/mL)	FGF 23 (ng/L)	TRP (%)	TMP/GFR
Case 1	109	30	808	2	9	16	90	75	1.97
Case 2	113	15	642	2.2	8.8	18	79.5	77	1.86

Table 2: Biochemical data at 12 months follow up

	eGFR (mL/min)	VIT D (25 OH) (ng/mL)	ALP (IU/L)	P (mg/dL)	Ca (mg/dL)	PTH (pg/mL)	FGF 23 (ng/L)	TRP (%)	TMP/GFR
Case 1	111	75	259	3.7	9.5	22		85	3.3
Case 2	194	64.91	289	3.7	9.1	23.31		87	3.2

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LUMASIRAN TREATMENT IMMEDIATELY AFTER BIRTH IN PRIMARY HYPEROXALURIA TYPE 1: NEVER TOO SOON

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**Background and Aims:** We present the case of a newborn affected by Primary hyperoxaluria type 1 (PH1) treated with Glycolate Oxidase (GO) RNA-interfering Lumasiran 6 at birth followed with Oxalate and Glycolate serial assessment.

**Method:** Homozygous mutation AGXT c.731T > C9 [p.Ile244Thr] was found at 11 wks of pregnancy on chorionic villus for family history. Parents are heterozygous, first cousins. The first child PH1-affected, required dialysis at 2mo of life, kidney-liver transplant at 14mo had multiple comorbidities. Mother blood Oxalate(BOx), Glycolate(Gly) and Urinary Oxalate(UOx) during pregnancy were normal (3 umol/L; 4 umol/L; 35 umol/mmol). Birth weight 4120 g; Length 49.9 cm (99<sup>o</sup> centile for gestational age). Apgar score 9/9. AGXT mutations confirmed at birth.

**Results:** Ox on cord blood was 15 umol/L (nv < 10), on amniotic fluid 55 umol/L (nv 19-71), on first urine 401 umol/mmolCr (nv < 400 umol/mmolCr). BOx at 6hrs rose to 32 umol/L, Gly to 107 umol/L, UOx to 573 umol/mmolCr. Serum Creatinin was normal (0.3 mg/dl) At 6 hrs of life he was treated with Lumasiran 6mg/kg sc. Hyperhydration (240 ml/kg/day) was maintained iv for 16 days associated to oral water, K- citrate and Pyridoxin 10 mg/kg/day. BOx, assessed every 48hrs, peaked at 108 umol/l (nv < 10) at day 6, (supersaturation level 50 umol/L), then gradually declined (65-56-62 umol/L at 10-20-30 days). Lumasiran 6 mg/kg was repeated at 30 and 60 days according to schedule, then 3 mg/kg monthly. After 2 doses BOx declined (31-17 umol/L at 45-60 days) reaching upper-normal limit 12 umol/L after 3 doses and normal level 6 umol/L after 4 doses. UOx in spite of Lumasiran early start rose to 4173 umol/mmolCr (nv for age < 300 umol/mmolCr) at 13 days and declined to 765 umol/mmolCr after 3 doses and to 335 umol/mmolCr after 4. BGly and UGly initially paralleled Ox then increased after each dose. Renal US showed only minimal hyperechogenic spots during the first 2 mo without signs of nephrocalcinosis/stones. Renal function at 4 mo is normal (sCreat 0.2 mg/dl); child growth on the higher centiles; no adverse events.

**Conclusion:** BOx and UOx serial analysis showed a latency in GO inhibition of at least 15 days. Extremely high level of UOx and BOx, far higher than supersaturation level, were reached, in spite of normal renal function, hyperhydration, B6 and citrate supplementation. Prompt Lumasiran start associated to aggressive supportive therapy is required to avoid irreversible nephrocalcinosis.

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**BUR-CL207, AN OPEN-LABEL, MULTICENTRE, NON-RANDOMISED STUDY TO ASSESS THE SAFETY, TOLERABILITY, PHARMACOKINETICS AND EFFICACY OF BUROSUMAB IN INFANTS WITH X-LINKED HYPOPHOSPHATAEMIA: SUMMARY OF PARTICIPANT ENROLMENT**

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**Aims:** X-linked hypophosphatemia (XLH) is a rare (prevalence of 1:20,000–1:60,000), progressive, genetic renal phosphate-wasting disorder caused by variants in PHEX, and characterised by elevated fibroblast growth factor 23 (FGF23) levels, leading to osteomalacia and rickets [1,2]. Early treatment initiation with oral phosphate and active vitamin D was found to improve height outcomes in children with XLH who were < 1 year at initiation compared with those ≥ 1 year [3]. Burosumab is a recombinant fully human monoclonal antibody that inhibits FGF23, improving serum phosphate levels, bone mineralization, symptoms, growth and function in children. It is licensed in Europe to treat XLH in children and adolescents aged 1 to 17 years with radiographic evidence of bone disease, and in adults. Here we describe the trial design and enrolled participants of the BUR-CL207 study, which was designed to evaluate the safety, tolerability, pharmacokinetics and efficacy of burosumab in infants, an age group not previously investigated.

**Methods:** Infants (< 1 year) with genetically-confirmed XLH and hypophosphatemia were eligible for this study. The total treatment period is up to 48 weeks. Participants were split across three cohorts: Cohort 1 and 2 had infants ≥ 6 ≤ 12 months when initiating burosumab (starting doses of 0.4 and 0.8 mg/kg, respectively). Cohort 3 had infants < 6 months when initiating burosumab (starting dose of 0.4 mg/kg). The primary endpoint is safety and the secondary endpoints are pharmacokinetics and efficacy of burosumab in infants.

**Results:** Enrolment of 16 participants across 5 countries (8 hospitals) completed on 7 Sep 2022. Geographical distribution: France n = 6, United Kingdom n = 4, Italy n = 3, Spain n = 2, Austria n = 1. There were 3 participants in Cohort 1, 8 in Cohort 2 and 4 in Cohort 3. To date, 13 participants have completed the study; “last patient out” expected Oct 2023, database lock Nov 2023 and study report Mar 2024.

**Conclusion:** The BUR-CL207 study will provide important safety, pharmacokinetics and efficacy data for burosumab in infants with XLH, an age group not previously investigated.

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Disclosures

Kyowa Kirin Pharmaceutical Development Ltd is Sponsor of the BUR-CL207 study and this abstract.

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**SCHIMKE IMMUNO-OSSEOUS DYSPLASIA: EXPANDING PHENOTYPE**

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**Aims/Purpose:** Schimke immuno-osseous dysplasia (SIOD) is a rare autosomal recessive disease characterized by T-immunodeficiency, steroid-resistant nephrotic syndrome and poor prognosis with early mortality mainly due to infections and stroke. The aim of study was to review genetic, clinical-laboratory features and outcome of our cohort of children with SIOD.

**Methods:** Retrospective observational study includes pediatric SIOD patients from Primary Immunodeficiency Registry (n = 23, 21 families; 17M); analysis of genetic (available for 20 pts), clinical, immunological (CD3+, CD19+, T-cell receptor excision circle (TREC) and kappa-deleting recombination excision circle (KREC), IgA, IgG, IgM blood levels, available for 14 pts) data was performed.

**Results:** The diagnosis of SIOD was established at median age 4[3;5] yrs in relation to SRNS/high proteinuria in most cases (q = 0.82). SMARCAL1 variant c.2542G > T p.Glu848Term was found in 8 pts (q = 0.4) in homozygous and in 8 children (q = 0.4) in the compound-heterozygous state, resulting in the allele frequency of 58%. Along with typical manifestations (prominent growth retardation (q = 1), multiple pigmented macules (q = 1), photophobia (q = 0.6), laterally displaced capital femoral epiphysis (q = 0.75), cerebral ischemic events (q = 0.43)), non-immune pancytopenia, CACUT, sensorineural deafness, infantile arterial hypertension were revealed in 3 (q = 0.13), 5 (q = 0.22), 1 (q = 0.04), 2 (q = 0.09) children, respectively. All patients had severe CD3+ lymphopenia, extremely low or absent TREC values and normal CD19+, KREC, IgA and IgM values. IgG blood level was decreased in most pts (q = 0.78) due to high proteinuria (r = 0.7, p < 0.001). Autoimmune thyroiditis was revealed in 4 pts (q = 0.17); 1 children had oropharyngeal EBV+ B-cell lymphoma. Overall, 10 pts are currently alive; 13 are deceased (Me age of death 8[5;12] yrs), including 5 who had HSCT/renal transplantation.

**Conclusion:** Our data demonstrates the high rate of SMARCAL1 c.2542G > T variant, severe impaired T-cell immunity with apparently normal B-cell function in our cohort of pts. CACUT and non-immune pancytopenia may be a part of SIOD phenotype. Autoimmune thyroiditis is a main autoimmune complication in SIOD children.

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EVALUATION OF CONGENITAL NEPHROGENIC DIABETES INSIPIDUS CASES WITH AVPR2 MUTATION: A SINGLE CENTER EXPERIENCE

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**Aims/Purpose:** Congenital nephrogenic diabetes insipidus (NDI) is the inability of the kidneys to concentrate urine due to unresponsiveness to vasopressin. Genetically, a loss-of-function mutation is seen in the vasopressin2 receptor (V2R) or the aquaporin2 channel (AQP2). This V2R-related mutations are located in the AVPR2 gene on the Xq28 chromosome and show X-linked recessive inheritance (2). AVPR2 NDI, which is due to the mutation, is seen in 1/250000 of boys.

**Methods:** 6 male patients with AVPR2 mutation, followed up in our center with the diagnosis of NDI, evaluated by their clinical and laboratory findings retrospectively through outpatient clinic files.

**Results:** Partial NDI was considered in one of our patients. He was diagnosed at the age of 9 complained of urinary incontinence and was found to be polyuric at the time of admission. In other NDI cases, hypernatremia was detected due to complaints such as Constipation, vomiting, fever, frequent urination. Other 5 patients were diagnosed in infancy, and 4 of our patients was less than a month old at the time of diagnosis. All of the patients were non-responders to the desmopressin suppression test. Hyperkalemia accompanied by hyperphosphatemia and borderline hypermagnesemia was detected in 50% (n = 3) of the patients, In one patient, hypokalemia, hypophosphatemia, hypomagnesemia has been observed. No electrolyte disturbance was detected in our patient with partial NDI. Hydrochlorothiazide started in all patients. Indomethacin treatment added to the 3 patients in follow-up. One of our patients hydrochlorothiazide treatment was discontinued due to borderline hypercalcemia. In the 6 patients presented in our study, 5 patient's AVPR2 mutations were not defined in the literature.

**Conclusion:** Nephrogenic diabetes insipidus should be considered especially in infants with hypernatremia. In older age groups, partial forms may present with symptoms of urinary incontinence, polyuria and may be accompanied by other electrolyte disturbances.



# POSTER SESSION 2A

## Dialysis and Transplantation

Sa-P 155

## AMBULATORY BLOOD PRESSURE MONITORING IN 40 KIDNEY TRANSPLANT PATIENTS

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**Introduction:** Hypertension is a common complication in post-renal transplantation. Ambulatory blood pressure monitoring (ABPM) is the best method of assessment as it can help to detect alterations that might not be observed in the consultation room.

**Aims/Purpose:** Describe ABPM findings in children being followed for kidney transplant in our centre.

**Methods:** Retrospective and preliminary observational descriptive study in patients with their first renal transplant who underwent an ABPM study.

**Results:** ABPM was performed in 40 patients, 72.5% male and 55% from cadaveric donor. Median age at transplantation was 7 years (IQR: 6.75). 19 patients (47.5%) were under antihypertensive treatment prior to recording. There were 18 patients (55%) with hypertension on ABPM (group 1): 9 had masked hypertension revealed by ABPM and in the other 9 the consultation finding was confirmed. 10 of the 18 patients (55.5%) were receiving antihypertensive treatment at the time of recording and, of these patients, 3 were diagnosed with masked hypertension. A total of 72% had lost the dipping pattern and almost half had left ventricular hypertrophy (47%). 22 patients had no hypertension on ABPM (group 2). 9 patients were under antihypertensive treatment. 73% had no nocturnal dipping. Statistical analysis revealed no significant differences between groups (group 1; group 2) in the following variables: recipient age ( $6.83 \pm 4.35$ ;  $8.86 \pm 4.24$  years; p-value: 0.145), donor age ( $22.67 \pm 13.14$ ;  $24.55 \pm 14.58$  years; p-value: 0.674), glomerular filtration rate estimated according to Schwartz ( $71.43 \pm 23.94$ ;  $66.31 \pm 22.78$  ml/min/1.73m<sup>2</sup>; p-value: 0.49) and time since transplantation ( $55.86 \pm 42$ ;  $76.28 \pm 54.19$  months; p-value: 0.187). Only 2 cases had renal artery stenosis (1 in each group).

**Conclusion:** 50% of our children with confirmed hypertension have poor blood pressure control. Given the necessity of controlling hypertension and the high incidence of masked hypertension, ABPM is an essential complementary test for the management of kidney transplant recipients.

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EARLY PROTEINURIA AFTER RENAL TRANSPLANTATION IN CHILDREN, WHAT IS ITS CLINICAL SIGNIFICANCE?

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**Aims/Purpose:** Proteinuria after renal transplantation is considered a strong predictor for poor graft function in adults. However, data in pediatric population remain scarce. The primary aim of this study was to characterize the proteinuria occurring after transplantation and assess its association with graft function.

**Methods:** In this prospective cohort, all patients that underwent renal transplantation at Schneider's Children Medical Center of Israel during the years 2017-2019, were followed for a period of 1-year. Demographic, laboratory and clinical data were collected. Correlation studies and logistic regression models were performed to assess association between the degree of proteinuria during follow-up and renal function.

**Results:** 44 patients (mean age  $11.2 \pm 5.3$  years) completed 1-year of follow-up. Significant proteinuria (urine protein/creatinine  $> 0.5$  mg/mg) was present in all the patients in the immediate post-transplantation period and normalised by 2 months in most of them (figure 1). This early proteinuria consisted primarily of albumin and was not associated with decreased graft function at 1-year post-transplantation. However, early proteinuria was correlated with persistent proteinuria with increasing magnitude over time (figure 2). Persistent significant proteinuria 6 months after transplantation was associated with poor graft function at 1-year post-transplantation (eGFR  $< 60$ ); OR [95%CI] for significant proteinuria at 7-9 months and 10-12 months post-transplantation; 15.000 [1.541-146.022] and 9.750 [1.635-58.150], respectively (figure 3). Persistent proteinuria was negatively correlated with serum albumin levels and high blood pressure, and positively correlated with primary disease recurrence.

**Conclusions:** Proteinuria in the immediate post-transplantation period is prevalent and is not associated with decreased graft function at 1-year post-transplantation. However, significant proteinuria persisting beyond 6 months is associated with poor graft function and increased morbidity at 1-year of follow-up.

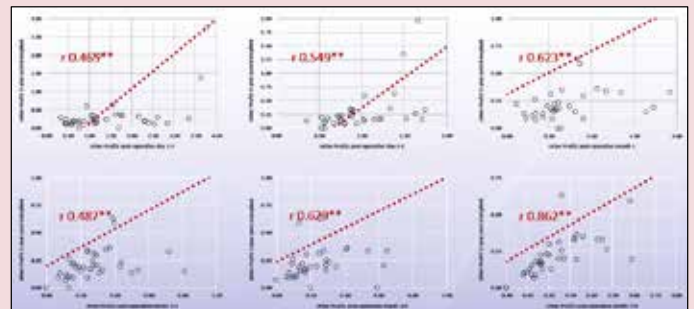
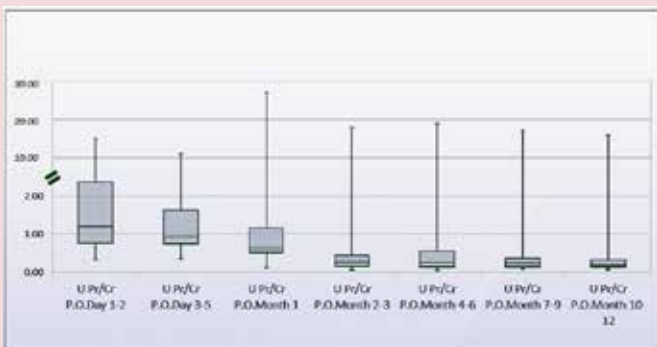


Figure 1: Distribution of proteinuria (urine protein/creatinine ratio (mg/mg)) within study cohort throughout follow-up period. P.O. (post operative).

Figure 2: Correlation coefficients between proteinuria throughout follow-up period and proteinuria at 1-year post-transplant. \*\*p-value < 0.01.

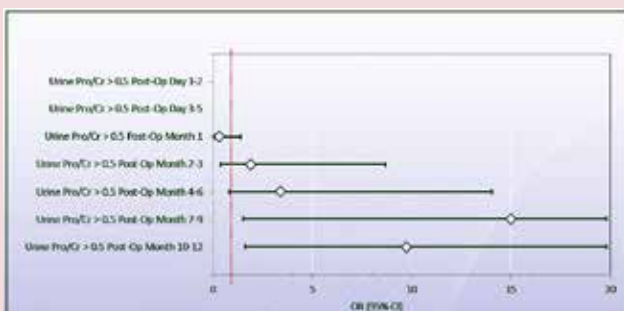


Figure 3: Association between significant proteinuria (urine protein/creatinine  $> 0.5$  mg/mg) throughout follow-up period and decreased graft function (eGFR  $< 60$ ) at 1-year post-transplant. Odds Ratio (OR) for first week post-transplant are not presented as all patients demonstrated significant proteinuria during this time period.

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## BILATERAL CORTICAL NECROSIS: CASE REPORT

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**Introduction:** Acute renal failure is characterized by the abrupt failure of the kidneys to regulate water and electrolyte homeostasis. ARFs in childhood due to hemolytic-uremic syndrome, postinfectious acute glomerulonephritis, or dehydration are reversible, but a small percentage may progress to chronic renal failure. Bilateral cortical necrosis is an uncommon cause of acute renal failure that can be caused by obstetrical, viral, or toxic disseminated intravascular coagulation. It's caused by chronic renal ischemia or widespread microvascular damage.

**Materials and Methods:** We received two cases of severe acute renal failure following traffic crashes in two kids aged 3 and 7 years old, with no known medical history initially supported for abdominal injuries compounded by shock and kidney failure, just a few months apart.

**Results:** The diagnosis of bilateral cortical necrosis was made in the first kid after renal biopsy revealed the persistence of renal insufficiency despite prompt sufficient nephrology care, and in the second child owing to a CT scan. The two children are currently undergoing hemodialysis in preparation for a kidney transplant from a living relative. The three leading causes of acute renal failure in children in developing countries are: hemolytic-uremic syndrome (31%), glomerulonephritis (23%), and postoperative sepsis/prerenal ischemia (18%). In contrast, for industrialized countries, the three most common causes are: intrinsic renal disease (44%), post-operative septic shock (especially after open heart surgery) (34%), and organ/bone marrow transplantation (13%).

**Conclusion:** Cortical and tubular necrosis may occur following hemorrhagic shock, severe dehydration, crush injuries, thermal burns, and septic shock. Adequate early management could limit the damage and especially the transition to chronic renal failure.

Keywords: Acute Renal failure, dialysis, cortical necrosis, Children.

Sa-P 158

**DIVERSITY OF RENAL TREATMENT PATHWAYS IN NATIONAL CHILD HEALTH SYSTEMS OF 48 EUROPEAN COUNTRIES: A SURVEY COMMISSIONED BY 55 ESPN MEMBERS**

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**Aims/Purpose:** Two previous surveys conducted by the European Society of Pediatric Nephrology (ESPN) in 1998 and 2017 showed substantial variation in renal care across European countries. This third survey included a questionnaire aimed at identifying further national differences in the design and organization of pediatric renal care pathways across 48 European countries.

**Methods:** An ESPN Council-endorsed Web-based survey was sent to representatives of 48 national pediatric nephrology societies in Europe. The questionnaire included 11 questions on treatment pathways and care for three pediatric kidney diseases: Acute kidney injury, urinary tract infection, and nephrotic syndrome.

**Results:** During normal working hours, patients with acute kidney injury in the community were admitted to secondary and tertiary care hospitals. On weekends, there was a shift to immediate referral to university pediatric hospitals, where they were treated by pediatric intensivists and pediatric nephrologists. Pediatric dialysis facilities for the treatment of AKI were available in 47 (98%) of the countries; one country required cross-border care. University children's hospitals were directly or indirectly involved in the treatment of AKI in 58% of countries; 18% of countries reported immediate referral to tertiary care pediatric hospitals, while 29% of countries reported collaboration with specialized pediatric nephrology centers and other facilities, including adult nephrology. Care pathways across countries varied not only during standard hours but also at night and on weekends outside normal working hours. Care pathways for children with UTIs included eight different types of caregivers during the day. Outside of normal working hours, there was a shift from primary care to general outpatient polyclinics and hospitals. In 69% of countries, children with nephrotic syndrome were cared for by pediatric nephrologists in hospitals.

**Conclusion:** This survey has highlighted the problems of gaps and fragmentation in national health services that affect the health care of European children with kidney disease. The risk of delayed or inadequate referral of children with kidney disease—particularly AKI—to pediatric nephrologists and the diversity of patient pathways outside of normal working hours were the weak links in the care chain.

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### MAY THURNER'S SYNDROME IN A PAEDIATRIC KIDNEY TRANSPLANT RECIPIENT

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**Aims/Purpose:** May-Thurner syndrome (MTS) is caused by compression of the left common iliac vein (VIC) between the right iliac artery and the fifth lumbar vertebra. The syndrome occurs three times more often in women, but the exact incidence is unknown due to common asymptomatic presentation. When symptomatic, it presents by swelling and pain of one extremity, but also deep vein thrombosis, venous ulcers, varicose veins and pulmonary embolism.

**Methods:** We present the case of a 20-year-old male with a kidney transplant who has developed May-Thurner syndrome.

**Results:** Our patient was diagnosed with neuroblastoma of the right adrenal gland at the age of 9 months. Chemotherapy was administered, but because of the spread of the neuroblastoma to the blood vessels, an excision of an adrenal tumour was made. He developed AKI caused by hypoperfusion of both kidneys due to thrombosis of the right renal artery and left renal vein. Thrombectomy with reconstruction of the vessels was performed, followed by peritoneal dialysis for one month. Although neuroblastoma treatment protocol resulted in sustained remission, the chemotherapy and radiation induced chronic renal failure up to grade V. Therefore, a living donor kidney transplantation (the mother's left kidney) to the patient's right iliac fossa was performed at the age of 12 years. After 2 years, he presented with acute swelling of the left leg and therapy with LMWH was initiated. A Doppler ultrasound ruled out DVT, heparin was discontinued, while acetylsalicylic acid therapy, an elastic bandage and elevated position of the leg were advised. Ultrasonography of the scrotum, a lymphoscintigraphy, tumour markers, and coagulation examination were all unremarkable. MR TOF angiography demonstrated ligamentous obliteration of the left VIC for a length of approximately 5 cm (from the site of compression of the right AIC to the left AIC), which finally led to a diagnosis of MTS. A stent was placed in the left VIC via a transjugular approach along with anticoagulation therapy. In addition, the patient continuously completes manual lymphatic drainage along with the use of an elastic compression stocking. This has led to decrease in the circumference of the left leg, which is still oedematous, but with no other symptoms attributable to the disease.

**Conclusion:** May-Thurner syndrome is uncommon in adult and even less common in the paediatric population. MRI or CT venography are recommended diagnostic methods. Thrombolysis, stent implantation and/or anticoagulation therapy are the treatment of choice for thrombosis in the setting of the syndrome. Moreover, even without thrombosis, stent implantation is recommended to prevent the complications and reduce symptoms. It is important to suspect and diagnose MTS in patients with renal transplant, since there are situations when the kidney must be transplanted to the left side, where MTS may directly affect the graft.

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ACUTE KIDNEY INJURY IN A ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANT RECIPIENT

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BK polyomavirus (BKPyV) infection is observed in approximately 40% of allo-HCT patients. The typical presentation of BKPyV infection in HCT patients is late-onset hemorrhagic cystitis. Although it is not observed very often, BKPyV nephropathy is included in the etiology of AKI. In this case report we present acute kidney injury due to BKPyV nephropathy in a girl who had underwent allo-HCT.

**Case:** An 11 year 8 month old girl, who had underwent allo-HCT five months ago due to Fanconi aplastic anemia, was referred because of elevation of serum creatinine levels. She has been using prescribed medications ruxolitinib 10 mg/d and cyclosporin 30 mg/d, acyclovir, voriconazole, and ciprofloxacin. Her non-invasive blood pressure was 110/90 mmHg (118/73 mmHg 95 p). There was no evidence of hypovolemia or oedema on physical examination. Laboratory data revealed anemia and thrombocytopenia (bicytopenia present since allo-HCT). Serum creatinine was 1.18 mg/dL and estimated glomerular filtration rate was 70 mL/min/1.73m<sup>2</sup>. There were no schistocyte and other hemolysis findings in the blood smear, and the lactate dehydrogenase (LDH) level was normal. Pathological examination revealed none of the 8 glomeruli had signs of sclerosis or mesangial hypercellularity. In the tubulointerstitial area, lymphocyte-dominated moderate-severe inflammation and mild-moderate tubular atrophy were observed. Fibrosis index is between 25-50% Marked virally induced tubular epithelial lysis, denudation of tubular basement membranes. (Figure 1A) In immunohistochemical study, nuclear expression of SV40 T antigen is detected in tubular epithelial cells (Figure 1B). According to Banff 2018 polyomavirus classes is Class 2 (pvl:2 (1% = positive tubule ducts = 10%) Ci:2 (25% = interstitial fibrosis = 50%)). Plasma BK virus load was 1.3X10<sup>5</sup> copies/mL, urine BK virus load was 1X10<sup>7</sup> copies/mL. According to the BKPyV viral load and biopsies findings, the cause of the patient's AKI was evaluated as BKPyV nephropathy.

**Conclusion:** BK virus infections after Allo-HCT may present as nephropathy. BKV nephropathy should be included in the etiology of AKI.

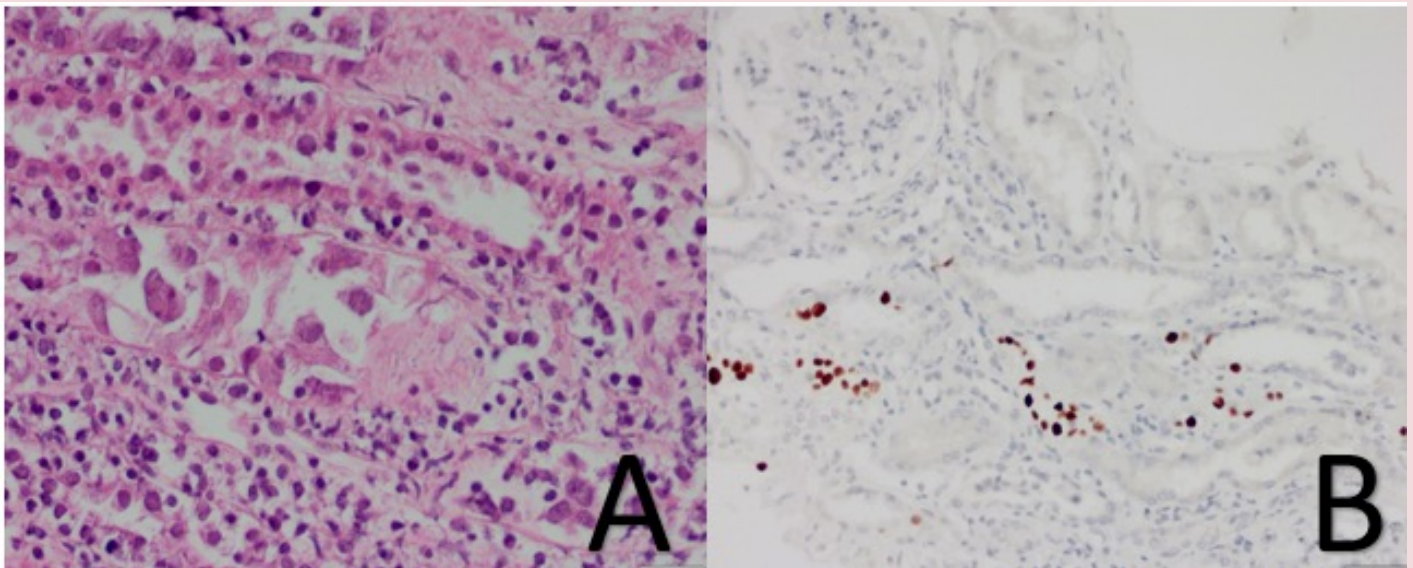


Figure 1: A: (H&E, x400) Marked virally induced tubular epithelial lysis, denudation of tubular basement membranes, marked interstitial inflammation is observed. B: (IHC, x200) Nuclear expression of SV40 in tubular epithelial cells confirmed infection of epithelial cells with BK virus.

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**A PROSPECTIVE STUDY OF ACUTE KIDNEY INJURY (AKI) RECOGNITION AND MANAGEMENT SINCE THE INTRODUCTION OF AKI E-ALERTS IN A TERTIARY PAEDIATRIC HOSPITAL**

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**Aims/Purpose:** AKI is defined as a rise in creatinine more than 1.5 times the baseline or age specific upper limit of normal. AKI is associated with increased mortality, increased length of hospital stay, risk of progression to CKD and associated costs. AKI e-alerts launched on 21/6/2021 and the trust AKI guideline published on 9/7/2021. A daily AKI huddle flagging patients with e-alerts to the nephrology consultant was introduced and a regional AKI clinic was launched. These measures aim to improve recognition and management of AKI.

**Methods:** A prospective audit including all inpatients from 21/6/2021 to 30/6/2022 with an AKI e-alert. Patients on dialysis, NICU and PICU were excluded. Data was collected from electronic records and management each month was compared to the trust AKI guideline.

**Results:** The overall incidence of AKI was 1% during the audit period. There were 132 episodes of AKI affecting 109 patients. 65.9% had AKI stage 1, 15.2% had AKI stage 2 and 18.9% had AKI stage 3. Recognition of AKI within 24 hours varied by month from 45%–100%. Documentation of the 3Ms (monitor, maintain and minimize) on admission was 18%–88% and 24 hourly documentation of the 3Ms was 21% to 86%. Mean time to recovery was 3–9 days. 85% of patients were followed up appropriately.

**Conclusion:** There was initial improvement in identification of AKI within 24 hours and management as per guideline following the e-alert launch and education to raise awareness but this was not consistent across the year. The daily huddle is invaluable in identifying patients. Patients are being appropriately followed up in AKI clinic. There is a need for ongoing education and consideration for the role of an AKI clinical nurse specialist.



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## HAEMOGLOBIN CAST NEPHROPATHY: THE FORGOTTEN CAUSE OF ACUTE KIDNEY INJURY IN CHILDREN

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**Introduction:** Intravascular haemolysis describes the breakdown of red blood cells within the vasculature resulting in the release of haemoglobin into the circulation. Haemoglobinemia then leads to acute kidney injury by various mechanisms. Herein, we report 2 cases of acute kidney injury secondary to haemoglobin cast nephropathy.

**Case Illustration:** *Case 1:* 7 year old boy with good past health presented with intermittent fever for 1 month followed by recent onset of pallor, jaundice and dark coloured urine. Blood parameters suggested intravascular haemolysis (haemoglobin 6.7 g/dL, low haptoglobin, positive direct Coombs test, high indirect bilirubin, reticulocytosis, raised lactate dehydrogenase and spherocytosis on peripheral blood film) and acute kidney injury. Serum creatinine peaked at 353  $\mu\text{mol/L}$  and he needed dialysis in view of his oliguria and poor solute clearance. He has Parvovirus associated immune haemolytic anaemia. Intravenous methylprednisolone was given for the rapidly declining kidney function. Kidney biopsy showed acute tubular injury with intratubular eosinophilic cast. He had then recovered well with normal serum creatinine. *Case 2:* 14 year old boy with known Hb S- Beta Thalassemia and intermediate G6PD activity, presented with pallor, jaundice and abdominal pain. He was hypotensive and there was massive splenomegaly. Initial haemoglobin was 4.6 g/dL. Soon, he developed non-oliguric AKI with highest creatinine 375  $\mu\text{mol/L}$ . A diagnosis of acute splenic sequestration crisis with intravascular haemolysis was made. Kidney biopsy showed dense eosinophilic intraluminal casts with unremarkable glomeruli. There were no immune deposits seen. He recovered well with supportive therapy and did not require dialysis. He too had recovery of kidney function.

**Discussion:** Haemoglobin cast nephropathy is a rare occurrence in children. Destruction of erythrocytes releases free haemoglobin that is filtered by the glomerulus and enters the tubules. The nephrotoxic effect of heme is caused by multiple mechanisms such as decreased renal perfusion, injury to renal tubules and intratubular cast. Treatment is mainly supportive in nature and measures should aim to halt the haemolysis.

**Conclusion:** The outcome of haemoglobin cast nephropathy remains favourable. Most patients recover their kidney function.

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## INCIDENCE AND OUTCOMES OF COVID-19 INFECTION IN PEDIATRIC TRANSPLANT RECIPIENTS

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**Aims/Purpose:** Evidence from adult studies has shown an increased risk for severe manifestations of COVID-19 infection even in vaccinated renal transplant recipients treated with immunosuppressive agents, however data on the pediatric population are limited.

**Methods:** We retrospectively analyzed the incidence and clinical course of PCR confirmed SARS-CoV-2 infection in a cohort of 20 (13 males/7 females) pediatric renal transplant recipients. In the vaccinated patients we measured spike protein of SARS-CoV-2 IgG antibody using chemiluminescent microparticle immunoassay (Architect/Alinity, Abbott). IgG results  $\geq 50$  AU/ml were considered positive.

**Results:** 17/20 were vaccinated with the BNT162b2 Covid-19 mRNA vaccine and 3/20 patients declined vaccination. 13 patients received 2 vaccine doses and 4 patients 3 doses. 11/17 patients had positive antibody titre (mean 2209,26 AU/ml) and 6/17 patients had negative antibody titre. 14 patients developed PCR confirmed COVID-19 disease; 11/17 vaccinated patients (mean time 6 m post vaccination) and 3/3 of the unvaccinated patients. The mean post vaccination antibody titre of the patient that acquired COVID-19 was 3067,33 AU/ml and the mean antibody titre of the patients that didn't have disease was 1741,22 AU/ml ( $p = 0.53$ ). After approval of remdesivir for treatment of COVID-19 infection, 5 patients received remdesivir as per our local protocol for immunocompromised patients. None of our patients developed pneumonia nor oxygen requirements. The mean symptom duration was 3 days (range 1-7 days) in the vaccinated patients and 2.6 days (range 2-3 days) in the unvaccinated patients. The major symptom was rhinitis in 11/14 patients while fever  $> 38$  C had 6/14 patients, low grade pyrexia  $< 38$  C 3/14 patients, cough 5/14 patients, diarrheas 2/14 patients headache 2/14 patients and anosmia/loss of taste 2/14. 2 patients developed rejection, both 6 months after COVID-19 disease.

**Conclusion:** The incidence of COVID-19 infection in the immunocompromised pediatric renal transplant recipients is high after vaccination, however the course of the disease is very mild.

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ACUTE KIDNEY INJURY IN INFANTS WITH GESTATION AGE LESS THAN 32 WEEKS

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**Aims/Purpose:** Acute kidney injury (AKI) is a common occurrence in the neonatal intensive care unit. Neonatal AKI associated with adverse outcomes, rise in mortality, especially in premature infants. Some work has confirmed a significant association between low birth weight, early gestational age, and AKI. The aim is to diagnose acute kidney injury in premature infants with gestational age < 32 weeks, based on the study laboratory markers - cystatin C (Cys C) in serum, lipocalin (NGAL) in urine.

**Methods:** We examined 65 premature infants who had signs of injury of kidney with gestational age < 32 weeks. The group of comparison included 25 premature newborns who were born without signs of kidney injury. Blood and urine samples were obtained at 2-4 days of life.

**Results:** In 76.9% ( $p < 0.05$ ) of infants with gestational age < 32 weeks Apgar score less than 4 points at 1 minute of life, this score remained at 5 minutes of life in half of infants. The severity of the condition after birth in infants with gestational age < 32 weeks was caused by severe respiratory disorders (78.5%), neurological symptoms (43.1%), 53.9% of infants had circulatory insufficiency, 12.3% - necrotizing enterocolitis. At the first days of life, the level of creatinine in the serum of infants with gestational age < 32 weeks was Me 107.4 [89.4; 124.8]  $\mu\text{mol/l}$ , and at the 7th day of life the level of creatinine was 4 times higher than the level of children group of comparison (Me 212.84 [159.6; 236.9]  $\mu\text{mol/l}$  against Me 66.57 [54.8; 72.6]  $\mu\text{mol/l}$ ,  $p < 0.01$ ). The level of Cys C in the serum of infants with gestational age < 32 weeks significantly exceeded this level in infants of the group of comparison (in infants with gestational age < 32 weeks -2.50 [2.14; 3.26] ng/ml, group of comparison - 0.62 [0.52; 0.77] ng/ml),  $p < 0.01$ . The value of NGAL in the urine of infants with gestational age < 32 weeks - Me 96.03 [38.6; 131.23] ng/ml UCr against Me 25.9 [8.24; 44.64] ng/mg UCr in infants of the group of comparison ( $p < 0.01$ ).

**Conclusion:** Levels of cystatin C in serum and level of lipocalin in urine are early and sensitive markers of kidney damage in premature infants with a gestational age < 32 weeks which exposed to perinatal hypoxia. On the 2-4th day of life, there was a significant increase level of the studied indicators, in contrast to serum creatinine.

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**PEDIATRIC KIDNEY TRANSPLANTATION: FOCUS ON GRAFT SURVIVAL AND CURRENT TRANSITION CARE**

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**Introduction:** The transition from pediatric to adult medical services is an important time in the life of an adolescent or young adult with a kidney transplant. Failure of proper transition can lead to medical non-adherence and subsequent loss of graft and return to dialysis. The aim of this study was to assess the survival of kidney grafts received in the childhood and the outcomes after transition to the adult nephrological service.

**Materials and Methods:** The study included all children who received a kidney transplant in Belarus for the period 2009–2021. Survival was assessed according to Cox model.

**Results:** We retrospectively analyzed 125 patients (79 males and 46 females) with median age 13,6 (IQR 9.2; 16.7) years on time of kidney transplantation, 2 of them received the second graft in the childhood. The time of follow up was 8,0 (IQR 4.7; 10.5) years. There were 6 (4.7%) primary non-functioning grafts (excluded from the study). In 21 cases (17.4%) there were a loss of kidney graft function: 6 in the childhood and 15 in the adulthood – 8 of them died: 4 children and 4 adults. The grafts survival rates of 1-year, 5-year and 10-year were 95%, 84%, 79%, respectively. 66 patients out of 119 were transferred to the adult service. 77% (51/66) patients have a functioning graft on December 31, 2021. 10 (15.2%) of 15 graft losses were due to patient non-adherence to medical prescriptions. Most cases of losses (n = 11) were in the first 3 years after the transition: 1 year – 6, 2 years – 3, 3 years – 2. It should also be noted that 4 graft losses occurred in patients who were transferred to adult service less than 1 year after surgery.

**Conclusions:** The transition from pediatric to adult medical care is a challenging process for adolescents after kidney transplantation. Timing should be individualized, according to the adolescent's neuro-cognitive and development, social status. Patients must be medically stable without new comorbidities. Pediatric follow-up should be for a minimum 1 year after a transplantation. While in developed countries there are programs for transferring patients to adult service, in developing countries such programs are at the planning stage.

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PLEURAL EFFUSION SECONDARY TO EVEROLIMUS IN A PEDIATRIC KIDNEY TRANSPLANT PATIENT

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**Introduction:** mTORi (mammalian target of rapamycin inhibitors) are macrolides obtained from the fungus *Streptomyces hygroscopicus*. Its use as an immunosuppressant in kidney transplantation has increased due to its lower nephrotoxicity and antilymphoproliferative action, which has been associated with a lower risk of tumors and infections. However they also have side effects.

**Clinical case:** An 8-years-old patient with chronic kidney disease secondary to kidney dysplasia and bilateral reflux. An anticipated cadaveric donor kidney transplant was performed. She received induction immunosuppression with basiliximab, TK, mycophenolate (MMF), and methylprednisolone and maintenance immunosuppression with TK, MMF and prednisone. Two months after transplantation, polyomavirus BK was detected, so MMF was changed to everolimus. Six months later, she went to the emergency department because she had abdominal distension and kidney graft pain. Hypoventilation was noted in the right hemithorax. A blood test showed normal kidney function and the urine sediment was negative. The abdominal ultrasound showed free fluid in the right iliac fossa and pelvis, the chest X-ray a white lung and the chest ultrasound a right pleural effusion. She received empirical antibiotic and a thoracentesis was performed. The drained fluid was a transudate.

**Etiological study:** echocardiography without evidence of cardiac dysfunction, normal ultrasound and liver function, normal thyroid function, moderate proteinuria but normal serum albumin, negative antibodies study, negative quantiferon, respiratory arrays, PCR for *S.pneumoniae*, VH6, VH7 and VH8. In pleural effusion ADA, culture for mycobacteria, bacterias and fungi, CMV, EBV and adenovirus were negative. A chest tomography and nuclear magnetic resonance excluded pulmonary thromboembolism and tumor. The pharmacological cause was considered, so everolimus was stopped. A progressive improvement was observed. During the follow-up serial ultrasounds showed no data of pleural effusion.

**Discussion:** Lymphedema and visceral effusions have been reported as a rare side effect of mTORi in transplant recipients. In pediatric patients, the use of mTORi has been exceptionally associated with lymphedema in limbs. However there are no cases of visceral effusions described in the literature. In our case, the presence of pleural effusion was related to everolimus since other etiologies were excluded and the process disappeared after discontinuing the drug. It is postulated that mTORi prevent lymphangiogenesis by inhibiting proliferation of lymphatic endothelial cells (VEGF). They also produce an increase in vascular permeability and vasodilation.

**Conclusions:** After excluding other causes, the pharmacological one must be taken into account in kidney transplant patients affected by visceral effusions. The suspension of the medication usually solves the process.

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## MOYAMOYA DISEASE IN A HEMODIALYSIS PATIENT WITH BARDET BIEDL SYNDROME

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**Aims/Purpose:** Bardet Biedl syndrome (BBS) is a ciliopathy which is characterized by retinal dystrophy, polydactyly, obesity, hypogonadism, intellectual disability, cardiovascular abnormalities, and renal structural abnormalities. Moyamoya disease (MMD) is a chronic cerebrovascular disease of unknown etiology characterized by progressive stenosis or occlusion of the main cerebral arteries forming the circle of Willis. Here we reported a hemodialysis patient with BBS and MMD.

**Case report:** A fourteen-year-old boy diagnosed with BBS and chronic kidney disease was admitted to emergency department due to a sudden onset of weakness in his left arm and leg. Neurological examination of the patient revealed paresis in the left upper and lower extremities with a positive left Babinski sign. Cerebral magnetic resonance (MR) imaging showed a wide acute ischemic changes extending from the right periventricular area to the parietal vertex. Sequelae of old infarct at the level of left centrum semiovale were observed. In cerebral MR angiography, right internal carotid artery after the lacerum segment, and left internal carotid artery is occluded from the cervical segment entering the cross-section, bilateral middle cerebral artery and anterior cerebral artery show collateral weak filling. These findings were found to be compatible with moyamoya disease. Low molecular weight heparin (Enoxaparin) was started as treatment. On the 15th day of the treatment, Enoxaparin was discontinued, and acetylsalicylic acid was started. Follow-up was done with physiotherapy. At the end of eight weeks of rehabilitation, the patient was able to walk with the orthosis.

**Conclusion:** To our knowledge, this was the first reported case of moyamoya disease in a hemodialysis patient with Bardet-Biedl syndrome. Moyamoya disease may be the cause of acute ischemic infarction in hemodialysis patients presenting with sudden neurological symptoms, therefore imaging methods should be performed in detail in patients.

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**INCIDENCE AND OUTCOME OF NEONATAL ACUTE KIDNEY INJURY (AKI) BASED ON MODIFIED KIDNEY DISEASE IMPROVING GLOBAL OUTCOMES (KDIGO) CRITERIA**

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**Aims/Purpose:** Neonatal AKI, as defined by KDIGO criteria is common worldwide. However, despite its prevalence, there is a paucity of data about the incidence and outcomes of babies diagnosed with AKI, particularly from UK centres.

**Aim:** To review the demographics and outcomes of babies diagnosed with AKI.

**Methods:** A retrospective review was performed of all babies admitted to a London tertiary neonatal unit with at least 3 serial creatinine measurements between January 2019 and December 2019. Laboratory creatinine levels for each infant were amalgamated with demographic data from Badgernet. KDIGO criteria was define AKI and its severity. Data was analysed using SPSS 28.

**Results:** 73 out of 348 infants (21%) were identified to have any stage of AKI with 51% extremely premature infants born at < 28 weeks developed 1 or more episodes of AKI (Table). Female gender was more likely to be diagnosed with AKI (M vs F 18.1% vs 24.8%). Those who developed AKI were of significantly lower median (IQR) GA: 29.6 (25.6–35.9) wks vs. 36.4(31.9–39.1) wks, and significantly lower median (IQR) BW:1200 (695–2485) gm vs. 2400 (1370–3190) gms. Of those with AKI, 58% (42/73) were diagnosed within 1 week of age. A higher proportion of those with AKI died (AKI 15/73 (20.5%) vs Non-AKI 10/275 (3.6%),  $p < 0.001$ ).

**Conclusion:** Our data shows slightly lower rates of AKI but higher proportion with early AKI in comparison with previous epidemiological study (AWAKEN) looking at AKI in newborn infants. The development of AKI was associated with increased mortality.

Table: GA and BW categories and AKI

		Total (n)	AKI (any)	Early AKI < 7 days	Late AKI > 7 days	AKI Stage 2 or 3
GA (wks)	< 28	68	35	18	17	12
	28-32	62	13	9	4	2
	33-36	73	8	3	5	4
	Term	145	17	12	5	8
BW (kg)	< 1	71	31	14	17	12
	1-1.5	52	10	7	3	1
	1.5-2.5	74	14	9	5	5
	> 2.5	150	18	12	6	8

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- <https://kdigo.org/guidelines/acute-kidney-injury/>
- Jetton et al. Incidence and outcomes of neonatal acute kidney injury (AWAKEN). Lancet Child Adolesc Health 2018.

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## pRIFLE FOR EVALUATION OF AKI IN CHILDREN

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**Introduction:** Pediatric RIFLE (pRIFLE) is a modified version for the setting of AKI in children. The Risk, Injury, Failure, Loss and End-stage renal disease (RIFLE) classification determines the stage of AKI based of serum creatinine level or glomerular filtration rate (GFR) and urine output.

**Aim of study:** To know the etiology and all features of all cases of AKI in Pediatric Hospital at UHC "Mother Teresa" Tirana, Albania during January –december 2019. Evaluation of AKI applying pRIFLE.

**Materials and Method:** We studied all cases of AKI hospitalized in on year in PICU. Evaluation of AKI was made by pRIFLE. The follow-up was done for 3 months.

**Results:** 26 patients were enrolle in the study, 16 males ang 10 females. 1-5years old children were most affected(10 cases). Etiology of AKI was: prerenal in 58%, renal in 38%, postrenal in 4% of all cases. Applying the pRIFLE scale at the entrance: Risk 6 patients, Injury 12 patients, Failure 8 patients. The average hospital stay was 18 days. 11 patients required replacement therapy. 3 patients died, 21 had complete recovery, 2 left with renal sequelae.

**Conclusion:** pRIFLE scale helps for an early detection of AKI and its application rise the incidence. A better evaluation of AKI can improve the management.



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**ANURIC PATIENT WITH PRIMITIVE NEUROECTODERMAL TUMOR SUCCESSFULLY TREATED WITH CHEMOTHERAPY ASSOCIATED N-ACETYL CYSTEINE – LONG TERM OUTCOME**

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**Aims/Purpose:** The data concerning patient with acute renal failure due to malignant neoplasm who requires aggressive chemotherapy including ifosfamide are scarce. Here we report a 10 year old girl with massive pelvic primitive neuroectodermal tumor (PNET) and anuria treated successfully with standard hemotherapy dosage combined with N-acetylcysteine (NAC).

**Case report:** A 10 year old girl admitted at the University Children Hospital for further diagnostics and treatment of abdominal mass. On admission the girl presented with generalized edema, large amount of ascites and anuria. Abdominal ultrasound revealed large pelvic and retroperitoneal mass with bilateral hydronephrosis and renal parenchyma involvement. Urinary bladder was compressed with tumor lesions and large amount of peritoneal liquid were seen. Partial tumor extirpation including bilateral adnexectomy was performed and PNET diagnosis was confirmed. According to the half-time of applied drug elimination (CWS 2004 protocol for high risk patients VAIA III), we prescribed certain HD regimen. On day 1 she received ifosfamide (IFO) based therapy and NAC (IV dosage: 150 mg/kg loading dose over 60 minutes of continuous infusion, 50 mg/kg over 4 hours, 100 mg/kg over 16 hours). She underwent dialysis after 24 hours. No adverse reaction was seen. On day 2, 19 hours after ifosfamide and NAC, she underwent dialysis. On day 3, ifosfamide without NAC was applied. But, after 12 hours, she manifested with face fasciculations and electroencephalogram confirmed encephalopathy. Therefore, dialysis was started earlier, 15 hours after ifosfamide infusion. After the first day of chemotherapy, her diuresis dramatically improved and normalized after three days so dialysis was stopped. After 13 VE III block, 3.5 month post first operation, she reoperated and several rest tumors were removed. She completed intensive chemotherapy after 7.5 months., and two months later PET scan showed no residual tumor. At the most recent follow up, 13 years after disease onset, she is in complete remission with normal kidney function and mild proteinuria treated with enalapril.

**Conclusion:** This case underlies that aggressive chemotherapy for PNET is possible in a child with anuric acute renal failure. NAC may protect against IFO-induced nephrotoxicity without interference with its antitumor activity.

# POSTER SESSION 2B

## CKD

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## LIVER AND KIDNEY ULTRASOUND ELASTOGRAPHY IN PAEDIATRIC PATIENTS WITH MILD CHRONIC KIDNEY DISEASE AND HYPERTENSION

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**Aims/Purpose:** Ultrasound elastography is an ultrasound technique; a method of measuring tissue elasticity properties that is being increasingly researched in various fields in the paediatric population. The aim of our study was to assess usability of ultrasound elastography in paediatric patients with hypertension or chronic kidney disease (CKD) in relation to anthropometric measurements, laboratory studies and other functional or imaging studies applied in cardiovascular health. Additionally, ultrasound elastography results were interpreted according to obesity status. Overall, the aim of our study was to assess the usability of ultrasound elastography in cardiovascular risk assessment in children and young adults at higher risk for subclinical atherosclerosis.

**Methods:** A total of 129 children, adolescents and young adults were included in the study; 46 subjects with CKD stage 1 or 2 (Group 1) with mildly affected kidney function, 50 participants with hypertension (Group 2) and 33 healthy children, adolescents and young adults to provide a control group. In all, anthropometric, laboratory and some functional studies indicating increased cardiovascular risk along with liver and kidney elastography were performed.

**Results:** In both groups, liver elastography parameters were increased compared to the control group: Group 1 vs. control group with  $p = 0.007$  for speed module and  $p = 0.006$  for pressure module, and Group 2 vs. control group with  $p = 0.001$  for both modules. In kidney elastography, the only difference was for the speed module in Group 1 compared to the control group ( $p = 0.049$ ). Kidney elastography parameters were significantly higher in Group 2 when compared to Group 1. Additionally, all participants were divided according to overweight and normal-weight status, where both liver and kidney parameters were significantly higher in group of overweight/obese subjects.

**Conclusion:** Ultrasound elastography of liver and kidney is feasible in paediatric patients with either mild chronic kidney disease or hypertension showing increased liver stiffness parameters in both groups, further aggravated by obesity. Along with overweight, kidney stiffness increased indicating a negative effect of clustering cardiovascular risk factors leading to decreased kidney elasticity. Further research on ultrasound elastography is needed.

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## EFFECT OF COMBINING NATIVE AND ACTIVE VITAMIN D IN PAEDIATRIC CHRONIC KIDNEY DISEASE–MINERAL BONE DISEASE

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**Aims/Purpose:** Vitamin D deficiency and insufficiency are common in chronic kidney disease [1]. This study aims to determine this prevalence in our paediatric dialysis (CKD5D) cohort and the effect of native and active vitamin D combination therapy in chronic kidney disease–mineral bone disease.

**Methods:** All CKD5D children were analysed in this retrospective cohort study at Hospital Sultan Ismail JohorBahru from 2017 to 2022. Active vitamin D (alfacalcidol/rocaltriol) was given for persistently above target iPTH with native vitamin D (cholecalciferol) supplementation if  $25(\text{OH})\text{D} \leq 75\text{nmol/L}$  [2,3]. Bone health blood parameters were studied every 3 to 6 monthly for 1 year. Vitamin D insufficiency and deficiency were defined as  $50\text{--}75\text{nmol/L}$  and  $< 50\text{nmol/L}$  [2].

**Results:** 34 children aged 4 to 18 were included (19 male, 15 female). A third ( $n = 13$ ) had congenital anomalies of the kidney and urinary tract. 70% ( $n = 24$ ) were on peritoneal dialysis and 30% ( $n = 10$ ) on chronic haemodialysis modality (median dialysis duration of 30 months). 85.3% had suboptimal  $25(\text{OH})\text{D}$  (26.5 % insufficient, 58.8 % deficient), ranging from 5 to 118.8 nmol/L. Malay ( $p = 0.015$ , OR: 3.0), female ( $p = 0.043$ , OR: 5.6), and less than 13 years ( $p = 0.003$ , OR: 4.9) were risk factors identified. With combination therapy, there was a significant rise in  $25(\text{OH})\text{D}$  (median 70.9;  $z = -3.1$ ,  $P = 0.002$ ); half achieved a sufficient level by 1 year with no vitamin D toxicity ( $> 250\text{ nmol/L}$ ) [4] at study end. Alkaline phosphatase improved (median 324;  $z = -2.4$ ,  $p = 0.018$ ), correlating strongly with iPTH reduction ( $r = 0.85$ ,  $p < 0.001$ ) (median 26.5,  $p = 0.095$ ). Calcium and phosphate remained stable. Satisfactory increment in height was seen (median 132.5,  $z = -4.0$ ,  $p = < 0.001$ ).

**Conclusion:** There is a high prevalence of low  $25(\text{OH})\text{D}$  in children on dialysis especially among Malay, female and younger children. Native and active vitamin D combination therapy improve bone health parameters.

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**INDICATIONS, FINDINGS AND COMPLICATIONS OF PERCUTANEOUS KIDNEY BIOPSIES IN PAEDITRIC PATIENTS. EXPERIENCE OF A REFERRAL HOSPITAL**

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**Introduction and Purpose:** Kidney biopsy is an essential tool for the diagnosis of many renal conditions. It allows not only optimizing and monitoring the treatment but also establishing a prognosis. The ultrasound-guided performance have reduced the complications rate in both native and transplanted kidney biopsies.

The objective of this study was to analyze the experience in performing kidney biopsies in a tertiary pediatric center, focusing on the main indications, technical procedure, histological findings, success rates and complications.

**Material and Methods:** We performed a retrospective descriptive study of patients < 18 years, who underwent a percutaneous kidney biopsy in the Pediatric Nephrology Unit of our institution, between 2007 and 2021. We analyzed demographic and clinical data, description and complications of the procedure and the histological findings. The variables were expressed in total/percentages (qualitative) and median/range (quantitative).

**Results:** 186 biopsies were performed, 70 in women. The median age was 12.2 years (range 0.8-18.4). One hundred biopsies were performed in native kidneys, 73 in cadaveric grafts and 13 in living-donor grafts. The main indications were steroid-resistant nephrotic syndrome and impaired graft function.

In most cases the 18G needle was used (90.9%) and two shots were given (64.5%). The median number of obtained glomeruli was 17 (range 2 - 73). Conscious sedoanalgesia (midazolam + ketamine) in Pediatric Nephrology ward was performed in 145 cases (78%), with no serious related side effects. Valid material was obtained in 182 cases (97.8%). The main findings were minimal change disease and acute cellular rejection. After biopsy, 34 cases developed macrohematuria and 3 required blood transfusions. There were 4 urinary retentions, 1 suture dehiscence and 1 transplantectomy. Postbiopsy ultrasound was performed only in 23 cases, who previously had developed clinical complications. There were no fistulas, infections or post-hospital discharge complications.

**Conclusions:** Percutaneous kidney biopsy is a safe procedure in pediatric population. Conscious sedoanalgesia in ward setting is safe and valid, avoiding the side effects of general anesthesia. Performing the postbiopsy ultrasound only in selected patients is a valid approach.

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## CAKUT IN CHILDREN BETWEEN 0 AND 4 YEARS, ABOUT PROSPECTIVE STUDY

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**Introduction:** Congenital anomalies of the kidney and urinary tract « CAKUT remains the first etiology of chronic renal insufficiency occurring in children and the initiation of a supleance treatment (Dialysis and transplantation) especially in early childhood, unfortunately we do not have national figures and no study has been made in this direction.

**Materials and Methods:** To determine the etiologic profile of CAKUTs and to assess their frequencies, their epidemiological characteristics, interest of antenatal diagnosis, their methods of taking in charge, as well as the economic cost of the latter. A prospective and descriptive study was carried out from July 2017 to July 2019, including 215 children aged between 0 and 4 years who did not present a malformative syndrome.

**Results:** Idiopathic hydronephrosis as the most common anomaly found in 40.9% of cases, followed by renown refluxing nephropathies posing a huge problem of management given the high frequency of occurrence of urinary tract infections with vesicoureteral reflux in 37.7% and the Mega-ureter in 11.2 cases, or antibiotic therapy was adopted in 48.8% of children for a period of 25.31 months on average in order to reduce the occurrence of urinary tract infections and thus delay the onset of renal failure over time. term which is the most formidable in this category of children. It was also noted that despite the performance of the new ultrasound devices, the prenatal diagnosis of CAKUT was only made in 40% of cases and unfortunately only 12.8% of positive DANs were made early, that is to say at the end of the first and second trimester. Reconstructive surgery is performed in 67% of cases, noting complications in 8.4% of cases and lethality in 0.9%.

**Conclusion:** The care of children with CAKUT can be significantly improved if better awareness of obstetricians about antenatal diagnosis and especially its precocity, and early guidance, thus creating a circuit would allow an overall improvement of CAKUTs in Algeria.

Keywords: CAKUT, Chronic Renal failure, renal replacement therapy, Children.

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## EFFICACY AND SAFETY OF FENOLDOPAM IN TREATMENT OF HYPERTENSIVE CRISES IN CHILDREN: A RETROSPECTIVE STUDY

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**Background and Aim:** Hypertensive urgencies and emergencies are life-threatening conditions associated with high mortality and morbidity. The most recent guidelines provide indications about treatment of these conditions. Fenoldopam is a dopaminergic drug and a possible treatment for hypertensive crises, although no studies on its efficacy on children are currently available.

**Methods:** We retrospectively studied the use of Fenoldopam to treat hypertensive crises in children who were admitted to the PICU and Pediatric Nephrology of Padua Children Hospital between January 2010 and December 2022. Patients aged 1 months to 18 years who presented an increase of systolic or diastolic blood pressure over 95<sup>th</sup> percentile+30 mmHg with or without associated acute symptoms were included in the study.

**Results:** We included 102 Fenoldopam infusions, performed in 74 patients, 60% males. Patients' mean age was 10 years (+5.7) and 80% of children had a previous diagnosis of CKD, while 20% presented AKI. At the time of Fenoldopam initiation, 53 patients already received antihypertensive medications. Indication for Fenoldopam was hypertensive urgency in 77%, while acute neurological symptoms – indicating a hypertensive emergency – were present in 10% of patients. Median duration of infusion was 115 hours (IQR range 76–302 hours), with a mean dose of 0.8 mcg/kg/min (+0.5 mg/kg/min). The treatment was associated with a reduction of initial BP > 10% and > 20% in 64% and 33% of patients, respectively. Non-responders were 36%. Responders were treated with higher Fenoldopam/kg/dose (> 20% 0.45 vs 0.35 mcg/kg/min,  $p = 0.016$ ; > 10% 0.50 vs 0.15 mcg/kg/min  $p = 0.001$ ). The normalization of BP at 24h and 48h occurred in 20% and 34% of cases, respectively. In 77% of patients BP resulted well-controlled at the end of infusion. All patients with a hypertensive emergency presented a resolution of symptoms within 8 hours after the beginning of Fenoldopam infusion. Neurological symptoms secondary to hypertension developed in only two patients during Fenoldopam infusion. Sixty% of patients received > 2 additional anti-hypertensive drugs, and seven patients required a surgical treatment of hypertension (renal artery stenting, nephrectomy). Hypotension occurred in 6%, hypokalemia in 13%, with no further significant adverse events. The ultrasound Doppler renal resistive index performed in 43 patients did not show any variation during the first 72 hours of Fenoldopam infusion.

**Conclusions:** Our study suggests that Fenoldopam is an effective and safe drug in the initial management of hypertensive urgencies-emergencies in children at an initial dose of 0.5 mcg/kg/min, with a low incidence of hypotension and other adverse events.

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## NEUTROPHIL EXTRACELLULAR TRAPS FORMATION IN CHILDREN WITH URINARY TRACT INFECTIONS

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**Introduction:** Urinary tract infection are frequent bacterial infection in childhood. Despite low mortality, UTI, represent the second most common cause of sepsis. Current diagnosis is based on the assessment of clinical picture, examination of laboratory inflammatory activity, and urine sediment along with urine culture. Early diagnosis and treatment might prevent most feared consequences such as hypertension, proteinuria, renal scarring and finally progression to chronic kidney disease. Neutrophils as the first line defender fight against pathogens via different strategies including neutrophil extracellular (NETs) formation. NETs are web-like structures made up of DNA coated with antimicrobial proteins. Besides fighting against pathogens, NETs might act pro-inflammatory and damage surrounding tissue. The aim of this study was to evaluate the role of NETs in children with UTI.

**Methods:** According to inclusion criteria (CRP above 50 mg/l, significant bacteriuria defined as  $\geq 50\,000$  colonies of *E. coli* per mL of catheterized urine, pyuria), 98 children (aged 1.1 years) were enrolled in the study. Fifty healthy children (aged 3.6 years) without previous UTI episodes were enrolled in the control group. Total extracellular DNA (ecDNA) concentrations were determined using fluorescent method (Qubit dsDNA HS Assay Kit, Invitrogen). Nuclear (ncDNA) and mitochondrial DNA (mtDNA) were quantified by real-time PCR. Cathelicidin and myeloperoxidase (MPO) were evaluated using commercially available assays (Human Myeloperoxidase DuoSet Elisa Kit, R&D Systems; LL-37 Human Elisa kit, Hycult Biotech). Moreover, UTI was induced in mice with attenuated NETs formation (n=18) and in normal WT mice (n=15).

**Results:** Despite no significant differences in plasma ecDNA between groups, all measured markers of NETs formation in urine including total ecDNA (4-times), ncDNA and mtDNA (3-times), cathelicidin (2-times) and MPO (19-times) were significantly higher in children with UTI compared to healthy controls. Additionally, there were positive correlations of urinary cathelicidin and MPO with ecDNA in urine ( $r=0.56$ ,  $p\leq 0.001$ ;  $r=0.53$ ,  $p\leq 0.001$ ) and pyuria ( $r=0.27$ ,  $p\leq 0.05$ ;  $r=0.29$ ,  $p\leq 0.05$ ). Further, mice with attenuated NETs formation had higher bacterial dissemination in bladder (20-times) and kidneys (300-times) than WT mice.

**Conclusions:** Elevated urinary concentrations of markers of NETs formation ecDNA, cathelicidin and MPO and their mutual correlations reveal activation and subsequent NETosis of neutrophils in urinary tract. Individual components of NETs might stimulate activation and migration of other immune cells, contributing to formation of "vicious circle". Increased bacterial dissemination in mice with attenuated formation of NETs suggest that their formation is required in an early phase of inflammation.

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**NON-FATAL METFORMIN ASSOCIATED LACTIC ACIDOSIS IN A GIRL WITH NON-DIALYZED CHRONIC KIDNEY DISEASE AND NON-INSULIN DEPENDENT DIABETES MELLITUS**

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**Aims/Purpose:** To report a case of metformin-associated lactic acidosis (MALA), a rare but serious condition, in a 14-year-old girl with non-dialyzed chronic kidney disease (CKD) and non-insulin dependent diabetes mellitus (NIDDM).

**Case Report:** A 14-year-old patient, a known case of CKD, NIDDM and dyslipidemia who had been treated with sodium bicarbonate, metformin and human insulin for 18 months, was brought to her local hospital with shortness of breath, palpitations and vomiting. She was lethargic, afebrile, tachypneic, tachycardic, hypertensive and had Kussmaul breathing. The laboratory investigations showed blood urea nitrogen (BUN) 68.0 mg/dL, creatinine 12.53 mg/dL, Na 141 mEq/L, K 6.7 mEq/L, Cl 92 mEq/L, and HCO<sub>3</sub><sup>-</sup> 5 mEq/L. (Lab tests two months prior to this presentation: BUN 57.2 mg/dL, creatinine 5.26 mg/dL, Na 141 mEq/L, K 4.7 mEq/L, Cl 102.8 mEq/L, HCO<sub>3</sub><sup>-</sup> 21.1 mEq/L). Blood sugar was 55 mg/dL, K 6.7 mEq/L, arterial blood gas pH 7.038, pCO<sub>2</sub> = 5 mmHg, and lactate 19.55 (0.56–1.39) mmol/L. She had acute kidney injury with preexisting CKD, and was treated with intravenous glucose, sodium bicarbonate, respirator support and suppository calcium polystyrene sulfonate, and referred to our hospital. She arrived at our hospital 9 hours later. After examining her referral history, we thought she could have MALA. The initial treatment consisted of adjusting the rates of sodium bicarbonate fluid, glucose, and insulin depending on the levels of serum bicarbonate and glucose. She was also given calcium gluconate, suppository of calcium polystyrene sulfonate, ceftriaxone and respiratory support. While we were considering continuous renal replacement therapy (CRRT)/hemodialysis (HD), at the 7th hour after arrival her laboratory results began to improve, with arterial blood pH of 7.361 and lactate level lowering to 11.7 mmol/L, and the CRRT/HD was put on hold. Her lactate level and serum bicarbonate continued to decline, and both reached normal levels at the 25th hour.

**Conclusion:** MALA is a rare but life-threatening condition in NIDDM patients using metformin. Metformin should be adjusted carefully in patients with renal impairment or other current illnesses, particularly if they have gastrointestinal symptoms or other conditions that can cause hypovolemia. In non-CRRT/HD situations, optimal supportive care, including adequate reduction of serum potassium, alkali therapy and respiratory support, and avoiding hypotension will be able to achieve a favorable result within 24 hours.

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## COMPERISON EVALUATION OF URINARY MARKERS IN CHILDREN WITH OBESITY

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**Aims/Purpose:** Obesity may lead to kidney injury in adults. There are now certain diagnostic markers for this injury in the early stages. Purpose of our study was to study urinary kidney injury markers: KIM-1, NGAL,  $\beta$ 2-m, IL-18 in healthy children and patients with obesity.

**Methods:** We investigated 50 healthy children (control group) aged 10 years [10-14] and 34 patients with exogenously constitutional obesity at the same age. All patients had BMI > 2 SDS. Obesity of 1st stage had 12 children (35.3%), 2nd stage – 13 patients (38.2), 3d stage – 8 children (23.5%) and 4th stage was diagnosed in 1 boy (2.9%). Control group of children as well as children with obesity had no any kidney diseases. They have normal parameters of urine, blood creatinine, ultrasound examination of kidney. Urinary markers measured by ELISA methods. The results were presented as median and interquartile range – Me [Q1; Q3]. Comparison between groups was performed using Kolmogorov-Smirnov test.

**Results:** In children with obesity urinary KIM -1/UCr was significantly higher than in control group of children: 1442.0 pg/mg [856.5- 2433.3] and 135.9 pg/mg [60.0- 248.7],  $p < 0.001$ . Level of NGAL /UCr also was higher in patients -1.27 ng/mg [0.46- 9.57], in healthy children it was 0.17ng/mg [0.03- 0.8],  $p < 0.01$ . Parameter of IL-18 /UCr was 0.07 pg/mg [0.04- 0.1] in children with obesity and in control group – 0.04 pg/mg [0.03- 0.05],  $p < 0.005$ . Urinary  $\beta$ 2-m /UCr was not differ in patients and healthy children: 4.1 mkg/mg [1.54- 9.68] and 4.6 mkg/mg [1.75- 9.73],  $p > 0.05$  correspondently.

**Conclusion:** Urinary KIM-1, NGAL, IL-18 may have diagnostic value for functional changes in the tubular system of the kidneys in children with obesity. Urinary  $\beta$ 2-m may be changed only for late stages of kidney involvement connected with obesity.

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## INTRACARDIAC THROMBUS IN A CHILD WITH NEPHROTIC SYNDROME

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**Introduction:** Nephrotic syndrome (NS) is defined by nephrotic range proteinuria, hypoalbuminemia ( $< 25$  g/L), edema and hyperlipidemia. The most common cause of NS in children is minimal change disease. Nephrotic syndrome seen in the first 3 months of life is defined as congenital nephrotic syndrome (CNS) and it is usually due to a genetic defect. Loss of coagulation factors cause hypercoagulability and thromboembolic complications can be seen in NS patients. Renal-vein thrombosis, deep vein thrombosis and pulmonary embolism are common thromboembolic complications. Intracardiac thrombus is a very rare and life-threatening complication of NS. We present a case of intracardiac thrombus in a child with CNS.

**Case:** A 4-year old female patient with nephrotic syndrome and end stage kidney disease (ESKD) admitted with respiratory distress. She is a refugee patient who has been on peritoneal dialysis for 2 years and her treatment compliance was poor due to social problems. On physical examination she had minimal pretibial oedema, her oxygen saturation was 95%, respiratory rate was 18/min, heart rate was 98/min with 2/6 systolic murmur. Chest X-ray showed cardiomegaly, bilateral paracardiac infiltrations with atelectasia on the right lung. Rhinovirus was weak positive on nasal swab test. Laboratory exam revealed urea 177 mg/dL, creatinine 6.78 mg/dL, albumin 2.8 g/L, Hb 7.4 g/dL. After peritoneal dialysis with hypertonic fluids, her volume status and respiratory distress improved. Echocardiography revealed left ventricular hypertrophy with failure of mitral valve and dilatation of left heart, ejection fraction was 56%. Troponin T 106 was ng/L, Pro-BNP was 22.633 pg/ml. Milrinone treatment was started. On daily echocardiographic examination, left atrial thrombus was detected on the 4. day of the treatment. Enoxaparin sodium treatment was started. PT, PTT, INR levels were normal. Anti cardiolipin IgM, IgG levels and Factor 5, 8 levels were normal. After 1 month with anticoagulant therapy, thrombus was dissolved successfully without need for surgical intervention and cardiac functions improved.

**Discussion:** The hypercoagulability in NS is multifactorial. Loss of anti-coagulation factors with urine, corticosteroid use, immobilization, associated infections are the main reasons for thromboembolic events. The incidence of thromboembolic complications is 3% among children. Majority of intracardiac thrombus can be treated with anticoagulants and thrombolytic therapies but if there is high risk of detachment and embolization surgical interventions may be needed. On daily echocardiography by checking the diameter and mobility of the thrombus and cardiac functions, along with effective peritoneal dialysis, we treated our patient conservatively.

**Conclusion:** Intracardiac thrombus is an infrequent but serious complication of nephrotic syndrome in children. It can be clinically silent, echocardiographic examination should be done in patients with NS especially in children with ESKD during infections.

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## THE RATE OF PROGRESSION OF CHRONIC KIDNEY DISEASE IN CHILDREN TO THE END STAGE AND AFFECTING FACTORS

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**Aims/Purpose:** Chronic kidney disease (CKD) is a worldwide health problem which incidence and prevalence keep going to increase. Risk factors for progression of CKD are defined as modifiable and non-modifiable. The aim of this study is to determine the risk factors for progression of chronic kidney disease in children.

**Material and Methods:** 70 children aged 0–18 years, with at least two years of follow-up and stage 2–4 chronic kidney disease were included in the study. CKD progression was defined as about more than %25 decline in glomerular filtration rate in two years follow-up. Patients were divided in to two groups as progressive and nonprogressive. In these two groups modifiable and nonmodifiable progression risk factors were analyzed. Demographic characteristics and laboratory test results were obtained from patient medical records.

**Results:** There were 29 (41%) female and 41 (59%) male in the study. Mean age of the patients was  $97.8 \pm 62.4$  months. This study is consisted of forty one progressed patients and twenty nine non-progressed patients. Late age of disease onset and presence of metabolic acidosis were found to be significantly risk factors affecting progression. Moreover, there was no statistically significant difference in gender, primary disease, chronic kidney stage, registration glomerular filtration rate, anemia, bone mineral metabolism disorders, hypertension, dyslipidemia, the presence of proteinuria and growth between two group ( $p > 0.05$ ).

**Conclusions:** Our findings showed that late age of disease onset and the presence of metabolic acidosis are associated with the progression of chronic kidney disease in children.

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**EVALUATING KIDNEY INJURY AFTER ACUTE PYELONEPHRITIS: GUIDELINES CHANGED, WHAT ABOUT THE RESULTS? A RETROSPECTIVE SINGLE-CENTER STUDY**

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**Aims/Purpose:** In the last decade, guidelines for pediatric screening after an episode of acute pyelonephritis have tended to limit the performance of dimercaptosuccinic acid (DMSA) scan to screen for kidney scar formation. This retrospective study aims to evaluate the cases of scarring when DMSA was performed after each episode of acute pyelonephritis compared to the current rate where DMSA scan is performed only in cases with abnormal ultrasonography, high-grade vesicoureteral reflux (VUR), or in atypical and recurrent urinary tract infections (UTIs).

**Methods:** We conducted a retrospective study of two periods, 2014 to 2015 with 2021 to 2022, comparing the difference in indications and the cases of kidney scarring detected with a DMSA scan, performed in the Nuclear Medicine Department of our hospital. Details of patients' history and diagnostic ultrasound before the DMSA scan were also included.

**Results:** According to the American Academy of Pediatrics (AAP), ultrasound evaluation was done after the first UTI. During the 2014–2015 period, 111 DMSA scans were performed, and 79 of them were performed, approximately, 6 months after acute pyelonephritis. In 37 of 79 cases (~46.8%), VUR ≥ grade 3 was detected with voiding cystourethrography. In 22 cases (~27.8%), kidney scars were detected. During the 2021–2022 period, 57 DMSA scans were performed, and 23 of them were performed, approximately, 6 months after acute pyelonephritis. In 21 of 23 cases, VUR ≥ grade 3 was detected with voiding cystourethrography. In 16 cases of 23 (~69.6%), kidney scars were detected with a DMSA scan.

**Conclusions:** Following older guidelines which included performing DMSA scan after each episode of acute pyelonephritis, about three times as many scans were conducted to detect a much smaller percentage of scar cases (27.8% vs 69.6% accordingly), but finally the same number of kidney scarring cases in equal time periods were noted. According to international guidelines, detection of kidney scarring is achieved to a satisfactory degree, omitting DMSA scans in the acute phase of a UTI where it is now not recommended, avoiding the implications of isotope exposure, injections, staff time and expense.

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## ACUTE PYELONEPHRITIS IN CHILDREN: PREDICTORS OF RECURRENCE AND EFFECTIVENESS OF ANTI-RELAPSE THERAPY

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**Introduction:** Acute pyelonephritis (APN) is considered one of the most serious bacterial illnesses in childhood. The episode of APN and its recurrence are associated with the development of nephrosclerosis, arterial hypertension and chronic kidney disease. The aim of this study to determine the predictors of recurrence of APN in children and evaluate the effectiveness of anti-relapse therapy.

**Material and Methods:** A retrospective analysis of 563 medical records of inpatient patients with acute pyelonephritis in the 2nd Children's Hospital in Minsk for the period 2017-2021 was carried out. All children were divided into 2 groups: 1st – < 2 years old (n = 225) with a median age of 0.6 (IQR 0.3; 1.1) year and 2nd – 2-17 years old (n = 338) with age of 9.1 (4.4; 15.3) years. Each group was divided into subgroups: with and without recurrence. Anti-relapse therapy was provided in 96% of patients of group 1 (the drug of choice in 69.4% – cefuroxime) and 42.9% of the second (furazidine in 70.4%). Voiding cystourethrography was performed in 177 (78.6%) patients in group 1 and 84 (24.8%) in group 2. Vesicoureteral reflux (VUR) was detected in 57 (32.2%) children in group 1: 1-2 degrees – in 36 (20.3%) and 3-5 degrees – in 21 (11.9%), in group 2 – in 28 (33.3%): 22 (26.2%) and 6 (7.1%) respectively.

**Results:** Recurrence of APN was observed more often in children of group 1 compared with group 2: 30 (13.3%) and 28 (8.3%) (p = 0.053). The use of intravenous antibiotics alone for the first episode of pyelonephritis was more frequently associated with relapse compared with a stepwise therapy: intravenous then oral antibiotics intakes in both age groups: 1st – 32.0% vs. 11.0% (p = 0.008) and 2nd – 22.4% vs. 5.8% (p = 0.001) respectively. VUR was associated with relapse: in subgroups of the 1st group with relapse – 57.7% patients had VUR and without relapse – 27.8% (p = 0.003) but not in the 2nd group: 42.1% vs. 30.8% (p = 0.36) respectively. VUR with higher degrees (3-5) was associated with recurrence more frequently than VUR with low degrees (1-2): in the 1st group – 43% vs. 17% (p = 0.030) and in the 2nd – 67% vs. 18% (p = 0.038). Anti-relapse therapy did not affect the recurrence rate both age group: in the 1st – 13.0% with vs. 22.2% without prevention (p = 0.34), and in the second: 10.3% vs. 6.7% respectively (p = 0.23).

**Conclusion:** Our study confirms the previously identified dependence of the presence of vesicoureteral reflux with the development of relapse of acute pyelonephritis in children. Intravenous antibiotic therapy is more often associated with a response than stepwise: intravenous with a change to oral. It was also confirmed that there was no connection between the development of recurrence and the implementation of anti-relapse antibiotic therapy.

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## SOLITARY FUNCTIONING KIDNEY IN CHILDREN : EPIDEMIOLOGY, RISK FACTORS AND COMPLICATIONS

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**Aim/Purpose:** The aim of this study is to determine the epidemiology, risk factors, evolution and complications of solitary functioning kidney (SFK) in children.

**Methods:** A retrospective study carried out in the pediatric department of Sahloul's hospital in Sousse, all children diagnosed with solitary functioning kidney over the period dating between 2010 and 2023 were included in the study.

**Results:** 17 patients were diagnosed with SFK over a period of 13 years. 67% of the them were male. Consanguinity rate was of 31.3% and 25% of patients had a family history of chronic kidney disease (including SFK (5.8%), polycystic kidney disease (5.8%), renal lithiasis (11.7%), nephrotic syndrome (5.8%)). All patients were born from pregnancies held without any dysgravidia, without recourse to nephrotoxic drugs, with a full-term delivery in 94% of cases and normal birth weight. 37.5% of the patients presented episodes of urinary tract infection which were recurrent for 17.6% of them. SFK was associated in 65% of cases with anomalies of the kidney and urinary tract and 11.6% of patients had a history of congenital heart disease associated to SFK. Single congenital kidney was the most frequent subtype (68.8% of the cases), it was discovered in the postnatal period in 37.5% of cases, the mean age at onset was equal at 7 months with extremes ranging from 15 days to 14 years. Acquired single kidney was observed in 31.3% of the cases, most common etiology was urethra-vesical reflux (23.5%). 88% of patients had compensatory renal hypertrophy at the time of diagnosis. 17.6% of patients presented with renal failure at diagnosis (eGFR less than 90 ml/min). During the course of the disease, 11.7% of patients developed glomerular proteinuria with a delay of 4 years from the time of diagnosis, 5.8% of them developed hypertension and 17.6% progressed to end-stage renal failure, renal replacement therapy was required in two thirds of these cases.

**Conclusion:** Pediatric patients with SFK are renal anomalies that deserve special attention. Monitoring for signs of kidney injury is therefore recommended throughout life to manage eventual complications and improve the prognosis of patients.

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REVERSIBLE RENAL IMPAIRMENT DUE TO ACQUIRED HYPOTHYROIDISM IN A CHILD WITH ADCK3 MUTATION

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**Background:** The effect of thyroid metabolism on renal function in children has rarely been mentioned in the literature. It is known that primary hypothyroidism is associated with a consistent increase in serum creatinine levels. Thyroxine replacement therapy completely restores euthyroid status and kidney function. So, patients with moderately reduced kidney function should be carefully evaluated for signs and symptoms of hypothyroidism and thyrotropin levels.

**Case Report:** A 5-year-old boy was determined to have ADCK3 mutation during screening upon diagnosis of coenzyme Q deficiency due to ADCK3 mutation in his brother. At 9-year of age he presented with edema in lower extremities and elevated serum creatinine [1.23 mg/dl (normal 0.5-0.75)] and decreased creatinine clearance (44 ml/min/1.73m<sup>2</sup>). At the same time serum T4 was decreased and TSH was elevated (Table 1). Renal ultrasonography and tubular functions were normal; there was no proteinuria. The patient was commenced on levothyroxine treatment with gradual improvements in thyroid and renal functions. Four months later, all parameters were totally normalized.

Table 1: Serial serum creatinine, T4 and TSH levels during thyroxine treatment

	Initial values	6th week	2nd month	3rd month	4th month
TSH <sup>1</sup> (mIU/L)	> 48.6	> 47.6	> 47.6	17	2.2
FT4 <sup>2</sup> (ng/dL)	0.25	0.37	0.70	0.78	1.21
Creatinine (mg/dL)	1.23	0.84	0.75	0.55	0.43
Dose of levothyroxine (µg)	12.5	25	37.5	50	50

<sup>1</sup>Normal levels 0.38-5.33; <sup>2</sup>Normal levels 0.5-1.51

**Conclusion:** Renal injury in association with ADCK3 mutations has not been reported. Decreased creatinine clearance in association of hypothyroidism and improvement of renal function during treatment with thyroxine suggest that renal injury in this patient is secondary to hypothyroidism. Renal impairment due to hypothyroidism has been attributed to hypothyroid myopathy, hemodynamic changes, decreased myocardial contractility and cardiac output. As a result, serum TSH levels should be checked in patients with unexpected renal impairment even in the absence of other symptoms of hypothyroidism.



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INVESTIGATING THE IMPACT OF PHYSICAL ACTIVITY ON MENTAL HEALTH: A SYSTEMATIC REVIEW AND META-ANALYSIS

Test 11, Test 22

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**Aims/Purpose:** Background: Physical activity has long been associated with numerous health benefits. In recent years, the focus has shifted towards investigating the impact of physical activity on mental health outcomes. While several studies have examined the relationship between physical activity and mental health, the results have been mixed. This systematic review and meta-analysis aims to investigate the impact of physical activity on mental health outcomes.

**Methods:** We conducted a comprehensive search of electronic databases including PubMed, EMBASE, and PsycINFO from inception to September 2022. We included studies that examined the relationship between physical activity and mental health outcomes in adults. The quality of the included studies was assessed using the Cochrane Risk of Bias tool. We performed a meta-analysis using a random-effects model to estimate the pooled effect size.

**Results:** A total of 35 studies met the inclusion criteria, including 15 randomized controlled trials and 20 observational studies. The studies included a total of 12,572 participants. The pooled effect size showed a significant association between physical activity and mental health outcomes ( $p = 0.001$ ). Specifically, physical activity was associated with a reduction in symptoms of depression (Hedges'  $g = -0.46$ , 95% CI:  $-0.61$  to  $-0.31$ ) and anxiety (Hedges'  $g = -0.39$ , 95% CI:  $-0.55$  to  $-0.23$ ). Physical activity was also associated with improved quality of life (Hedges'  $g = 0.36$ , 95% CI:  $0.22$  to  $0.51$ ).

**Conclusion:** Our findings suggest that physical activity is associated with improved mental health outcomes, including a reduction in symptoms of depression and anxiety, and improved quality of life. These findings have important implications for the development of interventions aimed at promoting physical activity as a means of improving mental health outcomes. Future research should focus on investigating the optimal types, duration, and intensity of physical activity that are most effective for improving mental health outcomes.

Clones	d/4 with	d/4 without	d/7 with	d/7 without
IRCA 130	1678 A a	1829 A a	1387 B a	1386 B a
IAC 41	1811 A a	1729 A a	1771 A a	1229 B a
IAC 35	1819 A a	1579 A a	1653 A a	1764 A a
PB 235	1709 A a	1578 A a	1729 A a	1170 B a
IAC 15	1527 A a	1564 A a	1442 A a	1386 A a
IRCA 18	1562 A a	1433 A a	1551 A a	1372 A a
PB 260	1528 A a	1355 A a	1463 A a	1390 A a
IRCA 111	1368 A a	1257 A a	1603 A a	1254 A a
RRIM 600	1478 A a	1169 B b	1636 A a	1205 B a
PB 330	1311 A a	1056 B b	959 B b	762 a B
PB 252	1041 A b	1000 A b	824 A b	828 A b
RO 38	610 A b	455 A c	390 A c	402 A b

Means followed by same uppercase letter in the line and lowercase letter in the column do not differ by Scott-Knott test ( $\alpha = 0.058$ )

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**NEONATAL HYPOCALCEMIA AND MATERNAL HYPERCALCEMIA: EXPLORING THE POTENTIAL CONNECTION TO PARATHYROID ADENOMA AND CASR MUTATIONS**

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**Aims/Purpose:** This study aims to investigate the relationship between neonatal hypocalcemia and maternal hypercalcemia, and to explore potential genetic predispositions related to parathyroid adenoma and CaSR mutations in mothers.

**Methods:** Neonates presenting with late-onset ( $\geq 3$  days) hypocalcemic tetany or seizures, low serum total calcium, high serum phosphorus, and inappropriately low or normal iPTH levels suggestive of hypoparathyroidism were prospectively enrolled. Hypomagnesemia, high phosphate intake, and kidney function impairment were excluded. Following enrollment, all mothers were evaluated for potential causes of neonatal hypocalcemia.

**Results:** Seven full-term newborns (six males, one female) and their mothers were enrolled. All newborns were diagnosed with transient hypoparathyroidism secondary to maternal hypercalcemia. To investigate the cause of maternal hypercalcemia, maternal serum calcium, phosphorus, iPTH levels, urine calcium, urine creatinine, and parathyroid scans were assessed. Six mothers were found to have parathyroid adenoma, and one exhibited low urine calcium excretion, subsequently confirmed to have a CaSR loss-of-function genetic mutation. All newborns were treated with oral calcium gluconate combined with cholecalciferol or calcitriol. After approximately 3 months of treatment, serum calcium and phosphate levels normalized. Following parathyroidectomy in mothers with parathyroid adenoma, serum calcium levels normalized, but elevated iPTH levels persisted for months. The mother with the CaSR loss-of-function mutation exhibited persistent high iPTH levels.

**Conclusion:** This study underscores the importance of evaluating maternal calcium homeostasis in cases of neonatal hypocalcemia and highlights a potential genetic association between neonatal symptoms and maternal parathyroid adenoma and CaSR mutations. Further research is warranted to understand the genetic basis and optimize management strategies for both conditions.

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## EVALUATING RISK FACTORS FOR CHRONIC KIDNEY DISEASE IN CHILDREN WITH SICKLE CELL DISEASE

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**Aims/Purpose:** Sickle cell anemia is a common genetic disorder resulting from a simple base pair substitution in the  $\beta$ -globin gene at position 6, resulting in a change from glutamic acid to valine. Forming abnormal Hb S. Over time children with sickle cell anemia at risk of developing sickle cell nephropathy leading to CKD and ESRD in early adulthood. We evaluated Risk factors of CKD in children with SCA.

**Methods:** We evaluated 69 children with Sickle cell Disease age 1-14 years attending outpatients' pediatric hematology clinic. Laboratory measurement included CBC, Reticulocyte count, renal panel and Serum Cystatin C. Glomerular filtration rate estimated using serum creatinine Modified Schwartz formula and Serum Cystatin C using filler equation. Urine albumin/cr ratio measured for all subjects.

**Results:** Total number of patients studied were 69 patients. Mean age was 8.5 years with ( $\pm$  3.6 SD). Mean serum Hb 9.0 gm/dL ( $\pm$  0.62 SD), plts  $336 \times 10^9$  /L ( $\pm$  157 SD), Wbcs  $9.5 \times 10^9$  /L ( $\pm$  3.3 SD) and reticulocyte 7.8% ( $\pm$  4.3% SD). There was Highly significant difference between Mean e-GFR Cyst-C Compared to e-GFR Cr 122 ml/min Vs 161 ml/min,  $p < 0.05$ . Micro-albuminuria is detected in 12 (17%) of 69 Children with SCA.

**Conclusion:** Estimation of GFR using serum Cr overestimate the GFR in children with sickle cell anemia Micro-albuminuria a Manifestation of sickle cell nephropathy is present in children 1-14 years and need follow up in this age group.

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### CLINICAL CASE OF A PATIENT WITH HNF1B-ASSOCIATED NEPHROPATHY

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**Introduction:** HNF1b is an associated multisystem disease with autosomal dominant inheritance due to heterozygous mutations in hepatocyte nuclear factor 1beta (HNF1B), manifested by lesions of the liver, pancreas, kidneys, neurological disorders and anomalies in the development of the reproductive system. HNF1B nephropathy is an umbrella term for various phenotypes of kidney disease, including congenital malformations of the kidneys and urinary tract (CAKUT), tubular disorders, and cystic kidney disease that result from a heterozygous mutation of the HNF1B gene located on chromosome 17q12 and encoding a transcription factor HNF-1 $\beta$ .

**Materials and Methods:** A 6-year-old girl was examined in the Nephrology Department of the Veltishchev Institute of Russian National Research Medical University named by N.I. Pirogov, where she underwent a complete clinical, laboratory and genetic examination.

**Results:** As a result of molecular genetic examination, 2 heterozygous mutations of the PKHD1 gene and a heterozygous mutation of HNF1b, leading to the p.Ile125Thr amino acid substitution, were identified. The child has diffuse changes in the renal parenchyma, including cystic formations in the cortical and medullary layers, the presence of an aberrant renal artery on the left, a decrease in the volume of the kidneys, and bilateral reflux nephropathy. There is no urinary syndrome, an increase in beta-2 microglobulin in the urine up to 2131.8 mcg/day, the glomerular filtration rate for cystatin C is 69 ml/min/1.73m<sup>2</sup>, which corresponds to stage II of chronic kidney disease. In the study of the hormonal profile of the blood, a decrease in insulin to 3.4 mIU/ml, c-peptide to 0.74 ng/ml was revealed. Also, the child has valgus deformities of the lower extremities as a result of osteoporosis. Currently, renoprotective therapy with ACE inhibitors is being carried out with a positive effect.

**Conclusion:** This observation confirms that all patients with early-onset combined kidney damage should undergo a comprehensive clinical examination, including molecular genetic methods, which is important for determining the tactics of patient management and prognosis of the disease.

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## TRANSITION OF HYPERTENSIVE CHILDREN AND ADOLESCENTS FROM PEDIATRIC TO ADULT CARE: INSIGHTS FROM THE ADULT PERSPECTIVE

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**Aims/Purpose:** Transition usually implies a progressive process from paediatric care responsibility to shared paediatric and adult care providers. In the light of increasing awareness of hypertensive youth that frequently present with comorbidities and secondary causes of HTN we aimed to assess transition practices from paediatric to adult health care among European Society Hypertension (ESH) Excellence Centres from the adult hypertension specialists' perspective.

**Methods:** A 22-question survey was sent out to the leaders of all ESH Excellence Centres. Only one answer per excellence centre from the corresponding leader was permitted. The survey was launched in July 2022 and 3 reminders were sent within 4 weeks intervals.

**Results:** Forty-nine ESH Excellence centres leaders responded to the survey, almost all (98%) affiliated in hospital settings. Specific transition clinics do not exist in 64% of the settings. The median number of young adults diagnosed with hypertension in childhood who are transferred per year from paediatric clinics to ESH Excellence Centres is 5 (IQR 2–13). Chronic kidney disease and renovascular disease are the most common causes of secondary hypertension. In 66% of the centres, the transition process is limited to written medical history (transfer letter) from paediatric clinics and only 23% reported coordinated visits at paediatric and adult clinics. The main criterion for patient transfer to adult clinics is patient age (87% of the centres) with transfer age being at 18 years in 75% of the centres, while 20% reported transfer ages younger than 18 years. In only 9% of the centres patient self-management skills are assessed to decide readiness for transfer to adult clinics. In 84% of the centres lead adult physicians are involved in the transition process. ESH 2016 guidelines hypertension staging scheme in children and adolescents blood pressure is used in 52% of the centers, while 21% use the adult ESH/ESC 2018 staging scheme to assess blood pressure status in children and adolescents. Adherence is considered as one of the main challenges during transition process as reported by 68% of the centres, lifestyle by 66% as well as patients' lack of understanding of their condition by 50%, and psychosocial issues by 50% of the centres. Fifty-one % of the centres modify treatment after transfer according to adult recommendations, 93% for uncontrolled hypertension and 75% to change in single (combination) pill.

**Conclusion:** Coordination and communication between paediatric and adult units is needed for effective transition into adult health care. Upcoming adult and paediatric hypertension management guidelines need to address challenges and differences between paediatric and adult practices.

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## JUVENILE NEPHRONOPHTHISIS IN 2 SIBLINGS PRESENTING WITH ESRD IN YOUNG AGE

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**Aims/Purpose:** Case report of 2 siblings from non-consanguineous parents who presented with end stage renal disease (ESRD) early in their life secondary to Juvenile Nephronophthisis (NPHP).

**Results:** 2-year, 8-month old girl was admitted for severe non-hemolytic anemia. On admission she was pale. Respiratory rate was 70/min, heart rate 101/minute, spO<sub>2</sub> 93%. Blood pressure (BP) was 147/98mmHg. She had no hepatosplenomegaly. No edema and no skin rash. She was short and skinny (Height Z-score -1.8). Her urine output was 1 ml/kg/hr, which was normal. Initial laboratory tests showed hemoglobin of 57 g/L, WBC 9.8, creatinine 480 umol/L, urea 42 mmol/L, albumin 35 g/l. She also had a severe metabolic acidosis (pH 7.27, HCO<sub>3</sub> 11, pCO<sub>2</sub> 23). Her Urinalysis showed nephrotic range proteinuria (protein/creatinine 1.07 g/mmol), low specific gravity (1.010). Urine microscopy was negative. eGFR (Schwartz formula) was 8 ml/min/1.73m<sup>2</sup>. Her renal US showed size of both kidneys at the upper limits of normal, increased echogenicity of the parenchyma with loss of corticomedullary differentiation. No mass or cystic lesions were noted. Kidney biopsy showed 13 of the 25 glomeruli were completely sclerosed. There was focal segmental fibrosis, increased mesangial cells and mesangial matrix. Some glomeruli showed periglomerular fibrosis. There was moderate to severe patchy atrophy of tubules, some groups of tubules show microcystic dilatation of the lumen. Interstitial fibrosis was affecting at least 50% of the cortex. Electron microscopy: hypertrophy of the podocytes. Some of the glomerular basement membranes showed lamellations. There were no electron dense deposits. Working diagnosis was collapsing FSGS. Our patient started hemodialysis and was later successfully transplanted. She was enrolled in the research study which included whole exome sequencing. This genetic exam revealed mutation in INVS gene which was in keeping with diagnosis of Juvenile Nephronophthisis. Her younger brother presented with similar symptoms two years later and his genetic testing showed the same mutation. He also received renal transplant. Renal function of both sibling is normal.

**Conclusion:** NPHP is a rare AR disease, most likely the most common cause of ESRD in young children and is likely underdiagnosed. Patients with NPHP typically have a “bland” urinalysis without evidence of proteinuria, hematuria, or cellular elements until the late stage, when proteinuria may develop into secondary glomerulosclerosis. We suggest that all infants and toddlers with unclear cause of ESRD should be tested for NPHP.

# POSTER SESSION 2C

## CAKUT

Sa-P 191

## A FAMILIAL CASE OF RARE STAR MULTIGENIC SYNDROME

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**Aims/Purpose:** STAR syndrome is a rare monogenic disorder manifesting itself by a combination of malformations: foot syndactyly, telecanthism, anal-genital anomalies and renal malformations. The disease in female probands is caused by heterozygous mutations in the CCNQ gene (OMIM #300708), leading to a complete loss of functional activity of the protein product, cyclin M. Impaired activation of cyclin-dependent kinase CDK10 leads to a defect in the formation of the CDK10/CycM complex, which phosphorylates and controls the stability of the ETS2 oncoprotein.

**Methods:** The girl was examined in the Department of Nephrology of the V.E. Veltishev Research Institute of Pediatrics, N.I. Pirogov Russian Medical University, where she underwent a complete clinical, laboratory, and genetic examination.

**Results:** Molecular genetic study revealed a 5-bp deletion in exon 2 of the CCNQ gene c.160\_164del, p.(Ile53Profs\*2), resulting in a shift in protein reading frame starting at amino acid 53, and premature termination of protein product translation right after that. Phenotypic features of the disease manifested as: telecanthism, high back of the nose, complete syndactyly of the 3rd, 4th and 5th toes of the left foot, partial syndactyly of the right foot and clinodactyly of the little fingers. The child also has: aplasia of the left kidney, Fraley syndrome on the left, megaureter, detrusor-sphincter dyskergia, bladder diverticulum, reduced glomerular and tubular renal function with the development of chronic kidney disease stage II. In the mother of the girl, hypoplasia of the left kidney, hypoplasia of the labia minora, syndactyly and telecanthism were noted. Phenotypic differences in this mother-daughter pair were normal indicators of physical development and absence of anogenetic malformations. The study of X chromosome inactivation in both the daughter and the mother revealed a non-random inactivation of a common allele with the number of CAG repeats of the AR gene equal to 24.

**Conclusion:** This observation confirms that the core of the clinical picture of the STAR syndrome is a complex of facial microanomalies, syndactyly of the feet, anal-genital and urinary anomalies. The phenotypic features of this case were the absence of short stature and anus atresia typical of STAR syndrome, probably due to differences in point mutations of the CCNQ gene or its deletion.



Sa-P 192

**THE NUT WAS CRACKED: A PECULIAR CASE OF PERSISTENT HEMTURIA IN AN OMANI CHILD**

**Dana Al Nabhani<sup>1</sup>, Munya Alshikh Abubakar<sup>2</sup>, Nidaa Al Naamany<sup>2</sup>, Saleh Baawain<sup>3</sup>, Mohammed Abdalnasser Obaid<sup>1</sup>**

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**Aims:** Hematuria is a common presentation in children. Detailed history, examination and proper investigations usually yields the diagnosis. Vascular causes such as nutcracker syndrome (NCS) is one of the least frequent causes of hematuria. It is overlooked due to the non-specificity of its symptoms. Our aim is to describe the dilemma in a child presenting with chronic painless microscopic hematuria. Also the clinical features and Investigations that helped in revealing the diagnosis are described. Finally we aim to shed light on this rare clinical entity to increase the awareness and prevent over investigation.

**Methods:** A 5-year-old boy who was evaluated for chronic persistent painless microscopic hematuria. After the routine hematuria work up a cause could not be identified.

**Results:** Upon specific request to screen for NCS by means of Doppler Ultrasound (DUS) it was found that the Left Renal Vein (LRV) was significantly compressed at the level of the superior mesenteric artery (SMA), which was suggestive of NCS. A CT scan confirmed the diagnosis.

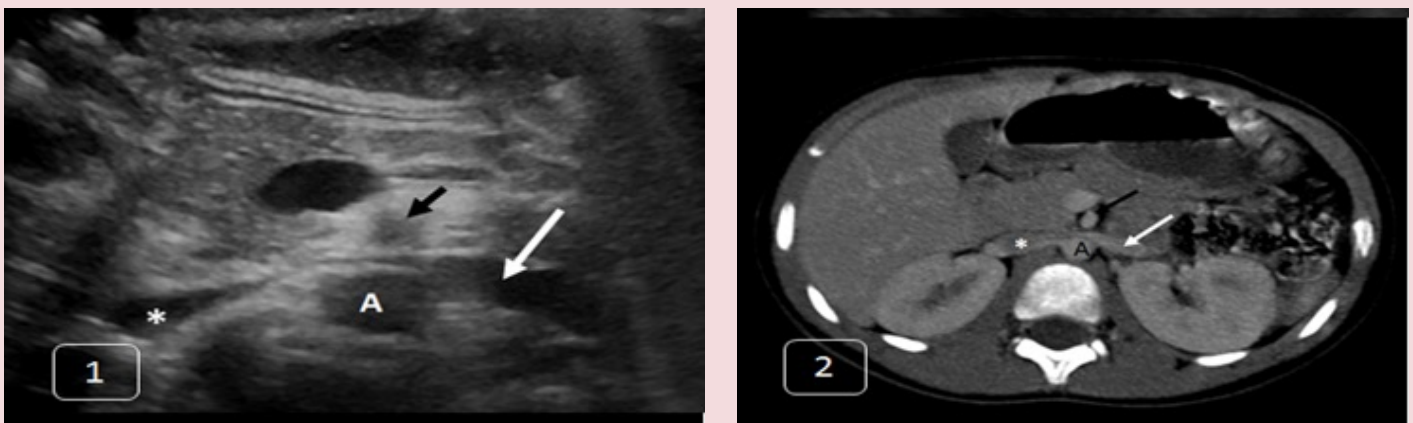


Figure 1: Corresponding axial section of abdominal ultrasound (1) and contrast enhanced CT (2) through the left renal vein (white arrow) as it passes to the inferior vena cava (\*) between the superior mesenteric artery (black arrow) and the abdominal aorta (A). The left renal vein is severely compressed between the superior mesenteric artery and the abdominal aorta.

**Conclusion:** Nutcracker Syndrome is a rare cause of persistent hematuria. This vascular entity should be considered in the differential diagnosis if a detailed medical history, physical examination and extended investigations yielded no clear diagnosis. Presentation can be with asymptomatic microscopic hematuria or other nonspecific symptoms as abdominal pain. Imaging with a renal doppler ultrasound aimed to specifically look for NCS and CT scan are required for making a diagnosis. Management is supportive and depends on the severity of symptoms.

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**BIMODAL, CONTINUOUS AND NON-INVASIVE ASSESSMENT OF LOWER URINARY TRACT FUNCTION IN CHILDREN – PRESENTATION OF PROJECT OBJECTIVES AND PRELIMINARY RESULTS**

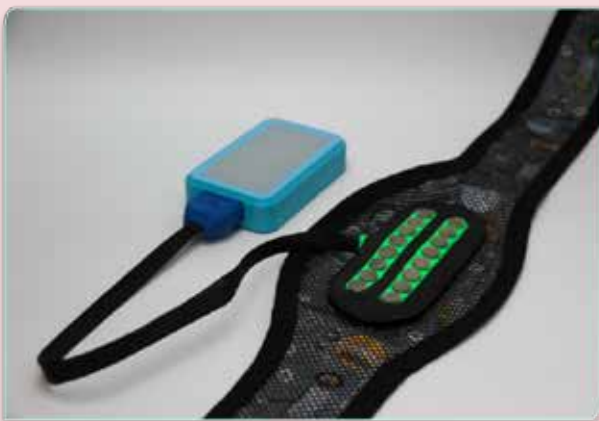
**Marcin Tkaczyk<sup>1</sup>, Marek Krakós<sup>1</sup>, Małgorzata Stańczyk<sup>1</sup>, Monika Pawlak-Bratkowska<sup>1</sup>, Krzysztof Strzecha<sup>2</sup>, Wołodymyr Mosorow<sup>2</sup>, Tomasz Rymarczyk<sup>3</sup>**

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**Aims:** Non-invasive diagnosis of urinary tract function in children is a challenge for the clinician. The demand for such diagnostics applies both to patients with anatomical urinary tract damage – such as neurogenic bladder and lower urinary tract defects – but also to children with purely functional disorders without organic damage. To date, non-invasive methods for monitoring urinary tract function include micturition diary assessment, uroflowmetry studies and ultrasonography. These are inaccurate, dependent on many variables and provide data over a short time period. The invasive method, urodynamic testing, due to its invasive nature, has a narrow application in practice and at the same time has the character of a short examination and the result is highly dependent on the experience of the person performing it.

The aim of this presentation is to present assumptions and the initial stage of implementation of the design and manufacture of a diagnostic device providing information on the function of the child's urinary tract in a non-invasive and continuous manner over a period of several hours.

**Methods:** The design and manufacturing phase of a portable device recording electrical potentials from the child's pelvis and simultaneously recording ultrasound results was carried out. A design and prototype of a sensor mounting undergarment was developed.



**Results:** To date, a device recording bioelectrical and ultrasound activity data with a set of electrodes and ultrasound sensors has been designed and fabricated. Pilot recordings of the bioimpedance test have been performed in a group of 10 volunteers recording the results at time intervals of 30 min over a 2-hour test interval.

**Conclusions:** The prototype of a portable device for continuous recording of electrical potentials together with multisensor ultrasound evaluation is intended to expand the possibilities of non-invasive assessment of lower urinary tract function in children who would not be qualified for invasive urodynamic examinations. POIR.04.01.04-00-0045/20

Key words: Lower urinary tract, functional assessment, non-invasive testing

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**EVALUATION OF RISK FACTORS FOR ACUTE PYELONEPHRITIS AND PERMANENT RENAL DAMAGE (RENAL SCARRING) IN CHILDREN UNDER 2 YEARS OF AGE WITH A FIRST FEBRILE URINARY TRACT INFECTION**

**Aikaterini Gkrepi<sup>1</sup>, Vasileios Giapros<sup>2</sup>, Spyros Tsiouris<sup>3</sup>, Anastasios Serbis<sup>1</sup>, Vasileios Xydis<sup>4</sup>, Ekaterini Siomou<sup>1</sup>**

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**Aims/Purpose:** To study possible predictive factors for acute pyelonephritis (APN) and renal scarring in children  $\leq$  2 years of age hospitalized with a first documented febrile urinary tract infection (UTI).

**Methods:** 60 patients  $\leq$  2 years of age and 63 age-matched controls were prospectively included in the study. On admission, the neutrophil count, serum levels of creatinine, CRP, ESR, cystatin C and 25OHD were evaluated. The patients were divided in two subgroups based on acute DMSA (technetium 99m-dimercaptosuccinic acid) scan, those with a normal DMSA and those with a DMSA indicating APN. The subgroup of patients with abnormal acute DMSA had a follow-up DMSA scan after 6 months to evaluate for renal scarring.

**Results:** APN was found in 28/60 (46,6%) children. The children with an abnormal DMSA scan was of significant higher age than those with a normal DMSA ( $p = 0.02$ ). The children with APN had significantly higher CRP ( $p < 0.01$ ) and ESR ( $p < 0.05$ ) and lower 25OHD ( $p < 0.01$ ) levels compared with those with normal DMSA. Only 5 children without lesions found to have serum vitamin D  $< 30$  ng/ml, while more than half of children with renal damage in acute DMSA had vitamin D level  $< 30$  ng/ml. The correlation between 25OHD level and APN was independent of age, fever duration and CRP/ESR level, implying that low vitamin D level is an independent predictor of acute renal damage in children with febrile UTI, with a specificity of 77% and sensitivity of 53%. Cystatin C levels did not differ significantly between the patient and control groups. Renal scarring was found in 9/27 (33.3 %) of children with APN. CRP levels  $> 100$  mg/L during APN were found more frequently in children with renal scarring, comparing to those with no renal scarring ( $p < 0.01$ ). VUR grade  $\geq 3$  was found only in children with renal scarring.

**Conclusion:** Vitamin D levels were found to be an independent predictor of acute renal damage in children with APN. Cystatin C was not found to be a predictive factor for renal damage. CRP levels  $> 100$  mg/L during APN and the presence of VUR grade  $\geq 3$  were associated with renal scarring.

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**FOSFOMYCIN PROPHYLAXIS CAN REDUCE THE RISK OF SEVERE RECURRENT URINARY TRACT INFECTIONS REQUIRING HOSPITALIZATION IN CHILDREN WITH COMPLEX URINARY TRACT MALFORMATIOS**

**Małgorzata Stańczyk<sup>1,2</sup>, Monika Pawlak-Bratkowska<sup>1</sup>, Anna Jander<sup>1</sup>, Barbara Puczko-Nogall, Agnieszka Seraficka<sup>3</sup>, Marcin Tkaczyk<sup>1,2</sup>**

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**Introduction:** Urinary tract infections (UTIs) with resistant bacterial strains are one of the most troublesome problems in children with severe congenital anomalies of the kidney and urinary tract (CAKUT).

**Aim:** We present the results of non-standard prophylactic treatment with fosfomycin of infants with complex urinary tract malformations.

**Material and Methods:** It was a retrospective analysis of data of 5 male infants after urological interventions due to complex CAKUT. The frequency of UTIs, their aetiology and course, frequency and duration of hospitalization due to UTIs, prophylaxis and treatment outcomes were analysed.

**Results:** The mean follow-up period was 16 months. Mean number of UTIs during observation was 5 (2-6). Infections with multi-drug resistant strains were observed in all patients before commencing fosfomycin prophylaxis, on average 21 days after urological procedure. Due to recurrent UTIs with highly resistant or reduced susceptibility strains, despite standard prophylaxis, we introduced fosfomycin in 50-70 mg/kg dose once a day for 4-9 months what reduced frequency of infections (3.6 vs 1.0,  $p = 0.01$ ), infections with decreased susceptibility strains (3.6 vs 0.0,  $p = 0.00006$ ) and need for hospitalizations (3.6 vs 0.2,  $p = 0.003$ ). Fosfomycin was introduced after 2-5 UTIs, at the mean age of 7 months, after mean of 4 months of ineffective standard prophylaxis. We didn't record any significant adverse effects of the treatment or bacterial resistance development.

**Conclusions:** In children with urinary tract malformations, and in particular with a history of urological interventions, in the case of recurrent UTIs with strains of reduced susceptibility to antibiotics, several months of non-standard prophylactic treatment with fosfomycin may be considered.

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## IGA NEPHROPATHY WITH BILATERAL HYDROCALICOSIS

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**Objective:** Presentation of a child with IgA nephropathy, and bilateral hydrocalycosis, with consideration of treatment options

**Methods:** Disease detection, follow-up, and previous treatment

**Case report:** In a previously healthy six-year-old child, the appearance of macrohematuria and proteinuria suddenly occur without worsening the overall renal function. The initial diagnosis showed IgA nephropathy, histologically consistent with focal segmental necrotizing glomerulonephritis and cellular crescents in 17.5% of glomeruli. She was treated with corticosteroid and supportive therapy, after which proteinuria normalized, but microhematuria remained. Already at that time, bilateral cystic changes of all calyces of both kidneys were noticed, which proved to be permanent on ultrasound examination of the kidney imaging. Kidney scintigraphy with Tc-99m DMSA after one year showed multiple “cold” zones of both kidneys, more on the left kidney. Functional magnetic resonance urography (fMRU) at the age of 14 revealed bilateral hydrocalycosis. Global renal function remained stable within normal GFR for now.

**Conclusion:** Even today there is still no approved and effective therapy for IgA nephropathy. The possible treatment with dapagliflozin or sparsentan is considered with IgA nephropathy progression [1]. Regarding the treatment of hydrocalycosis, many questions remain open. Potential endoscopic treatment is not an option. We are open to suggestions.

### References

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ACUTE URINARY RETENTION WITHOUT APPARENT CAUSE IN 14 YEARS OLD GIRL – DIAGNOSTIC AND THERAPEUTIC DIFFICULTIES

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**Introduction:** Acute urinary retention is a rare problem in children, the etiology is varied, and in about 10% of cases – unknown. It is more common in boys and is most often associated with inflammation of the urinary tract or mechanical obstruction, including concomitant constipation. Less common causes include injuries and infections of the urinary tract and malignancies in the lumbosacral region.

**A case report:** We present a case of a 14-year-old, previously healthy girl, who presented with urinary retention. The episode was preceded by hematuria and abdominal pain, then the changes in urine subsided, but the girl was unable to pass urine – the urinary bladder was catheterized, resulting in an outflow of 900 ml of urine. Initially, after catheterization and initiation of  $\alpha$ -blocker and oxybutynin, improvement was obtained. After a week, urinary retention occurred again – then the symptoms did not subside. Urodynamic evaluation revealed a lack of bladder sensation and detrusor activity, as well as increased sphincter tone. The patient was placed in a permanent suprapubic urine diversion. The neurological examination and the complete examination of the central nervous system by magnetic resonance imaging showed no abnormalities. The result of the nerve conduction study was normal. The cerebrospinal fluid was normal, but IgG antibodies reacting with recombinant sulfatide antigens were found. Suspecting an autoimmune process, three sessions of immunosuppressive treatment were performed followed by no clinical effect. Subsequently, distigmine and baclofen were added to the therapy – within a week the girl's bladder urge returned and she was able to pass urine on her own. The entire diagnostic and therapeutic process lasted 6 months.

**Conclusions:** Persistent urinary retention in a previously healthy child causes great anxiety and discomfort for the child. Rapid diagnosis is possible, but in idiopathic cases, adjusting the appropriate therapy is a challenge and requires close cooperation between a urologist, a nephrologist and a neurologist. If the procedure fails, the whole picture should be re-analysed and related to the most basic knowledge about the innervation of organs affected by the disease process.

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VASCULAR MALFORMATION OF THE KIDNEY AS A CAUSE OF SEVERE INFANTILE ARTERIAL HYPERTENSION: A CASE REPORT

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**Aims/Purpose:** The aim of our report is to present a case of infantile onset arterial hypertension and describe diagnostic issues which have been faced.

**Methods:** We present a case of severe Arterial hypertension due to unilateral Vascular malformation at renal hilum diagnosed in 5-month-old boy treated at 2nd Minsk Children's Hospital.

**Results:** The patient was initially admitted at infectious disease hospital because of vomit, loss of appetite and irritability. Mother reported of loss of appetite and poor weight gain one month prior. EchoCG revealed decreased LVEF and hypertrophy of both ventricles raising the suspicion of heart failure due to hypertrophic cardiomyopathy and the boy was transferred to cardiac surgery ICU. Nephrotic range proteinuria was found and the patient was transferred to the nephrological hospital with the suspected diagnosis of congenital nephrotic syndrome (NS). However no evidence of NS was further present except for proteinuria which has returned to mild level on appropriate hypotensive therapy within 2 days. No albumin transfusion was needed. Arterial hypertension detected since first days at the hospital was present through day and night with max of 142/84 mmHg. Four-component hypotensive therapy was required. Renal US revealed normal sized kidneys with no structural abnormalities. Anechogenic round shaped structure was found retroperitoneally at the right side close to the distal pole of the right kidney. The structure was found to be 10x12 mm with clearly seen hyperechogenic capsule and uneven surrounding tissue, no blood flow was detected in the structure. MRI with contrast was performed and retroperitoneal extrarenal malformation was detected on the right side (most likely benign in nature: highprotein/hemorrhagic cyst? Dermoid? Retroperitoneal lymphangioma?). Laparoscopic intervention for surgical removal of vascular malformation (presumably aneurism) of renal hilum was performed. Histological examination revealed a segment of a large venous vessel with the hyalinosis of it's wall and a thrombus formation in it's lumen. After the surgery the doses of hypotensives were reduced by 50% and after 10 days the patient's AH was managed with two-component hypotensive therapy. EchoCG revealed significant improvement – hypertrophy of interventricular septum and posterior left ventricular wall became less compared to preoperative parameters (Z-score +2.66 and +2.81 vs +5.44 and +4.36, respectively). Two months postoperatively patient is normotensive on two-component therapy. Control ultrasound and abdominal MRI didn't reveal any abnormalities.

**Conclusion:** Infantile AH is difficult to be diagnosed due to non-specific manifestations including irritability, poor appetite and weight gain. Every infant should have blood pressure measured if unexplained irritability and poor weight gain is present.

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**PANCAKE KIDNEY IN A 7-YEAR OLD GIRL – CASE REPORT**

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**Background:** Renal ectopia and fusion anomalies are congenital anomalies of the kidney and urinary tract (CAKUT) that are usually asymptomatic and detected incidentally. Patients with those anomalies present a higher risk of complications like urinary tract infections and urolithiasis. Pancake kidney (PK) is one of the rarest type of CAKUT. It is described as a complete fusion of the superior, mild and inferior poles of both kidneys in the pelvic cavity. Each kidney has its own excretory system with two ureters that do not cross the midline.

**Case presentation:** Almost 8-years old girl was admitted to our department due to suspicion of the ectopic kidney. Two different ultrasound examinations failed to visualize the left kidney. The girl has never presented any urinary symptoms. Computed tomography with urographic phase was performed, which showed fused kidneys situated in the right iliac fossa, anterior to the aortic bifurcation – a picture typical for the pancake kidney. The renal pelvises were pointed abdominally. Pelvicalyceal systems and ureters were undilated and both ureters entered the bladder in a typical location. A single renal artery was visualized arising from the abdominal aorta just above its bifurcation, on its abdominal surface, then dividing into the right and left renal arteries. There were two separate renal veins, the wider one on the left side, both draining into the superior vena cava.

**Conclusions:** This case presents the clinical picture of a rare renal malformation – pancake kidney. Imaging plays a key role in diagnosis of renal anomalies. In this case, only a CT scan gave a full urinary tract visualization. The diagnosis of a pancake kidney may be associated with an increased risk of urolithiasis or recurrent urinary tract infections. In addition, every renal anomaly is associated with an increased risk of developing chronic kidney disease. Hence regular kidney-function evaluation tests and regular blood pressure monitoring were recommended.



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### 13-YEAR-OLD MALE PATIENT WITH RETROCAVAL URETER, APPLYING WITH MACROSCOPIC HEMATURIA

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**Aims/Purpose:** Retrocaval ureteral anomaly is a developmental anomaly of the inferior vena cava and defines the course of the ureter surrounding the inferior vena cava. Although it is a congenital disease, patients usually become symptomatic in the third or fourth decade. Hematuria, flank pain, upper urinary tract infections and nephrolithiasis may be seen. Here, we present a patient who presented with macroscopic hematuria, flank pain and acute kidney injury.

**Methods:** The patient with solitary kidneys, who had irregular follow-up until age 13, presented with the complaint of sudden onset of macroscopic hematuria and flank pain. At admission, the hemoglobin value was 5.6 g/dl and the potassium value was 7.8 mEq/L. While the left kidney was not detected on USG, the AP diameter of the renal pelvis in the right kidney was 66 mm, and the renal pelvis was filled with hematoma. A nephrostomy catheter was inserted in the patient and it was observed that the hematoma in the renal pelvis descended to the bladder. Erythrocyte suspension was given for his anemia and hemodialysis was performed due to hyperkalemia that did not respond to medical treatment. Conventional angiography was performed to determine the localization of bleeding due to ongoing macroscopic hematuria but no bleeding focus was detected. Since there was no response to the tranexamic acid administered through the nephrostomy catheter and the bleeding continued, the patient was taken to the operation. The hematoma in the kidney was evacuated and a double J catheter was inserted. Steroid, fresh frozen plasma and IV tranexamic acid treatments were applied. No hematological problem was detected in the examinations performed for the bleeding etiology of the patient.

**Results:** On cystoscopy, it was observed that the renal pelvis was dilated, and after the pelvis turned laterally, it progressed transversely and turned medially again. It was thought to be compatible with the retrocaval ureter.

**Conclusion:** If hydronephrosis is mild in children with retrocaval ureter, it can be followed without surgical intervention. However, severe cases of hydronephrosis with symptoms require surgical intervention. Since our patient was asymptomatic in the follow-ups, surgical treatment was not considered.

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### DIURETIC RENOGRAPHY IN PEDIATRIC HYDRONEPHROSIS: A RETROSPECTIVE SINGLE-CENTER STUDY

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**Aims/Purpose:** In children with hydronephrosis, mercaptoacetyltriglycine-3 diuretic renography (99mTc-MAG3) is used to assess differential kidney function, the perfusion into the kidneys and drainage out of them through the ureters into the bladder. The aim of our study is to examine whether an ultrasound of the urinary tract system adequately identifies those patients who need further investigation.

**Methods:** We retrospectively reviewed the 99mTc-MAG3 scan findings performed in the Nuclear Medicine Department of our hospital, and medical records of pediatric patients with hydronephrosis who were at follow-up between 2020-2023.

**Results:** During 2020-2023 period, 142 pediatric patients (male/female (%): 63/37) underwent 99mTc-MAG3 scan after kidney ultrasonography evaluation. Pediatric patients with hydronephrosis but without vesicoureteral reflux, urolithiasis or a known obstructive nephropathy were enrolled in this study [n = 61, male/female (%): 80/20]. The median age of the children was ~3.4 years of age, with 34 (~55.7%) of them having an obstructive pattern on 99mTc-MAG3 scan.

**Conclusions:** The combination of ultrasound and 99mTc-MAG3 scan provides the necessary anatomical and functional information to follow the degree of obstruction and to decide between surgical intervention and conservative follow-up.

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## BLADDER-BOWEL DYSFUNCTION IN CHILDREN WITH RECURRENT URINARY TRACT INFECTION

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**Aims/Purpose:** Urinary tract infection (UTI) is one of the most common infectious diseases in the pediatric population. Up to 30% of pediatric patients experience a recurrence after the first episode of UTI. An important task in the management of children with recurrent UTI, is to identify underlying bladder-bowel dysfunction (BBD), which is an important risk factor for recurrent UTI. The aim is to evaluate the prevalence of BBD for toilet-trained children which had a recurrent UTI.

**Methods:** We included 46 children (31 boys, 15 girls) with a median age of 5.8 years (range 5 to 6.3) who had recurrent UTI (more than 2 recurrence). The group was characterized regarding urinary tract anomalies, recurrent UTI. BBD is defined as the combination of lower urinary tract dysfunction and constipation as suggested by the International Children's Continence Society (ICCS) standardization document. Function of bladder/bowel was investigated using a validated questionnaire for children and post-void residual urine assessments. To assess BBD, we administered the Dysfunctional Voiding Scoring System (DVSS) questionnaire to parents of children who were reportedly fully toilet trained (for both bladder and bowel). We used the cutoffs: girls with a score of  $\geq 6$  and boys with a score of  $\geq 9$  were considered to have BBD. Abnormal values residual urine  $\geq 10\%$  of bladder capacity.

**Results:** According to the bladder-bowel questionnaire BBD had 21 children (45.6%) with recurrent UTI, in 80.9% (17) it was girl. The most frequent urinary symptoms reported in children with BBD were urinary urgency in 15 (71.4%), withholding maneuvers (pee dance, squatting, crossing legs) in 17 (80.9%), and daytime wetting in 13 (61.9%); 19 (90.5%) reported either daytime wetting or withholding maneuvers. Among children with BBD 16 (76.2%) reported frequent painful defecation and 5 (23.8%) reported  $< 3$  bowel movements per week over the last 8 weeks. Post-void residual urine was abnormal in 9 patient (19.6%). In children with BBD during the first year of life in 52.4% (11 child) was diagnosed vesicoureteric reflux (VUR) all grades, in 5 children (23.8%) – hydroureteronephrosis, PUJ, 5 child had no urinary tract anomalies.

**Conclusion:** Almost half of preschool children (5–6 y.o.) with recurrent UTI had BBD. In 76.1% child with BBD also had a history of urinary tract anomalies. Very important to investigate children with recurrent UTI, urinary tract anomalies for BBD.

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## DESCRIPTION OF SYMPTOMS AND HEALTH STATUS OF PATIENTS WITH POSTNATAL CONFIRMED POSTERIOR URETHRAL VALVE IN OUR CLINIC

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**Aims/Purpose:** The purpose of the abstract is to present analysis and study on features and prognosis of patients with posterior urethral valves in Children's New Clinic in Tbilisi, Georgia as our clinic serves the largest part of nephrology patients of pediatric age across the country.

**Methods:** This is a descriptive study. Records of patients with PUV at the children's new clinic (Tbilisi, Georgia) were reviewed. Inclusion criteria were all patients who had radiological diagnosis of PUV with voiding cystourethrogram (VCUG) and renal ultrasound. Data such as age, age at presentation, voiding abnormality, recurrent fever, ballotable kidney, palpable bladder, failure to thrive, UTI, anemia, hypertension, UTI causing bacteria, VUR, hydronephrosis, CKD, ablation, megaurether, diagnose pre/postnatal were collected. Patients were managed between the pediatric nephrology and pediatric surgical units.

**Results:** There were 11 patients. They were all boys. The age ranges from 1 to 15 years. The patients mean age at presentation is 1 year. Clinical findings at presentation include: Age – 1-15years, age at presentation – 1 month-3 years, voiding abnormality – 36%, recurrent fever – 27%, ballotable kidney – 0%, palpable bladder – 27%, failure to thrive – 36%, UTI – 73%, anemia – 45%, hypertension – 18%, UTI causing bacteria – 64% – *E. coli*, 18% – *klebsiella*, VUR – 54%-high grade, 9%-mild, hydronephrosis-64% moderate, 9%-severe, CKD-36% progressing from mild to severe (Stage V), ablation-100%, megaurether-36%, diagnose prenatally-64%, postnatally-36%. Initial management instituted were continuous bladder drainage by urethral catheterization (9%) and cutaneous ureterostomy (18%) and none had vesicostomy. The outcome of the patients showed that 18% survived on dialysis (0% received peritoneal dialysis and 18% received hemodialysis). The remaining 82% of patients are doing well and are being prepared for transplantation.

**Conclusion:** By observing our patients, we can conclude that the management and treatment of the disease in prenatally informed patients is relatively successful and effective. Prenatal surgical intervention due to hydronephrosis has never been performed in our country, despite the recently discovered opinion that it does not have a significant effect in preventing future complaints.

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**MONITORING KIDNEY FUNCTION OF CHILDREN WITH CONGENITAL ANOMALIES OF THE KIDNEY AND URINARY TRACT- THE EXPERIENCE OF AN SINGLE CENTER IN WEST PART OF ROMANIA**

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**Aims/Purpose:** Chronic kidney disease prevalence among children is rising worldwide. Nowadays, the best glomerular filtration rate estimation (eGFR) formulas in children use serum creatinine and Cystatin-C. Renal scintigraphy is a complementary investigation following biological markers. We report the differences in estimating GFR in children with congenital anomalies of the kidney and urinary tract (CAKUT).

**Methods:** We performed a retrospective study including 40 patients with CAKUT admitted at the "Louis Turcanu" Emergency Children Hospital Timisoara between January 2018 and December 2022. All the patients had serum creatinine measurement and renal scintigraphy using Tc-99m Diethylenetriamine pentaacetate (Tc-99m-DTPA).

**Results:** Out of 40 patients with mean age  $98.5 \pm 67$  months (12 months old youngest and 294 months old the oldest respectively), 55% were males. Mean creatinine level was  $48.1 \pm 39.9$  micromoles/l with an average eGFR of  $104.6 \pm 29.7$  ml/min/1.73 square meters (Bedside Schwartz formula). All patients underwent renal scintigraphy scan using Tc-99mDTPA. The eGFR mean value using scintigraphy was  $128.15 \pm 47.5$  ml/min/1.73 square meters. Comparing eGFR values using paired sample t-test, scintigraphy eGFR was higher than Schwartz eGFR ( $p = 0.006$ ). In five children, we measured serum Cystatin-C levels at the time with serum creatinine and renal scintigraphy. In this lot of five patients, eGFR using Schwartz formula was  $71.03 \pm 42.9$  ml/min/1.73 square meters, while eGFR using Cystatin-C was  $58 \pm 34$  ml/min/1.73 square meters and eGFR using renal scintigraphy of  $115 \pm 99$  ml/min/1.73 square meters. Statistical significance was not reached in this lot of patients due to small number. On one hand eGFR using renal scintigraphy overestimated renal function and on the other hand eGFR using Cystatin-C appeared to be lower in patients with CAKUT.

**Conclusion:** In patients with CAKUT, renal scintigraphy can play a major role in long-term follow-up, as these patients are at high risk of renal scarring and progression to kidney failure. One should careful use renal scintigraphy eGFR in assessing kidney function due to its overestimation in pediatric patients. Cystatin-C is a better kidney function marker, but remains expensive in most countries. Children with CAKUT should have periodic kidney function evaluation using the most handful method.

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**CLINICAL IMPLICATIONS OF THE CONGENITAL SOLITARY FUNCTIONING KIDNEY IN CHILDREN – A COHORT OF PEDIATRIC PATIENTS FROM A SINGLE CENTER**

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**Aims/Purpose:** Abnormal renal development that results in lack of function or development of one of the kidneys is known as congenital solitary functioning kidney (CSFK). In this retrospective descriptive study we aim to analyze the clinical evolution and risk factors that predispose to progressive chronic kidney disease (CKD) in children under 18 years old with CSFK as a result of unilateral renal agenesis (URA), multicystic dysplastic kidney (MCDK) and renal aplasia (RA).

**Methods:** A total of 103 patients with CSFK evaluated in our centre during 2018–2023 were recruited. We analyzed the presence of compensatory enlargement of the CSFK, the presence of additional CAKUT and extra-renal malformations, other possible risk factors known in the literature to be causative for CKD progression (history of prematurity, obesity, hypertension, proteinuria) and renal function (latest GFR estimated by bedside Schwartz formula or by renal scintigraphy).

**Results:** In our group of 103 patients (42 females and 61 males), 3 well characterized sub-categories of CSFK were identified: URA 76.69% (79), MCDK 22.33% (23) and RA 1.94% (2). 22 patients (~21%) have additional CAKUT and 18 patients (~17%) have extra-renal malformations (involving the heart, the musculoskeletal system and genital tract). The group was divided in 3 subgroups by age: 0–5 years old (33 patients), 5–10 years old (22 patients) and 10–18 years old (48 patients). We analyzed the risk of developing proteinuria (3/33 patients 0–5 years old, 5/22 patients 5–10 years old, 9/48 patients 10–18 years old) and hypertension (only 2 patients from the 10–18 years old subgroup). ~58% of the patients (60) have a reduction of GFR < 90 ml/min/1.73 mp, ~12% (12 patients) have a significant reduction of GFR (< 60 ml/min/1.73 mp), while 3 of the patients (2.9%) experienced ESKD. All the 3 patients with ESKD presented with additional CAKUT on the solitary kidney, history of prematurity and without compensatory enlargement of the single functioning kidney on ultrasound. A significant reduction of GFR (< 60 ml/min/1.73 mp) was mostly correlated with the presence of CAKUT and the absence of compensatory enlargement of the solitary kidney.

**Conclusion:** A CSFK is a common developmental defect that predisposes to proteinuria, hypertension and CKD as a consequence of hyperfiltration. Congenital and environmental factors that may influence the clinical outcome are already described in the literature, but further research is needed to identify the predisposing factors that may differentiate the small subset of children with CSFK at a higher risk of developing adverse renal outcomes.

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## MULTICYSTIC DYSPLASTIC KIDNEY IN CHILDREN : EPIDEMIOLOGY, CLINICAL FEATURES AND FOLLOW UP

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**Aim/purpose:** We aim to evaluate the clinical features of patients with multicystic dysplastic Kidney (MCDK) followed in our pediatrics department.

**Methods:** A retrospective study was conducted in the pediatric department of Sahloul's hospital of Sousse. All patients with MCDK followed in our department between 2015 and 2023 were included in the study. The demographic, clinical, laboratory and radiological data were collected from different files of patients than evaluated.

**Results:** 24 children with MCDK were enrolled in the study with a sex-ratio = 1. A high consanguinity rate was observed (62.5%). 95.8% of patients had no family history of chronic kidney disease. Only half of patients had antenatal diagnosis at a mean term of 26.29 weeks of gestation (range, 21-33 weeks). Mean age of the first consultation was  $2.92 \pm 4.34$  years and age at first post-natal ultrasonography was equal to  $0.81 \pm 0.7$  years. MCDK was bilateral in 79.2% of cases, located in left and right sides in 50% and 33% respectively. Contralateral kidney was normal in only 37% of cases and 12% presented with associated liver cysts. MCDK was syndromic in 29.2% of cases associated to a failure to thrive in 33.3% of children. At diagnosis, 12.5% of children had confirmed hypertension, average diuresis was equal to  $1.6 \pm 0.9$  ml/Kh/h. Cystography was performed in 66.7% of patients and showed urethra-vesical reflux in 25.1% of cases. During follow-up, 25% developed compensatory hypertrophy of the contralateral kidney, 50% had a chronic kidney failure with renal replacement therapy required in 25% of cases. 8.3% of patients deceased

**Conclusion:** MCDK follows a benign course with relatively few sequelae in majority of cases, serious complications can occur, thus patients should be closely followed up and conservatively managed to prevent evolution to end stage renal disease.

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**PEDIATRIC URINARY TRACT DILATIONS: DATA FROM A MULTICENTER RETROSPECTIVE OBSERVATIONAL STUDY**

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**Aims:** In pediatric age, ultrasound (US) findings of urinary tract dilation (UTD) are very frequent. Indeed, there is great variability in the management of these patients. This study aims to evaluate the prevalence of obstructive pathology and vesicoureteral reflux (VUR) and recognize the prognostic factors of UTDs, that can guide the subsequent follow up.

**Methods:** This is a multicenter retrospective observational study involving a cohort of children treated for UTD at the Pediatric Nephrology Units in Bologna, Milan, Modena, and Naples between 2000 and 2019. Inclusion criteria were the presence of a postnatal US documenting a UTD and related measurements, and at least one other US performed during follow-up. The patients were divided into three groups based on the time of diagnosis: group A patients with a prenatal diagnosis, group B patients with a diagnosis made after a urinary tract infection (UTI), and group C patients with diagnosis due to an incidental finding. For the whole cohort, data relating to the first postnatal diagnostic US documenting the UTD were collected. In addition, data relating to US performed during the follow-up and second level examinations (voiding cystourethrography and/or renal scintigraphy if performed) were collected for all patients.

**Results:** A total of 1784 children were enrolled: group A n = 1214, 68%; group B n = 266, 15%; and group C n = 304, 17%. Regarding the US findings: mono- and bilateral pelvic dilations and unilateral and bilateral calyceal dilations were significantly more frequent in group A (p 0.0004, p 0.0000001, p 0.00000002, p 0.002, respectively); while unilateral and bilateral ureteral dilations were significantly more frequent in group B (p 4.5e-11 and p 0.00000005). After the first diagnostic US, 54.8% of children underwent second-level examination. Both scintigraphy and voiding cystourethrography were significantly more frequently performed in group B (77.1% vs. A 45.9% and C 32.2%, p = 2.2e-16; 54.1% vs A 42.4% and C 30.6%, p 0.00000009). Obstructive pathology was more frequent in group A (45.2% vs B 21.5% and C 30.1%, p 0.0000003), while VUR of grade 3 or higher was more frequent in group B (48.8% vs A 27.1% and C 35.7%, p 0.0000001), the same was true for bilateral VUR (28.3% vs A 15.6% and C 17.3%, p 0.0004).

**Conclusion:** The etiological causes underlying UTDs can be grouped into two families of urological anomalies, obstructive uropathy and VUR, which differ in time of onset, clinical presentation, and US findings. The former is significantly more frequent in prenatal diagnosis; the second is significantly more frequent after UTI diagnosis, while the incidental postnatal findings generally do not have great clinical significance. These data show how the association between prognostic factors and modality of onset can be used as an indicator to choose the most suitable follow-up and standardized diagnostic management.



# POSTER SESSION 2D

## Transplantation

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**ROLE OF EBV IN DEVELOPMENT OF ADENOTONSILLAR HYPERTROPHY IN KIDNEY TRANSPLANTED CHILDREN: A RETROSPECTIVE STUDY**

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**Background:** Post-transplant Lymphoproliferative Disease (PTLD), a unifying term for a broad spectrum of lymphoid proliferations, represents the most important malignant complications and has been correlated to primary Epstein-Barr virus (EBV) infections in most cases. In children PTLD often presents in the Waldeyer's ring in the form of lymphoid hyperplasia, a precursor of the most aggressive types of PTLD; however, the incidence and the meaning of adenotonsillar hypertrophy in this population have not been determined making it difficult to distinguish a benign condition from a possible PTLD. For these reasons, some authors have recommended performing diagnostic adenotonsillectomy in all solid organ transplant recipients presenting with adenotonsillar hypertrophy apart from symptoms.

**Objective:** Contribute to determine the incidence and meaning of adenotonsillar hypertrophy in pediatric solid organ transplantation recipients and try to identify risk factors associated to its development.

**Methods:** Retrospective analysis of pediatric kidney transplant recipients treated at our institution between January 2005 and December 2021 was conducted to identify patients who underwent adenoidectomy and/or tonsillectomy in the post-transplantation period and to evaluate the presence of PTLD in the pathology specimens. We also assessed whether EBV seronegativity at time of transplantation and age at transplantation were related to adenotonsillectomy or diagnosis of PTLD.

**Results:** 215 patients were included, 9% underwent adenoidectomy and/or tonsillectomy after transplantation, of these 35% showed signs of early PTLD in the pathological specimen, nobody showed signs of more advanced types of PTLD. EBV seronegativity and younger age at time of transplantation were statistically related to adenotonsillectomy and presence of PTLD. We conducted univariate and multivariate analysis which showed that EBV seronegativity at time of transplantation was an independent risk factor for adenotonsillectomy.

**Conclusion:** Pediatric kidney transplant recipients who are EBV seronegative at the time of transplantation are at increased risk to develop adenotonsillar hypertrophy requiring surgery compared to EBV seropositive recipients, in agreement with previous studies. We also found that EBV seronegativity is a risk factor independent from age at transplantation, underlying the critical role of EBV in the development of adenotonsillar hypertrophy in these patients.

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**THE CHALLENGES OF UNDERTAKING PAEDIATRIC KIDNEY TRANSPLANTATION IN LOW- AND MIDDLE-INCOME COUNTRIES: THE TRANSPLANT LINKS COMMUNITY EXPERIENCE**

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**Aims/Purpose:** Paediatric end-stage kidney failure (ESKF) is a global problem. Kidney transplantation (KTx) is the gold-standard treatment, but is largely unavailable to children in low and middle income countries (LMICs). Transplant Links Community (TLC) is a UK charity mentoring centres in LMICs seeking to start paediatric KTx (PKTx) programmes. We present TLC's 15 year experience supporting emerging services in 3 LMICs.

**Methods:** Qualitative data were obtained from case studies and observations by TLC and its partner centres. Supporting quantitative data were collected from TLC and partner centre records.

**Results:** Over 15 years TLC has assisted 3 centres in the Caribbean. After initial contact by clinicians in LMICs, TLC provided support through team visits and ongoing UK-based mentoring. Challenges identified in establishing PKTx were multiple, varied between countries and invariably involved lack of investment (Table). Such issues had no quick solutions, indicating that commitment is needed over years for PKTx programmes to become sustainable. 16 live-related (usually parental) transplants have been performed. Patients received either peritoneal or haemodialysis (via CV catheter) pre-KTx. Causes of ESKF included obstructive uropathy, vesicoureteric reflux, chronic glomerulonephritis and congenital kidney dysplasia. Patient outcomes have been mixed, highlighting challenges that follow the initiation of PKTx (Table). There were no early postoperative deaths or graft losses in the first year. However, 7 patients returned to dialysis 2.5 -13 years post-KTx; biopsies included cellular rejection and chronic allograft and BK nephropathies. 7 patients have functioning grafts, with eGFRs 16 - 116 ml/min. 3 patients subsequently died, two with functioning grafts.

Table: Challenges experienced by TLC

Initial challenges	Long-term challenges
<ul style="list-style-type: none"> <li>·Local government funding and will to develop services</li> <li>·Identifying local teams with paediatric nephrology, urology and KTx expertise</li> <li>·Sub-optimal management of CKD</li> <li>·Identifying healthy donors</li> <li>·Reliable supplies of medication and surgical equipment.</li> <li>·Causes of ESKF often unknown</li> </ul>	<ul style="list-style-type: none"> <li>·Turnover of key staff</li> <li>·Variable level of clinical care</li> <li>·Inconsistent political support</li> <li>·Variable availability of immunosuppression</li> <li>·Social issues, clinic non-attendance and non-compliance</li> <li>·Infrastructure for data collection</li> </ul>

**Conclusion:** PKTx should not be restricted to resource-rich countries and the achievement of TLC-mentored centres in performing KTxs, albeit in small numbers, demonstrates that barriers to initiating PKTx can be overcome. While sustainability requires stakeholder commitment over many years, partnerships can make KTx available to children globally. Even so, the international renal community needs to support LMIC colleagues in lobbying governments to ensure healthcare planning addresses the needs of paediatric ESKF patients.

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## ANESTHESIA AND ICU PRACTICE IN PEDIATRIC KIDNEY TRANSPLANTATION; A EUROPEAN SURVEY

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**Aims/Purpose:** Pediatric kidney transplantations (PKT) are performed in relative low numbers, even in expertise centers. Despite the high perioperative risk profile of both patient and procedure, international guidelines for anesthesia care are lacking. Furthermore, local guidelines show inconsistency particularly in hemodynamic (HD) monitoring, -targets and -support. Especially in small children receiving an adult donor kidney, hemodynamic changes are considerable and support of blood pressure and kidney perfusion can be challenging. Aim of our study was to investigate anesthesia and ICU practices in European PKT expertise centers. These data can be used for an international consensus guideline.

**Methods:** International survey. An anonymized link was sent from a Castor database to contacts in European reference centers. Inclusion criteria were; medical doctor in anesthesia, ICU or pediatric nephrology working in a PKT expertise center and signed informed consent. Questions considered center information and topics considering surgery, anesthesia and ICU practice. Data were analyzed using descriptive statistics.

**Results:** The survey was completed by 25 replicants, from ten countries. Replicants represented anesthesiologists (52%), pediatric nephrologists (32%) and ICU doctors (16%). 68% of centers perform more than 10 PKT a year of which less than 30% in acceptors < 5 yrs. In only 24% of centers, the majority of PKT is with living donor. In 36% of centers, a team of diverse surgical specialists performs the PKT. When the acceptors weight is below 15-20 kg, all centers anastomose the donor kidney on aorta and caval vein. Perioperative HD therapy is guided by central venous pressure (CVP; 68%), arterial blood pressure (ABP; 90%) and cardiac output (CO; 32%). Most centers use intra-arterial BP measurements and CVP- or CO guided HD therapy in the youngest acceptors. HD targets vary between centers, although ABP targets show the least variation. Albumin, isotonic crystalloids and norepinephrine are the most reported fluids and vasopressor used to reach targets. Around reperfusion, furosemide and/or mannitol are given per protocol in most centers (both 58%). Postoperative care is mainly located in pediatric ICU; the youngest acceptors always go to ICU. In 20% of centers, per protocol the youngest ventilated postoperatively for 1 or 2 days.

**Conclusion:** The results of our survey reveal a variety in anesthesia and ICU practices in European PKT centers. Diversity is most apparent in CVP- and CO-targets, use of furosemide and mannitol, and type of surgical specialist performing the transplantation. These data can be a starting point to form a network and a consensus guideline; [www.ankitc.eu](http://www.ankitc.eu)

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## ANTIBODY RESPONSE TO SARS-COV-2 VACCINATION IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS: A SINGLE CENTER EXPERIENCE

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**Aims/Purpose:** Organ transplant recipients are a priority for vaccination against COVID 19, due to increased risk of severe disease. As in adults, a reduced antibody response is expected also in immunocompromised children. Therefore we aimed to evaluate antibody (Ab) response to Sars-COV2 vaccination among a cohort of pediatric kidney transplant recipients (pkt).

**Methods:** We retrospectively analyzed Ab response in 22 pkt recipients who received at least 2 doses of mRNA Sars-Cov2 (Comirnaty, Pfizer) vaccine between 2021 and 2022. Collected data included demographic characteristics, number of vaccine doses, immunosuppressive medication regimen at the time of vaccination, Ab response, defined as quantitative measurement of IgG Ab against the spike protein of SARS-CoV-2 (Anti-S) by a chemiluminescence immunoassays (CLIA, DiaSorin LIAISON SARS-CoV-2 Trimerics) and expressed as BAU (Binding Antibody Unite).

**Results:** 22 patients were evaluated (average age 18.35 yrs, 17 male). Immunosuppression at the time of vaccination consisted of FK506 with MMF in 12 patients (54.54%) and mTOR inhibitors in 6 patients (27.27%), FK506 alone in two patients (9.09%), MMF with CsA in 1 patient (4.54%) and with Belatacept and in another patient (4.54%). All received prednisone daily or every two days. Of these patients, 6 (27.3%) contracted COVID-19 infection before anti-S dosage and then were excluded. 2 participants (12.5%) were tested for anti-spike (anti-S) Ab after the fourth vaccine dose, 12 (75%) after the third dose and 2 (12.5%) after the second dose. Based on IgG levels, we stratified Ab response as negative (for Anti-S < 4.76), inconclusive (4.76-53 BAU) low (53-241 BAU) medium (241-832) or high (> 832 BAU). Based on Ab levels, we found a high vaccine response in 14 patients (87.5%), a low response in one patient (6.25%); only the patient receiving Belatacept had no Ab response.

**Conclusion:** In our experience most patients (87.5%) had a high response to vaccination. Our results seem to be in contrast with a reduced Ab response described in organ transplant recipients. However, the high Ab response found in our population can be explained by the time of Ab measurement (mostly after the 3 vaccine doses). Moreover, we confirm a low immune response in pkt recipients receiving Belatacept. Our results suggest that immunogenicity increased after 3 doses and is unaffected by immunosuppressive therapy, except for those receiving Belatacept. However, further studies are needed to assess Sars-COV2 vaccine immunogenicity in this population.

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## HLA DESENSITIZATION FOR RETRANSPLANTATION IN AN ADOLESCENT WITH FOCAL SEGMENTAL GLOMERULOSCLEROSIS

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**Aims/Purpose:** Both the high rate of graft recurrence in focal segmental glomerulosclerosis (FSGS) and HLA sensitization hinder access to kidney transplantation as well as the guarantees of success. It is necessary to adapt the usual protocols and use therapeutic tools that improve the chances of survival of these patients.

**Methods:** We review the electronic medical history of a patient with FSGS and anti-HLA antibodies for a second transplant.

**Results:** We present the clinical case of an adolescent girl who started at 14 years of age with a steroid-resistant and multidrug-resistant nephrotic syndrome with a biopsy of FSGS. The etiologic study, including genetic, was negative. She progressed to end-stage chronic kidney disease within one year. She started chronic hemodialysis program until first deceased donor transplant. The initial evolution was favorable (creatinine decreased from 9.5 mg/dl to 2.3 mg/dl in the first 24 hours) with no data of recurrence. The first week she had a cellular rejection type III that did not respond to treatment (bolus methylprednisolone and thymoglobulin), requiring an urgent transplantectomy due to massive bleeding on day +9. She sensitized to HLA with a Panel Reactive Antibodies (PRA) of 100%. Therefore, after 18 months on hemodialysis and 6 months on the deceased donor waiting list, HLA desensitization was performed. She received immunoglobulins (2 g/kg at weeks 0 and 4) and rituximab (375 mg/m<sup>2</sup> at week 2). The PRA decreased to 97% without finding donor after 6 months on the waiting list. It was planned to repeat the same treatment (immunoglobulins and rituximab) preceded by 5 sessions of plasmapheresis (PF). In the second session of PF, a transplant alert was received. Induction was performed according to the usual protocol, with modifications: rituximab was added and alemtuzumab was substituted for basiliximab. The current donor shared a B\*35 antigen with the previous donor for whom the recipient had never generated antibodies. The recipient also had antibodies against A\*01,\*24:02 and DRB1\*14, which with HLA desensitization dropped from mean fluorescence intensity (MFI) of 3000 to less than 1000. The transplantation was uneventful. After 9 months of follow-up, creatinine levels remained at 1.5–1.7 mg/dl (glomerular filtration rate around 50 ml/min/1.73m<sup>2</sup>). She has had infectious complications and IB cellular rejection with good response to treatment.

**Conclusion:** HLA desensitization techniques can offer a valid therapeutic option in hyperimmune patients who have no short-term alternatives. Evidence-based pediatric studies are needed to have unified protocols.

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COMPLICATIONS OF THERAPEUTIC APHERESIS IN CHILDREN WITH KIDNEY DISEASE

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Therapeutic apheresis (TA) is an extracorporeal treatment that selectively eliminates harmful substances. Although, it is an effective treatment in renal diseases, information about side effects is insufficient. In this study, we aim to evaluate the complications encountered in children with kidney disease who underwent therapeutic apheresis.

**Method:** The medical records of children with kidney disease treated with therapeutic apheresis between January 2007 and August 2022 in our department were reviewed retrospectively. Patient with missing data and non-nephrological diseases were excluded.

**Results:** 108 children, 51 boys (47.2%) with a median age of 14 years (1–18) and median body weight of 38 kg (6–90) were included in the study. A total of 1214 sessions of apheresis, including 1147 sessions of therapeutic plasma exchange (TPE) and 67 sessions of immunoadsorption (IA). Primer diagnosis were as follows: acute humoral rejection 65.9%, hemolytic uremic syndrome 14.6%, nephrotic syndrome 14.1%, glomerulonephritis 4.2% and desensitization before renal transplantation 1.2%. Of the total 1214 sessions, 17 different complications developed in 58 (4.8%) sessions, and 53 sessions (4.6%) could not be completed due to these complications (Table 1). The patients with TPE had more complications than patients with IA (5.1% vs. 0%,  $p = 0.070$ ). The incidence of complications was higher in patients aged 3–6 years compared to other age ( $p = 0.031$ ). Multivariate analysis modeled on age and hemoglobin values found increased risk of complications with increased hemoglobin (Hb) value (OR 1.250, 95% CI 1.093–1.429,  $p < 0.001$ ); The cutoff value of Hb for development of complications was calculated as 9.75 g/dL with a sensitivity of %59.1 and specificity of 57.2% (AUC: 0.576, CI: 0.50 – 0.64,  $p = 0.015$ ).

Table 1: Distribution of complications associated with therapeutic apheresis

Complications (n = 58)	n (%)
Technical problems (scarce flow, bleeding, access malfunction,...)	24 (41.4)
Allergic reactions (urticaria, itching, angioedema)	15 (25.9)
Others (headache, chest pain, vomiting, hypotension,...)	14 (24.1)
Citrate intoxication (hypocalcemic contraction)	3 (5.2)
Severe reactions (anaphylaxis)	2 (3.4)

**Conclusion:** In our study, we found the frequency of complications in TPE procedures to be around 5%; about half of the complications were technical problems. We observed that the risk of complications increased in patients between the ages of 3–6 years and with a Hb level above 9.75 mg/dL.

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## THE IMPACT OF IMMUNOSUPPRESSIVE THERAPY ON PUBERTAL DEVELOPMENT AND LONG-TERM OUTCOMES IN PEDIATRIC RENAL TRANSPLANTATION

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**Objectives/Purpose:** In children undergoing kidney transplantation, the anti-rejection therapy may be associated with serious side effects on the long-term. Among these, anomalies in puberty, hormonal balance and growth disorders represent underrecognized and, thus, underestimated complications.

**Methods:** We run a systematic review in PubMed, Embase and Cochrane databases, from inception to November 2022, looking for studies providing any evidence of the effects of immunosuppression on growth and pubertal development in children undergoing kidney transplantation. Studies were collected with no language, follow-up or population restriction. Study quality was evaluated by the Newcastle-Ottawa scale.

**Results:** From an initial set of 154 potentially relevant studies, we finally included 22 papers fully matching the clinical question and the reference population. Twenty studies were retrospective while only two were prospective observational studies. Of these, 13 analyzed the impact of immunosuppression in childhood on fertility and pubertal development while the remaining focused on bone growth and maturation. We found hypogonadotrophism to be frequently reported in uremic children with anti-rejection therapy causing at first an improvement in growth which is usually followed by a progressive slowdown and a delay in puberty, especially in individuals born small for gestational age. Body disproportion after immunosuppressive therapy was also frequently reported. The dose, exposure time, category of the immunosuppressant (particularly sirolimus and cyclophosphamide), the time from transplantation and the eGFR were the most relevant individual modulators of such effects. The quality of the studies was on average mild to moderate.

**Conclusion:** Detrimental effects of immunosuppressive therapy on growth and puberty are frequently reported among children receiving a kidney transplant and should therefore be considered as a major concern. Optimization of anti-rejection therapy, early identification of individuals at higher risk, optimal planning of complementary GnRH therapy and more focused research on this issue are advocated to improve outcomes in such a particular population setting.



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**MEDIUM TERM OUTCOME OF DE NOVO DSA TREATED WITH OPTIMISED IMMUNOSUPPRESSION FOLLOWING KIDNEY TRANSPLANTATION IN CHILDREN**

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**Aims/Purpose:** Development of de novo Donor specific antibodies (DSA) is associated with reduced graft survival in children following kidney transplantation (KT). There is little data on the optimum management of these children who develop DSA.

**Aims:** To study the outcome of children treated with optimised immunosuppression following detection of de novo DSA following KT.

**Methods:** A retrospective single centre study of all children who developed de novo DSA following KT January 2020 to January 2023. DSA were checked because of a clinical indication or as part of annual assessment. Optimisation of IS involved triple IS - aiming for tacrolimus trough levels of 5–8 mcg/l, MMF dose of 600 mg/m<sup>2</sup> /dose and prednisolone 5–10 mg daily.

**Results:** 12 children (10 male) developed de novo DSA 0.3 – 10.7 years following KT. The age at development of DSA was 3.3 – 14.9 years. 10 were living donor recipients and 2 were from deceased donors. The mean mismatch was 1:1:1 at A, B and DR. All developed class II HLA DSA with 7 against DQ, 1 against DR and 4 against both DQ and DR. The median MFI was 12337 (range 5312 – 33733). Graft biopsy was performed because of impaired function in 5 children. 2 demonstrated Banff TCMR (IA and IIA), 2 had CAMR with IFTA 2–3 and 1 child developed acute AMR. The eGFR at DSA detection was 58ml/min/1.73m<sup>2</sup> (range 20 – 118). There were issues with adherence to treatment in 3 children and in 2 IS was reduced due to viraemia and MMF intolerance. At the time of development of DSA 10 children were on tacrolimus and MMF, 1 on tacrolimus monotherapy and 1 on tacrolimus, MMF and prednisolone. The median tacrolimus level at the time of detection of DSA was 4.0 mcg/l (range 2.2 – 6.3) and the median MMF dose was 220 mg/m<sup>2</sup>/dose (range 175 – 310). In terms of treatment, the children with biopsy proven rejection received 3 doses of intravenous methylprednisolone and were then commenced on triple IS. At the latest follow up 1.3 – 12.2 years following KT and 1.6 years (range 1 – 2.5 years) following detection of DSA, the eGFR is 51 (range 33 – 91) ml/min/1.73m<sup>2</sup> and 2 children have proteinuria and 2 have hypertension. In terms of DSA, the MFI has reduced in 9 children by a median of 74% (range 20 – 89%). In 3 the level of DSA had dropped to a level considered negative. One child developed mastoiditis following increased IS. There have been no graft losses or mortality.

**Conclusion:** Optimisation of IS appears to reduce levels of DSA and stabilise graft function in the medium term. Longer term data and prospective studies are required to confirm these findings.

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## PAEDIATRIC RENAL DIETETIC INPUT POST RENAL TRANSPLANT: A SURVEY OF PARENTS/CARERS

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**Aims/Purpose:** It has been suggested by KDOQI that assessment of growth, nutrient intakes and physical activity levels should continue in children post renal transplant to ensure the best outcomes. A recent survey by our team identified that, due to staffing levels and funding, paediatric dietitians from the 13 UK paediatric renal centres are unable to regularly review these patients in the outpatient setting. There is limited published data on parental/carer views regarding paediatric dietetic services post-transplant.

**Methods:** We surveyed parents/carers of children currently attending our post renal transplant outpatient clinics using an electronic survey.

**Results:** The majority of parents/carers (89%) reported a preference for the initial dietetic advice post-transplant to be given face to face by the paediatric renal dietitian, of which 47% would also like an information leaflet. Overall, parents/carers felt that an information leaflet (53%) and video (21%) would be useful. The majority of parents/carers (83%) would like regular dietetic reviews for their child. With regard to the frequency for these consultations, 38.9% would like 6 monthly reviews whilst 27.8% and 16.7% preferred yearly or 3 monthly reviews respectively. The remainder reported a preference for a review on request service (11%) with only one parent/carer noting that their child did not require regular dietetic input. Fifty-three percent of parents/carers reported no concerns with their child's nutrition or weight; 18% reported concerns with large amounts of weight gain post-transplant and 12% reported concerns that their child was experiencing difficulties gaining weight. Feedback from parents/carers on the type of post-transplant dietetic service they would like for their child included dedicated dietetic support in the early weeks and months post-transplant with dietetic input thereafter to be available on request. Other themes included frequent reminders on foods to be avoided, updates on new research in post-transplant nutrition and support with healthy eating.

**Conclusion:** This single centre survey identified that the majority of parents/carers surveyed felt there was a need for regular paediatric dietetic input for their children post-transplant, ideally every 6 to 12 months. Funding is required in this area of patient care as, due to issues with staffing levels, dietetic services are currently unable to provide this service in the UK.

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**FOCAL SEGMENTAL GLOMERULOSCLEROSIS ASSOCIATED WITH SCABIES IN A PEDIATRIC KIDNEY TRANSPLANT PATIENT**

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**Aims/Purpose:** Before the 1980s scabies complicated by nephropathy was common in disadvantaged populations living in tropical and subtropical regions. In the last years, incidence rate of scabies decreased due to the improved sanitary conditions. Nowadays, it is very important to make an early diagnosis of scabies infection and to start appropriate treatment especially in immunosuppressed patients.

**Methods:** Here, we present the case of 8-year-old boy with bilateral renal dysplasia who received kidney transplant in 2016, admitted into the nephrology ward with diffuse red papules and persistent pruritus associated with worsening of renal function and proteinuria and with hypertension. In his history, there were two past episodes of kidney transplant rejection (first acute cellular, second humoral), scarce compliance to prescriptions and residual mild proteinuria (urine protein-to-creatinine ratio, UPCR 0.5) secondary to his chronic kidney damage. One month before admission, the patient had started to present generalized pruritus and itching especially at night. The initial laboratory tests showed: creatinine 1,8 mg/dL (baseline creatinine values 1,2 mg/dl), mild dysproteinemia and the UPCR was 5. Renal ultrasonography disclosed no abnormalities. After dermatologist's inspection a diagnosis of scabies was confirmed and the patient was placed on contact isolation and treated with local application of permethrin. In the following days, a renal biopsy was performed which revealed the coexistence of a chronic transplant glomerulopathy and FSGS, modest inflammatory lymphomonocytic infiltrate without tubulitis. Immunofluorescence showed granular glomerular capillary and mesangial staining for IgG, IgA, IgM, C3, C1q. No signs of interstitial nephritis were found. The symptom of skin pruritus significantly improved within two weeks. In the following month, UPCR and creatinine decreased to the value of 1.3 and 1.4 mg/dl respectively.

**Conclusion:** To the best of our knowledge, this is the first report where scabies resulted in a FSGS. Glomerulopathy associated with scabies could be misdiagnosed. Early diagnosis is necessary considering that it can lead to severe renal damage. Therefore, physicians need to pay close attention to the symptoms of skin pruritus in immunosuppressed patients presenting with worsening renal function and proteinuria.

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## EVALUATIONS OF CARDIAC FUNCTIONS BY SPECKLE-TRACKING ECHOCARDIOGRAPHY IN PEDIATRIC PATIENTS UNDERGOING RENAL TRANSPLANTATION

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**Aims/Purpose:** Although kidney transplantation (KTx) is the best treatment for end-stage chronic kidney disease and improves prognosis, these patients are at risk for cardiovascular disease due to ongoing metabolic processes, hypertension, and medications used. This study aimed to document dysfunction at an early stage using methods such as two-dimensional speckle-tracking echocardiography (STE).

**Methods:** 23 KTx and 23 healthy age and gender-matched children were evaluated. Conventional echocardiography and 2-dimensional STE were applied to the cases. Left ventricle (LV), total global longitudinal strain (TGLS), and total global strain (TGS) were measured. Instant blood pressures of all patients were evaluated.

**Results:** When blood pressure measurements were compared, it was seen that the z-scores of the systolic blood pressure measurements of the patient group were higher, but there was no statistical difference ( $p = 0.05$ ). However, a diastolic difference was observed ( $p = 0.015$ ). In echocardiographic measurements, the left ventricular mass index of the patient group was high ( $p = 0.046$ ). However, there was no difference between the two groups in terms of ejection fraction and relative wall thickness ( $p = 0.113, 0.928$ ). The longitudinal global strain values in the apical four-chamber, three-chamber, and two-chamber views and the total global strain values were significantly lower in the patients. There was a statistically significant difference ( $p < 0.05$ ).

**Conclusion:** The mechanism of persistent hypertension in the post-transplant period was still unclear. With STE, contractile defects can be demonstrated without end-organ damage. STE can help identify subclinical left ventricular dysfunction in patients with normal conventional echocardiography. Although there is no problem in ejection fraction or wall thickness in patients, it is advantageous to show that there is a problem in myocardial contractility in the early period with STE, in the prevention of morbidity and mortality.

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## A RARE CLINIC IN COMPLICATED URINARY TRACT INFECTION: EMPHYSEMATOUS PYELONEPHRITIS

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**Aims/Purpose:** Complicated urinary tract infections (UTIs) are clinics that are difficult to recognize and treat. Here, we present a case who presented with sepsis and was diagnosed with emphysematous pyelonephritis despite no UTI during renal transplantation follow-up.

**Methods:** A 4-year-old girl who had undergone a renal transplant 3 years ago due to congenital nephrotic syndrome was admitted with complaints of fever and vomiting. On physical examination, capillary refill time was long and tachycardic. It was learned that the hypotensive patient had a sluggish appearance and no urine output. WBC was 21400/mm<sup>3</sup> and NEU was 16300/mm<sup>3</sup> in complete blood count. While basal creatinine was 0.4 mg/dL, it was 0.7 mg/dL at admission. The CRP value of the case without ion imbalance was determined as 203mg/L. Lactic acidosis was detected in the blood gas of the patient, and the density was 1005 and +3 leukocytes in the routine urinalysis.

**Results:** Abdominal ultrasonography performed for abdominal pain was evaluated as emphysematous cystitis due to the presence of air in the bladder. However, because the patient was septic and receiving immunosuppressive therapy, non-contrast abdominal computed tomography (CT) was performed to confirm the diagnosis. Emphysematous pyelonephritis was diagnosed in the case, in which air was detected in the transplanted kidney on CT. The patient was started on meropenem, teicoplanin, and amikacin treatment. With appropriate hydration and antibiotic therapy, the clinic resolved within 48–72 hours. *Escherichia coli* growth was observed in the urine culture. *Escherichia coli* is the most common cause of emphysematous pyelonephritis. Intravenous antibiotic therapy was completed in 14 days and a voiding cystourethrogram was performed. Vesicoureteral reflux was detected in the patient who had no history of UTI so far.

**Conclusion:** Emphysematous pyelonephritis is a rare but important clinical entity among complicated UTIs. It is a clinic that should be kept in mind, especially in elderly, diabetic, and immunocompromised patients. Nevertheless, emphysematous pyelonephritis should be considered in immunosuppressive cases, even if the age is younger.

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**FOLLOW-UP OF TURKISH CHILDREN WITH RENAL TRANSPLANTATION IN INFANCY PERIOD: A SINGLE CENTER EXPERIENCE**

**Cemaliye Başaran<sup>1</sup>, Özgür Özdemir-Şimşek<sup>1</sup>, Gökçen Erfidan<sup>2</sup>, Belde Kasap-Demir<sup>1,3</sup>, Seçil Arslansoyu-Çamlar<sup>4</sup>, Demet Alaygut<sup>4</sup>, Fatma Mutlubas<sup>4</sup>**

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**Aims/Purpose:** In our study, we aimed to present the follow-up of our patients who were followed up in our center and who underwent renal transplantation in infancy.

**Methods:** The files of patients who underwent renal transplantation in infancy were reviewed retrospectively. Age of transplantation, type and duration of renal replacement performed before transplantation, weight at the time of transplantation, height, type of donor, early and late complications after transplantation, rejection histories, treatment and interventions, growth status in the follow-up after transplantation and biochemical examinations in all these periods were evaluated.

**Results:** We had a total of 8 patients who underwent renal transplantation. One patient was followed up with cystic kidney disease, two patients with renal dysplasia, two patients with congenital nephrotic syndrome, one patient with cystinosis, one patient with chronic kidney disease secondary to hemolytic uremic syndrome, and the primary diagnosis of one patient was unknown. Peritoneal dialysis was applied to 6 patients before transplantation, while preemptive transplantation was performed on 2 patients. Five of the patients were transplanted from a living donor and three from a cadaver. The weight of the patients at the time of transplantation ranged from 6.7–13 kg and the mean age of transplantation was  $23.3 \pm 6.9$  months. Unilateral or bilateral nephrectomy was performed in all patients. The mean follow-up period of the patients after transplantation was  $79.5 \pm 63.7$  months. In the follow-up, 2 patients developed acute rejection and 4 patients had EBV or CMV infection. All patients had positive growth developments in the post-transplant period. The mean weight SDS before transplantation was  $-1.37 \pm 1.20$ , while the mean height SDS was  $-2.24 \pm 1.52$ . In the last visit of the patients, mean weight SDS were  $0.33 \pm 3.48$ , and current height SDS were  $-0.43 \pm 4.27$ .

**Conclusion:** Contrary to what was reported in previous studies, acute rejection was rare in our patients, and infections are the most common complication. Therefore, we think that more care should be taken when giving immunosuppressive therapy to infants.

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**OBINUTUZUMAB IN FOCAL SEGMENTAL GLOMERULOSCLEROSIS RECURRENCE AFTER PEDIATRIC KIDNEY TRANSPLANTATION: A CASE REPORT**

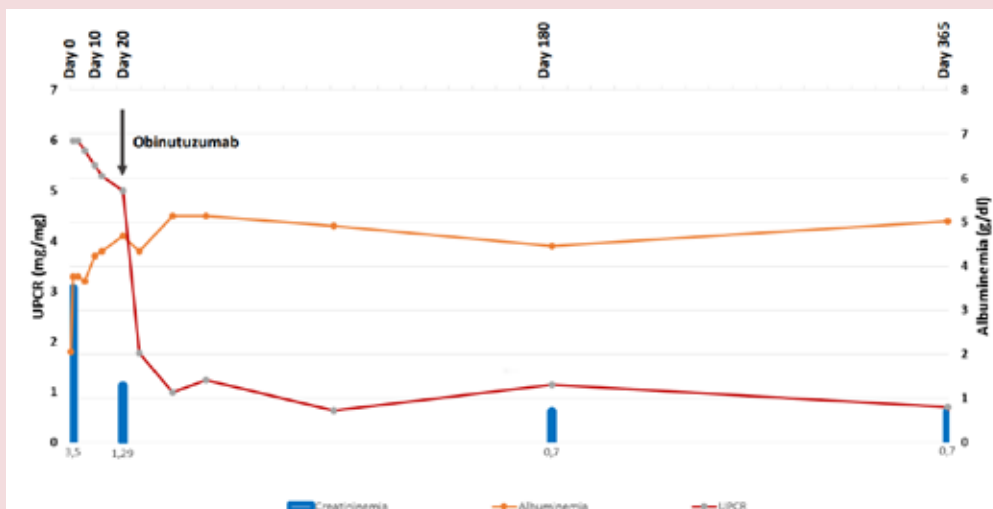
Francesca Semeraro<sup>1</sup>, Luca Antonucci<sup>2,3</sup>, Marina Vivarelli<sup>2</sup>, Manuela Colucci<sup>4</sup>, Raffaella Labbadia<sup>2</sup>, Andrea Cappoli<sup>2</sup>, Angela De Luca<sup>5</sup>, Carmine Pecoraro<sup>5</sup>, Francesco Emma<sup>2</sup>, Isabella Guzzo<sup>2</sup>

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**Aims / Purpose:** SRNS is responsible for more than 10% of ESKD in children and FSGS is the most common histological finding. Its recurrence after kidney transplantation is frequent and associated with poor outcome [1]. Its treatment is challenging without a standardized protocol, based only on case series and reports. Plasma exchange, infusion of rituximab, high doses of cyclosporine, immunoabsorption and LDL apheresis are possible options [2]. Our work aims to describe a child successfully treated with Obinutuzumab in a FSGS recurrence after kidney transplantation.

**Methods:** A 3 years old boy was admitted in our center for a steroid resistant nephrotic syndrome (SRNS) treated with steroids, calcineurin inhibitors, rituximab, ofatumumab and plasmapheresis without remission. Genetic test was negative and kidney biopsy revealed FSGS. He rapidly developed ESKD with need for peritoneal dialysis at age of 6 years, and underwent kidney transplantation from living donor at age of 8 years. Twelve hours after transplantation he developed dramatic FSGS recurrence with an anuric AKI, poorly treated with high doses of steroids, cyclosporine, rituximab, immunoabsorption, and plasmapheresis three times per week. After collegial discussion we decided to administer Obinutuzumab as rescue therapy.

**Results:** After about one week, a clinical and laboratory response occurred, proteinuria reached sub-nephrotic range (UPCR 1.78 mg/mg) with a subsequent reduction in plasmapheresis frequency twice a week. Six months after transplantation proteinuria was reduced (UPCR 1.24 mg/mg). One year after transplantation proteinuria was stably low (UPCR 0.7 mg/mg) and plasmapheresis frequency was further decrease to once per week (Fig. 1).



**Conclusions:** The use of Obinutuzumab (II generation humanized anti-CD 20 antibody) is recently reported in autoimmune glomerulonephritis such as membranous nephropathy and lupus nephritis [3]. There is a single study outlining its efficacy in association with daratumumab in pediatric SRNS [4]. As far as we know, this is the first pediatric case of FSGS recurrence on kidney graft treated with Obinutuzumab, and based on our experience, it could reveal a valid therapeutic option. Further studies are required to clarify its use in these category of patients.

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POST-TRANSPLANT COMPLICATION: LEIOMYOMA AND EARLY FOLLOW-UP

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**Aims/Purpose:** Many complications, especially infections, are expected after kidney transplantation. Malignancies are one of these complications and patients should be followed in this regard. Here, a 3-year-old girl who was diagnosed with leiomyoma in her 2nd year after transplantation will be presented.

**Methods:** A 3-year-old girl, who had undergone kidney transplantation for congenital nephrotic syndrome 2 years ago, was admitted to the emergency department with complaints of fever, cough, and deterioration in her general condition. Physical examination revealed tachypnea, tachycardia, prolonged capillary filling time, decreased lung sounds, and bilateral rales at the bases. The patient was evaluated for sepsis. Blood and urine cultures were taken. A bilateral chest X-ray was taken and bilateral nodules of different sizes were seen. There was leukocytosis and neutrophilia, and c-reactive protein and sedimentation were also very high. High-resolution lung computed tomography was performed on the patient. Nodules were evaluated in favor of infection. Amikacin, meropenem, and teicoplanin were started because the patient was septic.

**Results:** Antibiotherapy was completed in 14 days for the patient whose fever regressed at 48 hours of treatment, acute phase reactants tended to regress, and became clinically stable. However, tuberculosis and *Nocardia* were excluded in terms of opportunistic infections in the patient who did not show radiological improvement. The cyst was evaluated by the radiologist as suspicious for a hydatid cyst and nodule exploration was performed in the case. The pathology result was evaluated as leiomyoma. EBER staining was requested and it was found positive. It was evaluated as Epstein-Barr virus (EBV) associated leiomyoma, but EBV DNA was negative. In accordance with the literature, mycophenolate mofetil was discontinued and everolimus was started. Tacrolimus and oral steroid treatment were continued as usual. In the case followed for 1 year, no growth was observed in the nodules.

**Conclusion:** Many complications, including malignancies, can be seen in the long term after transplantation. Patients should pay attention to the post-transplant lymphoproliferative disease and other malignancies should be kept in mind.



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## ADEQUACY OF KIDNEY BIOPSIES IN CHILDREN: A SINGLE CENTRE STUDY

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**Aims:** Percutaneous kidney biopsy is an essential procedure performed in the diagnosis and management of paediatric kidney disease. We aimed to study the adequacy of attained native and transplant biopsy specimens within our centre.

**Methods:** We retrospectively studied the outcome of 207 kidney biopsies performed during a five-year period. All biopsies were performed by a paediatric radiologist under general anaesthesia with an 18 G needle by ultrasound-guidance. A paediatric nephrologist was present during the procedure performing an ocular inspection of the biopsy. In native kidneys a biopsy was regarded adequate when 10 or more glomeruli were present and marginally adequate if fewer glomeruli were described but diagnosis could be set. An adequate transplant biopsy was defined according to the Banff 97 classification of renal allograft pathology having 10 or more glomeruli and at least two arteries. A marginally adequate sample was defined as a biopsy with at least 7 glomeruli and one artery. Adequate cortex had to be present in the examined material.

**Results:** 203 (98%) of the biopsies were assessed as adequate (87%) or marginally adequate (11%). Transplant biopsies were assessed as adequate in 68% compared to native biopsies in 92%. A total of 4 (2%) specimens were considered inadequate, all of them in transplant biopsies. One transplant biopsy had an inadequately low number of glomeruli whereas the other biopsies had a low number of arteries or insufficient amount of cortex.

**Conclusions:** The kidney biopsy procedure in our centre provided a high number of adequate samples. Transplant biopsies were likely evaluated as less adequate due to the distinct classification system for transplant biopsies.

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DOSE DEVELOPMENT OF DNDSA ACCELERATE KIDNEY ALLOGRAFT FAILURE IN CHILDREN?

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**Aim/Purpose:** The development of de novo Donor specific Antibodies (dnDSA) has been linked with graft rejection and dysfunction in paediatric kidney transplant recipients. Routine surveillance for DSA is thought by some to have no clear role in the presence of normal allograft function in kidney transplant recipients. There are limited data on development of dnDSAs and graft dysfunction and allograft failure. We aim to understand the development of allograft dysfunction and failure in children who develop dnDSAs.

**Method:** 10-year retrospective observational review was carried out for all the children (= 18 years of age) who underwent kidney transplantation at a tertiary centre. Data were collected through electronic patient records and included patient demographics, donor and recipient characteristics and post-transplant course including rejection episodes, dnDSA surveillance, progression of eGFR and immunosuppression changes.

**Results:** Preliminary analysis identified 46 children (20 female and 26 Males) who had a kidney transplant at a mean age of 10 years (SD 4.8). Median follow-up time was 3 years (IQR:2). 10 patients (22%) developed dsDSAs, 27 patients (58%) did not develop any dsDSAs throughout their follow-up and 9 patients were excluded as no data on dnDSAs were available. 60% (6/10) of patients in dsDNA group had a decline in eGFR to a mean 30ml/min/1.73m<sup>2</sup>(SD 18), whereas 40% (5 /27) of children with no DSAs developed a mean eGFR of 35 ml/min/1.73m<sup>2</sup> (SD 13) over the follow-up period (p = 0.2). Biopsy proven rejection episodes were noted more in the dnDSA group as compared to no dnDSA group (30% vs 18%, p value: 0.08).

**Conclusion:** Our interim analysis did not find any statistically significant difference in the eGFRs of children with kidney allografts who developed dnDSA and those who did not at the last follow-up. This study is the first step towards understanding this cohort and developing future directions in research to understand kidney allograft failure.

	Follow-Up		3 months	6 months	1Year	2 Year	3 Year	4 Year	
Total (46)	Developed dnDSA (10)	eGFR**	< 50	3	1	2	2	2	1
			50-90	1	1	0	1	3	1
			> 90	0	0	0	1	0	0
		Viremia***	Yes	2	1	1	4	3	1
			No	2	1	1	0	2	1
		Rejections	Number	1	0	1	1	0	0
	Proteinuria		Yes	2	1	0	2	2	1
		No	0	0	0	0	1	0	
	No dnDSAs Developed (27)	eGFR	< 50	9	9	8	10	9	4
			50-90	10	15	10	14	12	8
> 90			16	12	19	6	3	4	
Viremia		Yes	19	16	27	22	19	11	
		No	16	20	10	8	5	4	
		1	1	1	1	0	0	0	
Rejection		= 2	0	1	0	0	0	0	
		1	1	1	1	0	0	0	
proteinuria		Yes	10	13	12	16	13	9	
		No	2	0	1	1	1	1	

\*\*eGFR ml/min/1.73m<sup>2</sup> - \*\*\* includes EBV,CMV,BK and JC

# POSTER SESSION 2E

# Glomerular Disorders

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## IMPACT OF COVID19 PANDEMIC ON HEMOLYTIC UREMIC SYNDROME EPIDEMIOLOGY IN CHILDREN – PRELIMINARY RESULTS OF A SINGLE CENTRE STUDY

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**Introduction:** Various case reports have shown that COVID-19 infections may lead to new episodes or relapses of hemolytic uremic syndrome (HUS). Aim of the project was the assessment of COVID19 pandemic in the context of HUS epidemiology in children in our centre.

**Methods:** In retrospective analysis all HUS cases having been treated in Department of Pediatric Nephrology and Hypertension Jagiellonian University Collegium Medicum in Kraków within 3 years prior (HUS-3) and 3 years after (HUS+3) COVID19 pandemic outbreak - were included. The time cut off point was settled on Jan 1-st 2020. STEC (typical) HUS was diagnosed when genetic material of Enteropathogenic (EPEC), Enterohemorrhagic (EHEC), Shiga Toxin *Escherichia coli* 1 or 2 (STEC 1 or2) in patient's stool or anal swab was confirmed; whereas atypical HUS was diagnosed when the result of stool test was negative and ADAMTS13 activity was above 10%. In groups comparison for groups cardinality - Fisher's exact test was applied, while for detailed data - t-Student's test; for groups having been positively verified about Gaussian distribution - Shapiro-Wilk test and Wilcoxon rank sum test for other groups were applied.

**Results:** In the study 41 new cases (HUS-3:14 and HUS+3:27) - were included. Annual morbidity in HUS+3 vs HUS-3 was 1.9 - times higher (9 vs 4.7). Mean hospitalization duration (HUS+3: 36.6 vs HUS-3: 21.2 days) was statistically insignificant (NS), however mean time spent in intensive care unit (ICU) was 10-times longer (17 vs 1,7 days), and the number of children that must have been treated in ICU in HUS+3 group was significantly higher than in HUS-3 population (7.14% vs 44.4%; p = 0.03). which reflects more severe disease course. The mortality (about 7%) was NS between groups. Children in HUS+3 group were younger (mean 52.2 vs 73.5 months) but the difference was NS; similarly no statistically significant distinctions in terms of: 1/sex, 2/eGFR values at admission, 3/diarrhoea in medical history, 4/blood the stool, 5/concomitant respiratory infection, 6/concomitant neurological symptoms, 7/the fact of oligo-anuria, 8/hypertension, 9/the need of renal replacement therapy - were ascertained.

**Conclusions:** COVID19 pandemic might have impacted on the incidence of new paediatric HUS cases with more severe clinical course but did not impact on their survival rate. The study needs to be continued.

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## PERCUTANEOUS RENAL BIOPSY FINDINGS IN A TERTIARY REFERRAL CENTER

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<sup>1</sup>Pediatrics, <sup>2</sup>Pediatric Nephrology, <sup>3</sup>Pediatric Radiology, Ankara University, Ankara, Turkey

**Aims/Purpose:** Ultrasound-guided percutaneous renal biopsy is a basic method used in the diagnostic and prognostic evaluation of children with renal disease. In this study, we aimed to evaluate the indications, results and complications of percutaneous renal biopsies performed in our clinic in the last 10 years.

**Methods:** Native and transplant percutaneous kidney biopsies performed in our center between January 2010 and January 2020 were included in the study. Patients were examined retrospectively through archive files and hospital operating system. The study was approved by the Ankara University Faculty of Medicine Ethics Committee.

**Results:** We found that, 237 percutaneous renal biopsies were performed in 202 patients (105 males) with a mean age of  $10.54 \pm 5.05$  years. Among them 194 (82%) were native biopsies and 43 (18%) were transplant biopsies. The most common indications for native renal biopsy were proteinuria (22.6%), systemic diseases (21%) and nephrotic syndrome (20.4%). Proteinuria was found in the majority (96%) of the patients who underwent biopsy, hematuria in approximately half and impaired renal function tests in one third. In the analysis of biopsy results, glomerular diseases (53%) were the most common pathology followed by systemic disease involvement (22%). Focal segmental glomerulosclerosis was the most common primary glomerular disease followed by IgA nephropathy. Almost all transplant renal biopsies were performed due to increased creatinine levels (81.4%) and the most common pathological finding was acute or chronic rejection with a frequency of 62.8%. Recurrence of primary disease was detected in 7%, and drug toxicity in 11.6% of the biopsies. A total of 52 (21.9%) complications were observed after biopsy procedures. The most common complication was perirenal hematoma (21%), and macroscopic hematuria was observed in three patients (1.2%).

**Conclusions:** Percutaneous renal biopsy is an important procedure that gives clinicians the chance to make a definitive diagnosis in a wide spectrum of diseases in patients presenting with severe complaints such as edema, hypertension, and hematuria in childhood. It is a very safe and useful method with extremely low complication rates.

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URINARY COMPLEMENT FACTOR D AS A POTENTIAL INDICATOR OF PERSISTING PROTEINURIA IN CHILDREN WITH IGA VASCULITIS

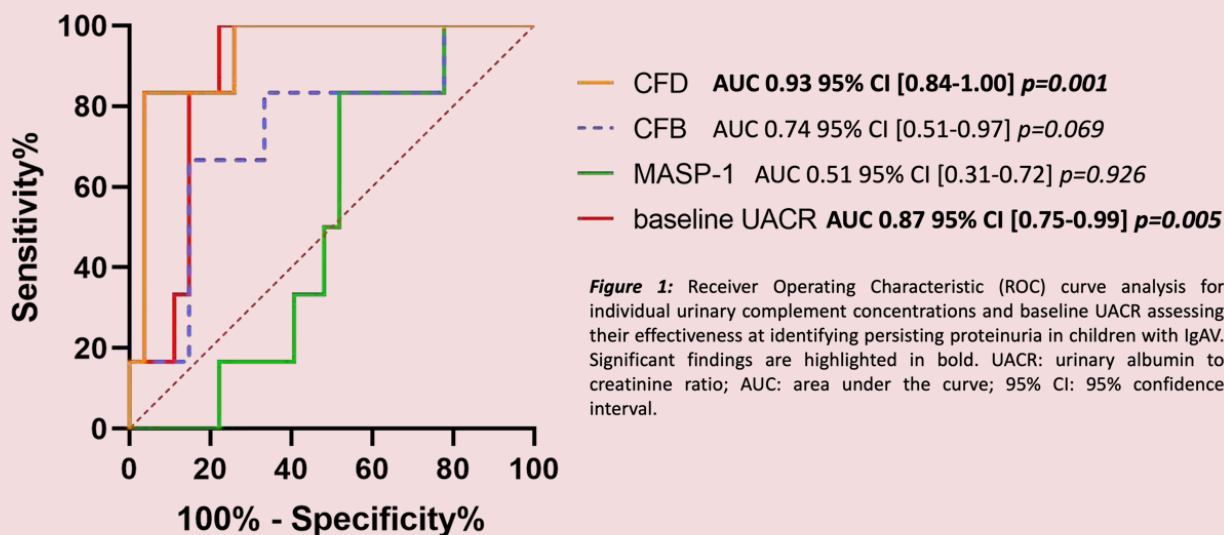
Julien Marro<sup>1</sup>, Andrew Chetwynd<sup>1,2</sup>, Jennifer Hawkes<sup>1</sup>, Sarah Northey<sup>1</sup>, Louise Oni<sup>1,3</sup>

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**Aims/Purpose:** Nephritis is a recognised complication of IgA vasculitis (IgAV; HSP) with 1-2% risk of kidney failure. The pathophysiology of nephritis is largely unknown, recent evidence suggests the complement system is involved. The aim of this study was to quantify urinary products of the alternative and lectin complement pathways in children with IgAVN and their ability to predict outcomes.

**Methods:** Children with IgAV and healthy controls (HCs) were recruited to the IgA vasculitis study (Alder Hey Children's Hospital, Liverpool, UK). Participants were subgrouped according to proteinuria: IgAV with nephritis (IgAVN) or IgAV without nephritis (IgAVwoN). Urinary quantification of complement factor D (CFD), factor B (CFB) and MBL-associated protease 1 (MASP-1) were performed using ELISA. All patients were followed-up for  $\geq 6$  months, primary outcome was persisting proteinuria (urinary albumin to creatinine ratio  $> 30$  mg/mmol). Data (mean  $\pm$  SD) was normalised to urinary creatinine. Exploratory ROC analysis was conducted to assess the predictive value for persistent proteinuria.

**Results:** In total 50 children were included (IgAVN,  $n = 15$ ; IgAVwoN,  $n = 20$ , HCs,  $n = 15$ ) with a mean age of  $8.5 \pm 3.7$  years old. Urinary CFD and CFB concentrations were significantly increased in children with IgAVN ( $3.5 \pm 5.46$   $\mu$ g/mmol;  $25.6 \pm 27.6$   $\mu$ g/mmol respectively) compared to IgAVwoN ( $0.4 \pm 0.4$   $\mu$ g/mmol,  $p = 0.002$ ;  $9.2 \pm 11.5$   $\mu$ g/mmol,  $p = 0.007$ ) and HCs ( $0.3 \pm 0.2$   $\mu$ g/mmol,  $p < 0.001$ ;  $5.1 \pm 5.9$   $\mu$ g/mmol,  $p < 0.001$ ). Urinary MASP-1 concentrations were significantly increased in patients with IgAVN ( $116.9 \pm 116.7$  ng/mmol) compared to HCs ( $41.4 \pm 56.1$  ng/mmol,  $p = 0.006$ ). Mean follow-up ( $n = 33$ ) was  $17.8 \pm 17.5$  months (range [6.0-79.0]) and 6 IgAVN patients had persisting proteinuria at last review. Urinary CFD was excellent at identifying persisting proteinuria (AUC 0.93; 95% CI [0.84-1.00];  $p = 0.001$ ) whilst urinary CFB and MASP-1 were non-significant (Figure 1).



**Figure 1:** Receiver Operating Characteristic (ROC) curve analysis for individual urinary complement concentrations and baseline UACR assessing their effectiveness at identifying persisting proteinuria in children with IgAV. Significant findings are highlighted in bold. UACR: urinary albumin to creatinine ratio; AUC: area under the curve; 95% CI: 95% confidence interval.

**Conclusion:** Components of the alternative and lectin complement pathways are increased in the urine of children with IgAVN and may constitute potential therapeutic targets. Our exploratory results suggest urinary CFD may be a promising indicator of persisting proteinuria that warrants further analysis in larger longitudinal studies.

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**CLINICAL, LABORATORY AND GENETIC CHARACTERISTICS, TREATMENT AND OUTCOME OF CHILDREN WITH HUS DURING COVID-19 PANDEMIC: EXPERIENCE FROM TERTIARY REFERRAL CENTRE**

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**Aims/Purpose:** The global pandemic of COVID-19 made substantial changes on modes of transmission for many infectious and infections related diseases. Moreover, the SARS-CoV-2 virus has been shown to interfere with almost all body systems and mechanisms, including immunological and coagulation cascade, with a possibility to cause thrombotic microangiopathy in a susceptible host. Nevertheless, the studies examining the aetiology, clinical and laboratory findings, as well as outcome of HUS patients during the pandemic are lacking.

**Methods:** Retrospective study of consecutive patients treated for symptoms and signs suggestive of HUS in referral centre for paediatric nephrology of Republic of Croatia from November 2020 to January 2023.

**Results:** Out of 15 patients (median age 17 months, 11 female), 5 had Shiga toxin producing *Escherichia coli* (STEC) and 1 *Streptococcus Pneumoniae* (SP) induced HUS. Moreover, 2 patients had HUS in the setting of COVID-19, 1 associated with Influenza A and 1 with Parvo B19 virus. The genetic testing revealed disease causing mutations in 2 patients (1 with COVID-19), 2 had variant of unknown significance along with variant reported as a risk factor (1 with influenza A), and 4 had polymorphisms reported as a risk factor for developing aHUS (1 with COVID-19). The most common presenting symptom was vomiting (67%), followed by diarrhoea (60%) and fever (53%). CNS was affected in 3 patients, lungs in 2 and pancreas in 1. CRRT was required in 5 and plasmapheresis was employed in 9 patients. Finally, 5 patients received complement inhibition therapy (4 Ravulizumab, 1 Eculizumab) during the first week after the disease onset (median 5 days). This treatment was used for less than 6 months in 3 and permanently in 2 patients. With the exception of SP induced HUS patient, who maintained increased levels of creatinine, all of the other patients had favourable outcome with median of 28, 7 and 15 days to reach lower reference range normal for Hb, PLT and creatinine, respectively, as well as sustained remission during the follow up (median of 8 months).

**Conclusion:** While STEC remains the single most common cause of HUS, our data have shown that during the COVID-19 pandemic other aetiologies became more common, with SARS-CoV-2 emerging as a new possible trigger for HUS in patients predisposed with genetic background. In our cohort, children with SARS-CoV-2 and influenza induced HUS were treated with C5 inhibitors, at least until the results of genetic testing became available. Although little is known about the detailed characteristics and most appropriate treatment modality for those patients, our results indicate that short term complement inhibition might be a valuable option.

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## LONG TERM OUTCOMES IN IGA VASCULITIS: SINGLE CENTRE EXPERIENCE

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IgA vasculitis (IgAV) is a small vessel vasculitis, characterized by IgA deposits presenting between 2–10 years (incidence 3–26 cases 100 000), associated with renal involvement in 20–30% of cases. The risk of progression to chronic kidney disease (CKD) is small although it may increase in presentations with nephrotic syndrome and/or renal failure. In recent years it has been proposed to be more aggressive in treatment as historically it had been considered a benign entity.

A descriptive, retrospective study was designed to describe the long-term evolution of patients with a diagnosis of IgAV referred to our clinic from 1983 to 2022.

We reviewed 91 patients (43 males) with mean age 8.1 (SD = 2.79 years) and median follow-up 11.5 (1–5 years). At the beginning of the cutaneous symptoms 49% had urinary alterations and 50% received steroids due to extrarenal indication.

All were referred for persistence/appearance of urinary signs (15% hematuria, 81% hematuria and proteinuria, 3% isolated proteinuria; 14% proteinuria in nephrotic range), 5% decreased glomerular filtration rate (GFR) and/or 9.8% arterial hypertension. In 13 cases the diagnosis was confirmed by biopsy.

After our evaluation 10 patients received immunosuppression (10/10 methylprednisolone, azathioprine 2/10, cyclophosphamide 2/10). 75/91 continued follow-up, and 22% received ACE inhibitors. Throughout evolution 14 presented outbreaks of macroscopic hematuria. At the end of follow-up 49% were in remission with normal GFR, 20% maintained microhematuria, 22% proteinuria, 76% of them were controlled with ACE inhibitors. 4 developed CKD: 1 dialysis 3 years after presentation and 3 with borderline GFR (81–85 ml/min/1.73m<sup>2</sup>). In our historical series a low percentage of patients were biopsied or received immunosuppression. Although 22% maintain low grade proteinuria, GFR evolution has been favorable, apart from 1 patient who had a rapidly progressive renal failure. The clinical impact of persistent urinary alterations must be evaluated in longer term studies.



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**HEREDITARY FORM OF THROMBOTIC THROMBOCYTOPENIC PURPURA WITH NOVEL GENETIC VARIANTS AS A CAUSE OF THROMBOTIC MICROANGIOPATHY: A CASE REPORT FROM PEDIATRIC NEPHROLOGY PRACTICE**

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**Introduction:** thrombocytopenia and microangiopathic hemolytic anemia with creation of microthrombi are characteristic for thrombotic microangiopathy (TMA). Although this process might affect any body system it is one of the most common causes of acute kidney injury in children. Despite distinct mechanism, the clinical manifestations are shared between most common primary forms, hemolytic uremic syndrome (HUS) and thrombotic thrombocytopenic purpura (TTP), opting for a wide diagnostic workup.

**Methods:** We present a case of a 20-month-old girl with TTP.

**Results:** A previously healthy 20-month-old girl with severe thrombocytopenia, mild hemolytic anemia with few schistocytes, along with microhematuria and proteinuria, was referred to department of pediatric nephrology due to suspected TMA. Her family and past medical history were unremarkable with only brief and resolved thrombocytopenia in the neonatal period. She had no signs of acute kidney injury and no other symptoms aside from mild respiratory tract infection. The standard evaluation for TMA revealed very low levels of ADAMTS13 (= 1%), suggesting TTP. Antibodies directed against ADAMTS13 were negative. Plasmapheresis with FFP substitution was immediately started with rapid amelioration of platelet and hemoglobin count. Genetic testing exposed two variants in ADAMTS13 gene, c.3655C > T, p.(Arg1219Trp) classified as pathogenic, and previously undescribed c.536C > T, p.(Thr179Ile) classified as a VUS and predicted to be deleterious, thus confirming hereditary TTP. Although literature data is still inconclusive, we decided to initiate prophylactic FFP infusions every 3 weeks. Nevertheless, a day before her second planned infusion, the patient had another relapse triggered by influenza A viral infection, which completely resolved after FFP administration. In further course, FFP was administered every 2 weeks, with no new relapses.

**Conclusion:** While HUS is the most common form of TMA encountered in everyday pediatric nephrology practice, due to distinctive mechanisms and management, it is important to be alert for other underlying causes as well. Our case highlights the importance of further genetic testing and phenotype correlation in hereditary TTP and adds to the growing body of evidence for the beneficial role of prophylactic FFP infusions.

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## MCPGGAAC HAPLOTYPE FOLLOWING ATYPICAL HEMOLYTIC UREMIC SYNDROME (AHUS) – EXPERIENCE OF THREE SOUTH EASTERN EUROPEAN COUNTRIES

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**Objective:** Follow-up evaluation of patients with MCPggaac haplotype with/without complement inhibition therapy.

**Methods:** We present a retrospective multicenter study of eight pediatric aHUS cases with the MCPggaac haplotype collected from three different countries: Croatia, Bosnia, Herzegovina, and North Macedonia.

**Results:** MCPggaac haplotype was found to be in the majority among aHUS mutations in regional populations. All aHUS onset started at a pediatric age at a median of 33 months (IQR 24.25 – 73.50 months). The average follow-up time was 151 months (IQR 58.50 – 255.0 months). Two patients were transferred to adult care. The median age of the first relapse was 10 months (IQR 9 – 30 months), and complement blockade was applied at the age median of 92 months (IQR 36–252 months) with an average number of relapses before complement blockade with eculizumab at 2.8 episodes. The average onset time of proteinuria was after the 4.4th relapse without therapy. Due to the inaccessibility to complement blockade therapy, one child has 11 relapses and now has renal insufficiency starting after 7th relapse. Most of the relapses occurred within a median of 17.5 months (minimum 8 months and 48 months maximum) since the onset of the disease (6/8 patients), as shown by the Kaplan–Meier survival curve.

**Conclusions:** Although MCPggaac haplotype onset and relapse can achieve remission by renal replacement therapy without complement inhibition, the disease can relapse quickly. If complement inhibition is not applied within 4–5 relapses, proteinuria and chronic renal failure will occur.

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GENETIC ATYPICAL HEMOLYTIC UREMIC SYNDROME IN CHILDREN: 10- YEAR EXPERIENCE FROM A TERTIARY CENTER

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**Aims:** Atypical hemolytic uremic syndrome (aHUS) is a rare disease. This study aimed to describe clinical profile, management, and outcome of aHUS patients admitted to our center between 2012- 2022.

**Methods:** We performed a retrospective analysis of data from medical records of aHUS patients younger than 18 years. A Next Generation Sequencing (NGS) panel of genes for aHUS was performed. Clinical features, genetic and complement serology results, therapeutic interventions, and outcomes were reviewed. Children with a confirmed STEC infection were excluded.

**Results:** Five cases of aHUS were included (3 male), median age 116 months (18-124). 60% had diarrhea at onset. In four patients we documented mutations in genes of the alternative complement pathway; 2 had anti-CFH antibodies. CFHR1-3 deletion without anti-CFH antibodies (patient 4, table 1) was not considered pathologic. 3 patients received eculizumab. Median time for eculizumab initiation was 6 days (5-30). Both patients with anti-CFH antibodies required hemodialysis despite plasma infusions (PI) but remitted completely at 13 and 30 days post eculizumab initiation, respectively. Eculizumab was later withdrawn (once anti-CFH < 1000 AU/ml) patients were started on MMF and steroids). The patient with MCP variant had 2 relapses (46 and 60 mo after initial episode). During the second one he required haemodialysis yet responded completely on day 16 of eculizumab treatment. The drug was discontinued after 6 months. Two patients did not receive eculizumab as 1 was treated before eculizumab era and remained on hemodialysis and 1 remitted with PI. Complications included vein thrombosis (n = 2), and transaminitis which is a rare side effect of eculizumab.

**Conclusion:** In this small cohort, all patients responded completely to eculizumab with no severe adverse effects. It is crucial to start eculizumab immediately after diagnosis. Genetic studies in aHUS are a valuable tool for planning duration of treatment with eculizumab according to the mutation.

Table 1: Clinical characteristics, management and outcome of aHUS patients

	Pt 1	Pt 2	Pt 3	Pt 4	Pt 5
Gender	M	F	M	F	M
Age at onset (months)	124	116	108	18	23
Prior infection	yes	Yes	yes	yes	Yes
Diarrhea	yes	No	No	yes	Yes
C3	normal	Low	low	normal	Low
Complement Gene affected	CFH mutation	CFHR3-1 deletion	CFHR3-1 deletion	CFHR3-1 deletion	MCP heterozygous
Anti-CFH antibodies	no	Yes	yes	no	no
Kidney biopsy	no	No	No	Thrombotic microangiopathy	No
Plasma exchange (PE) /infusions (PI)	PE	PI	PI	PI	PI
Hemodialysis	yes	yes	yes	no	Yes
Eculizumab	no	yes	yes	no	yes
Immunosuppressive treatment	no	MMF, steroids	MMF, steroids	no	No
Complications	no	jugular vein thrombosis	Transaminitis	no	Cephalic vein thrombosis, transaminitis
Relapses	no	No	no	no	2
Outcome	Kidney failure	Complete response	Complete response	Complete response	Complete response

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## IGA NEPHROPATHY AND SCHONLEIN-HENOCH PURPURA NEPHRITIS IN CHILDREN: COMPARISON OF CLINICAL AND BIOPTIC FEATURES, RISK FACTORS AND PROGNOSIS

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**Aims/Purpose:** It is still not known if IgA Nephropathy (IgAN) and IgA Vasculitis Nephritis (IgAVN) are different entities or the spectrum of the same disease.

**Methods:** This is a retrospective study on 26 children < 18 years with IgAN and 34 with IgAVN who performed renal biopsy between the 1st January 2009 and the 31st December 2019 at the Pediatric Nephrology and Dialysis Unit of IRCCS Azienda Ospedaliero-Universitaria in Bologna. Clinical, laboratoristic and bioptic data were compared between the two cohorts at disease onset, biopsy time and different time point, with a minimum follow up of 12 months. Renal outcome was defined as the persistence of proteinuria (UPr/UCr > 0.2 mg/mg) and/or eGFR reduction < 90 ml/min/1.73m<sup>2</sup> at last follow-up.

**Results:** IgAN patients were older at disease onset, compared to IgAVN patients (11.3 ± 2.9 vs 8.2 ± 2.9 anni, p < 0.05); in addition, time from disease onset to biopsy was longer for IgAN ones (11.3 ± 2.9 vs 8.2 ± 2.9 anni, p < 0.05). At biopsy time, IgAVN cohort had higher proteinuria and minor albuminemia levels (2.68 ± 2.42 vs 0.73 ± 1.02 mg/mg, p < 0.05 and 3.75 ± 0.61 vs 4.31 ± 0.35 g/dl, p < 0.05, respectively). Recurrent isolated macrohematuria was more frequent in IgAN cohort (46.2%), while nephrotic proteinuria was prevalent in IgAVN patients (44.1%). Comparing renal biopsy using MEST-C score, endothelial hypercellularity (E1) and crescents (C1) were significantly more frequent in IgAVN patients (61.7 vs 30.8% e 55.9 vs 26.9%, p < 0.05). The mean follow-up was 4.1 ± 2.3 years; 46.1% of IgAN and 8.8% of IgAVN had UPr/UCr > 0.2 mg/mg, while an eGFR < 90 ml/min/1.73m<sup>2</sup> was present in 11.5% of IgAN and 2.9% of IgAVN patients. The Kaplan Meier analysis showed a cumulative probability of proteinuria resolution at 5 years significantly worst in IgAN cohort compared to IgAVN (87.9 vs 42.7% respectively, p = 0.032). In IgAN cohort no clinic-biopic prognostic factors were found, while in IgAVN patients nephritic syndrome, ISKDC IIIb-VI classes and C1 presence at renal biopsy are correlated with a worst renal prognosis.

**Conclusion:** IgAN is a chronic, slowly progressive disease, while IgAVN has a more severe and acute clinical onset but with a better renal outcome. This reinforces the hypothesis that they are two different entities, rather than the spectrum of a single disease.

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THE FACES OF THROMBOTIC MICROANGIOPATHY IN CHILDREN – SUPPORTIVE VERSUS TARGETED THERAPY – OUR EXPERIENCE

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**Aims/Purpose:** The syndrome of thrombotic microangiopathy (TMA) is a clinical-pathological entity characterized by microangiopathic hemolytic anemia, thrombocytopenia, and end organ involvement. It comprises a spectrum of underlying etiologies that may differ in children and adults. To report the incidence of TMA in children in the western part of Romania and how current strategies are influencing outcomes.

**Methods:** We conducted a multiyear, single-center, retrospective observational study in the ‘Louis Turcanu’ Emergency County Hospital for Children in Timisoara, Romania. Data were extracted from the electronic data base between first of January 2014 until 31 December 2022. 22 patients met the diagnosis criteria. The study was performed in accordance with the World Medical Association and the Hospital’s Ethics Committee.

**Results:** Out of the 22 patients (mean age  $40.33 \pm 50.05$  months), 9 were males (40.9%), 16 children were coming from the urban areas (72.72%) and 5 cases were atypical HUS (21.77%). From the typical HUS lot, 58.8% had a positive Shiga toxin. 63.63% children required a form of renal replacement therapy, 86.36% required intensive care admission. In a multiple regression model only intensive care unit days correlated to hospitalization ( $p = 0.001$ ,  $r = 0.8895$ ). Although Eculizumab was administered to all atypical HUS patients, 2 reached kidney failure dependent of dialysis. Early initiation of Eculizumab within the first 2 weeks reduced blood transfusions, time on dialysis and hospital stay. One patient received Eculizumab in the first 24 hours thus renal recovery was obtained without the need of dialysis. The average hospital stay was  $24.36 \pm 16.94$  days with almost two thirds of the admissions being in the intensive care unit ( $16.81 \pm 13.86$  days). 6 months after HUS episode, all patients resumed normal renal function (except the 2 dialysis dependent patients), proteinuria was encountered in 8 cases, arterial hypertension was still present in 4 cases and 3 patients were followed up in the gastroenterology department for inflammatory bowel disease (1 patient) and cholangitis (2 patients). Death occurred in 2 typical HUS patients with severe neurologic involvement (brain death).

**Conclusion:** 1 out of 5 patients with HUS was atypical. Typical HUS patients are prone to high morbidity and mortality rates in the lack of specific treatment. Eculizumab is safe and an effective treatment for atypical HUS.

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**CLINICOPATHOLOGICAL AND PROGNOSTIC FEATURES OF IGA NEPHROPATHY AND IGA VASCULITIS NEPHRITIS WITH UTILIZATION OF A COMPUTER BASED PREDICTION ALGORITHM**

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**Aims/Purpose:** Immunoglobulin A (IgA) nephropathy (IgAN) and IgA vasculitis (IgAV) nephritis (IgAVN) have similar pathophysiological backgrounds and have quite variable clinical presentations. They generally progress slowly in children and some patients end up with end-stage renal disease in adulthood. To predict the prognosis of IgAN patients studies have been carried out that used computer-based prognosis estimation algorithms. This study was conducted to evaluate the clinicopathological and prognostic features of IgAN and IgAVN patients followed at Hacettepe University Department of Pediatric Nephrology by also using a computer based prognosis estimation algorithm.

**Methods:** Patients with biopsy proven IgAN and IgAVN with at least 6 months of follow-up between January 2005 and December 2021 were included. Patient demographics, clinical, laboratory, and biopsy findings were recorded from hospital files. Computer-based prognosis prediction algorithm QxMD was used in patients with at least 5-year follow-up.

**Results:** There were 27 IgAN and 48 IgAVN patients. Fifty-two percent of IgAN patients were male and the median age of diagnosis was 12 years. Fifty-four percent of IgAVN patients were male and the median age of diagnosis was 8 years. Complete remission was seen in 23 (85%) IgAN patients after a median follow-up of 40 months and 43 (90%) IgAVN patients at a median follow-up of 35.5 months. Only one patient with IgAN (3.7%) had end-stage renal disease at last follow-up. Computer-based prognosis prediction algorithm (QxMD) found a high risk of eGFR decline for 5 out of 18 patients with IgAVN and 5 year-follow-up, and a genuine eGFR decline was observed in 2 of them. Whereas in 6 IgAN patients with 5-year follow-up, the risk was calculated low and accordingly a genuine eGFR decline was not observed. In IgAN patients significant relationship with poor prognosis was observed with low serum albumin levels ( $p = 0.011$ ), severe proteinuria ( $p = 0.032$ ) at diagnosis, and duration to achieve remission ( $p = 0.035$ ) while in IgAVN, duration to achieve remission ( $p = 0.001$ ), segmental glomerulosclerosis ( $p = 0.009$ ) and presence of crescents in biopsy ( $p = 0.034$ ) were found related to poor outcomes. When IgAN and IgAVN patients were compared, in IgAVN; age at diagnosis was found to be lower ( $p = 0.002$ ), nephrotic proteinuria at diagnosis more common ( $p = 0.001$ ), serum albumin levels lower ( $p = 0.001$ ), crescents in biopsy ( $p = 0.017$ ) and immunosuppressive treatment used ( $p = 0.014$ ) more frequent.

**Conclusion:** Although IgAN and IgAVN share similar pathophysiological features they differ in important clinical and prognostic aspects. There still is a need for prospective, large scaled studies also using computer-based prognosis prediction algorithms to make treatment strategies based on risk scoring in childhood IgAN and IgAVN.

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## PULMONARY ARTERY AND RENAL VEIN THROMBOSIS AS MANIFESTATIONS OF MEMBRANOUS NEPHROPATHY IN A 16-YEAR-OLD GIRL

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**Aims/Purpose:** Membranous nephropathy (MN) is a rare histologic entity in children that contributes to ~ 5% of pediatric nephrotic syndrome (NS) cases. Thromboembolic complications (TC) in NS are observed in about 2 - 3% of children and generally occur during treatment in the course of the disease, while their presentation as the first manifestation is occasional. Here we report a case of an adolescent girl who presented with pulmonary artery and renal vein thrombosis and subsequently diagnosed as MN.

**Methods:** Case report

**Results:** A 16-year-old girl with no specific medical history but back and knee pain and fatigue for two months was consulted with abdominal pain, vomiting, and diarrhoea that started two days before and with recently occurred chest pain, breathing difficulty, and syncope. In the initial physical examination, dyspnea and central cyanosis were observed. Peripheral oedema was not existing. While the chest radiograph and the electrocardiogram did not reveal any specific abnormalities, the echocardiography showed dilatation of the right ventricle and pulmonary hypertension. Onwards the thorax CT-angiography indicated massive pulmonary thromboembolism with thrombosis at the distal right pulmonary artery and both lobar pulmonary artery branches. The lower extremity doppler ultrasonography (USG) did not reveal any pathologies, but the abdominal doppler USG showed a thrombus occluding the left renal vein completely. At this point, the laboratory examination confirmed the diagnosis of NS with proteinuria (477 mg/m<sup>2</sup>/h), hypoalbuminemia (1.59 g/dl), and hyperlipidaemia (triglyceride: 255 mg/dl and total cholesterol: 232 mg/dl). Since the scintigraphy revealed normal DMSA uptake and homogeneous distribution in the parenchyma of both kidneys and serial renal Doppler USG imaging showed flow in the renal parenchymal veins, it was predicted that collateral veins developed, and the process was in the subacute period. With prompt initiation of anti-thrombotic therapy, recanalization occurred. Subsequently, the kidney biopsy supported the diagnosis of MN. No secondary cause of MN could not be detected. PLCE2 antibody was negative. In MN treatment, 600mg of bolus methylprednisolone was given for three consecutive days, and the therapy continued with tacrolimus. The initial symptoms of the patient resolved in days, and an improvement in proteinuria (spot urine protein/kreatinin level decreased to 0.8 mg/mg) and hypoalbuminemia (serum albumin level increased up to 3.18 g/dl) was observed in two weeks.

**Conclusion:** In NS, TCs may occur not only in veins but also in arteries. As thromboembolic events can be its initial presentation, an awareness regarding TCs of NS is essential for all pediatric nephrologists.

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**A RARE CASE: OVERLAPPING C3 GLOMERULOPATHY AND THROMBOTIC MICROANGIOPATHY**

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**Aims/Purpose:** C3 glomerulopathy (C3G) are rare childhood pathology caused by a defect in the alternative complement pathway. Thrombotic microangiopathy (TMA) is a different clinical entity and is a thrombotic process with vessel wall damage. The coexistence of C3G and TMA is rare and the case described here is special in this respect.

**Methods:** An 8-year-old male patient with no known disease was admitted with complaints of abdominal pain and decreased urine output. On physical examination, her blood pressure was 190/100 mmHg ( $> 95p+12$  mmHg), tachycardia, and tachypneic. The patient with +3 pretibial edema was anuric. Laboratory tests revealed urea was 183 mg/dL and creatinine was 4 mg/dL. There was no ion exchange. C3 0.76 g/L (N:0.9-1.8) and other immunological markers were negative. Urine analysis revealed specific gravity, 1044; protein, + 2; and erythrocytes, + 2, and urine microscopy showed dysmorphic erythrocytes. COVID-19 PCR and IgM were negative and the patient's IgG was positive, there was no history of COVID-19.

**Results:** A kidney biopsy was performed and then 30mg/kg/day pulse methylprednisolone (PMP) treatment was started for 3 days. A biopsy result of the case was compatible with C3 glomerulopathy. Only +2 C3 stained in DIF. However, there were findings compatible with TMA in light microscopy. In light of these findings, eculizumab was given to the patient who was on hemodialysis and received 3 doses of PMP since hospitalization. 24 hours after the first dose of eculizumab, the urine output began to increase and biochemical parameters began to decrease. He did not receive dialysis after eculizumab and diuresis returned to normal on day 6. No mutations related to the complement pathway were detected in genetic tests. He is being followed up with eculizumab treatment and is receiving oral steroid and mofetil treatment. Laboratory tests are within the normal range.

**Conclusion:** Although C3G is a rare clinical entity in childhood, it has been reported to overlap with TMA in the literature. They are limited in number and in the form of case reports in the literature.



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**RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS IN A PATIENT WITH RENO-PULMONARY INVOLVEMENT: ADULT PATHOLOGY ONLY?**

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**Aims/Purpose:** Anti-glomerular basement membrane antibody (anti-GBM) disease is a very rare small vessel vasculitis in pediatrics, caused by the presence of antibodies directed against GBM and alveolar basement membrane (ABM), which presents as rapidly progressive glomerulonephritis (RPGN) and/or alveolar hemorrhage.

**Methods:** We present the case of a patient diagnosed with anti-glomerular basement membrane antibody disease.

**Results:** 8-year-old girl, no history of interest, consulted the emergency department for prostration and pallor, presenting the previous days with epigastralgia without other associated symptoms. No edematization and she reported preserved diuresis. Constant findings: tachypnea, hypoxemia (SatO<sub>2</sub> 89%) and hypertension (138/89 mmHg). Physical examination: poor general condition and cutaneous-mucous pallor, crackles in the right lung base and pansystolic heart murmur. Blood analysis: severe non-hemolytic anemia (Hb 4.1 mg/dl), acute renal damage (urea 249 mg/dl, creatinine 10.78 mg/dl) with hyperkalemia (K 6.7 mmol/l) and metabolic acidosis. Proteinuria in nephrotic range (IPr/Cr 5 mg/mg) and microhematuria. The study was completed with a chest X-ray showing signs of acute pulmonary edema, cardiomegaly and peripheral cottony infiltrate in right fields suggestive of alveolar hemorrhage. An abdominal ultrasound was performed showing globular, hyperechogenic kidneys with loss of corticomedullary differentiation. A red blood cell transfusion was administered. A bladder catheter was placed and oligoanuria was observed despite diuretic treatment. He was transferred to the PICU for placement of a hemodialysis catheter and empirical treatment with methylprednisolone (300 mg/m<sup>2</sup>/day, 3 doses) was administered. Renal biopsy was performed after 48 hours: necrotizing glomerulonephritis with active and chronic lesions, with positive immunofluorescence for linear IgG in GBM. With the diagnostic orientation of anti-GBM antibody disease treatment with cyclophosphamide and plasmapheresis is associated. The detection of anti-GBM antibodies in the analytical controls is repeatedly negative, and the presence of pANCA antibodies is confirmed. A bronchoalveolar lavage confirming the presence of hemosiderophages with a satisfactory evolution. She persists in ESRD requiring RRT until she receives a renal transplant at 10 years of age.

**Conclusion:** Anti-GBM disease is a rare cause of ESRD in pediatrics. The serologic spectrum is variable, antibodies may not be found in plasma (12%) or may be found together with ANCA (10-50%). Renal biopsy is essential to establish the diagnosis and prognosis of the disease.

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### HYPOCOMPLEMENTEMIC GLOMERULONEPHRITIS OR HYPOCOMPLEMENTEMIA WITH GLOMERULONEPHRITIS?

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**Aims/Purpose:** Postinfectious glomerulonephritis (APIGN) is the most common cause of acute glomerulonephritis (AGN) and glomerular hematuria worldwide in pediatrics, with most of the manifestations usually resolving in 2 weeks, with persistent proteinuria 6–8 weeks, decrease of complement (C3) 10–12 weeks and microhematuria 12–24 months.

**Methods:** Cases that present deviations on this evolution force to raise the differential diagnosis with other ANG with C3 decrease (glomerulonephritis by C3 or systemic pathologies like SLE). We present a case with a torpid evolution.

**Results:** 4-year-old patient consulted for macrohematuria of 10 days of evolution and oliguria in the last 48h, who had presented a febrile episode 2 weeks earlier. Mild bilateral palpebral edema and stage II hypertension together with nephrotic proteinuria (iPr/Cr 4.4 mg/mg). Blood tests showed normal renal function parameters and negative antibodies, hypocomplementemia with decreased C3, normal C4 and elevated ASLO. He was admitted for blood pressure control, receiving furosemide and nifedipine. In subsequent controls, normalization of proteinuria and decrease of hematuria was observed, with persistence of low C3 levels after 12 weeks of follow-up, so a renal biopsy was indicated. The results showed a mesangial proliferative glomerulonephritis with only C3 deposits and no scarring or necrotizing lesions. Ultrastructurally we identified small nodular deposits predominantly in mesangium and very isolated paramesangial/parietal deposits. Ultrastructural findings ruled out a dense deposit disease and raised the possibility of a C3 glomerulopathy/evolved postinfectious glomerulonephritis/glomerulonephritis in remission. Nephritic factor was negative. A genetic study of the complement found a heterozygous variant of the C3 gene (aberrant protein) that would justify the partial deficit of C3. Same mutation was found in both the father and his sister. She has had no new flares during follow-up, with negative proteinuria and hematuria.

**Conclusion:** APIGN has an excellent prognosis with complete remission in 95% and infrequent recurrences; other pathologies should be suspected in case of recurrences or torpid evolution. Our case was oriented as an episode of APIGN in a patient with genetic complement deficiency, justify the persistently low C3 values without associated abnormal complement activation.

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COMPLICATIONS OF ULTRASOUND-GUIDED KIDNEY BIOPSY IN CHILDREN: SINGLE CENTER EXPERIENCE

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**Aims/Purpose:** The current study aims to evaluate and explore the complications that happened after percutaneous kidney biopsy in children and associated risk factors.

**Methods:** A retrospective record-based study was conducted by reviewing the medical records of children with post-ultrasound-guided percutaneous kidney biopsy complications at King Saud Medical City, a tertiary hospital in Riyadh, Saudi Arabia during the period from May 2014 to June 2021. Data were extracted using pre-structured data collection sheet. Data collected included children's age, gender, primary disease, laboratory findings, and kidney complications with needed management.

**Results:** The study identified 76 children who had undergone 86 ultrasound-guided percutaneous kidney biopsies in the study period and fulfilled the inclusion criteria. Children's ages ranged from 1 years to 15 years with a mean age of  $7.3 \pm 4.0$  years old. Most of the study children had nephrotic syndrome (61.6%; 53), followed by glomerulonephritis (25.6%; 22). Thirty-five (40.7%) children developed at least one of the complications. The most-reported complication was microscopic haematuria (32.6%; 28), followed by gross haematuria (3.5%; 3), Flank pain was reported among 3 (3.5%) children also and hematoma (1 child), only 2 children (3.9%) among those who had no complications recorded. Haemoglobin drop  $> 2$  g/dl compared to 3 of those who had complications with no statistical significance ( $p = .365$ ). Prothrombin time was significantly higher among children who had renal complications than others who had not ( $11.7 \pm 1.8$  vs.  $10.8 \pm 1.2$  seconds;  $p = .022$ ).

**Conclusion:** Suggestive by the low need to intervene in complications, ultrasound-guided percutaneous kidney biopsy is a relatively safe procedure in children. Even in the most commonly observed complication, i.e. hemorrhagic ones, blood transfusion is rarely needed.

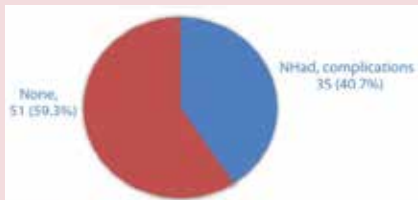


Figure 1: Prevalence of complications after ultrasound-guided kidney biopsy in children.

Table 1: Distribution of complications after ultrasound-guided kidney biopsy in children by their bio-demographic data

Bio-demographic data	Had complications						p value
	All cases (n = 86)		Yes (n = 35)		No (n = 51)		
	No	%	No	%	No	%	
<b>Primary disease</b>							
Nephrotic syndrome	53	61.6	15	42.9	38	74.5	.001*
Glomerulonephritis	22	25.6	17	48.6	5	9.8	
Chronic kidney disease of unknown etiology	5	5.8	1	2.9	4	7.8	
Hemolytic uremic syndrome	3	3.5	2	5.7	1	2.0	
Transplant rejection	3	3.5	0	0.0	3	5.9	
<b>Age in years</b>							
1-5	31	36.0	4	11.4	27	52.9	.001*
6-9	26	30.2	12	34.3	14	27.5	
10-15	29	33.7	19	54.3	10	19.6	
<b>Gender</b>							
Male	40	46.5	7	20.0	33	64.7	.001*
Female	45	53.5	28	80.0	18	35.3	
<b>BP centile%</b>							
50 <sup>th</sup>	16	18.6	9	25.7	7	13.7	.428
90 <sup>th</sup>	29	33.7	10	28.6	19	37.3	
95 <sup>th</sup>	31	36.0	11	31.4	20	39.2	
99 <sup>th</sup>	10	11.6	5	14.3	5	9.8	
<b>SBP</b>							
Mean $\pm$ SD	111 $\pm$ 12.0		110.2 $\pm$ 12		108.1 $\pm$ 10.9		.001*
<b>DPB</b>							
Mean $\pm$ SD	69.0 $\pm$ 9.0		70.2 $\pm$ 9.4		68.2 $\pm$ 8.7		.320

P = Pearson  $\chi^2$ ; \*Independent t test; \*p = 0.05 significant

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## ECULIZUMAB IN STEC-HUS: A PARADIGM SHIFT IN THE MANAGEMENT OF PAEDIATRIC PATIENTS WITH NEUROLOGICAL INVOLVEMENT

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**Background:** Eculizumab for the treatment of atypical haemolytic uremic syndrome (HUS) is a standard of care. Central nervous system (CNS) involvement in Shiga toxin-producing *Escherichia coli* (STEC)-HUS is associated with increased morbidity and mortality. There is no consensus on the use of plasma exchange and/or Eculizumab. We report a series (n = 4) of children with CNS involvement in STEC-HUS with excellent outcomes after treatment with Eculizumab only and supportive therapies.

**Methods:** A retrospective chart review of patients with CNS involvement in STEC-HUS, managed with supportive therapies and Eculizumab only.

**Results:** Four patients (75% female) with a median age of five years and eleven months (IQR: 23.5–105.5 months) were admitted to a tertiary paediatric nephrology centre with CNS involvement in STEC-HUS. Neurological symptoms presented between days two and seven of illness and included ataxia, altered mental status, visual symptoms and seizures. All had abnormal MRI brain at presentation. All received two doses of Eculizumab, one week apart (dosing according to weight). Resolution of neurological symptoms was evident at a mean of 60 hours post-administration (range: 24–72 hours). The median length of paediatric intensive care unit (PICU) admission was only 1.5 days (IQR: 0.5–3.0 days). Though not published in previous paper, the median length of PICU stay was 6 days (IQR: 4–12.5 days), prolonged due to PLEX sessions, sedation, and intubation associated with PLEX. All patients have complete renal and neurological recovery at 12-month follow-up.

**Conclusion:** We present a case series of four children with STEC-HUS and CNS involvement, managed with Eculizumab only, in lieu of plasma exchange (as per our previous policy). The marked improvement in symptoms in our cohort supports the use of Eculizumab, rather than plasma exchange in CNS-involvement of STEC-HUS.

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**THROMBOTIC MICROANGIOPATHY (TMA) IN A PATIENT WITH ECMO SUPPORT**

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**Aims/Purpose:** Thrombotic microangiopathy (TMA) is a group of disorders characterized by damage to the vascular endothelium mediated by activation of the alternative pathway of complement primarily or secondary to environmental factors and/or triggers. The complement system is also triggered upon initiation of extracorporeal support (ECMO).

**Methods:** We present a case of TMA in a patient with ECMO support.

**Results:** A 12-year-old girl, previously healthy, without drug treatment, recent immunizations or family history of interest. She was admitted to the PICU due to acute symptoms of hypoxemic respiratory failure that required intubation. During initial stabilization, severe cardiac dysfunction with 4-minute cardiorespiratory arrest and subsequent initiation of ECMO. On admission, progressive pancytopenia with nadir values of Hb 9.7 gr/dl, platelets of  $55,000 \times 10^9/L$  and leukopenia of  $200 \times 10^9/L$ , prior to ECMO. It was associated with oliguria, mild renal dysfunction (eGFR by Schwartz 73 ml/min/1.73m<sup>2</sup>), without hematuria, leukocyturia, but severe proteinuria (U Prot/Cr 5 gr/gr). After PCR, anuria requiring renal replacement therapy. Ultrasound with severe bilateral and symmetrical decrease in the doppler signal and exclusively in renal flow, being almost imperceptible at the arterial level. Presence of hemolysis data on extracorporeal support (decreased haptoglobin, increased LDH), decrease in C3 (33.9 mg/dl) with normal C4 and elevation of the soluble membrane attack complex (C5sb9) 694.77 mg/dl (standard 127–303). The clinical diagnosis of suspected TMA is established, and treatment is started, urgent empirical treatment with Eculizumab. Subsequently, bilateral renal blood flow improved at 8 days, diuresis started at 2 weeks and withdrawal of support with CRRT at 6 weeks. ECMO support for 49 days. After removing extracorporeal support, a renal biopsy was performed, which confirmed the diagnosis of TMA. Molecular and genetic study of complement in progress.

**Conclusion:** TMA are a group of disorders characterized by damage to the vascular endothelium mediated by activation of the alternative pathway of complement primarily or secondary to environmental factors and/or triggers. It is important to maintain a high diagnostic suspicion in incomplete cases and start treatment early to reduce morbidity and mortality and preserve renal function. In the case that we present, renal failure with absence of renal blood flow was key for diagnosis and early initiation of treatment.

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## ASSESSMENT OF PROGNOSIS AND PREDICTORS OF PROGNOSIS IN PATIENTS WITH IMMUNOGLOBULIN A NEPHRITIS

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**Aims:** Immunoglobulin A nephritis (IgAN) is the most common primary glomerulonephritis in the world and one of the leading causes of end-stage renal disease (ESRD). It is thought that the determination of clinical and histopathological findings that can predict patients at risk of progression to ESRD in the early period will contribute to better management of the disease.

**Methods:** This study was conducted by retrospectively examining the data of 34 patients with IgAN and 33 patients with Immunoglobulin A vasculitis nephritis (IgAVN) who were followed up for at least 6 months by Istanbul University Istanbul Faculty of Medicine, Division of Pediatric Nephrology. Patients with IgAN had low GFR ( $\leq 90$  ml/min/1.73m<sup>2</sup>) and normal at the end of the follow-up, those with and without proteinuria at the end of the follow-up and those with MEST-C score  $\geq 3$  and MEST-C score of  $< 3$  were divided into subgroups.

**Results:** At the end of the follow-up, 14.7% (n = 5) of 34 patients with IgAN had a GFR  $< 90$  ml/min/1.73m<sup>2</sup>, while the rate of patients with GFR  $< 60$  ml/min/1.73m<sup>2</sup> was 5.9% (n = 2). The rate of complete remission of proteinuria was significantly lower and the rate of presence of proteinuria at the end of the follow-up was significantly higher in the patient group with low GFR at the end of follow-up. (respectively, p = 0.037, p = 0.037). There was no significant difference between the groups with a MEST-C score of  $\geq 3$  and a group with a MEST-C score of  $< 3$  findings at the time of diagnosis and at the end of follow-up (p > 0.05). The rate of patients with GFR  $< 90$  ml/min/1.73m<sup>2</sup> at the end of follow-up in the IgAVN group was 3% (n = 1). In this group, the rate of complete remission of proteinuria at the end of follow-up were significantly higher than the IgAN group, and presence of proteinuria at the end of follow-up was significantly lower than the IgAN group (p = 0.002, p = 0.005, respectively).

**Conclusions:** In patients with IgAN, it was thought that the presence and degree of proteinuria that continued during the follow-up was the most important clinical determinant in predicting the prognosis, rather than the proteinuria level at the time of presentation. It was thought that the renal prognosis of patients with IgAVN was better than the patients with IgAN. In order to more accurately determine the prognosis in patients with IgAN diagnosed at childhood required long follow-up periods extending to adulthood.

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## COMPLEMENT C5 INHIBITORS... USEFUL IN TYPICAL HEMOLYTIC UREMIC SYNDROME?

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**Purpose:** The emergence of complement C5 inhibitors (eculizumab, ravulizumab) has clearly changed treatment and prognosis of patients with atypical hemolytic uremic syndrome. Regarding its benefit in typical hemolytic uremic syndrome there is considerable controversy. The aim of our work is to present our experience with the use of these drugs in patients with typical hemolytic uremic syndrome, trying to analyse which patients could benefit from their administration.

**Methods:** We reviewed the cases of typical hemolytic uremic syndrome admitted to our hospital in the last 2 years, microbiologically confirmed (with isolation of Shiga toxin or Shiga-like toxin (verotoxin)), without identified genetic alterations related to the development of complement-mediated atypical hemolytic uremic syndrome, and in which it was decided to administer a complement C5 inhibitor, depending on the clinical course of the patients.

**Results:** During last 2 years complement C5 inhibitors were administered in 3 patients with typical hemolytic uremic syndrome. All of them were male. The first one was 14 months old at debut, presenting as a complication associated with hemolytic uremic syndrome seizures and irritability, so it was decided to administer eculizumab (2 doses in total). The second was a 6-year-old boy who, after presenting with status epilepticus, was administered ravulizumab (2 doses in total). After administration, both patients had a good clinical course, without new seizures, did not require chronic antiepileptic treatment and did not show any alterations in the imaging tests performed. The last patient was a 5-year-old boy who was given ravulizumab (1 dose in total) due to a complication of severe pancolitis. After its administration, he presented improvement in hematological parameters (hemoglobin and platelets), but did not have much improvement in pancolitis.

**Conclusion:** The concept that Shiga toxin or Shiga-like toxin (verotoxin) may activate complement directly, providing a rationale for therapeutic complement blockade in typical hemolytic uremic syndrome with severe complications. The use of complement C5 inhibitors, after analysing our results, in patients diagnosed with hemolytic uremic syndrome with a poor clinical course, could be a therapeutic option to be taken into account, especially in those with neurological involvement, as it could improve the evolution of these patients. This benefit is less clear in other systemic disorders, such as pancolitis.

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A CASE REPORT OF CHILD WITH SENIOR-LOKEN SYNDROME AND COMORBIDITIES

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**Background:** Senior Løken syndrome (SLS) is a rare (1-9/1,000,000) autosomal recessive ciliopathy characterized by nephronophthisis (NPHP) and retinal dystrophy, that lead to end-stage renal disease and irreversible vision loss. Diagnosis is often late as it has no pathognomonic signs and symptoms.

**Aims/Purpose:** We report a case of patient with Senior-Løken syndrome, type 1 diabetes and heavy menstrual bleeding.

**Methods:** Retrospective analysis of the patient's medical data was made.

**Results:** The 16 years girl admitted to the hospital because of asthenia and hypovolemia evolved from heavy menstrual bleeding. Laboratory examination showed severe anemia (serum hemoglobin 70 g/l) and renal impairment (serum creatinine 270 µmol/l) with unremarkable urinalysis. Ultrasonography showed slightly increased parenchymal echogenicity in kidneys. Non-specific changes were observed in kidney biopsy. Horizontal nystagmus, strabismus, hypermetropia, photophobia and type 1 diabetes were diagnosed in early childhood. Optic nerve atrophy was initially suspected; however, later progressive rod-cone retinal dystrophy was diagnosed, with impaired night vision, concentric visual fields constriction, non-recordable Ganzfeld ERG a- and b-waves and retinal pigmentary changes. Whole exome sequencing (WES) showed pathogenic homozygous frameshift variant in IQCB1 gene (NM\_001023570.4) c.825\_828del, p.(Arg275fs). The genetic testing confirmed Senior-Løken syndrome (MIM # 609254, ORPHA:3156) diagnosis. Genetic testing of the family showed that parents and two sisters are carriers of the gene mutation. Despite of adequate treatment, renal impairment was gradually progressing.

**Conclusion:** 1. Senior-Løken syndrome and type 1 diabetes are not common in children. 2. Genetical testing of the family members of affected person would help to make early diagnosis of the disease and make better prevention in progression of symptoms of the disease. 3. Ophthalmic symptoms were the first to appear, therefore timely genetic evaluation of retinal dystrophy would have contributed to the diagnosis of systemic disease.



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## ALTERATIONS IN GLOMERULAR FILTRATION MARKERS WITHOUT ALTERATIONS IN KIDNEY FUNCTION

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**Introduction:** The assessment of estimated glomerular filtration rate (eGFR) in patients with childhood neoplasms is important. This value is used to adjust different prescriptions in light of their frequent nephrotoxic effects. We present two cases with an alteration in the filtration rate according to cystatin C calculation but within normal range according to the creatinine calculation and nuclear medicine techniques

**Case report:** The first patient is an 11-year-old girl with acute myeloid leukaemia, whom, prior to the start of treatment, showed an alteration in cystatin C of 2.74 mg/l (eGFR by Filler 30 ml/min/1.73m<sup>2</sup>), despite serial creatinine levels within the normal range (0.55–0.65 mg/dl, eGFR by Schwartz 95–105 ml/min/1.73m<sup>2</sup>). Analytical study ruled out the presence of thyroid disorders and the use of corticoids. Renal ultrasound showed a slight non-specific parenchymal echogenicity. Finally, the GFR was measured by Cr-EDTA: 102 ml/min/1.73m<sup>2</sup>, confirming a normal GFR. The second patient was a 12-year-old boy also with acute myeloid leukaemia, who had received an allo-transplant of haematopoietic progenitors 1 year earlier, referred to the clinic for progressive worsening of renal function due to high cystatin C levels (1.44 mg/l, GFR by Filler of 61 ml/min/1.73m<sup>2</sup>) and creatinine within normal levels (0.43 mg/dl, GFR by Schwartz 137 ml/min/1.73m<sup>2</sup>). Initially, the discrepancy was ascribed to baricitinib and acyclovir nephrotoxicity. Laboratory analysis ruled out thyroid disorders and the patient did not receive corticotherapy. His glomerular filtration rate was <sup>99m</sup>Tc-DTPA of 135 cc of plasma/minute/1.73m<sup>2</sup>, within the normal range.

**Conclusion:** Cystatin C can be an unreliable marker filtration marker in the context of leukemia. Nuclear medicine techniques are an alternative for the calculation of glomerular filtration rate in patients with discrepancies between different markers.

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## CHRONIC KIDNEY DISEASE RELATED TO WT1 GENE: A REPORT OF THREE CASES

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**Aims/Purpose:** Pathogenic variants of the WT1 gene may cause several genetic conditions involving progressive renal function impairment. These rare conditions are not commonly seen in everyday practice, therefore we believe more awareness should be raised. In addition, this report will serve as an overview of our improving capabilities to diagnose and manage such patients.

**Methods:** This is a case report of three pediatric patients who, during the period between 2002 and 2022, were treated in our centre due to chronic kidney disease related to the WT1 gene.

**Results:** 1st case (10 months) presented with Wilms' tumour, hypertension, and hypoalbuminemia. Kidney biopsy showed signs of focal segmental glomerulosclerosis (FSGS). The patient was female, karyotype 46,XX. Genetic analysis revealed a missense mutation in the WT1 gene, confirming Denys-Drash syndrome. The patient's kidney function deteriorated and peritoneal dialysis was initiated. She was treated for sepsis and peritonitis several times in the following years. The patient passed away at the age of 9 years due to sepsis following kidney transplantation. 2nd case (1 year) presented with 46,XY sex differentiation disorder. Surgical removal of the ovotestes and vaginoplasty were performed. At the age of 8 years, she was hospitalised with end stage kidney disease. FSGS was discovered in the kidney biopsy. Peritoneal dialysis was performed until kidney transplantation. A frame shift mutation was discovered in the WT1 gene, with a clinical diagnosis of Frasier syndrome. With continued care, she has recently reached 18 years of age with a well-functioning transplant kidney. 3rd case (36 days) presented with generalised oedema, hypoalbuminemia, and anuria. Peritoneal dialysis was started. The patient's karyotype is 46,XY with normal female genitalia and persistent Müllerian ducts. A pathogenic missense variant was detected in the WT1 gene, Denys-Drash syndrome was diagnosed. At the age of 3 months, bilateral nephrectomy was performed. The patient continues receiving peritoneal dialysis.

**Conclusion:** WT1 nephropathy has led to end stage kidney disease in all three cases. Kidney transplantation appears to be the most preferable mode of treatment. Early clinical manifestation provides additional challenges in managing the condition.

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CONGENITAL NEPHROTIC SYNDROME: EXPERIENCE FROM A SINGLE CENTER

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**Aims/Purpose:** Congenital nephrotic syndrome (CNS) is a rare congenital disease presenting in the first three months of life. Children with CNS requires intensive supportive treatment and is associated with high morbidity and mortality. Our main aim was to evaluate all admissions with CNS with focus on age at presentation, gender, treatment, genetic cause and outcome.

**Methods:** Retrospective survey of admissions in children below 1 year of age with the diagnosis CNS in the period 2005–2020.

**Results:** Ten children (2 males) were identified. Diagnosis was made at a median age of 2 weeks (range: at birth – 8). The presenting symptom in all was oedema, with severe proteinuria and median albumin levels of 16 g/L (10–23). Birthweight was median 2577 g (1175 – 3075). Term birth was seen in 6/10 patients. A genetic cause was found in 9/10: NPHS1 (n = 4), WT1 (n = 3), LAMB2 (n = 2). One child died before genetic testing. Consanguineous marriage was identified in three families. One child with NPHS1 mutation was confirmed with the rare variant with muscular dystonia and athetosis (NPHS1+MDA). Five children died at a median age of 21 weeks (range 3–60). Causes of death were septicemia, termination of treatment and sudden cardiac death. Treatment was done according to guidelines. Six children started peritoneal dialysis. Four children were transplanted at a median age of 16 months (range 15–18), two were nephrectomised prior to transplantation. So far, all the transplanted children have good transplant function, two had rejections and two post transplant lymphoproliferative disease. One child has supportive and palliative care (NPHS1+MDA).

**Conclusion:** CNS is a rare condition, and only 10 children were diagnosed during a 15 year period at the largest center in Norway. NPHS1 mutation was the most common genetic cause, followed by WT1 and LAMB2 mutation. The mortality was high, 50% (n = 5), and three died due to severe infection. Four children have been successfully transplanted.

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**GIRLS WITH X-LINKED ALPORT SYNDROME: RISK OF THE DISEASE PROGRESSION**

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**Aims/Purpose:** X-linked Alport syndrome (XLAS) is a progressive, hereditary disorder of basement membranes leads to kidney failure in males. In females, XLAS has an unpredictable prognosis due to one of the X chromosomes inactivation. The aim of study was to compare XLAS' manifestations and disease progression by gender.

**Methods:** Clinical (blood pressure (BP), hearing acuity, ophthalmoscopy) and laboratory data were obtained from girls (n = 52) and boys (n = 88) with genetically confirmed XLAS included in retrospective single center study. BP  $\geq$  95% by age and height was defined as a blood hypertension (BH). Proteinuria (Pr), nephrotic Pr (nPr) and reduced GFR were defined by urine protein excretion  $>$  100 mg/m<sup>2</sup>/day, Pr  $>$  1000 mg/m<sup>2</sup>/day and eGFR  $<$  90 ml/min/1.73m<sup>2</sup> (Schwartz bedside), respectively. There was no difference in Me age of girls and boys at last observation (13.5(8;17) vs 14(10.5;17) yrs).

**Results:** There was no difference in frequency of BH (0.5 vs 0.52), gross hematuria (0.33 vs 0.47), proteinuria (0.56 vs 0.79), retinopathy (0.13 vs 0.23) between girls and boys. The rate of hearing loss (0.15 vs 0.43, p = 0.002), nPr (0.02 vs 0.36, p = 0.001), decreased GFR (0.17 vs 0.44, p = 0.03) and risk of kidney disease progression (OR = 3.8, 95%CI 1.66;8.74) were higher in boys.

**Conclusion:** Girls with XLAS are at risk, (although less than boys) of extrarenal and renal disease progression during childhood and require monitoring similar to boys.

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## BARAKAT SYNDROME FROM CHILDHOOD TO ADULTHOOD

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**Introduction:** Barakat syndrome (HDR) is a rare genetic disorder which is characterized by hypoparathyroidism ("H"), neurosensory deafness ("D"), renal disease ("R") and is inherited with autosomal dominant pattern. It is caused by mutations on the GATA3 gene. This syndrome can be misdiagnosed due to the phenotypic diversity and the genetic heterogenicity of the cases that have been recorded.

**Aim:** Case presentation of a teenage boy that has been observed from childhood due to a hypoparathyroidism and progressively he presented with decrease in acoustic acuity and renal disease.

**Case presentation:** An 18-year-old male has been monitored due to hypoparathyroidism. The diagnosis was established at the age of 1.5yo when hospitalized due to febrile convulsions and thus hypocalcemia was discovered. His hypoparathyroidism was confirmed and was treated with alfacalcidol and calcium. At the age of 9 yo, the patient was referred to the nephrologist, due to his increased creatinine 1mg/dl, where was also found a CrCl 143.3 ml/min/1.73m<sup>2</sup> and cystatin C 1.28 mg/dl. The renal ultrasound showed kidneys with a small asymmetry, as well as a normal DMSA scan. At the age of 12yo he ceased his medication and thus he developed hyperphosphatemia 9 mg/dl, hypocalcemia 7.4 mg/dl, hypercalciuria/24h: 5.1 mg/kg and mild proteinuria (P/Cr: 0.43). In a kidney ultrasound, it was revealed a nephrocalcinosis Grade I. He therefore started a low phosphorus diet, alphacalcidol and calcium carbonate. Concerning his hypercalciuria, it was prescribed potassium citrate. The previous results brought the suspicion of the Barakat syndrome, leading to further investigation of his hearing acuity that showed sensorineural bilateral mild deafness. In the genetic research that was performed, a pathogenic variant was identified in GATA3. In the end of his monitoring creatinine levels reached 1.4mg/dl, cystatin C came up to 1.42 mg/d while his CrCl became 102.5 ml/min/1.73m<sup>2</sup>. At the age of 17yo, in the kidney ultrasound was found a small asymmetry in the size of the kidneys with bilateral hyperechogenicity and medullary nephrocalcinosis Grade I.

**Conclusion:** Barakat syndrome is a medical state that demands a lifelong regular endocrinological and nephrological follow up. In cases of hypoparathyroidism, it is crucial to evaluate the kidney function since in this syndrome the renal involvement and hearing acuity appear in a later stage of life. GATA3 genetic studies should also be performed in every suspected case to exemplify the diagnosis of this uncommon medical disorder.

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## NUTCRACKER SYNDROME: INITIAL FINDINGS AND LONG-TERM FOLLOW-UP RESULTS

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**Aims/Purpose:** Nutcracker syndrome (NCS) is defined by compression of the left renal vein (LRV) between the aorta and the superior mesenteric artery (SMA) and may present with various symptoms. There is insufficient knowledge about its natural course and uncertainty in the choice of diagnostic and treatment options in pediatric patients. This study aimed to evaluate the clinical, laboratory, radiological findings and follow-up results of pediatric patients with NCS.

**Methods:** The medical records of the patients were retrospectively investigated, and their demographic features, presenting symptoms, laboratory and radiological findings were recorded.

**Results:** In the last 10 years 130 patients (88 females) with NCS were detected with a mean follow-up of  $31.11 \pm 26.89$  months. The mean age at diagnosis was  $12.10 \pm 2.88$  years. Body mass index percentile was below  $< 5$  in 36% of the cases. At the diagnosis 23.3% of the patients had left flank and/or abdominal pain, 6.9% had macroscopic hematuria and 2.3% had left-sided varicocele. The most common laboratory finding was nephritic proteinuria (97.6%), followed by microscopic hematuria (18.4%). Left renal vein doppler ultrasonography (DUS) was performed in all patients. The mean ratio of the diameter of the hilar portion of the LRV to that of the aortomesenteric portion in the supine and upright positions was  $5.32 \pm 3.19$  and  $9.13 \pm 9.73$ , respectively. The mean ratio of the peak velocity between the two sites of the LRV was  $4.94 \pm 2.50$  and  $8.63 \pm 4.04$  respectively. Signs of compression of the LRV were more evident in patients with NCS, when visualized in a vertical position. There was no difference between DUS values of symptomatic and asymptomatic patients at the time of presentation ( $p = 0.05$ ). All patients have been followed conservatively, hematuria and/or proteinuria had resolved in 51 of the 114 patients (44.7%). 53 patients underwent a follow-up DUS examination after a mean period of  $40 \pm 21.5$  months. The median peak velocity and diameter ratios of the LRV in the upright position decreased significantly when compared with the initial findings. Normal DUS findings were noted in 15 patients at the final evaluation and clinical and laboratory features of these patients were completely recovered.

**Conclusion:** NCS should be considered in unexplained proteinuria and/or hematuria, especially in slim children and during adolescence. In the follow-up laboratory findings resolved in approximately half of the patients, and DUS findings improved significantly. Our results support conservative management in children as a first-line treatment approach.

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RENAL INVOLVEMENT AS THE MAIN PRESENTATION OF INFLAMMATORY BOWEL DISEASE: A CASE REPORT

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**Purpose:** Extra-intestinal manifestations of inflammatory bowel diseases (IBD) are common and occur in approximately 25–40% of cases. These may precede, be concomitant, or follow gastrointestinal symptoms<sup>1</sup>. Renal involvement in children with IBD is rare (1–2% of cases). Reported renal findings include nephrolithiasis, glomerulonephritis, interstitial nephritis, and entero-vesical fistula<sup>2,3,4</sup>. Furthermore, drugs used for treating IBD (i.e., mesalazine) can cause renal damage<sup>3</sup>. Herein, we report an unusual case where kidney involvement was the presenting symptom of a patient with IBD.

**Methods:** A 17-year-old healthy female patient first presented with unilateral panniculitis of a knee, which was treated with piperacillin-tazobactam and ibuprofen. During the hospital stay, renal function progressively declined (serum creatinine 1.9 mg/dl, eGFR 38.1 ml/min) without overt proteinuria, hematuria, or evidence of autoimmune disorders. In the hypothesis of drug-induced interstitial nephritis, the patient was treated with prednisone, to which she partially responded with an eGFR increase of 54.7 ml/min. However, at the 3-month follow-up visit, kidney function deteriorated again (eGFR 33.1 ml/min). A kidney biopsy was performed.

**Results:** The kidney biopsy revealed a granulomatous interstitial nephritis (Figure 1). Extensive investigations were performed to rule out causes of granulomatous disease. Finally, the patient underwent an esophagogastroduodenoscopy (EGDS) and a colonoscopy. The microscopic examination of the colon mucosa showed active chronic inflammation, glandular damage and numerous granulomas (Figure 2), establishing the diagnosis of IBD with kidney involvement. The patient was treated with methylprednisone boluses followed by oral prednisone tapering, methotrexate, and adalimumab. After 2 years, eGFR is stable (65 ml/min, CKD stage II).

**Conclusions:** This rare case illustrates that occasionally, symptoms related to kidney involvement prevail over intestinal symptoms in patients with IBD.

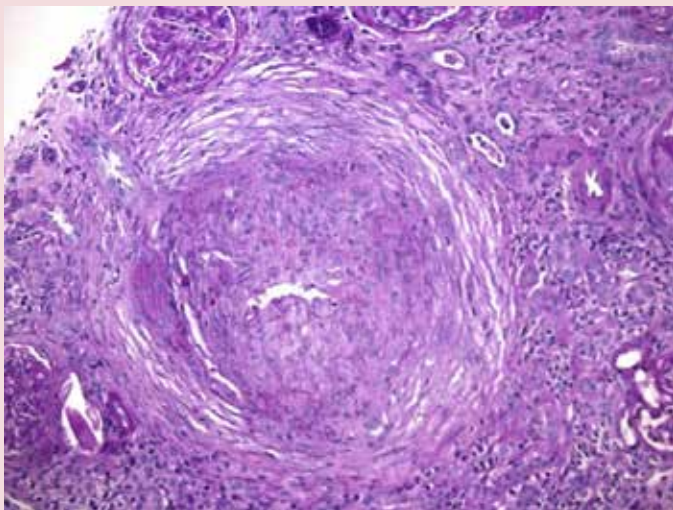


Figure 1: Granulomatous interstitial nephritis.

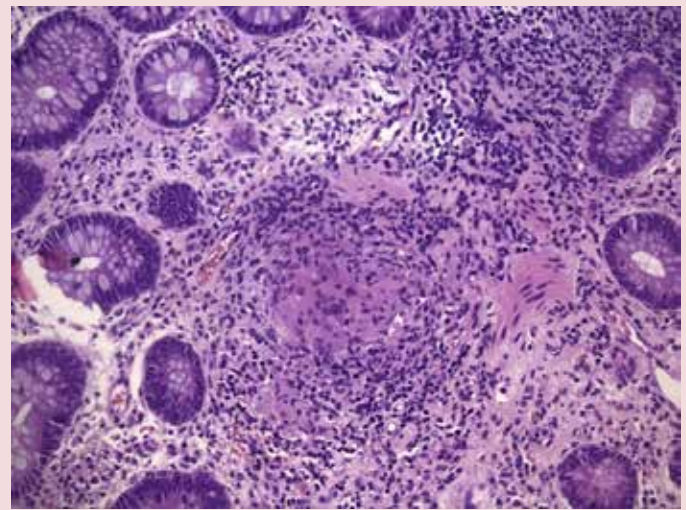


Figure 2: Granulomas in the colic mucosa.

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## A NOVEL RENAL PHENOTYPE IN SHUKLA-VERNON SYNDROME

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**Background:** Shukla-Vernon Syndrome (SVS; OMIM #301029) is an X-linked neurodevelopmental disorder caused by pathogenic variants in BCORL1, a transcriptional co-repressor. To date, only 4 pedigrees (7 cases) are reported in the literature. SVS is usually characterised by global neurodevelopmental delay, seizures, behavioural difficulties, and dysmorphic features including facial and digital anomalies. We describe the first patient who presents with an additional renal malformation not explained by other genetic mutations. We expand the SVS phenotype by proposing a novel association of SVS with congenital anomalies of the kidney and urinary tract (CAKUT).

**Methods:** The index case was a 4.5 year old male who underwent detailed phenotyping to establish clinical features. Whole exome sequencing (Twist Core Human exome/Illumina NextSeq/Novaseq) and bioinformatics were used to identify and validate discoverable genetic mutations. BCORL1 RNA and protein expression patterns were examined in human kidney and genitourinary tract (GTEx and Human Protein Atlas).

**Results:** Parents were non-consanguineous and there was no family history of CAKUT or cardiac anomaly. The proband had incomplete bilateral cleft lip and palate, neurodevelopmental delay and characteristic SVS-associated dysmorphic facial and digital features. In addition, he had unilateral renal agenesis and bilateral undescended testes. Other novel features were bicuspid aortic valve, patent ductus arteriosus, atrial septal defect, scoliosis and hemivertebrae. Trio whole exome sequencing (WES; 23,244 genes) detected a de novo pathogenic mutation NM\_021946.4c.2752C > T p.Gln918Ter resulting in premature truncation of the BCORL1 protein. No other renal disease associated mutations were detected. BCORL1 is expressed in the human kidney tissue, specifically the collecting duct and tubular cells. Furthermore, association of BCORL1 mutations with mesonephric carcinoma indirectly supports a role in kidney organogenesis.

**Conclusion:** We uniquely expand the known SVS phenotype to include CAKUT as well as cardiac and skeletal anomalies: features not previously identified in association with SVS. As such, we propose that imaging and assessment of kidney function should be considered in children diagnosed with SVS. In view of phenotypic variability and possibility of incomplete expression, testing for BCORL1 gene mutations might also be considered in cases of CAKUT.



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## EVALUATION OF THE PEDIATRIC PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS BY PULSE WAVE ANALYSIS

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**Introduction:** The relationship between cardiovascular diseases and juvenile idiopathic arthritis (JIA), one of the most common chronic inflammatory diseases in childhood, is unclear. This study aims to compare the noninvasive markers of arterial stiffness (AS) like pulse wave velocity (PWV) and augmentation index (AIx) values of children with JIA and healthy control group.

**Materials-Method:** It is a single-center prospective case-control study. While patients with JIA followed up for at least six months were included in the study, the cases with systemic JIA were excluded. Peripheral and central blood pressure (BP) values, PWV and AIx data were obtained with Mobil-O-Graph ambulatory BP measuring device. After the participants rested in a quiet room for about 10 minutes, three consecutive measurements were taken at 30-second intervals, and the averages of these measurements were analyzed. Echocardiography was performed within the same week, and left ventricular mass index (LVMI) was obtained.

**Results:** A total of 46 patients with JIA and 65 healthy children were included. The mean age of patients was 13.5 (6.4–17.9) years, and 56.5% were male. The mean age at diagnosis of JIA was 10.1 ± 4.8 years, and the disease duration was 22.4 (6–170) months. 27.8% of the patients had five or more joints involved. 58.7% of the patients were using a biological agent. In the control group, the mean age was 12.2 (6.6–17.9), and 53.8% were male. Age, gender, height-body weight-body mass index SDSs of the patient and control groups were similar. Systolic, diastolic, mean arterial pressure (MAP), pulse measurements and their SDS values, central systolic and diastolic BP, central pulse pressure measurements were significantly higher in the patient group ( $p < 0.05$ ). While the AIx of both groups were similar, the PWV was significantly higher in the patients. There was no difference between LVMI values and LVMI z-scores between the groups.

**Conclusion:** Arterial stiffness helps to show endothelial dysfunction and predict cardiovascular diseases. In our study, peripheral and central blood pressure values and PWV, one of the AS markers, were found higher in patients with JIA, before the adverse effects of on the left ventricle developed.

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## MARCH HEMOGLOBINURIA IN AN ADOLESCENT WITH “MACROHEMATURIA”

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**Aims/Purpose:** March hemoglobinuria is caused by hemolytic mechanism induced by physical exercise like running, walking, karate or hand drumming. The intravascular hemolysis is typically mild without induction of anemia (estimated quantity of hemolyzed blood is only 6 to 40 mL/paroxysm), self-limiting (resolving within 24–48 hours), with severity depending on athlete population, as well as on number, frequency and intensity of ground contacts. This very rare disease usually has a benign clinical course except for recurring episodes and cases presenting with acute kidney injury (AKI). So far, no changes have been described in complement system, which we present in the case report.

**Methods:** Casereports.

**Results:** A previously healthy 15-year-old boy complained of suddenly arisen repeated attacks of dark urine. Urine tests were repeatedly positive for hemoglobinuria without erythrocyturia or proteinuria. He had always normal renal function and blood count. Two weeks before the first attack he had a cold and one week before the first attack he was vaccinated against meningococcus. The history of the patients revealed that all attacks were associated with antecedent long walking (6–8 km). Shortly after the paroxysms, we repeatedly confirmed high free serum hemoglobin (986 mg/l), higher schistocytes (0.5%), low haptoglobin (= 0.08 g/l), high LD (6.91 ukat/l), normal bilirubin. These laboratory abnormalities completely resolved within 24–48 hours. We excluded cold and nocturnal hemoglobinuria, pathology of erythrocytes or hemoglobinopathy and myoglobinuria. During the attacks we repeatedly found low alternative pathway of complement (8.52, N > 11.0), low C3 (0.74 g/l, N > 0.9) and high C5b-9 (max. 1058 ng/ml, N < 525). Until now, glomerular and tubular function and blood count are normal. Renal biopsy was not performed.

**Conclusion:** March hemoglobinuria is a very rare hemolytic disease that can occur after intense exercise, especially walking/running. Its exact pathomechanism is not fully understood. Our patient is the first reported case with detected changes in complement and we may only speculate about its role in local hemolysis.

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## URINALYSIS AS A TOOL FOR EARLY SCREENING OF SILENT NEPHROPATHY IN CHILDREN PRACTICING SPORT: A SINGLE CENTER EXPERIENCE

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**Aims/Purpose:** Microhaematuria is an early sign of different genetic and non-genetic nephropathies which can present with mild changes in urinary sediment and can go undetected in the lack of a high clinical suspicion. In Europe routine urinary tests are not recommended for screening in the paediatric population with the exception of laboratory workup for obtaining medical certificates for sport activities. Our aim was to evaluate the impact of urinalysis performed in this setting for the diagnosis of collagenopathies.

**Methods:** We retrospectively collected clinical and laboratory data of paediatric (< 18 years-old) patients who underwent genetic testing in the suspect of collagenopathies, as a third-level investigation at the end of the diagnostic process. These were patients referred to nephrological evaluation after occasional finding of microhaematuria, with non-conclusive second-level investigations (e.g. testing for autoimmunity). Genetic testing was performed by exome sequencing followed by bioinformatic filtering for genes associated with kidney diseases and reverse phenotyping, as previously described [1].

**Results:** Among 55 patients who underwent genetic testing in the suspicion of collagenopathies for the presence of familiar history of kidney diseases and/or extra-renal involvement (e.g. hearing loss), 22 (40%) were referred for occasional findings of microhaematuria at screening for sport medical certificates. Among those, 9 (40.9%, corresponding to 16.3% of total patients screened) had pathogenic variants leading to a conclusive diagnosis of collagenopathies. In 11 patients the test is currently ongoing while genetic tested negative in two patients.

**Conclusion:** Urinalysis is an inexpensive, potentially cost-effective test. Our data highlighted that almost 16% of our patients had an early diagnosis of collagenopathy before full phenotypic expression, allowing timely initiation of nephroprotective therapies. Moreover, this approach led to identification of otherwise undiagnosed family members, with a relevant impact on their prognosis. In our experience urinalysis screening in children practicing sport proved useful for detection of a population at risk for collagenopathies.

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### HYPOCOMPLEMENTEMIC NEPHROTIC SYNDROME: WHO IS WHO?

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**Aims/Purpose:** Alport Syndrome (AS) is the second most common hereditary kidney disease caused by alterations in type IV collagen genes, with varied symptoms, from asymptomatic or hematuria, proteinuria, sensorineural hearing loss and ocular involvement, to end-stage renal disease (ESRD).

**Methods:** Present a case of AS with atypical presentation.

**Results:** 14-year-old boy who, at age of 6, presented episode of generalized edema, nephrotic proteinuria (iPr/Cr 11.24 mg/mg), hematuria, hyperkalemia, hypoalbuminemia, elevated creatinine (0.77 mg/dl), metabolic acidosis, and hypocomplementemia (C3 175 mg/l, C4 230 mg/l) with normal autoimmune tests. Hypertension (HT) was documented, requiring treatment with nifedipine. The diagnosis was oriented to acute glomerulonephritis (GN) in the context of viral sickness. Renal biopsy was performed, obtaining data of post-infectious-GN with positive immunofluorescence (C3, IgG and IgM). He progressively recovered renal function, decreasing proteinuria and hematuria. Given persistence of HT, hyperkalemic metabolic acidosis with low renin activity and decreased transtubular potassium gradient (TTKG), diagnosis of type IV ATR/Gordon syndrome was proposed, initiating treatment with hydrochlorothiazide, achieving adequate evolution, without genetic confirmation. 3 years later, second episode of similar characteristics. Enalapril and amlodipine were added. However, due to persistence of C3 consumption, renal biopsy was made, diagnosing C3-glomerulopathy. During follow-up, the presence of hypocitraturia together with high lithogenic index was highlighted (no nephrocalcinosis/lithiasis) which has made it necessary to maintain treatment with potassium citrate. Progressive withdrawal of antihypertensives has been achieved until omitting them, as well as hydrochlorothiazide due to normalization of calciuria. Currently, he presents tubular damage with partial resolution and worsening of renal function (eGFR 50–70 ml/min/1.73m<sup>2</sup>), drawing attention to persistent hypomagnesemia, hypovitaminosis D, without proteinuria or hematuria, maintaining low GTTK. For all these reasons, it was decided to study the clinical exome, observing a mutation in COL4A3 in homozygosis, producing SA.

**Conclusion:** When faced with clinically variable diseases, the importance of genetic tests in the face of uncertain diagnoses is highlighted, and in this case, without usual clinical presentation (up to 40% ocular involvement and sensorineural hearing loss in childhood), masked by symptoms and analytical findings that led to a completely different pathology. Once the affected gene has been identified, a family segregation study is necessary to determine the inheritance pattern and to be able to provide genetic counseling, as well as prognosis and prevention of progression towards ESRD.

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ISOLATED NON-ORTHOSTATIC PERSISTENT PROTEINURIA IN A CHILD: DO NOT OVERLOOK CUBN VARIANTS

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**Background:** Isolated non-nephrotic proteinuria in older children and adolescents are most commonly orthostatic. Non-orthostatic proteinuria creates a challenge for the physicians. We describe an adolescent girl with persistent non-nephrotic proteinuria associated with homozygous CUBN variant.

**Case report:** A 12-year-old girl presented with isolated proteinuria discovered incidentally at 7 years of age. Physical examination disclosed a well-developed girl with normal blood pressure. Laboratory tests revealed normal urine sediment, non-orthostatic and non-nephrotic proteinuria, normal hemoglobin, serum creatinine, albumin, C3 and C4 levels. ANA was positive, but anti-dsDNA antibody was absent. Her parents were non-related and there was no family history of renal disease. She underwent a renal biopsy yielding non-specific findings. Genetic analysis for proteinuric renal diseases showed homozygous carboxy terminal c.10102A > G variant in CUBN gene. This variant has been reported to be a founder mutation in Turkish population. Urine  $\beta$ 2-microglobulin level was normal and microalbumin level was increased. Serum vitamin B12 level was slightly reduced with normal homocysteine level.

**Discussion:** Cubulin, in association with megalin and amnionless, is responsible for receptor mediated endocytosis of low molecular weight proteins and albumin in the proximal tubule. While amino terminal mutations of CUBN causes Imlerslund-Grasbeck syndrome characterized by low molecular weight proteinuria and megaloblastic anemia, carboxy terminal mutations are associated with isolated proteinuria. Renal biopsy has revealed focal segmental glomerulosclerosis in some of these patients. In addition, some patients received immunosuppressive medications. Thus, it is important to include CUBN for genetic testing in patients with isolated non-nephrotic proteinuria and normal kidney function to avoid invasive tests and unnecessary treatments.

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**A NOVEL DE NOVO TRIM8 VARIANT ASSOCIATED WITH CHILDHOOD -ONSET FOCAL SEGMENTAL GLMERULOSCLEROSIS AND FACIAL SYNDROMIC FEATURES, WITHOUT NEUROLOGICAL SYMPTOMS**

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**Aims:** To describe the pheno/genotype of a boy with a very rare genetic TRIM8 variant, as his presentation is different from previously published cases. To describe the effect of immunosuppressive therapy in a patient with monogenic focal segmental glomerulosclerosis (FSGS).

**Methods:** We describe an 11-year-old boy presenting with proteinuria and facial dysmorphism indicative of syndromic disease; Macrocephaly, frontal bossing, high anterior hairline, and low-set ears.

**Results:** At 8 years of age, our patient presented with albuminuria that within 18 months had progressed to an albumin/creatinine ratio (ACR) of 1830 mg/g. He had normal neurological development, no history of epilepsy and a normal CT scan of the head. Renal biopsy showed FSGS: of 23 glomeruli 4 showed complete and 4 focal segmental sclerosis. IF negative. Based on the syndromic features, a Whole Genome Sequencing was performed as trio analysis showing a de novo heterozygous variant, c.1485del, p. (Trp495\*) in TRIM8 (NM\_030912.3) associated with autosomal dominant FSGS. The variant introduces a premature stop. The variant has not been reported earlier, but previously reported pathogenic variants in TRIM8 cause protein truncation clustering within the last exon, indicating a correlation between the disease and loss of the TRIM8 C-terminal region [1,2]. To our knowledge, only one previous case of TRIM8-associated FSGS without neurological symptoms has been published [3]. Initially, our patient was treated with Enalapril. Following the biopsy result and a rise in ACR to 1830 mg/g, Deflazacort and Tacrolimus were added, resulting in a rapid partial response reducing ACR to 550 mg/g. Following the genetic result, Deflazacort has been weaned. Current e-GFR is 79 ml/min/1.73m<sup>2</sup>.

**Conclusion:** This case report reveals that the phenotype of TRIM8 mutations is expanding. Genetic testing for TRIM8 variants in children with FSGS is relevant even in the absence of neurological symptoms. Despite the genetic results, our patient seems to have some effect of treatment with immunosuppressants in combination with ACE inhibition. The treatment may delay the expected progression to ESKD.

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Sa-P 260

WT1 VARIANT PRESENTING EARLY IN LIFE WITH NEPHROTIC SYNDROME, END STAGE RENAL DISEASE AND CRYPTORCHIDISM

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**Aims/Purpose:** Pathogenic variants in WT1 have a wide phenotypic appearance including Nephrotic syndrome, ESRD, genital abnormalities and Wilms tumor [1]. Missense variants have a more severe phenotype [2]. Our aim is to increase knowledge of phenotypic variation associated with missense variants in the DNA-binding site of the protein.

**Methods:** We describe the genotype/phenotype of a boy presenting with nephrotic syndrome, ESRD and cryptorchidism at 6 weeks of age.

**Results:** At presentation his symptoms were vomiting and tachypnea for three days. Phenotypically a male with normal penis and scrotum but bilateral cryptorchidism. Heavy proteinuria, low plasma albumin, oedema and oliguric renal failure lead to a diagnosis of Nephrotic syndrome and ESRD. Renal replacement therapy was immediately initiated. Previous history: born mature with oligohydramnion, birth weight 3.540 g. Prenatal ultrasonography in early pregnancy was normal.

**Genetic findings:** Trio whole exome sequencing with analysis of a panel of genes involved in kidney diseases showed a de novo heterozygous missense variant in WT1 (NM\_024426.6): c.1400G > A (p.Arg467Gln). The variant has previously been reported in patients with testicular ectopia and steroid-resistant nephrotic syndrome [1]. Chromosome analysis showed a normal male karyotype, 46 XY.

**Further course of disease:** Seven months of age: bilateral nephrectomy was performed due to the risk of Wilms tumor. Renal histological findings were segmental and global glomerulosclerosis. No malignancy was found. Macroscopic the kidneys were hypoplastic (10–13 g each). Two years and eight months: Renal transplant with a living related donor was successfully performed. Two and a half years post-transplant renal function is stable eGFR 46 ml/min/1.73m<sup>2</sup>. Four years and 6 months: Preemptive removal of both intraabdominal nonfunctioning testes was performed due to the risk of gonadoblastoma. Histology showed streak gonads with germinal cell agenesis, no malignancy. Overall developmental delay and microcephaly is observed whether this is due to the mutation or infant ESRD is difficult to differentiate.

**Conclusion:** Missense variants in exons 8 and 9 of WT1 affecting the DNA-binding site of the protein have been shown to be associated with an earlier and more severe phenotype compared to variants in other parts of the gene, as illustrated by this case [1]. Phenotypic variants of Missense mutations have a 33% risk of developing Wilms tumor at a median age of 1.3 years [2]. As a tumor preventive strategy, we performed early bilateral nephrectomy and orchiectomy in the present case.

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# POSTER SESSION 2G

## Inherited Kidney Disorders



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**KIDNEY CONCENTRATING CAPACITY IN CHILDREN WITH AUTOSOMAL RECESSIVE POLYCYSTIC KIDNEY DISEASE IS LINKED TO GLOMERULAR FILTRATION AND HYPERTENSION**

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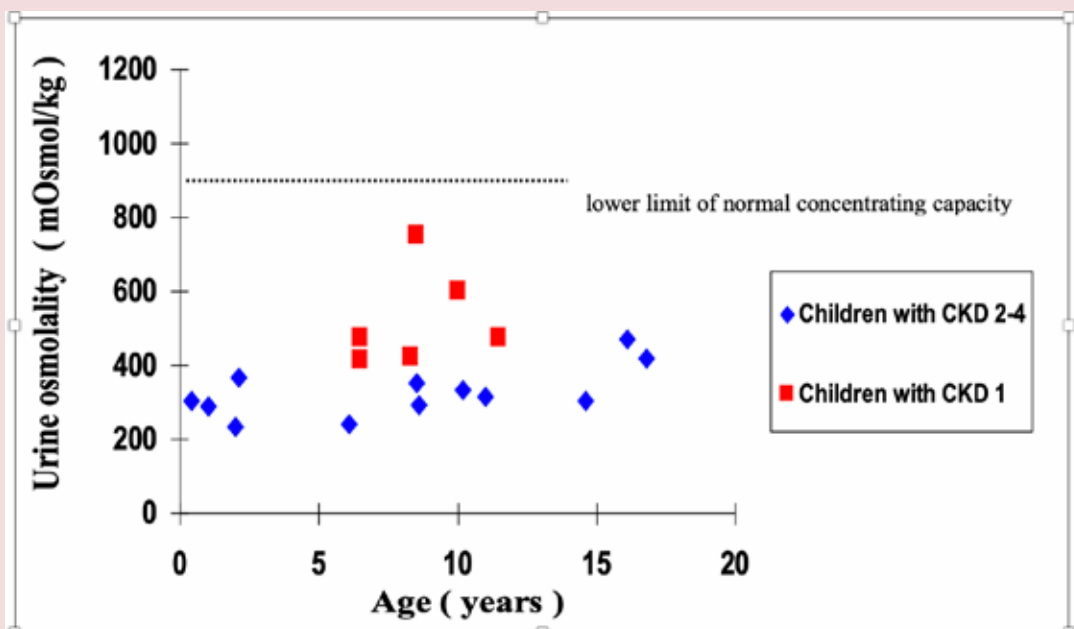
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**Aims/Purpose:** Impaired kidney concentration capacity is present in half of the patients with autosomal dominant polycystic kidney disease (ADPKD). The kidney concentrating capacity was further impaired within the animal model of autosomal recessive polycystic kidney disease (ARPKD). To date, only one small study has investigated it in children having ARPKD. Therefore we aimed to study the kidney concentrating ability in a larger cohort of children with ARPKD.

**Methods:** Eighteen children (median age 8.5 years, range 1.3–16.8) were retrospectively investigated. A standardized kidney concentrating capacity test was performed after the application of a nasal drop of desmopressin (urine osmolality > 900 mOsmol/kg). The glomerular filtration rate was estimated using the Schwartz formula (eGFR) and blood pressure (BP) was measured as office BP.

**Results:** Kidney concentrating capacity was decreased (urine osmolality < 900 mOsmol/kg) in 100% of children with ARPKD. The median urine osmolality after desmopressin application was 389 (range 235 – 601) mOsmol/kg {Figure}. Sixteen patients (89%) were defined as hypertensive based on their actual BP level or their use of antihypertensive drugs. The maximum amounts of urinary concentration correlated significantly with eGFR ( $r = 0.72$ ,  $p < 0.0001$ ) and hypertensive scores ( $r = 0.50$ ,  $p = 0.05$ ), but not with kidney size. Twelve patients (67%) were defined as having CKD stage 2–4. The median concentrating capacity was significantly lower in children within this group, when compared to children with CKD stage 1 possessing a normal eGFR (544 mOsmol/kg, range 413 – 600 mOsmol/kg vs. 327 mOsmol/kg, range 235 – 417 mOsmol/l,  $p < 0.001$ ).

**Conclusion:** Impaired kidney concentrating capacity is present in most children with ARPKD and is associated with decreased eGFR and hypertension.



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## TWO CASES OF ISOLATED PROXIMAL RENAL TUBULAR ACIDOSIS CAUSED BY SLC4A4 MUTATIONS

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**Aims/Purpose:** Our aim was to compare laboratory and clinical phenotype of 2 paediatric patients with genetically confirmed proximal renal tubular acidosis. Inherited isolated proximal renal tubular acidosis is an extremely rare disease with unknown prevalence mostly caused by autosomal recessive mutations in SLC4A4, the gene encoding the basolateral sodium-bicarbonate cotransporter (NBCe1). It is characterized by renal bicarbonate losses without impaired reabsorption of other solutes in the proximal tubule. Patients exhibit specific phenotypic abnormalities which include severe hypokalaemic metabolic acidosis with normal anion gap, growth and mental retardation, glaucoma, cataracts, corneal opacities (band keratopathy), basal ganglia calcification, elevated serum lipase and amylase, dentition defects and migraine headaches.

**Methods:** We retrospectively analysed clinical data, imaging, and laboratory tests of 2 patients from 2 different centres, both with genetically confirmed isolated proximal renal tubular acidosis. We evaluated and compared type and extent of organ involvement as well as administered treatment and its efficacy.

**Results:** We describe 2 female patients (aged 5 and 7 years, respectively) with previously unreported mutations of the SLC4A4 gene. Patient 1 (5-year-old) has homozygous mutation c.392dupA (p.Ala132Glyfs\*13) and Patient 2 (7-year-old) is a compound heterozygote with mutations c.1994\_1997delTGAC(p.Asp665Glyfs\*45) and c.2396A > C (p.Gln799Pro). Both patients presented in infancy with severe hypokalaemic normal-anion gap metabolic acidosis with subsequent need for massive alkali substitution. A common feature of the two patients is normal mental development, glaucoma, and zonular keratopathy with the need for repeated surgical interventions. Cataracts or intracerebral calcifications have not been demonstrated in any of them. Both patients were recently started on novel treatment with potassium citrate and potassium hydrogen carbonate in the form of prolonged-release granules, but metabolic acidosis in Patient 1 still remains very difficult to correct. Her severe growth retardation does not respond to growth hormone treatment. At the age of 4, she suffered an attack of acute pancreatitis with constant increase of serum pancreatic enzymes until today. Patient 2 responds better to alkali substitution. She however developed considerable dentition defects.

**Conclusion:** Due to the extreme rarity of the disease, more data are needed about the genotype-phenotype correlation, clinical course, and prognosis of patients with inherited isolated proximal renal tubular acidosis to improve their treatment and outcome. This would need broad international collaboration.

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CONGENITAL CHLORIDE DIARRHEA: DIAGNOSTIC DIFFICULTIES

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**Aims/Purpose:** Congenital chloride diarrhea (CCD) is a severe autosomal recessive (AR) disorder of electrolyte malabsorption manifested by profuse watery stool with massive loss of chlorides and dehydration.

**Methods:** We report results of own observation of patient with CCD.

**Results:** Boy was born in 04.2018 from second pregnancy at 35 weeks (weight 3620g, length 51 cm). At 23-25 weeks of gestation ultrasound (US) revealed high intestinal obstruction, left foot polydactyly and polyhydramnios. At 5 months of age the boy had a respiratory infection (RI) and was admitted to hospital. Metabolic alkalosis, hypokalemia and hypochloremia were revealed in acid-base status (ABS): (pH-7.58, cHCO<sub>3</sub>-34 mmol/l, SBE- 7.3 mmol/l, K<sup>+</sup> - 2 mmol/l, Cl<sup>-</sup> - 88 mmol/l). A diagnosis Tubulopathy (Bartter's syndrome N25.8) was made on the basis of complaints (weakness, refusal of feeding), history (first symptoms are due to an RI, prematurity, high intestinal obstruction and polyhydramnios on fetal US), examination (muscle hypotension), labs (metabolic alkalosis, hypokalemia, hypochloremia) and instrumental data (arterial hypertension, AG). Treatment: NaCl 4 mmol/kg/day and KCl 2 mmol/kg/day iv and per os, amlodipine 1.25 mg/24h. In 07.2019 DNA sequencing revealed heterozygous carriage of c.578C > T mutation in exon2 of the KCNJ1 gene described in type 2 Bartter's syndrome. During follow up the child had no problems with weight and height typical for tubulopathies. In 07.2021 complain of increase in stool up to 4 times a day for the last 3 months so celiac disease was excluded. Malabsorption, the presence of clinical features not characteristic for Bartter's syndrome (AG, normal weight and height) recommend a second genetic test to rule out co-morbidity of the urinary and gastrointestinal tract. Clinical genome sequencing identified SLC26A3 mutation characteristic of CCD. A diagnosis CCD type 1 with AR type of inheritance (OMIM:214700) was made. We recommended monitoring ABS, blood chemistry and urinalysis, orally 10% NaCl and 7.5% KCl, amlodipine 1.25 mg/24h. At present time the child is 4.5 yrs old with normal ABS, blood chemistry and urinalysis and doesn't have any problems with weight and height, normal stool.

**Conclusion:** This case reveals the difficulties with diagnosis of CCD. Antenatal history, correct interpretation of clinical and labs data, genetic testing, multidisciplinary approach contribute to timely diagnosis, adequate therapy and prevention of complications.

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EARLY MANIFESTATION BUT LATE DIAGNOSIS OF HNF1B NEPHROPATHY – A CASE REPORT

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The disease associated with a mutation of the HNF1B gene is rare. One of the characteristic disorders described in this entity is MODY5 diabetes, which usually becomes apparent in adolescence. Congenital anomalies of the kidneys and urinary tract, pancreatic and genital anomalies as well as hypomagnesemia and hyperuricemia are also characteristic of this disease. Here, we present a case with a rare manifestation of HNF1B nephropathy in order to facilitate timely diagnosis of further cases.

**Case report:** The girl was born at 32+6 weeks of gestation complicated by premature rupture of the amniotic sac. She was hospitalized in the intensive care unit due to respiratory distress syndrome. During the stay, significantly elevated blood glucose concentrations requiring insulin therapy were observed (up to the 5th day of life). The ultrasound examination performed at that time showed bilateral kidney dysplasia. Low concentrations of serum Mg (0.65–0.68 mmol/l) were noted. Up to 12 months of age, the girl was followed up mainly in the outpatient diabetes clinic where fasting blood glucose and HbA1c control tests were normal throughout the observation period. At the age of 4 years, she was consulted by pediatric nephrologist, and referred to hospital for further evaluation that revealed hyperuricemia (5.5 mg/dl). Metabolic tests of glucose homeostasis were found to be within reference range (HbA1c 5.07%). The family history of kidney diseases and glycemic disorders was negative. Due to the wide spectrum of abnormalities, including transient glycemic disorder, kidney dysplasia and disorders of Mg and uric acid metabolism, a suspicion of a disease related to the HNF1B gene mutation was raised. Genetic tests in the child confirmed the presence of deletion of this gene. The last check-up at the age of 4 years and 4 months showed no hyperglycemia; pancreatic  $\beta$ -cells reserve for insulin secretion was intact. Kidney function remained within normal limits. Conclusions: Transient neonatal diabetes mellitus is an unexpected manifestation of HNF1B disease, and its presence in the face of kidney anomalies may suggest HNF1B nephropathy.

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## CAN KIDNEY LENGTH PERCENTILES PREDICT ADPKD PROGRESSION?

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**Aims/Purpose:** We report the utility of 2D renal ultrasound in the paediatric patients with autosomal dominant polycystic kidney disease (ADPKD) in kidney length measurements for three different percentile adjusted for age, height and body mass area.

**Methods:** We report 9 cases with ADPKD from 'Louis Turcanu' Emergency County Hospital for Children in Timisoara, Romania. Data were extracted from the electronic data base between first of August 2016 until first of March 2023. Renal ultrasound was performed by the same operator using the same device. The study was performed in accordance with the World Medical Association and the Hospital's Ethics Committee.

**Results:** Out of the 9 patients (mean age 81.8 months  $\pm$  65.2), 3 were males (33.3%) and 4 (44.4%) had a positive family history. The mean serum creatinine level was 36.7  $\pm$  17.8  $\mu$ mol/l, GFR = 124.2  $\pm$  27.2 ml/min/1.73 square meters using Schwartz formula. 77.7% had bilateral cysts. The percentile of kidney length was assessed for age, height and body mass area. Although there were no statistical differences between age and height percentiles (76.9  $\pm$  20.5 vs 80.1  $\pm$  25.7,  $p$  = 0.73) nor between age and body mass area (76.9  $\pm$  20.5 vs 76.1  $\pm$  29,  $p$  = 0.9) nor for height and body mass ( $p$  = 0.57), one should notice the increased kidney length, over the 75% percentile adjusted for age, height and body mass area. 4 out of 9 patients had at least one urinary tract infection with only one patient being diagnosed with arterial hypertension and metabolic syndrome. Annual renal function and ultrasound assessment was performed in 5 patients. GFR increased from 126.8  $\pm$  20.2 ml/min/1.73 square metres to 145.8  $\pm$  30.6 ml/min/1.73 square metres ( $p$  = 0.29) with a slight increase in age renal length percentile (83.2  $\pm$  18.6% to 85.7  $\pm$  15.2%,  $p$  = 0.39).

**Conclusion:** Besides diagnosis, 2D renal ultrasound is a useful tool in assessing kidney length and percentile in the pediatric population. Even though our cohort is small, kidney expansion with associated hyperfiltration seems to start in early in childhood.

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**IDENTIFICATION OF NOVEL PROTEIN DISULFIDE ISOMERASE A6 MUTATIONS CAUSING SYNDROMIC POLYCYSTIC KIDNEY DISEASE WITH NEONATAL DIABETES: A CASE SERIES**

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**Aims/Purpose:** Protein disulfide isomerase A6 (PDIA6) is an unfolded protein response-regulating protein that regulates cell-cycle proteins, protein kinase R-like endoplasmic reticulum kinase and inositol requiring enzyme 1. Inactivation of PDIA6 gene in mice causes renal failure, skeletal abnormalities and diabetes. Here, we present three families with PDIA6 mutations who presented with polycystic kidney disease (PCKD), liver fibrosis, microcephaly, and type 1 diabetes mellitus (T1DM).

**Methods:** Three patients and their families underwent whole exome sequencing (WES), Sanger sequencing and Genome Analysis Toolkit for molecular testing and variant curation. Candidate gene variations were selected, categorized and reported. We extracted total RNA for real-time PCR analysis from all family members and 6 healthy controls.

**Results:** Case 1: A 4-year-old boy was born prematurely with respiratory distress, hypertension, PCKD, liver dysfunction, T1DM, left ventricular hypertrophy, cleft palate, inguinal hernia, and choroid plexus cyst. He has a number of dysmorphic features, in addition to muscle atrophy and dilated superficial veins. Case 2: A 7-year-old girl with PCKD, T1DM, and microcephaly who was born prematurely with congenital heart disease. She developed kidney failure, hypertension, gastroesophageal reflux, developmental delay and liver fibrosis. Case 3: A 1-year-old boy was born prematurely with intrauterine growth restriction, respiratory distress, hypertension, PCKD, T1DM and liver fibrosis. He has short limbs, a narrow chest, facial dysmorphic features and microcephaly. Imaging revealed a patent foramen oval with left-to-right shunting. The chromosomal analysis revealed no abnormalities. WES found no significant variations in clinically known ciliopathies. However, the additional research-based analysis revealed novel mutations in PDIA6 gene; two homozygous loss of function mutations in cases 1 and 2, and one homozygous missense variant in case 3, which was validated by Sanger sequencing.

**Conclusion:** This study establishes the association between novel PDIA6 mutations and PCKD. Hence, we recommend screening for PDIA6 mutations in children with PCKD and early-onset diabetes. Absence of PDIA6 protein may cause insulin-dependent diabetes, which is similarly linked to diabetes in other species.

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## A PAEDIATRIC COHORT OF HNF1B-RELATED-DISEASE

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**Aim:** Hepatocyte nuclear factor-beta (HNF1- $\beta$ )-related disease is a multi-system disorder characterized by a heterogeneous phenotype. The main renal features include hyperechogenic kidneys, renal dysplasia, kidney agenesis and renal cysts. Extra-renal symptoms include early-onset diabetes mellitus, hypomagnesemia, abnormal liver function, pancreatic hypoplasia, genital tract malformations, early-onset gout and behaviour disorder. Herein, we report the clinical presentation of a paediatric case series of HNF1 $\beta$ -related-disease followed-up in a single centre and with genetic diagnosis.

**Methods:** all patients with a pathogenic variant in the HNF1B gene were included. The following variables were collected: eGFR, blood pressure, renal ultrasound data, urogenital tract malformation, and behaviour disorders.

**Results:** 18 patients (11F:7M) were included in the study. Molecular analysis showed large deletions of ch17 encompassing the HNF1B gene in 5 patients, deletion of the entire gene (exon 1-9) in 8 patients, and missense substitutions in 5. The mean age at the first visit was  $1.4 \pm 2.1$  years, the mean follow-up was  $5.6 \pm 2.9$  years. Four patients (22%) had stage 2 chronic kidney disease, 15 (83%) had hyperechogenic kidneys. Of these, 9 also had microcysts and reduced cortico-medullary differentiation, and 7 (39%) had pelvic dilatation. During follow-up, progressive reduction in kidney size was observed in 5 patients (28%). Hypomagnesemia was detected in 8 children. Blood pressure was normal in 17/18 patients. No significant correlation was observed between blood pressure and kidney length or eGFR. A significant correlation was observed between kidney length and eGFR. Four children had a speech disorder and 8 behavioral disorder. In all these patients a 1-9 exons deletion or a large deletion of ch17 was found.

**Conclusion:** HNF1- $\beta$  gene should always be analysed in children with hyperechoic kidneys. The association of renal hypoplasia and/or dysplasia with speech or behavioral disorder is very suggestive of HNF1beta-related-disease.

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**HYPOMAGNESEMIA IN A CHILD WITH UROMODULIN GENE MUTATION: COEXISTENCE OR COINCIDENCE?**

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**Aims/Purpose:** Autosomal dominant tubulointerstitial kidney disease is a group of disorders that cause tubular atrophy, interstitial fibrosis, and chronic kidney disease (CKD). UMOD gene mutation is one of the diseases in this group and is rare in childhood, causing early-onset gout and slowly progressive CKD.

**Case:** Here, we reported a 6-year-old boy who presented with hypomagnesemia and metabolic alkalosis. In laboratory analysis, creatinine and uric acid values were normal. There was no family history of CKD or gout. There was an increase in bilateral renal parenchyma echogenicity in ultrasonography. Bartter type 3 and Gittelman syndromes were considered in the differential diagnosis, but no mutation was found in the genetic examination. The tubular gene panel confirmed that heterozygous mutation c.1124 G > A (p.R375Q) in the UMOD gene. His father was also found to have hypomagnesemia in the family screening. Therefore, the UMOD gene is also being studied from his father.

**Conclusion:** The present case emphasizes the importance of detailed genetic examination in children with the tubular disease with hypomagnesemia and the need to consider UMOD gene mutation in the differential diagnosis.



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AN INFANT WITH ALDOSTERONE SYNTHASE DEFICIENCY WHO WAS ERRONEOUSLY TREATED AS BARTTER SYNDROME

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**Background:** Isolated aldosterone synthase deficiency is a rare autosomal recessive disorder of impaired aldosterone synthesis caused by pathogenic CYP11B2 variants. The disease is characterized by hyperreninemic hypoaldosteronism leading to severe growth retardation, dehydration, hyponatremia, hyperkalemia and mild metabolic acidosis. Bartter syndrome, on the other hand, is a rare inherited salt-losing tubulopathy characterized by hyperreninemic hyperaldosteronism associated with polyhydramnios, premature birth, polyuria, growth retardation, and hypokalemic metabolic alkalosis.

**Case report:** A 6-month-old girl presented with severe failure to thrive (3030 g body weight). At one month of age, she had been hospitalized at a local hospital and followed up for 110 days due to feeding difficulty and respiratory distress. She was diagnosed as Bartter syndrome due to hyponatremia, polyuria (urine output ranged 2 to 5 ml/kg/h), alkalosis, and treated with oral salt and indomethacine without any benefit. She was an appropriate for gestational age term baby without a history of polyhydramnios. Evaluation of previous laboratory tests revealed normal serum creatinine, mild hyponatremia and hyperkalemia, respiratory alkalosis with normal to mildly decreased serum bicarbonate, and urine specific gravity of 1010. We stopped the medications and repeated the basic tests that revealed urine specific gravity 1020, serum glucose 102 mg/dL, Na 127 mmol/L, K 6.0 mmol/L, pH 7.45, HCO<sub>3</sub> 20 mmol/L, renin = 500 pg/mL (2.8-122) and aldosterone 50 pg/mL (35-300). Thus, we started fludrocortisone treatment with a diagnosis of isolated familial hypoaldosteronism. Clinical condition of the baby improved with this treatment. Genetic test revealed pathogenic compound heterozygous CYP11B2 variants (c.763G > T and c.788T > A) confirming the diagnosis.

**Discussion:** Hyporeninemic hypoaldosteronism resulting from isolated aldosterone synthase deficiency is a potentially fatal condition if the diagnosis and treatment is delayed. Hyperkalemia may be absent in 11% of cases. Metabolic acidosis may be mild or not apparent in some cases and compensation with respiratory effort may lead to misdiagnosis as in the present case. Thus, consideration of plasma K, renin and aldosterone levels are important in differential diagnosis of hyponatremic infants.

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KEEP IN MIND NEW GENE MUTATION IN AUTOSOMAL RECESSIVE POLYCYSTIC KIDNEY DISEASE: DZIPIL GENE

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**Aims/Purpose:** Autosomal recessive polycystic kidney disease (ARPKD) is a rare cystic kidney disease commonly caused by PKHD1 gene mutation, encoding fibrocystin. This disease presents perinatally or in childhood with enlarged kidneys, hypertension, varying degrees of kidney dysfunction and liver fibrosis in children. More rarely, DZIPIL gene mutation has been identified in patients with ARPKD. Patients with DZIPIL gene mutation have clinically similar features with PKHD1 related ARPKD, however liver involvement has been rarely reported. Here, we reported a case of ARPKD with DZIPIL gene mutation.

**Case:** A 6-year-old male patient was referred to pediatric nephrology department due to hypertension. He had normal kidney function with an estimated glomerular filtration of 123 ml/min/1.73m<sup>2</sup>. Urinary ultrasonography (US) and renal doppler US revealed multiple cysts in bilateral kidneys. No pathology was observed in the liver. Enalapril and amlodipine treatments were started for hypertension, respectively. There was consanguinity in the family history, there was no known kidney disease in the family. US was requested from parents and siblings and the results were normal. Genetic analysis was performed, and no pathogenic mutations were detected in PKD1, PKD2 and PKHD1 genes. A homozygous mutation (c.463C = T) in the DZIPIL gene was detected in whole-exome sequencing (WES). The patient was followed-up regularly in the past six years and he had normal kidney function with an eGFR of 120 ml/min/1.73m<sup>2</sup> in last visit. His blood pressure was within normal limits.

**Conclusion:** In this case, we wanted to emphasize that autosomal recessive kidney disease, which is mostly seen with PKHD1 gene mutation, may also be caused by DZIPIL gene mutation very rarely.

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**BARDET BIEDL SYNDROME TYPE 10 DEVELOPING END STAGE RENAL DISEASE IN INFANCY**

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**Aims/Purpose:** Bardet-Biedl Syndrome is a rare autosomal recessive disease characterized by retinal dystrophy, obesity, polydactyly, hypogonadism, and mental retardation. So far, 26 gene mutations have been identified. Here, we discussed a patient who needed peritoneal dialysis in infancy.

**Methods:** A newborn case with a birth weight of 2600 g born at 34th gestational week was admitted due to the increase in renal function tests (urea: 119 mg/dl, creatinine 2.2 mg/dl) detected during the follow-up. Medical history was remarkable for increased kidney sizes in the antenatal period and no consanguinity was defined between the parents.

**Results:** His current ultrasonography showed normal bilateral kidney sizes, bilateral increased echogenicity, and bilateral multiple cortical and medullary cysts with a maximum of 7 mm. On physical examination, he had polydactyly. The patient, who developed polyuria and polydipsia at three months of age was started on nonsteroidal anti-inflammatory therapy and thiazide due to vasopressin-resistant urinary concentration disorder. He was started on peritoneal dialysis program at the 6th month of age due to increased urea, creatinine and PTH levels. Bardet-Biedl syndrome type 10 (homozygous c.931T > G, p.Ser311Ala variant in BBS10 gene) was detected. In the 4th year of follow-up, he has nasal root flattening in physical examination, has head movements in a stereotypic pattern and retardation in mental developmental tests, but no hypogonadism, obesity or retinal changes in the eye examination yet.

**Conclusion:** Our patient confirms that Bardet-Biedl syndrome type 10 should be considered in cases with polydactyly and severe renal cystic abnormalities in the early infantile or even in the antenatal period.

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## CHARACTERISTICS OF LIVER DISEASE IN A MURINE ARPKD MODEL

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**Aims/Purpose:** Loss of fibrocystin (FPC) function causes autosomal recessive polycystic kidney disease (ARPKD). Besides enlarged cystic kidneys resulting in chronic kidney failure, ARPKD patients suffer from ductal plate malformation, leading to biliary disease and portal hypertension. Here, we analyze the liver phenotype in *Pkhd1*-knockout mice of different age and observe distinct, organ-specific hallmarks of disease development. Selective re-expression of FPC in embryonal liver eliminates cystic liver disease.

**Methods:** Livers (and kidneys) of male and female targeted mutation *Pkhd1*-knockout mice, homozygous and heterozygous for the *Pkhd1*-knockout allele as well as wildtype, were analyzed histologically at 8 weeks and 3 to 9 months of age with serum and urine samples taken before preparation. We address liver defects using tissue sections and selective mRNA/proteins analysis to identify the molecular signature of disease progression, and test the effect of FPC (re-)expression following Cre-based removal of the stop cassette in the *Pkhd1* gene.

**Results:** Analysis of relative organ weights indicates a stronger and earlier increase of liver than kidney weights in homozygous *Pkhd1*-knockout mice, aged 3, 6 and 9 months, as compared to controls, with no alterations in lung and heart weights. Organ function is mostly preserved in *Pkhd1*-knockout animals at all time points. In liver, we observe cyst formation originating from the bile ducts at 8 weeks, while female kidneys first show cysts at 3 months of age. In both organs, cyst development is associated with fibrosis, inflammatory processes and enhanced proliferation. Characteristic ductal plate malformation and Caroli syndrome in *Pkhd1*-knockout mice indicate embryonal origin of liver defects, and cholangiocytes show expression of CK14, a marker of the embryonal stage, reduced cilia formation, and altered functional properties. Periportal fibrosis is high in collagen type I, and alpha smooth muscle actin ( $\alpha$ SMA) marks activated hepatic stellate cells acting as myofibroblasts that surrounded biliary cysts. Lymphatic tailback is revealed by lymphatic vessel endothelial hyaluronic acid receptor (LYVE1) staining of heavily dilated vessels. In the liver, recruitment of immune cells comprises T-cells and M2 macrophages, epithelial expression of EGFR is increased, and there is no prominent nuclear localization of phosphorylated STAT3 in cyst lining epithelia as seen in cystic kidneys. Selective reactivation of the *Pkhd1* gene in liver results in healthy organs.

**Conclusion:** Hepatic disease in this murine ARPKD model is characterized by progressive cyst formation originating from the bile ducts comprising increased proliferation, inflammation, and periportal fibrosis. This model will allow analysis of disease related mechanisms and appears suitable for testing of therapeutic interventions in ARPKD associated liver disease.

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## HEALTH-RELATED QUALITY OF LIFE, MENTAL HEALTH AND CAREGIVER BURDEN IN CHILDREN WITH AUTOSOMAL RECESSIVE POLYCYSTIC KIDNEY DISEASE (ARPKD)

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**Aims/Purpose:** To examine whether established patient-reported outcome measures are suitable for capturing the impact of ARPKD in children and their families.

**Methods:** We assessed 44 children with ARPKD (40 families) with respect to patients' health-related quality of life (hrQOL) using PedsQL™ ESRD module) and mental health (strength and difficulties questionnaire (SDQ)) as well as family and caregiver burden (Impact on family score (IFS) und Ulm inventory of parental caregiver QOL (ULQIE)) and compared them to published data and 36 healthy control children matched for age and time (pandemic restrictions).

**Results:** Patients were aged  $9.5 \pm 5.9$  years (vs controls  $8.8 \pm 5.0$ ,  $p = ns$ ) and 21 (48%) were female (vs 19 controls (53%),  $p = ns$ ). Mean eGFR was  $81 \text{ ml/min} \cdot 1.73 \text{ m}^2$  (range 4–165); 7 received dialysis and 11 had functioning kidney transplants (KTX, 2 combined with liver transplants). Eight patients had developmental delay secondary to medical complications, while chronic illness was an exclusion criterion for healthy controls. 61 caregivers of affected children had the same gender-distribution (61% vs 60% mothers) and age (both  $42 \pm 7$  years) and number of dependent children ( $1.8 \pm 0.9$  vs  $2.0 \pm 0.8$ ) as 57 caregivers of healthy children. The mean proxy-reported PedsQL Total score was  $77.5 \pm 10.6$  (range 59–96). It correlated significantly to eGFR ( $r = 0.5$ ,  $p < 0.01$ , (also within the subpopulations pre- and post-KTX)). Parents reported greater mental health problems in their affected than in control children with a higher SDQ total score mainly due to higher scores in the hyperactivity and peer-interaction subscales. ULQIE revealed that parents of affected children had significantly lower levels of physical functioning, self-fulfillment and general QOL, but despite higher emotional burden scores they indicated similar satisfaction with family life. Impact on family scores were in a similar range to those of children with moderate to severe disabilities.

**Conclusion:** The good spread of PedsQL™ ESRD-scores and their correlation to renal function indicates that it captures significant aspects of ARPKD, however it may need further adjustment to include liver complications. All 4 chosen instruments revealed significant impact of ARPKD on hrQOL and mental health of affected children as well as family life and parental wellbeing in comparison to healthy controls. More problems with peer-interactions may also be due to more stringent shielding of chronically ill children from social contacts during the COVID pandemic compared to healthy children.

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**THE EXPERIENCE OF PAIN, QUALITY OF LIFE AND SYMPTOMS OF ANXIETY AND DEPRESSION IN ADOLESCENTS AND YOUNG ADULTS WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD)**

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**Aims/Purpose:** ADPKD is often still considered an ‘adult’ disease, with adults showing severe disease manifestations, pain, reduced quality of life (QoL) and increased psychosocial symptoms. Although ADPKD has mainly asymptomatic manifestations in childhood, the first aim of our study is to investigate QoL, pain, anxiety and depression in adolescents and young adults affected by ADPKD and compare scores to reference populations. Second, we aim to investigate the intra-familial relationship between the disease experience of the young person and disease experience and feelings about genetic disease transmission of their affected parent. Finally, we aim to develop a novel age- and disease-specific instrument (SAIL-ADPKD), that facilitates capturing these patient-centered aspects of ADPKD in future studies with adolescents.

**Methods:** We asked 11- to 25-year-old patients with ADPKD followed at UZ Leuven and age-matched healthy controls to complete surveys of pain (PROMIS pain interference short form) and QoL (PedsQL™ 4.0 generic core scales) and a behavioral screening questionnaire (Strengths and Difficulties Questionnaire (SDQ)). Parental burden of disease is captured with the ADPKD-IS (impact scale), ADPKD-PDS (pain and discomfort scale), SF36 (Short-Form 36) and a modified Genetic Psychosocial Risk Instrument (GPRI-ADPKD). With regard to the final aim, we created a novel instrument based on symptom frequency recorded in the APedKD registry, core outcomes defined in the multidisciplinary SONG-kids and SONG-PKD initiative, patient testimonies of pain as well as personal experience from pediatric ADPKD clinics. The questionnaire was improved by the feedback of psychologists, a psychometrician, a patient representative, and external experts in pediatric nephrology.

**Results:** Data collection will be finished in spring 2023. We firstly hypothesize that adolescents and young adults with ADPKD have a significant burden of pain due to ADPKD, reduced QoL and increased symptoms of anxiety and depression. Secondly, we hypothesize positive intra-familial associations. Finally, we will test whether the SAIL-ADPKD is a valid and reliable instrument, by analyzing internal consistency, test-retest reliability, and construct validity by convergence with the above-mentioned scores and correlation to measures of biochemical and radiological disease severity.

**Conclusion:** In summary, this study will add evidence on understanding and measuring disease burden in early ADPKD and deepen our understanding of the inter-generational aspects of disease experience in autosomal dominant disorders.

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## A RARE CAUSE OF FAILURE TO THRIVE

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The child at three years and six months old was admitted to the pediatric outpatient clinic due to nausea and vomiting accompanied by malnutrition and moderate dehydration. It was learned that she ate salt, drink a lot of water, and urinated a lot.

His perinatal history was unremarkable. The birth weight of the term baby was 3.2 kg. His parents were non-consanguineous. There was a sibling death history. She's been to hospitalization for dehydration before.

At our hospital admission; a physical examination revealed a weight of 10.1 kg (below 3rd percentile, SDS: -3.9), and a height of 91 cm (below 3rd percentile, SDS: -3). She had a dry tongue and dry lips. Arterial blood pressure was 90/50 mmHg. Hypokalemia, hypochloremia, hyponatremia, hypomagnesemia, hypophosphatemia, and hypocalcemia were found in laboratory examinations. However, serum creatinine level and estimated glomerular filtration rate were normal. The patient's urine output rate is 10 ml/kg/h. Urinary density was 1005. Urine electrolyte measurement showed a urinary potassium level of 35 mmol/L. There were proteinuria, hyperuricosuria, hypercalciuria, hypermagnesuria and a decrease in tubular reabsorption of phosphorus (TRP). The ultrasound examination revealed increased renal echogenicity. Parathyroid hormone was 137 pg/mL (high), and 25OHD was 3.8 ng/ml (low). Whole exome sequencing revealed a homozygous pathogenic mutation in c.371C > T(p.Pro124Leu) CLCNKB gene (OMIM 607364), and Bartter syndrome type 3 was diagnosed. And the patient also had nutritional 25OHD deficiency.

To our knowledge, this case is the first case describing type 3 Bartter syndrome without metabolic alkalosis.

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## NUTCRACKER SYNDROME AS A REASON TO VISIT THE OPERATING ROOM

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**Aims/Purpose:** Nutcracker syndrome is a rare, clinical condition caused by compression of the left renal vein between the superior mesenteric artery and the abdominal aorta. The clinical phenotype is highly variable, with the typical presentation being recurrent left flank abdominal pain, haematuria and proteinuria. Diagnosis is carried out by imaging studies, firstly abdominal ultrasound, requiring some of them complementary imaging studies to confirm the diagnosis. Doppler ultrasonography has been also commonly used for diagnosis. Treatment depends on the clinical manifestations and on the severity of the results and ranges from conservative treatment with oral analgesia to surgical intervention if needed.

**Methods:** We performed a retrospective review of two cases with nutcracker syndrome who required surgery due to the severity of their condition.

**Results:** Case report 1. 15-year-old boy on follow-up in the nephrology department for Nutcracker syndrome, diagnosed in the context of recurrent abdominal pain when an abdominal ultrasound was carried out. During workup, blood tests (normal renal function), urine analysis (mild proteinuria) and abdominal ultrasound were performed, with the left kidney showing hyperechogenicity and significant dilatation of medullary veins and renal vein that disappears at the level of the aorto-mesenteric clamp, with increased renal vein velocities. The study was completed with a computerized tomography angiography which confirmed the previously described severe stenosis of the left renal vein. Given these findings, surgical treatment was decided with transposition of the left renal vein, requiring reintervention 5 months later with stent placement due to clinical recurrence. Case report 2. 16-year-old girl diagnosed at the age of 14 with Nutcracker syndrome after polyuria and low back pain, initially treated as recurrent urinary tract infections, without microbiological confirmation. The functional and anatomical renal study by blood and urine tests, voiding cystourethrogram and abdominal ultrasound were normal except for mild microhaematuria and leucocyturia. The abdomino-pelvic CT scan was compatible with nutcracker syndrome, and conservative treatment with analgesia was initiated. After four months, she began with continuous low back pain and paresthesia in the lower limbs with no response to analgesia. Therapeutic approach was then reconsidered, and the patient was referred to Vascular Surgery, which confirmed the diagnosis by phlebography and underwent laparotomy surgery with reimplantation of the left renal vein into the inferior vena cava, with complete remission of pain.

**Conclusion:** Nutcracker syndrome is highly variable in terms of clinical presentation. Both imaging and kidney function as well as clinical development help to determine the different therapeutic approaches, varying from conservative treatment to surgery.



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**IDENTIFICATION OF A MISSENCE MUTATION IN THE CLDN19 GENE IN A PATIENT WITH OHSS AND EARLY ONSET CHRONIC KIDNEY DISEASE WITHOUT EYE INVOLVEMENT: A CLINICAL CASE**

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Familial hypomagnesemia with hypercalciuria and nephrocalcinosis (FHHNC) is a rare autosomal recessive disease of the renal tubules caused by mutations in the CLDN16 or CLDN19 genes encoding the claudin-16 and claudin-19 proteins, respectively. FHHNC is characterized by hypomagnesemia, hypercalciuria and nephrocalcinosis and progresses to renal failure. In patients with claudin-19 mutations, severe ocular involvement (macular coloboma, pigmentary retinitis, nystagmus, or visual loss) has been described.

The aim of our study was to demonstrate a patient with FHHNC with progressive decline in kidney function without eye damage.

In this report, we presented a 3-year-old girl (from consanguineous marriage (cousin sibs)) with polyuria, and polydipsia, laboratory examination revealed hypomagnesemia (blood Mg level - 0.62 mmol/l, hypocalcemia (Ca -1.86 mmol/l, decreased renal function - GFR - 67.6 ml/min/1.73m<sup>2</sup>; hypercalciuria, nephrocalcinosis, and renal stone. Taking into account nephrocalcinosis, hypomagnesemia, and decreased kidney function, a genetic study was conducted: a homozygous mutation in the CLDN19 gene was detected (missense mutation chr1:g.43204239G > A, (c.241C > T, p.Arg81Trp), validation of the CLDN19 gene (trio) was according to Sanger: a heterozygous mutation in the CLDN19 gene was performed in the proband father (c.241C > T, p.Arg81Trp) and mother (c.241C > T, p.Arg81Trp). The therapy includes: citrate, rovatinex, magnesium preparations.

In the dynamics of observation, hypomagnesemia persists, progressive decrease in kidney function (GFR - 52.9 ml/min/1.73m<sup>2</sup>), according to kidney ultrasound: nephrocalcinosis without dynamics, consultation of an ophthalmologist: pathology was not revealed.

**Conclusion:** the patient with a diagnosis of FHHNC, with a progressive decrease in kidney function at the age of 3 years (with a homozygous mutation in the CLDN19 gene detected) does not have eye lesions. Due to the fact that severe visual impairment is observed with a mutation in the CLDN19 gene, this child needs to be monitored by an ophthalmologist.

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## TUBULOINTERSTITIAL ACUTE KIDNEY INJURY IN PEDIATRICS: A SINGLE CENTER EXPERIENCE

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**Aim/Purpose:** Acute kidney injury (AKI) in children is a serious and often challenging condition. Its clinical management depends on the underlying kidney disease. Aim of this study was to investigate clinical characteristics and management of children with AKI of tubulointerstitial origin in a tertiary pediatric center in Italy.

**Methods:** We retrospectively reviewed the medical records of patients admitted over a 17-year period for intrinsic AKI with tubulointerstitial involvement, showed by polyuria, glycosuria, low-molecular weight (LMW) proteinuria, and without any clinical signs or symptoms of glomerular disease (gross hematuria, nephrotic-range proteinuria). We collected data on demographics, clinical course, biochemistry, kidney biopsy (if performed), treatment and long-term outcome.

**Results:** 32 patients were identified, 17 males, median age 13.5 years (IQR 12.0–15.0). Twenty-five of them reported recent drug assumption; symptoms at presentation were mainly aspecific (abdominal pain, nausea). Urinalysis at admission showed glycosuria and LMW proteinuria in 28% and 70.4% of the cases respectively. According to maximum creatinine values, reached in 1.5 days (IQR 1–3), 60% of patients were classified as stage 3 AKI, 37% as stage 2 and 3% as stage 1 AKI. No patients required kidney replacement therapy. Nine patients underwent kidney biopsy, with the diagnosis of tubulointerstitial nephritis (TIN) in all cases. Seventeen patients received steroid therapy: 10 with intravenous methylprednisolone followed by oral prednisone, and 7 with oral prednisone only. Kidney function improved quickly in all patients, LMW proteinuria normalized after a median time of 10 days (IQR 1–67.5). After a median follow-up time of 300 days (52.5–600), only 41% of patients had serum creatinine in the normal range, while 50% presented CKD stage 2 and 9% CKD stage 3a. No statistically significant differences were found in kidney function at admission and follow-up between biopsied vs non-biopsied patients and between children receiving vs not receiving steroids

**Conclusions:** we described a series of pediatric AKI cases of tubular-interstitial origin. Notwithstanding the limitations, our study underlines the consistent prognostic risk towards mild to moderate CKD (59%) of these patients and raised some doubts about the utility of kidney biopsy and steroid therapy.

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**URINE COMPOSITION AND LITHOGENIC RISK SHOW A CIRCADIAN VARIABILITY WHICH IS SIMILAR BETWEEN PEDIATRIC HEALTHY SUBJECTS AND STONE-FORMERS**

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**Aims/Purpose:** Urine composition can be vary modulated by oral intake, activity and individual intrinsic factors, often producing a circadian pattern. This variability can affect the individual risk for urinary crystallization along the day. Whether this variability is similar or different between healthy and stone-forming pediatric subjects is uncertain. We aim to describe the circadian variability in urinary parameters related to crystallization in children and adolescents comparing healthy individuals with stone-formers.

**Methods:** Twenty-six pediatric stone-formers aged 5-17 years old were recruited from the outpatient clinic in a tertiary care center. Twelve of them had been diagnosed with renal lithiasis and 14 ones presented with pre-lithiasic symptoms (hematuria, dysuria, overactive bladder or chronic abdominal pain related to urinary crystallization through a metabolic evaluation and discarding other potential causes). Eighty-seven healthy individuals of the same group of age were recruited from local schools as a control group. Spontaneous ambulatory 24-hour urine samples were obtained, fractioned in two consecutive 12-hour periods (daytime and overnight). Calcium, phosphate, magnesium, uric acid, oxalate, citrate, creatinine, pH and urine volume were measured for each period at a research specialized laboratory.

**Results:** In both groups, overnight excretion of phosphate and magnesium were higher; on the contrary, uric acid and citrate excretion, as well as pH and urine volume, were lower. Calcium and oxalate average excretion did not differ between both periods but we observed day to night differences according to each subject. Lithogenic risk was higher in the overnight period in both healthy and stone-forming subjects according to higher calcium to citrate ratio, as well as the previously mentioned higher phosphate excretion and lower pH, volume and citrate excretion (and, in some patients, higher calcium excretion).

**Conclusion:** An altered pattern of the circadian variability in urinary solute excretion does not seem to play a role in kidney stone formation, as it is similar in healthy subjects and patients. A higher overnight risk for stone formation is confirmed in this study.

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**PARAMETERS IN URINARY COMPOSITION FOR THE EVALUATION OF PEDIATRIC RENAL LITHIASIS CANNOT BE EXTRAPOLATED FROM 12-HOUR OVERNIGHT SAMPLES TO A 24-HOUR PERIOD WITHOUT RELEVANT BIAS. SPECIFIC REFERENCE VALUES ARE PROPOSED FOR 12-HOUR OVERNIGHT SAMPLES**

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**Aims/Purpose:** Collecting 24-hour urine samples can be complex for many patients. Shorter periods can be an alternative method. Extrapolation to a 24-hour period to compare with reference values is a common practice but its interpretation can be affected by circadian variability in solute excretion. We aim to compare extrapolated urinary solute excretion as well as urine volume from 12-hour overnight samples to real excretion obtained in 24-hour samples from pediatric healthy subjects and stone-formers.

**Methods:** Twenty-six pediatric stone-formers aged 5–17 years old were recruited from the outpatient clinic in a tertiary care center. Eighty-seven healthy individuals of the same age were recruited from local schools. Spontaneous ambulatory urine samples were obtained, fractioned in two consecutive 12-hour periods (daytime and overnight). Calcium, phosphate, magnesium, uric acid, oxalate, citrate and creatinine excretions and urine volume were measured for each period. Median excretions in 24 hours extrapolated from 12-hour overnight sample were compared with real 24-hour excretions for both groups of subjects. Urinary solute excretion and urine volume in the overnight period are described in healthy subjects.

**Results:** In healthy subjects, phosphate and magnesium excretions were overestimated by an 11 and 15%, respectively, and calcium, uric acid, oxalate, citrate excretions and urine volume were underestimated by a 3, 23, 9.5, 25 and 18%. In stone-formers, calcium, phosphate and magnesium excretions were overestimated by a 4, 20 and 13%, and uric acid, oxalate, citrate excretions and urine volume were underestimated by a 14, 13, 22 and 1%. Upper normal limit (p95) in 12-hour overnight period for stone promoters were: calcium 2.2 mg/kg, phosphate 13.2 mg/kg, uric acid 424 mg/1.73m<sup>2</sup>, oxalate 20.5 mg/1.73m<sup>2</sup>; lower normal limit (p5) for stone inhibitors were: citrate 1.6 mg/kg, magnesium 0.6 mg/kg.

**Conclusion:** Up to a 25% error was observed when extrapolating urinary solute excretion and urine volume from 12-hour samples to a 24-hour period. Specific reference values for 12-hour overnight samples are proposed.

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## CORRELATION AND CONCORDANCE IN URINARY INDEXES FOR THE EVALUATION OF PEDIATRIC RENAL LITHIASIS BETWEEN 12-HOUR OVERNIGHT SAMPLES AND 24-HOUR SAMPLES

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**Aims/Purpose:** Collecting 24-hour urine samples can be complex for many patients. Incorrect collection can derive in biased results. Shorter periods can palliate this problem and detect peaks of risk for crystallization. Interpretation of results from this samples compared to standard 24-hour ones is debatable. We compare urinary indexes in overnight 12-hour samples and over 24 hours regarding correlation and concordance.

**Methods:** Twenty-six pediatric stone-formers aged between 5 and 17 years old were recruited from the outpatient clinic in a tertiary care center. Eighty-seven healthy individuals of the same group of age were recruited from local schools. Spontaneous ambulatory 24-hour urine samples were obtained, fractioned in two consecutive 12-hour periods (daytime and overnight). Calcium, phosphate, magnesium, uric acid, oxalate, citrate, and creatinine were measured for each period. Urinary indexes for overnight 12-hour sample and 24 hours were compared regarding correlation (Spearman test) and concordance in detecting abnormal results according with reference values for 24-hour samples.

**Results:** In healthy subjects, correlation coefficients for calcium, phosphate, uric acid, oxalate, magnesium and citrate to creatinine ratios, and calcium to citrate ratio, were, respectively: 0.92, 0.86, 0.89, 0.90, 0.91, 0.92 and 0.92. In stone-formers, correlation coefficients were, also respectively: 0.87, 0.90, 0.76, 0.96, 0.92, 0.92 and 0.90. Most of abnormal results over a 24-hour period were also detected in overnight samples. Remarkable exceptions are 11% individuals with normal calcium-to-creatinine ratios in overnight samples when abnormal in 24 hours and 18% ones with abnormal calcium-to-citrate ratio in overnight samples when normal in 24 hours, both in the group of stone-formers

**Conclusion:** Correlations between indexes from overnight 12-hour samples and 24-hour samples were high for all parameters. Nevertheless, individual circadian pattern should be evaluated before using 12-hour samples for follow-up, especially for calcium. 12-hour samples can better detect increased calcium-to-citrate ratio which is thought to represent an increased lithogenic risk. Finally, specific reference values for 12-hour samples are needed to more reliably classify results as normal or abnormal.

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## NEPHROCALCINOSIS CAN DISAPPEAR IN INFANTS RECEIVING EARLY LUMASIRAN THERAPY: A REPORT ON 2 CASES

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**Background:** Lumasiran is the first RNA interference (RNAi) therapy approved for the treatment of primary hyperoxaluria type 1 (PH1). Here we report on the rapid improvement and even disappearance of nephrocalcinosis after early lumasiran therapy in two children.

**Case-Diagnosis/Treatment:** In patient 1, PH1 was suspected due to incidental discovery of nephrocalcinosis stage 3 in a 4-month-old boy with increased urinary oxalate (Uox) and glycolate (Ugly); lumasiran therapy was started before genetic confirmation. He also received hyperhydration through nasogastric tube, vitamin B6 and crystallization inhibitors. The patient displayed rapid decrease of UOx. Nephrocalcinosis started to improve 5 months after lumasiran initiation and disappeared at month 16 of therapy. Bilateral nephrocalcinosis stage 3 was diagnosed in patient 2 at the age of 10 months concomitantly to acute pyelonephritis. Uox and Ugly were elevated; lumasiran therapy was started before genetic confirmation associated to oral hydration, vitamin B6 and crystallization inhibitors. After one year of therapy, nephrocalcinosis has significantly improved from stage 3 to 1.

**Conclusion:** These two clinical cases illustrate the efficacy of early lumasiran therapy in infants to improve and even normalize nephrocalcinosis. As proposed in the 2023 European guidelines, the interest of starting treatment quickly as soon as PH1 is strongly suspected without waiting for genetic confirmation may have an impact on long-term outcomes.

Keywords: Primary hyperoxaluria, lumasiran, nephrocalcinosis, children

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COMPARISON OF RISK FACTORS FOR KIDNEY STONES AND RECURRENT KIDNEY STONES AMONG CHILDREN OF ELBASAN, ALBANIA

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**Aims/Purpose:** Urinary stone disease is increasing among pediatric age. This is a signal for pediatric nephrologists to investigate stone formation and prevention. Patients with kidney stones have some metabolic abnormalities, which are related to stone formation.

**Material and Methods:** We studied two groups of children. The first group of 62 children, 35 of them boys, arrived at our hospital with a kidney stone. The second group with 61 children, 33 of them male, arrived at our hospital with a recurrent kidney stone. The male/female ratio was 1.3:1 for the first group and for the second one was 1.17:1. We analyzed their records for clinical features, and their anamneses for positive family history of kidney stones. We examined their blood for urea, creatinine, uric acid and 24-hour urine in which we measured sodium, potassium, creatinine, calcium, citrate, oxalate, and magnesium. We evaluated Calcium/ Creatinine, Sodium/Potassium and Magnesium/Creatinine ratio. We compared the results found for the two groups.

**Results:** The most common clinical feature was abdominal pain 61% for children with a kidney stone and 43.9%, for kids with recurrent stone. Hypercalciuria was detected in 48% of kids in the first group and 79% of kids in the second group. Children with positive family history of kidney stones were 43.9% in the first group and 54.6% in the second group. We found a significant relationship between Calcium/Creatinine ratio and positive family for urolithiasis ( $p \approx 0.002$ ) and Calcium/Creatinine and Sodium/Potassium ratio ( $p \approx 0.001$ ) in both groups. Calcium/Creatinine ratio was 2.009 in the first group and 2.65 in the second group.

**Conclusion:** To detect and prevent lithogenic risk among children with kidney stones and recurrent kidney stones, metabolic evaluation of 24-hour urine remains an important determinant. In children with recurrent kidney stones, hypercalciuria and calcium/creatinine ratio are higher.

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## AGE-RELATED CLINICAL AND GENETIC CHARACTERISTICS OF IDIOPATHIC INFANTILE HYPERCALCEMIA TYPE 1 IN CHILDREN

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Idiopathic infantile hypercalcemia, type 1 (IIH1) is a rare autosomal recessive disorder caused by pathogenic variants in the CYP24A1 gene, which encodes 25-hydroxyvitamin D 24-hydroxylase, disrupt active vitamin D degradation. IIH1 characterized by hypercalcemia, low parathyroid hormone (PTH) serum level, hypercalciuria, nephrocalcinosis (NC) and/or urolithiasis. The aim of the study was to evaluate age-related clinical and molecular characteristics of IIH1 in Russian children.

**Methods:** We conducted retrospective two-centers longitudinal study of 20 children (9M/11F) with genetically confirmed IIH1. The median age of patients at the first follow up was 13.0 [10.0; 58.5] months. To identify age-related clinical features of the IIH1, patients were divided into 2 groups depending on the age at the time of the initial examination: group 1 included children < 24 months (n = 12), group 2 - children ≥ 24 months (n = 8). Molecular genetic analysis was performed in all patients using NGS.

**Results:** The most prevalent features of IIH1 were medullary NC (100%) and low PTH serum level (90%). Hypercalcemia was found in 75% of children, hypercalciuria in 60% of patients, urolithiasis in 20% of children with IIH1. According to the results of NGS, the most common CYP24A1 variants were p.Arg396Trp (55%) and p.Glu143del (40%). 4 novel CYP24A1 variants were identified: p.Gly78Val, p.Arg396Gln, p.Met99Thr, p.Gln471SerfsTer21. In patients examined up to 24 months, serum levels of calcium (Ca<sup>2+</sup> and total) were higher: 1.39 [1.35; 1.56] vs. 1.31 [1.24; 1.34] mmol/l (p = 0.013) and 2.9 [2.71; 3.74] vs. 2.45 [2.36; 2.52] mmol/l (p = 0.001), respectively, and serum level of PTH was lower: 7.9 [3.0; 12.7] vs. 14.6 [8.25; 15.85] pg/ml (p = 0.038) than in older children.

**Conclusion:** Medullary NC and low PTH serum level are prevalent clinical features of IIH1. Children aged < 24 months had higher serum level of calcium and lower serum level PTH compared with older patients. The severity and frequency of detection of the main clinical and laboratory characteristics of IIH1 depend on the age of patients, which must be taken in the differential diagnostic search in children with nephrocalcinosis/urolithiasis. The Russian cohort of children with IIH1 characterized by the same two “hot spots” variants in the CYP24A1 gene as European patients.



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MULTICENTER STUDY OF PATIENTS WITH MUTATIONS IN GENES POTENTIALLY CAUSING HYPERCALCEMIA

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**Aims/Purpose:** In recent years it has been known that mutations in the CYP24A1 gene (1,25-Dihydroxyvitamin D3 24-hydroxylase) cause hypercalcemia. Mutations in two other genes such as CaSR (calcium sensitive receptor) and SLC26A1 (solute carrier family 26 member 1) can also cause hypercalcemia. Our objective is to determine the clinical, biochemical and genetic characteristics of patients with mutations in CYP24A1, CaSR, SLC26A1 and heterozygous genes.

**Methods:** Multicenter study in which 9 patients (5V, 4M) with mutations in genes potentially causing hypercalcemia studied in nine Spanish hospitals were included. Various biochemical parameters were collected at diagnosis and at the end of the follow-up period.

**Results:** Four patients had mutations in CYP24A1, one in CASR, one in SLC26A1 and three had a heterozygous mutation in CYP24A1. Age at diagnosis was  $6.1 \pm 5.6$  years (range: 0.7-14.2). Two had normal ultrasound (CASR and SLC26A1 mutations) and the rest had ultrasound nephrocalcinosis. At diagnosis, eight patients showed calcemia levels above 10.5 mg/dl and a TRP between 82 and 95 ml/100 ml GFR. There was hypercalciuria in 5/9 (55.6%), hypophosphatemia in 3/9, lithogenic risk (elevated calcium/citrate ratio) in 2/9 (28.6%), concentration capacity defect in 7/9 (77.8%) and GFR less than 90 ml/min/1.73m<sup>2</sup> in 3/9 (33.3%). The treatment received was variable (in general, potassium citrate or thiazides together with potassium citrate). At the end of follow-up, the defect in concentrating ability persisted in seven patients and a reduction in GRF in two of them. In the two of the three cases in which calcitriol levels could be measured were higher than 120 pg/ml.

**Conclusion:** It is known that mutations in some genes can be associated with hypercalcemia with the consequence of nephrocalcinosis and/or renal lithiasis. The most frequent functional anomaly in these cases is the defect in renal concentrating capacity.

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**A MULTICENTER STUDY OF PATIENTS WITH NEPHROCALCINOSIS SECONDARY TO MUTATIONS IN THE GENES ENCODING TWO RENAL PROXIMAL TUBULAR PHOSPHATE TRANSPORTERS**

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**Aims/Purpose:** It is known that mutations in the genes encoding two proximal phosphate transporters cause hypophosphatemia, hypercalciuria and nephrocalcinosis. The SLC34A3 gene encodes type IIc Na<sup>+</sup>/Pi cotransporter; its mutations cause Hypophosphatemic rickets with hypercalciuria. The SLC34A1 gene encodes type IIa Na<sup>+</sup>/Pi cotransporter; its mutations cause nephrolithiasis/osteoporosis, hypophosphatemic rickets. Our objective is to determine the clinical, biochemical and genetic characteristics of patients with mutations in the SLC34A3, SLC34A1 and heterozygous genes.

**Methods:** Multicenter study in which 17 patients (7F, 10M) with ultrasound nephrocalcinosis studied in nine Spanish hospitals were included. Several biochemical parameters were collected at diagnosis and at the end of the follow-up period.

**Results:** Nine patients had mutations in SLC34A3, six in SLC34A1 and, two, a heterozygous mutation in SLC34A1. Age at diagnosis was  $5.3 \pm 3.9$  years (range: 0.1–15.5). At diagnosis, all but one patient showed a TRP less than 95 ml/100 ml GFR, hypercalciuria was present in 10/17 (58.8%), hypophosphatemia in 5/17 (29.4%), lithogenic risk (elevated calcium/citrate ratio) in 15/17 (88.2%), concentration capacity defect in 12/15 (70.6%) and GFR less than 90 ml/min/1.73m<sup>2</sup> in 5/16 (29.4%). The treatment received was variable (in general, potassium citrate, thiazides and potassium citrate or phosphate salts). There were no statistically significant differences between phosphatemia levels at baseline and at the end of follow-up. In contrast, in the second period GFR (Schwartz) was lower ( $105.6 \pm 8.5$  vs.  $90.9 \pm 30.3$  ml/min/1.73m<sup>2</sup>,  $p = 0.03$ ) and creatinine levels higher ( $0.47 \pm 0.19$  vs.  $0.66 \pm 0.19$  mg/dl,  $p = 0.01$ ). At the end of follow-up 9/15 (60%) showed reduced GFR.

**Conclusion:** In pediatric patients with nephrocalcinosis, the joint presence of hypercalciuria and hypophosphatemia should be investigated. If positive, mutations in the SLC34A3 and SLC34A1 genes are candidates. It is unknown whether the reduction of GRF is secondary to nephrocalcinosis or to other unknown mechanisms.

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## THE EFFECT OF CASR, CALCR, ORAI1, AND SCL13 GENE POLYMORPHISM ON THE DEVELOPMENT OF UROLITHIASIS IN TURKISH CHILDREN

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**Aims/Purpose:** No other study simultaneously examines the calcium-sensing receptor (CASR), Calcitonin receptor (CALCR), Calcium Release-Activated Calcium Modulator-1 (ORAI1), and Solute-Carrier-Family-13 Member-2 (SCL13A2) gene polymorphisms. Mutations of these 4 genes play a role in urolithiasis. Here, the clinical significance of polymorphisms will be evaluated by determining the presence of polymorphisms in urolithiasis patients and healthy children.

**Methods:** 100 pediatric patients aged 0-18 years diagnosed with urolithiasis and 64 healthy patients were evaluated. The patient group was evaluated in terms of laboratory tests, clinical follow-ups, and the presence of polymorphism. Only the presence of polymorphism was investigated in the healthy group.

**Results:** When the CASR, CALCR, ORAI1, and SCL13A2 gene polymorphisms were compared with the patient and healthy groups, no significant difference was found between the groups with no mutations and those with heterozygous/homozygous mutations (respectively  $p = 0.495, 0.382, 0.495, 0.258$ ). When CALCR, ORAI1, and SCL13A2 gene polymorphisms, homozygous mutations, and others were compared in the patient and healthy groups, respectively, no significant difference was found between the groups (respectively  $p = 0.183, 0.544, 0.508$ ). No homozygous CASR gene polymorphism was detected in both groups. In the patient group, polymorphisms could not be associated with recurrent urolithiasis, need for surgery, urinary pH, and hypercalciuria.

**Conclusion:** We investigated these 4 genes simultaneously in terms of genotype-phenotype for urolithiasis in Turkish children. However, we showed that it has no effect on healthy children and pediatric patients with urolithiasis. This is the first study to examine these gene polymorphisms in Turkish children.

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## EPIDEMIOLOGY AND RECURRENCE IN PAEDIATRIC UROLITHIASIS UNRAVELLED: A SINGLE CENTER EXPERIENCE IN UNITED KINGDOM

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**Aim/Purpose:** Whereas adult urolithiasis is frequently idiopathic, it is probable that risk factors for stone disease are more likely in children. We retrospectively reviewed all children who had undergone treatment for upper tract stones at our tertiary unit. We further investigated whether these risk factors were more prevalent in those with recurrent stones.

**Method:** All children undergoing surgery for renal or ureteric stones over the past 14 years, between 2008 to 2022 were retrospectively reviewed. Data was collected on number, position, size of stones and whether they were staghorn or present in transplant kidneys. Patient Risk factors included prematurity, comorbidity, family history and the presence of blood or urine chemistry abnormality. Statistical significance was taken at  $p < 0.05$  (two-tailed).

**Results:** 131 patients (55.7% boys) were identified with median (IQR) age 9.5 (4.7-13.6) years at time of surgery and subsequent follow-up of 42.9 (22.4-68.9) months. Multiple stones were present in 65, stone size (largest where multiple) was 10 (7-13), mm, unless a staghorn, of which there were 17. In 2, stones were present in transplants. UTI was the presentation in 34.4%. Metabolic abnormality for urolithiasis was found in 28.4%. Risk associations for urolithiasis included history of prematurity in 11.5%, other co-morbidity in 42%, anatomical renal tract anomaly in 21.4%, family history of urolithiasis 20.6%. Primary surgery was extracorporeal shock wave lithotripsy in 3, rigid ureteroscopy in 20, percutaneous nephrolithotomy in 39, and flexible ureteroscopy in 77. Stone recurrence was evaluated in 79 children who were completely clear of stone following treatment. Twelve (15.2%) children developed recurrence, and were significantly older when compared with those with no recurrence (median 12.1 versus 8.2 years respectively). Recurrence was significantly higher in children with multiple stones when compared to those with single stone at initial presentation (26.5% versus 6.7%,  $p = 0.015$  respectively). There was no difference in the rates in transplanted, staghorn, prematurity, structural anomaly, comorbidity, or family history between those with recurrence and those without. Nor was there a difference in presenting stone size, blood or urine biochemical testing.

**Conclusion:** We report metabolic stone disease in only a 1/3rd of children with urolithiasis. Stone recurrence was more frequently seen in older children and those presenting with multiple stones.

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## HYPERCALCEMIA: AN UNUSUAL MANIFESTATION OF AN HNF1 $\beta$ MUTATION

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**Aims/Purpose:** Mutations in the gene coding for Hepatocyte nuclear factor 1 $\beta$  (HNF1 $\beta$ ) may cause maturity-onset diabetes of the young type 5 (MODY5) and they are also encountered in a significant proportion of patients with various renal malformations. These mutations may cause several different phenotypes of varying severity. Usual clinical findings include pancreatic, kidney, liver and urogenital manifestations. Patients often present with renal cysts and/or increased echogenicity on renal ultrasound.

**Methods:** Our case is a girl currently 3.5 years of age, who had hypercalcemia along with multiple bilateral small renal cysts, increased renal echogenicity and relatively small kidney size at birth. Consequently, genetic testing (massive parallel sequencing) was performed at early infancy, which revealed an heterozygous HNF1 $\beta$  pathogenic truncating mutation (p.Q182\* (CAG > TAG). Due to the presence of hypercalcemia, several other candidate genes were tested for, and no other clear genetic cause of hypercalcemia was detected.

**Results:** During regular follow up the patient shows steady mild, asymptomatic hypercalcemia (serum total calcium levels: 11-11.9 mg/dl), which is accompanied by very low urine calcium (FeCa: 0.1%-0.6%) and inappropriately normal or mildly elevated PTH, with serum magnesium also within normal limits. The patient has a normal renal function (serum Creat.: 0.5mg/dl). A extensive endocrine work-up did not reveal any other cause for hypercalcemia and the thyroid/parathyroid ultrasound was within normal limits. According to the literature HNF1 $\beta$  mutations have rarely been associated with primary hyperparathyroidism and reduced calcium renal excretion. In particular, HNF1 $\beta$  was detected as a transcriptional repressor of PTH production, so patients with such mutations lose this HNF1 $\beta$ -mediated PTH regulation. Moreover, research data show that HNF1 $\beta$  also acts as a transcriptional activator of the calcium-sensing receptor (CaSR) in the kidney. Thus, HNF1 $\beta$  mutations may reduce CaSR activity, leading to an increase in tubular calcium reabsorption.

**Conclusion:** HNF1 $\beta$  mutations may present with various clinical phenotypes. Hypercalcemia is not a frequent clinical manifestation in children with these mutations. A thorough investigation did not reveal alternative causes for the raised calcium levels. Pediatric nephrologists should be aware of the diversity of HNF1 $\beta$  mutations clinical manifestations.

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HOW TO TALK SO PATIENTS WILL LISTEN – JOINT MOTIVATION FROM NEPHROLOGIST AND UROTHERAPIST INCERASES THE EFFECTIVNESS IN VOIDING DISORDERS IN CHILDREN

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**Aims:** In children over 5 years or those who have managed to get control of their bladder, most of voiding disorders are functional. A large part of these clinical problems undergo non-pharmacological treatment based on the principles of standard urotherapy. The aim of the study was to develop an effective method of urotherapy during a multidisciplinary visit (pediatric nephrologist + physiotherapist) in children with voiding disorders that initially failed to adhere to standard urotherapy presented by family doctors or specialists.

**Methods:** The study group consisted of 28 children aged 5-13 y – 15 girls, 13 boys. These were patients with micturition disorders – 54% reported day-time incontinence and frequent/urgent urination, in 18% the problem was also bed-wetting, 28% suffer from isolated night-time incontinence, 14% complains of bladder and bowel dysfunction (BBD). Parents of all patients admitted that they had heard about the standard lifestyle modification that could have improved the situation, but they failed to implement them. None of these patients received pharmacological treatment either before the visit or during the 3 of follow-up. All patients had a combined consultation with physician and urotherapist, during which they were thoroughly and vividly explained the principles of proper hydration throughout the day, the appropriate position during micturition, and the principles of relaxation of the pelvic diaphragm. The children were trained to behave appropriately while urinating. We helped parents choose the right aids (toilet seat covers, footrests) to help them maintain the correct position while urinating. In this way, the little patients became “trainers of their bladders”.

**Results:** 19 out of 27 patients (70.3%) achieved complete resolution of symptoms after 3 months our visit. 58% of this group suffer from day-time incontinence, 21% with enuresis, 21% combined day- and night-time voiding disfunction. All patients in this group admitted that they scrupulously followed the recommendations of effective urotherapy. 65% of this group were girls, 35% boys. X% of them showed an improvement in cystometry. In 5 patients (17.9%) partial relief of symptoms was achieved. All patients in this group had symptoms of overactive bladder. For all of them, the use of additional oxybutynin turned out to be an effective treatment. 3 patients (11%) did not experience improvement, but all admitted that they did not strictly follow the instructions given. Patients in this group had psychiatric comorbidities that made cooperation difficult. All of them where boys.

**Conclusions:** In children who initially failed to adhere to the therapy of functional voiding disorders, the key to the success is to incorporate a professional urotherapist to the multidisciplinary team and intensify training and motivation, rather than change the treatment.

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GENETIC TESTING IN CHILDREN WITH NEPHROCALCINOSIS: A SINGLE-CENTER COHORT STUDY

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**Aims/Purpose:** In children, nephrocalcinosis is mainly related to metabolic and inherited disorders, making the genetic testing essential to provide a specific diagnosis. The study objectives were to characterize the genetic profile of pediatric patients with nephrocalcinosis and to evaluate the genotype-phenotype correlations.

**Methods:** This retrospective study included 28 patients who had a radiological diagnosis of nephrocalcinosis and who underwent a genetic testing by the age of 18 years old (customized nephrocalcinosis/ nephrolithiasis panel or Whole Exome Sequencing).

**Results:** Genetic testing was positive in 89% (25 cases) and negative in only 11% (3 cases). However, in 5 cases, the diagnosis confirmed a neurological syndrome, and nephrocalcinosis was a known feature of it (Coffin-Siris and Williams syndrome) or was associated with the treatment (parenteral nutrition or antiepileptic drugs). Causative monogenic mutations were reported in 50% of the cases. The diagnosis was definite (only pathogenic or likely pathogenic variants) in 8 cases (28.5%), probable (a combination of pathogenic variants and variants of uncertain significance) in 2 cases (7%) and possible (only VUS) in 7 cases (25%). We also identified 4 patients (14%) with heterozygous mutations in autosomal recessive diseases, but who had a phenotype that was consistent with the genetic profile. The most frequent pathologies identified were idiopathic infantile hypercalcemia type 1 and 2 in 28.5% of the cases (5 patients with mutations in CYP24A1 and 3 patients with mutation in SLC34A1) and Bartter syndrome in 14% of the cases (type 1: SLC12A1 mutation in 3 patients and type 2: KCNJ1 mutation in 1 patient), followed by Dent disease (CLCN5 mutation) in 2 cases (7%), distal renal tubular acidosis (ATP6V1B1 mutation) in 2 cases (7%) and renal hypouricemia (SLC22A12 mutation) in 2 cases (7%). Regarding the genotype-phenotype correlations, we identified that a more severe degree of nephrocalcinosis (class III, according to the Hoyer classification) was associated with infantile hypercalcemia (homozygous or compound heterozygous mutations in CYP24A1 and SLC34A1) and distal renal tubular acidosis. We also observed that a more severe clinical evolution (failure to thrive, < 5th percentile of weight and height) was associated with Bartter syndrome type I and distal renal tubular acidosis, while the 2 patients with Dent disease had a more severe renal impairment (progression to CKD stage G3 during the observational period).

**Conclusion:** In our study, most of the patients had a mutation that could explain the nephrocalcinosis. The etiology was heterogenous, but the genetic testing was helpful to establish an early specific diagnosis and treatment. Gaining more insight into the correlations between the genotype and phenotype in nephrocalcinosis, we could provide predictive information about the disease evolution and prognosis.

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**EXTREMELY LOW URIC ACID LEVEL AND MEDULLARY NEPHROCALCINOSIS IN A CHILD: SLC2A9 MUTATION**

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**Aims/Purpose:** Renal hypouricemia (RHUC) is a rare inherited disorder characterized by impaired uric acid reabsorption in the proximal tubule and caused by mutations in SLC22A12 and SLC2A9 genes.

**Results:** A 6-year-old boy presented to the pediatric nephrology department with abdominal pain. His past medical history was unremarkable. He was not taking any medications. The physical examination and vital signs were normal. Renal ultrasound revealed bilateral medullary nephrocalcinosis. The laboratory tests revealed extremely low serum uric acid levels (0.3 mg/dl) and increased urinary excretion of uric acid. Proximal renal tubular acidosis was ruled out by normal urine analysis, blood gas and serum electrolyte levels. SLC2A9 gene was sequenced and revealed homozygous p.Arg380Trp (c.1138C > T) mutation. The patient was treated with potassium citrate. He was closely and regularly followed-up with renal ultrasonography.

**Conclusion:** Renal hypouricemia (RHUC) is a rare inherited disorder with increased urinary urate excretion resulting in low serum urate levels. Patients with renal hypouricemia is likely underdiagnosed, so it should be kept in mind in case of very low uric acid levels.



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## THE CLINICAL CHARACTERISTICS AND THE LONG-TERM OUTCOME OF CYSTINURIA; SINGLE CENTER EXPERIENCE

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**Aims/Purpose:** Cystinuria is a rare hereditary metabolic disease involving the defective transport of cystine and dibasic amino acids through the proximal renal tubules, causing stone formation in the urinary tract. Recurrent cystine stones may result in chronic kidney disease from recurrent renal injury. This study aimed to determine the clinical data, treatment responses, and long-term results of patients with cystinuria in our center.

**Methods:** The medical data of 11 patients diagnosed with cystinuria between 2001 and 2022 were retrospectively reviewed. Demographic data, clinical characteristics, laboratory results, and treatment responses were evaluated.

**Results:** Of the patients, 7 (63.6%) were female, and 4 (36.3%) were male. The median age at diagnosis was 12 months (4 months–12.5 years), and the mean follow-up duration was  $7.5 \pm 5.12$  years. The most common initial symptoms were urolithiasis and urinary tract infections, followed by abdominal pain. Five patients had acute kidney injury at diagnosis, and three underwent acute dialysis in admission. Seven patients (63.6%) had bilateral nephrolithiasis, and six underwent more than one urological procedure. Cystine level in the spot urine was significantly high at the time of diagnosis. Hypocitraturia was noted in 6 patients, hyperoxaluria in 3 patients, and none had hypercalciuria or hyperuricosuria. In addition to diet, increased hydration, and oral potassium citrate, tiopronin therapy was added. Seven patients had a stone-free period during the follow-up, while four had recurrent stone formation despite the treatment. During the COVID-19 pandemic, patients could not receive tiopronin therapy; captopril was started along with potassium citrate. Penicillamine was initiated in one patient. The urinary cystine level was normal under penicillamine therapy, and no stones or side effects were noted after the treatment switch. The 24-hour urinary cystine level was high in 4 patients in the last follow-up. All of our patients had normal glomerular filtration rate values except for one patient.

**Conclusions:** Cystinuria is a critical health problem in childhood. Patients require combined urological and pharmacological treatments to prevent stone recurrence and maintain renal function. Despite high urinary output and alkalinization, using cystine-binding drugs, D-penicillamine, and tiopronin effectively reduces free cystine levels and prevents stone formation or growth.

**Keywords:** Pediatric patients, cystinuria, cystine stone.

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## MONITORING OF PLASMA OXALATE IN AN ANURIC CHILD ON PERITONEAL DIALYSIS AND TREATED WITH LUMASIRAN FOR PRIMARY HYPEROXALURIA TYPE 1

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**Aims / Purpose:** Lumasiran is a subcutaneous RNA- interference (RNAi) therapy that reduces hepatic oxalate production by targeting glycolate oxidase in primary hyperoxaluria type 1.

**Methods:** Here we report on a case of infantile PH1 diagnosed at 3 months of age in December 2019. Irreversible anuria with kidney failure and nephrocalcinosis were present at diagnosis. Intensive peritoneal dialysis (PD) and conservative treatment were immediately begun. The first dose of lumasiran was given at 13 months of age as compassionate use since our patient could not be included in the ongoing industry-sponsored studies because of age, anuria and peritoneal dialysis. The dose and interval of administration were the same than the ones used in clinical studies.

**Results:** As expected, PD alone, even with an intensive strategy (20h/24 daily), did not decrease plasma oxalate (POx) levels, which in fact kept increasing (maximum of 192  $\mu\text{mol/L}$ ). After the introduction of lumasiran, POx levels decreased by 37% after the first 3 months of treatment and by 46% after 6 months of treatment. With the growth of our patient, we were able to begin hemodialysis (HD) 6 days per week at 21 months of age (POx at 107  $\mu\text{mol/L}$ ), and to add convective technique at 29 months. This dialysis strategy was followed by a slow decrease in POx levels below 100  $\mu\text{mol/L}$ . As observed in the clinical trials in HD, POx levels remained above 60  $\mu\text{mol/L}$ , which is proposed by some authors as the rate to reach to allow isolated kidney transplantation under lumasiran. With a follow-up of 13 months in HD, the persistent increased POx levels are probably related to systemic oxalosis that is progressively released from bone and is not impacted by RNAi therapies. Of note, our patient displayed only one low-trauma fractures just before the lumasiran initiation since diagnosis.

**Conclusions:** Lumasiran seems effective without side effects even in infants in PD, with an almost 50%-decrease in POx levels in this case. However, in severe PH1 with early anuria, it remains crucial to go on with intensive extra renal epuration to allow the clearance of the oxalate stored before diagnosis and in our case before the initiation of lumasiran treatment. Therefore, RNAi therapies should be initiated as early as possible in association with conservative measures and dialysis to avoid or to limit oxalate overload.

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## BONE AND MINERAL METABOLISM IN CHILDREN AND ADULTS WITH NEPHROPATHIC CYSTINOSIS

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**Aims/Purpose:** The pathophysiology of nephropathic cystinosis (NC) associated bone disease is poorly understood.

**Methods:** We examined serum/plasma concentrations of 8 bone markers and routine parameters of mineral metabolism in 63 children (mean age 10.8 years) and 40 adults (mean age 28.3 years) with NC by ELISA and autoanalyzer. Data are given as age- and sex-dependent z-scores as a function of estimated glomerular filtration rate (eGFR).

**Results:** Pediatric and adult NC patients with eGFR > 60 ml/min/1.73m<sup>2</sup> showed reduced z-scores for serum phosphate and calcium, and elevated bone-specific alkaline phosphatase (BAP) despite treatment for Fanconi syndrome. Hypocalcemia was more pronounced in children, whereas BAP z-scores were more elevated in adults (each p < 0.001). Intact and total fibroblast growth factor 23 (FGF23) and parathyroid hormone levels were suppressed in NC patients with eGFR > 60 ml/min/1.73m<sup>2</sup> (each p < 0.001). FGF23 z-scores progressively increased in parallel with decreasing eGFR, reaching 6 SD in patients with eGFR < 30 ml/min/1.73m<sup>2</sup>, while calcitriol levels progressively declined. The Wnt signaling inhibitor sclerostin was increased by 1 SD in pediatric but not in adult NC patients irrespectively of eGFR. The osteoclast marker tartrate-resistant acid phosphatase 5b (TRAP5b) was increased by 1 SD (children) and 2 SD (adults) independent of eGFR despite the absence of hyperparathyroidism in the majority of patients (each p < 0.001). Receptor-Activator of NF- $\kappa$ B ligand (RANKL), an inhibitor of osteoclast activity, was reduced by 1 SD in pediatric but not in adult NC patients. Finally, the RANKL inhibitor osteoprotegerin (OPG) was increased by 2 SD in children with eGFR < 30 ml/min/1.73m<sup>2</sup>, whereas adult patients consistently showed reduced OPG z-scores.

**Conclusion:** Pediatric and adult NC patients show hypophosphatemia, hypocalcemia, hypovitaminosis D, and increased osteoblast activity indicating persisting rickets/osteomalacia despite treatment for Fanconi syndrome. Increased osteoclast activity despite counter regulation via OPG/RANKL and suppressed PTH levels suggests a primary osteoclast defect in NC resulting in increased bone resorption, which is more pronounced in children compared to adult patients.

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## A RARE ASSOCIATION OF PROPIONIC ACIDEMIA AND NEPHROLITHIASIS

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**Introduction:** Propionic acidemia (PA) is an autosomal recessive metabolic disorder caused by deficiency of mitochondrial enzyme propionyl-CoA carboxylase (PCC). Impaired kidney function is a well-documented long-term complication in PA but there are only a few case reports regarding the association of kidney stones in PA. In PA, hyperglycinemia causes hyperoxaluria by increasing the excretion of oxalate and glyoxylic acid, which is the pre-product of oxalate, from the urinary tract. In addition, medical therapy for metabolic acidosis and essential amino acids may cause hypercalciuria. Hyperoxaluria, hypercalciuria and acidic urine may explain the formation of kidney stones in patients with PA. In this report, we present a case with PA and nephrolithiasis, and aim to draw attention to rare association of kidney stones and PA.

**Case:** A 10-month-old boy was admitted to our clinic because of vomiting. He was born full term by caesarean section with birthweight of 2500 grams. There is a third-degree consanguinity between the parents. He was the sixth child of a 32 year-old mother. The first baby died at the age of 14 days due to unknown reason. In the past history, at the age of eight days, hyperbilirubinemia, hypotonicity, decreased reflexes and poor sucking developed. His ammonia level was high and he was diagnosed PA with urinary organic acid analysis, plasma amino acids and Tandem mass spectrometry at the age of one month. At the admission, kidney stones were detected in both kidneys on urinary ultrasonography. Laboratory investigations revealed hyperoxaluria and hypercalciuria in 24-hour urine. The patient was treated with hydrochlorothiazide for hypercalciuria. He was followed-up by urinalysis and urinary ultrasonography regularly. At the age of one-year, obstructive stone was detected in the ureteropelvic junction of the right kidney and a double j stent was placed. Laser lithotripsy was performed by flexible ureterorenoscopy. Currently, there are no stones in the urinary ultrasonography. Urinary metabolites of the patient are normal and hydrochlorothiazide was discontinued.

**Conclusion:** Although it is very rare, it should be kept in mind that kidney stones may develop in patients with PA. Metabolic acidosis, hyperoxaluria and hypercalciuria may be risk factors for stone formation. Therefore, we suggest that these patients should be followed-up regularly by ultrasonography for kidney stones.

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