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ABSTRACTS

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ACPN210330O01 ASSOCIATION OF T-CELL HYPORESPONSIVENESS AND METABOLIC QUIESCENCE IN PATIENTS WITH SRNS

Ms. Chang Yien Chan[1,2], Dr Liangjian Lu[2], Dr Yaochun Zhang[1,2], Dr Sharon Teo[2], Dr Perry Yew Weng Lau[1,2], Dr Mya Than[1,2], Dr Kong Peng Lam[1,3,4,5], Dr Haishu Lin[6], Dr Kar Hui Ng Ng[1,2], Dr Hui Kim Yap[1,2]

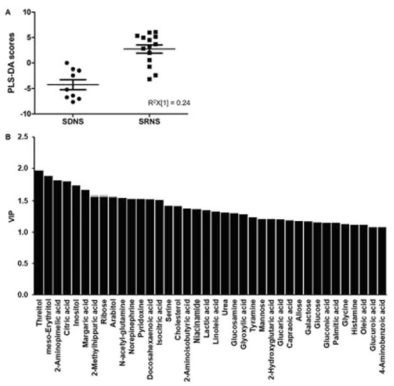
*[1]Department of Paediatrics, Yong Loo Lin School of Medicine, National University of Singapore, , Singapore, [2]Khoo Teck Puat-National University Children's Medical Institute, National University Health System, , Singapore, [3]Bioprocessing Technology Institute, Agency for Science, Technology and Research (A*STAR), , Singapore, [4]Singapore Immunology Network (SIgN), Agency for Science, Technology and Research (A*STAR), , Singapore, [5]Department of Microbiology and Immunology, Yong Loo Lin School of Medicine, National University of Singapore, , Singapore, [6]Department of Pharmacy, National University of Singapore, , Singapore*

Objectives: We have previously demonstrated that a subset of patients with focal segmental glomerulosclerosis display reduced T-cell response to in vitro stimulation, and this is associated with a favourable clinical response to Rituximab. T-cell hyporesponsiveness is increasingly recognized as a key attribute of T-cell exhaustion, which is a distinct T-cell state following sustained stimulation, e.g. autoimmune disease or chronic viral infection. T-cell exhaustion is also characterized by metabolic dysregulation, with a failure to enter an anabolic state through activation of biosynthetic pathways such as the pentose phosphate shunt. In this work, we compared the T-cell response to stimulation between patients with steroid-dependent (SDNS) and steroid-resistant nephrotic syndrome (SRNS) in relapse, and characterise the metabolic alterations associated with T-cell hyporesponsiveness.

Methods: Patients with childhood-onset SDNS (n=31) and SRNS (n=17) were recruited during relapse. T-cells were isolated from peripheral blood, and stimulated with ionomycin (1μg/ml), phorbol 12-myristate 13-acetate (PMA) (20ng/ml) and monensin sodium (6μM) in RPMI 1640 medium (Invitrogen Life Technologies, Carlsbad, CA, USA) for four hours at 37°C. Cells were isolated and intracellular CD69 and IFNγ measured. Metabolomic profiling was performed on culture supernatants (n=23) using GC-MS/MS, and analysed using Shimadzu Smart Metabolites Database (contains analytical conditions for the high-sensitivity detection of 475 metabolites). Differences in the metabolomic profile between SDNS and SRNS were first identified using PLS-DA (SIMCA), and pathway analysis was subsequently performed using MetaboAnalyst 4.0. All other comparisons were performed using Mann-Whitney U tests.

Results: Compared to patients with SDNS, SRNS patients had attenuated T-cell expression of CD69 (88±2.3% vs 91±3.1%, P=0.024) and IFNγ (1.9±0.73% vs 6.6±1.35%, P=0.016) following stimulation. Metabolomic profiling identified 93 metabolites in CD4 culture supernatant. A PLS-DA model yielded one fitted component, which was able to use 24% of the variability in metabolites measured (R2X) to explain 58% of the variation in steroid-response (R2Y) (Figure 1A). This was robust to internal cross-validation with a Q2 of 44%. Strikingly, 79 of 93 (85%) metabolites tended to be lower in SRNS compared to SDNS patients in keeping with metabolic quiescence. Pathway analysis of the 38 metabolites with VIP>1 (Figure 1B) implicated the biosynthetic pathways glyoxylate and dicarboxylate metabolism, ascorbate and aldarate metabolism as well as galactose metabolism (Benjamini-Hochberg P<0.05). Interestingly, the 2 metabolites with the highest VIP scores were the related molecules Threitol and Erythritol. These were reduced in SRNS compared to SDNS patients (P<0.001) and have recently been implicated as downstream products in the pentose phosphate pathway.

Conclusion: Compared to SDNS patients, SRNS patients have T-cells which were hyporesponsive to in vitro stimulation. This was associated with metabolic quiescence even following stimulation, with a failure to upregulate biosynthetic pathways including the pentose phosphate shunt. Taken together, this demonstrated that T-cell exhaustion is a key immunological correlate of steroid-resistant disease.



ACPN210330O02 CLINICAL PROFILE AND PREDICTIVE RISK FACTORS FOR CATARACT AND RAISED INTRAOCULAR PRESSURE IN CHILDREN WITH NEPHROTIC SYNDROME RECEIVING LONG TERM ORAL STEROIDS: AN OBSERVATIONAL STUDY

Mr. Hariharan Raja[1], Mr. Sriram Krishnamurthy[1], Mrs. Subashini Kaliaperumal[1], Mr. Pediredla Karunakar[1], Mrs. Bobbity Deepthi[1]

[1]*Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Pondicherry-605006, India., Pondicherry-605006, India, India*

Introduction: There is a paucity of data on ophthalmological complications in children with nephrotic syndrome on long-term oral steroids from India. Only one study from India described the effect of dose, duration of steroids and age of the patient on ocular complications in patients with nephrotic syndrome receiving long term steroids.

Objectives: The primary objective of the study was to evaluate the prevalence of ophthalmological complications (including cataract and glaucoma) among children with idiopathic nephrotic syndrome receiving oral steroids continuously for more than 6 months, while the secondary objective was to study the predictive risk factors for development of these ophthalmological complications.

Material and methods: This study was an observational study which included patients of age group 4 to 18 years with idiopathic nephrotic syndrome who received oral steroids continuously for more than 6 months and presented to the pediatric nephrology clinic. The enrolled subjects were evaluated using a standard protocol based on clinical features, ophthalmological and laboratory investigations. Data were collected in a predesigned proforma, and included age at onset of nephrotic syndrome, cumulative dose and duration of steroids and presence of ophthalmological complications including cataract and raised intraocular pressure (IOP) at presentation and follow-up.

Results: We evaluated 110 children with idiopathic nephrotic syndrome [frequently relapsing nephrotic syndrome [62 (56.4%)], steroid dependent nephrotic syndrome [23 (20.9%)] and steroid resistant nephrotic syndrome [25 (22.7%)]]. The age of the enrolled children [median [IQR]] was 9.17 [7, 12.67] years, while the duration of follow-up since the onset of nephrotic syndrome was 5 [3, 7] years. The prevalence of cataract was found to be 18.1 % (20 out of 110 cases). Nineteen (95%) of these children with cataract had posterior subcapsular cataract while one child had hypermature (5%) cataract. Among the children with cataract, visual acuity was less than 6/36 in 4 out of 20 (20%) children. Three children underwent cataract excision followed by intraocular lens implantation. The median (IQR) ages (years) at the onset of nephrotic syndrome among children with cataract [2.5 (2, 4) years] and those without cataract [4 (2.1, 6) years] were significantly different (p= 0.03). The median (IQR) cumulative dose of prednisolone intake (mg/m2) among children with cataract [28669 (21329.5, 33500)] was significantly higher as compared to the corresponding value among the children without cataract [14995.5 (10492, 19687)] (p<0.01). The median (IQR) cumulative duration (years) of prednisolone intake among children with cataract [4.3 (3.08, 5.16)] was also significantly higher in comparison to children without cataract [2.25 (1.33, 3.67)] (p <0.01). The profile of alternate immunosuppressants received among children with cataract (n=20) versus those without cataract (n=90) was not significantly different.

The prevalence of raised IOP was found to be 9.1% (10 out of 110 cases). The cumulative dose of prednisolone intake (mg/m2) [22359.5 (11574, 36240.6) versus 16898.5 (12154.5, 22484.1)] as well as the cumulative duration of steroid intake (years) [3.55 (1.48, 4.27) versus 2.14 (1.38, 3.63)] among children with and without raised IOP/glaucoma were not found to be significantly different. One enrolled subject developed hypertensive retinopathy.

Conclusions: The prevalence of cataract as well as raised IOP/glaucoma was high in our study population. The predictive risk factors for the development of cataract in children with nephrotic syndrome receiving long term oral prednisolone were the age of onset of nephrotic syndrome, cumulative dose and cumulative duration of steroid intake in the enrolled subjects. Based on the results of our study, we recommend a 6-monthly ophthalmological screening for detection of cataract and raised intraocular pressure in children receiving prolonged steroids for more than 6 months. Genetic factors contributing to development of cataract and glaucoma in children receiving prolonged steroids need further evaluation.

ACPN210330O03 ACUTE KIDNEY INJURY IN HOSPITALISED CHILDREN WITH SARS-COV-2 INFECTION: AN OBSERVATION FROM A RESOURCE LIMITED SETTING

Ms. Sanya Chopra[1], Dr. Abhijeet Saha[1], Dr. Virendra Kumar[1], Dr. Archana Thakur[1], Dr. Harish Pemde[1], Dr. Aditi Das[1], Dr. Ravitanya Sodani[1], Dr. Ankita Goel Sharma[1], Dr. Preeti Singh[1], Dr. Anu Gulati[1], Dr. Akanksha Mahajan[1], Dr. Kaveri Pandit[1], Dr. Suchitra Sehgal[1]

[1]*Lady Hardinge Medical College and associated Kalawati Saran Children Hospital, New Delhi, India*

Objective: Acute kidney injury (AKI) has been recognised as a significant risk factor for mortality among adults with SARS-CoV-2 infection. Primary objective of this study was to assess the prevalence of AKI in children with COVID19. The secondary objective was to identify risk factors for AKI and mortality in children in a resource limited setting.

Methods: We retrospectively reviewed the records of children, with laboratory confirmed COVID 19 infection admitted to our hospital from 1st March 2020 to 30th November 2020. AKI was defined by the 2012 Kidney Disease Improving Global Outcomes (KDIGO) criteria using serum creatinine. The baseline serum creatinine was estimated by the height independent method using the Hoste's equation. The stage of AKI was determined based on the change in the serum creatinine from baseline to the highest value noted during the hospital stay. Patients were also evaluated for associated complications including shock, pneumonia, encephalitis, myocarditis and multi system inflammatory syndrome in children (MIS-C). We compared the outcome in the AKI versus the non-AKI group to ascertain risk factors for development of AKI and mortality.

Results: A total of 64810 children were screened during the study period, 3412 with suspected SARS-CoV-2 infection were tested, 295 turned out to be positive and 105 (54 % boys) were hospitalised. The median age of presentation was 6 years with maximum (47.6%) in the 5-13-year age group. Majority of the children (76.2%) had an associated co morbidity with sepsis (44.8%) being most common. A total of 24 children (22.8%) developed AKI; 8 children progressed to stage 1(33.3%), 7 to stage 2 (29.2%) and 9 to AKI stage 3 (37.5%) respectively. Three patients subsequently required hemodialysis. The total leucocyte count (TLC) was significantly higher and the platelet count was lower in children with AKI. The difference in the peak serum creatinine among the AKI and non-AKI group was statistically significant (p value < 0.0001).

Sepsis (OR 3.394, p<0.01) and nephrotic syndrome (OR 12.8, p<0.01) were significant risk factors for development of AKI. Other risk factors included vasopressor support (OR 3.59, 95% CI, 1.37-9.40, p value< 0.007), shock at the time of presentation (OR 2.98, 95% CI, 1.16-7.60, p value 0.01) and the need for mechanical ventilation (OR 2.64, 95% CI, 1.04-6.71, p value< 0.03). Mortality was significantly higher in patients with AKI (OR 2.65, p<0.01). Of the 20 (19.0%) children diagnosed with MIS-C, seven (29.2%) developed AKI.

The overall mortality was 9.15 % (27/295) and 25.71% (27/105) for hospitalised children. Mortality was significantly high in children with AKI as compared to non-AKI patients (OR 3.088, p<0.023). On univariate analysis, hypoxia at admission (OR 3.843, p<0.003), need for respiratory support (OR 33.01, p<0.001) requirement of vasopressors (OR 56, p <0.001), pneumonia (OR 3.684, p<0.004), shock (OR 169, p<0.001),

encephalitis (OR 6.785, p <0.001) and myocarditis (OR 13.4, p<0.001) were significant risk factors for mortality. Binary logistic regression confirmed the presence of shock (OR 45.92; 95% CI, 3.44 -612.0, p value <0.004) and ventilation (OR 46.24; 95% CI, 1.6-1333.0 p value< 0.02) as statistically significant risk factors for mortality.On Kaplan-Meier survival analysis cumulative probability of survival in AKI patients was zero and 39% among non- AKI patients after 25 days of follow up.

Conclusion: The evolving knowledge about coronavirus and its role in development of AKI in the paediatric population highlights the importance of early recognition and intensive monitoring. Timely intervention with careful fluid balance and use of renal replacement therapy may reduce the risk of AKI, and thus mortality in these children.

Table. Risk factors for AKI.

	COVID 19 case n=105	AKI n=24(22.8%)	Non-AKI n=81(77.2%)	p value	Odds Ratio
Reason for Admission* n (%)					
Hypoxia	41(39.0)	8(33.3)	33 (40.7)	0.51	0.727
Pneumonia	35(33.3)	7(29.2)	28(34.6)	0.62	0.779
Shock	36(34.3)	13(52,2)	23(28.4)	**0.01**	**2.980**
Encephalitis	16(15.2)	6(25.0)	10(12.3)	0.13	2.367
Myocarditis	9(8.6)	4(16.7)	5(6.2)	0.10	3.040
Sepsis	47(44.8)	18(75.0)	38(46.9)	**0.01**	**3.394**
Nephrotic syndrome	4(3.8)	3(12.5)	1(1.2)	**0.01**	**12.8**
Exposure to nephrotoxic drugs	70(66.7)	16(66.7)	54(66.7)	1.0	1.0
Respiratory Support n (%)					
None	52(50.0)	9(37.5)	43(53.1)		
Need for Oxygenation	53(51.0)	15(62.5)	38(47.5)	0.19	1.842
Invasive	36(34.3)	13(54.2)	25(30.5)	**0.03**	**2.647**
Vasopressor support	34(33.3)	13(56.5)	21(25.6)	**0.007**	**3.590**
Mortality	27(25.7)	10(41.7)	17(20.9)	**0.01**	**2.650**
MIS-C	20(19.0)	7(29.2)	13(16.0)	0.15	2.154

ACPN210330O04 CLINICAL AND GENETIC LANDSCAPES OF PROTEINURIC KIDNEY DISEASES AMONG SOUTHEAST AND SOUTH ASIANS: THE DRAGON STUDY

Ms. Kar Hui Ng[1,2], Dr David Liangjian Lu[2], Dr Yok Chin Yap[3], Dr Duc Quang Nguyen[4], Dr Yiong Huak Chan[5], Ms Jun Li Ng[1,2], Dr Yao Chun Zhang[1], Dr Chang Yien Chan[1], Dr Mya Than[1,2], Dr Isaac Desheng Liu[2], Dr Sadaf Asim[6], Prof Khemchand N Moorani[6], Dr Bilquis Naeem[6], Prof Iftikhar Ijaz[7], Dr Thi Minh Tan Nguyen[8], Dr Ming Lee Lee[9], Dr Caroline Eng[9], Dr Syed Saimul Huque[10], Dr Yong Hong Ng[11], Dr Indra Ganesan[11], Dr Sing Ming Chao[11], Dr Siew Le Chong[11], Prof Puay Hoon Tan[12], Dr Alwin Loh[12], Dr Sonia Davila[13], Dr Vikrant Kumar[14], Ms Joanna Zhi Jie Ling[15], Dr Rajesh Babu Moorakonda[15], Dr Karen Mei Ling Tan[16], Dr Alvin Yu Jin Ng[16], Mr Kok Siong Poon[16], Prof Franz Schaefer[17], Dr Beata S Lipska-Zietkiewicz[18,19], Prof Hui Kim Yap[1,2]

[1]Department of Paediatrics, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore, [2]Khoo Teck Puat-National University Children's Medical Institute, National University Health System, Singapore, Singapore, [3]Hospital Kuala Lumpur, Kuala Lumpur, Malaysia, [4]Children's Hospital 1, Ho Chi Minh City, Vietnam, [5]Department of Biostatistics, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore, [6]Department of Paediatric Nephrology, National Institute of Child Health, Karachi, Pakistan , [7]King Edward Medical University, Lahore, Pakistan, [8]Children Hospital 2, Ho Chi Minh City, Vietnam , [9]Hospital Tuanku Ja'afar Seremban, Seremban, Malaysia, [10]Department of Paediatric Nephrology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh , [11]KK Women's and Children's Hospital, Singapore , Singapore , [12]Department of Anatomical Pathology, Singapore General Hospital, Singapore , Singapore , [13]Institute of Precision Medicine (PRISM), Duke-NUS and Singapore Health Services, Singapore, Singapore, [14]Cancer and Stem Cell Biology, Duke-NUS Medical School, Singapore , Singapore , [15]Singapore Clinical Research Institute, Singapore , Singapore , [16]Molecular Diagnosis Centre, Department of Laboratory Medicine, National University Hospital, Singapore, Singapore, [17]Division of Paediatrics Nephrology and KFH Children's Kidney Center, Center for Paediatrics and Adolescent Medicine, Heidelberg, Germany , [18]Clinical Genetics Unit, Medical University Of Gdansk, Gdansk, Poland, [19]Clinical Genetics Unit, Department of Biology and Medical Genetics, Medical University of Gdansk, Gdansk, Poland

Objectives: Monogenic etiologies have been reported in 25-30% of children with steroid-resistant nephrotic syndrome, which is an important cause of kidney failure. As multi-national studies are lacking in Asia, we established DRAGoN (Deciphering Diversities: Renal Asian Genetics Network) in 2015 to address this problem. We hypothesized that the genetic spectrum for Asian patients with glomerulopathies differs from other populations. This study aimed to describe the genetic and clinical spectrums of probands with suspected genetic glomerulopathies from South and Southeast Asia, and to identify predictors for a genetic diagnosis. To our knowledge, this is the first multi-national study based in Asia.

Methods: We recruited a prospective cohort of probands with nephrotic syndrome (NS) or persistent proteinuria presenting before 20 years old, with at least 1 feature that suggested genetic etiology: disease onset before 3 years, positive family history, parental consanguinity, extrarenal malformations, steroid resistance (initial or late-onset) and chronic kidney disease. The latter two were applicable only to those presenting with NS. Data on clinical features at first manifestation, family history, kidney histology, medications and responses, kidney function, extrarenal malformations and renal replacement therapy were collected and updated prospectively every 6 months. Targeted gene sequencing using SeqCap EZ Choice (NimbleGen Roche, Roche Sequencing and Life Science, USA) involving 144 genes were performed, of which 50 renal-related genes were analysed. The pathogenicity of the variants was evaluated based on the American College of Medical Genetics and Genomics (ACMG) guidelines. Demographic variables and variables at disease onset were used in the logistic regression to identify predictors for a genetic diagnosis. Receiver Operating Curve (ROC) analyses were performed to develop a scoring model to discriminate the Variant group. Statistical significance set at 2-sided p<0.05.

Results: We recruited 183 probands from 9 countries in Southeast (76.5%) and South Asia (21.9%). The largest ethnic groups were Chinese (32.4%), Vietnamese (23.5%), Pakistani (16.5%) and Malays (13.5%). Genetic diagnosis was established in 26 (14.2%) probands who were referred to as the Variant group. Thirty-three causative variants in 8 genes (5 autosomal recessive, 2 autosomal dominant, 1 X-linked) were classified as (likely) pathogenic. Twelve of these are novel. Genetic diagnoses involved COL4A5 (n=8, 4.4%), NPHS1 (n=5, 2.7%), NPHS2 (n=4, 2.2%), WT1 (n=4, 2.2%), COQ8B (n=2, 1.1%), TRPC6 (n=1, 0.5%), CUBN (n=1, 0.5%) and COL4A4 (n=1, 0.5%) genes. NPHS1 variants were commonest in patients presenting before 1 year while collagen IV (COL4A4 and COL4A5) variants, which accounted for one third of all pathogenic variants, were commonest in those presenting beyond infancy. Only 2 (22.2%) patients with collagen IV gene defects had sensorineural hearing loss and/or biopsy findings suggestive of Alport syndrome. Older age [6.2 (interquartile range (IQR) 10.7) vs 2.4 (IQR 3.2) years], hematuria (OR 4.1; 95% CI: 1.5-11.2)

and proteinuria in the absence of NS (OR 0.2; 95% CI: 0.1-0.6) at first manifestation were novel predictors of a genetic diagnosis, in addition to positive family history and extrarenal malformations. These predictors enabled us to develop a clinical score which is able to predict a genetic diagnosis in Asian children with a high negative predictive value of 97%.

Conclusions: We have identified genetic cause in 14.2% of Asian patients with suspected genetic glomerulopathies. Collagen IV genes were the commonest, suggesting these should be included in gene panels for Asians even in the absence of suggestive features. Unlike other cohorts, patients who presented at older age groups are more likely to have a genetic diagnosis. Other novel predictors included hematuria and proteinuria in the absence of NS. We developed a clinical score which may be useful in screening out genetic diseases in resource-poor settings, pending further validation.

ACPN210330O05 AMOT MUTATION CAUSES NEPHROPATHY BY REGULATING HNF4A PATHWAY

Mr. Yaochun Zhang[1,2], Miss Jannah Binti Ahmad Nurul[1,2], Dr. Haishu Lin[3], Dr. Zhenhua Hu[4], Dr. Hunziker Walter[4], Dr. Chan Chan[1,2], Mr. Liangjian Lu[1,2], Professor Hui Kim Yap[1,2], Associate Professor Kar Hui Ng[1,2]

*[1]Department of Paediatrics, Yong Loo Lin School of Medicine, National University of Singapore, , Singapore, [2]Khoo Teck Puat-National University Children's Medical Institute, National University Health System, , Singapore, [3]Department of Pharmacy, Faculty of Science, National University of Singapore, , Singapore, [4]Institute of Molecular and Cell Biology, Agency for Science, Technology and Research (A*STAR), Singapore*

Objectives: In a family with X-linked recessive glomerular and renal cystic diseases, we identified, using whole exome sequencing, a possibly pathogenic p.S50G variant in AMOT which encodes for angiomotin. AMOT plays an important role in tube formation and cell proliferation. Knockdown of Amot in zebrafish severely impaired the migration of intersegmental vessels and knockout of Amot in mice induced embryonic lethality. This study aimed to elucidate the function of this mutation.

Methods: Using CRISPR/Cas9 system, we created a rat line with a missense mutation corresponding to the patients. The phenotypes of Amot mutated (MUT) rats, including renal pathology, were compared with wild type control (WT). The cytoskeleton and function of the tight junctions were studied in ex vivo proximal convoluted tubular (PCT) cells and podocytes. Transcriptome regulation was analysed with RNA-sequencing and chromatin accessibility profiled with Assay for Transposase-Accessible Chromatin using sequencing (ATAC-seq). The rat plasma metabolomics were analysed using a targeted GC-MS/MS metabolites analysis platform. Statistical analysis was performed using Mann-Whitney U test.

Results: MUT rats developed significantly higher body weights compared to WT rats at age of 6 months (581 ± 37 vs 510 ± 41 g, P = 0.0278). MUT rats had increased albuminuria from 2 months old. They displayed severe glomerular abnormalities including podocyte hypertrophy, mesangial hypercellularity and focal segmental glomerulosclerosis (FSGS), as well as tubulointerstitial damage consisting of tubular dilatation, inflammatory infiltrates and fibrosis. Some MUT rats had macroscopic renal cysts from 3 weeks old. Podocytes in MUT rats showed extensive foot process effacement and detachment from the glomerular basement membrane.

In ex vivo podocytes, Amot mutation increased and disrupted F-actin expression, and increased the stress fibres formation even though cell stiffness was reduced. Tight junctions were disturbed as demonstrated by the perturbation in ZO-1 expression/distribution in ex vivo podocytes and PCT, as well as increased FITC-albumin flux across the PCT formed monolayer in Amot mutated cells. RNA-seq on ex vivo PCT revealed 231 upregulated and 202 repressed genes in MUT rats. In total, 118 signalling pathways, mostly metabolism pathways, were enriched on KEGG (Kyoto Encyclopedia of Genes and Genomes) pathway analysis. Hepatocyte nuclear factors (HNFs), including Hnf1, Hnf1b and Hnf4a, were enriched in the promoters of Amot mutation activated genes, suggesting the Amot mutation induced HNFs activation. In ATAC-seq, Hnf4a registered the first position in both known and de novo motifs. Additionally, Hnf1b, was also among the top 10 enriched motifs. These suggest the Amot mutation induced an increase in chromatin accessibility for HNF4a and Hnf1b transcription factors.

In metabolomics study, pentose and glucuronate interconversions and citrate cycle, which were among the RNA-seq enriched metabolic pathways, were enriched.

Conclusions: In conclusion, we reported a novel mutation on AMOT gene. The mutation caused a nephropathy involving glomeruli and tubules in patients and transgenic rats, possibly by regulating Hnf4a and Hnf1b and the subsequent pentose/glucuronate interconversions and citrate cycle metabolic pathway.

ACPN210330O06 RENAL MANIFESTATIONS AND OUTCOMES OF FILIPINO CHILDREN WITH COVID-19

Ms. Katrina Anne Cordova[1], Ms. Melissa Dator[1], Ms. An-an Pablita Emata[1], Mr. Francisco Anacleto, Jr[1], Ms. Dolores Bonzon[1], Mr. Eric Emmanuel Aragon[1], Ms. Lourdes Paula Resontoc[1]

[1]Philippine General Hospital, Manila, Philippines

Renal dysfunction is one of the complications of COVID-19 (coronavirus disease 2019) in children. The infection can lead to acute kidney injury (AKI), glomerulonephritis, or tubulopathies. There is currently no local data available on the renal manifestations of COVID-19 in the pediatric population. Therefore, this study aimed to describe the renal manifestations of COVID-19 in Filipino children and their outcomes.

A retrospective cohort study was conducted and included patients less than 19 years old less with COVID-19 diagnosed by reverse transcriptase polymerase chain reaction (RT-PCR) seen from March 1 to October 30, 2020. Descriptive statistics were used for the general data and were summarized in table.

A total of 37 COVID-19 positive pediatric patients were admitted at the Philippine General Hospital COVID-19 Ward. Ten patients exhibited kidney involvement. Among those with kidney involvement, 50% (n=5) had AKI, 30% (n=3) had tubular involvement, 40% (n=4) had proteinuria, and 70% (n=7) had hematuria. One patient had COVID-19-associated rhabdomyolysis-induced AKI. Eighty two percent (n=23) of the COVID-19 positive patients recovered. One non-dialysis chronic kidney disease (CKD) patient underwent kidney replacement therapy.

Children with comorbid conditions are at risk for COVID-19. COVID-19 can involve the kidneys through AKI, glomerulopathies, and tubulopathies. This is the first case series on Filipino children with COVID-19 with renal involvement including COVID-19-induced rhabdomyolysis with acute kidney failure. This is the first study investigating renal tubule involvement in children with COVID-19. Children with renal involvement have a good outcome. We recommend that children with COVID-19 should have baseline urinalysis and baseline kidney function tests.

ACPN210330O07 ANALYSIS OF CRITICALLY ILL PATIENTS RECEIVED INTERMITTENT HEMODIALYSIS IN PEDIATRIC INTENSIVE CARE UNIT: A 20-YEAR SINGLE CENTER STUDY

Ms. Hui Lan Chen[1,2,3], Dr. Yi-Hsuan Tang[1,3,4], Assistant Professor Chien-Hung Lin[1,4], Associate Professor Hsin-Hui Wang*[1,3,4]

[1]Department of Pediatrics, Division of Pediatric Immunology and Nephrology, Taipei Veterans General Hospital , Taipei , Taiwan, [2]Department of Pediatrics, Keelung Hospital, Ministry of Health and Welfare, Keelung,Taiwan, Keelung, Taiwan, [3]Institute of Emergency and Critical Care Medicine, School of Medicine,National Yang Ming Chiao Tung University, Taipei , Taiwan, [4]Department of Pediatrics, Faculty of Medicine, School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan

Abstract: Objectives:Acute kidney injury (AKI) may increase the risk of chronic kidney disease (CKD). Renal replacement therapy (RRT) has become an important supportive treatment for critically ill patients with AKI in intensive care unit (ICU). Intermittent hemodialysis (IHD) is one of the modalities for RRT treatment of critically ill patients with AKI. IHD is readily available, uncomplicated and highly effective in achieving solute removal by solute clearance and rapidly removes volume load by ultrafiltration. IHD is efficient modality to remove small dialyzable molecules (including blood urea nitrogen (BUN), creatinine (Cr), phosphorus, electrolytes, certain drugs and toxins) and it can be used in hemodynamic relatively stable patients in ICU. Our objective is to analyze the adequacy and outcome of IHD in critically ill patients to compare in two groups 2000 to 2009 and 2010 to 2020.

Methods: A retrospective study of the medical records of the patients who underwent IHD in the pediatric intensive care unit (PICU) between January 2000 to December 2020 was performed. Patients' demographic and clinical characteristics cause of AKI, length of ICU stays, indications of IHD were analyzed and compared in two groups (2000-2009 and 2010 -2020). Primary outcome was mortality.

Results: Total 107 patients who underwent IHD in the PICU during our study period. Studies were stratified into gender, age groups 0-1, 2-5, 6-10, 11-15,16-20, 21-30, and 30 years above based on mean age reported in the study. Mean age were 18.79 ±7.182 and 5.0 ± 2.55 in 2000-2009 and 2010-2020 group respectively. Two groups of mean BUN/Cr were 95.96 ± 51.64 / 8.52± 5.43 and 61.41 ± 47.02 / 5.78± 5.29, respectively. Overall mortality rate in 2010-2020 group and 2000-2009 group were 14.7% and 9.6%, respectively. Hospital length of stays and mortality rates were not different between the two groups (all $P > 0.05$). Sepsis is one of the most morbidities, 5 of 34 (73.5%) patients in 2010-2020 group compared with 25 of 73(34.2%) patients in 2000-2009 group.

Conclusions: In our study, gender and morbidities were not differ in both groups. Nevertheless, mean of BUN/ Cr, which were recorded before the initiation of IHD and mean age in 2010-2020 group lowered than 2000-2009 group. Creatinine production is related to muscle mass and the increase in levels with age. Younger age of patients (0-1year) which were more in 2010-2020 group (17.6% versus 0%) and it may be influenced the mean of BUN/Cr. These factors may explain why 2010-2020 group has lower levels than 2000-2009 group. In addition, morbidities did not differ in both groups and early initiation of IHD in critically ill patients may be benefit. However, we found that less patients those received IHD in our PICU after 2010. Most of the ICU patients are critically ill and hemodynamically unstable and those received RRT treatment with continuous veno-venous hemofiltration (CVVH) or continuous veno-venous hemodiafiltration, this might be the one possible reasons for less patients received IHD . Sepsis is the most important morbidity in critically patients in ICU with AKI and earlier intervention and more intensive RRT treatment may improve the outcome.

ACPN210330O08 PERSONALIZED SHARED DECISION-MAKING IN THE CHOICE OF DIALYSIS MODALITY IN CHILDREN WITH END-STAGE RENAL DISEASE

Ms. Hsin-Hui Wang[1,2,3], Ms. Meei-Chyi Guo[1,4], Mr. Yi-Hsuan Tang[1,2,3], Mr. Yen-Han Chou[5], Ms. Hui-Lan Chen[1,3,6], Mr. Chien-Hung Lin[1,2]

[1]Department of Pediatrics, Division of Pediatric Immunology and Nephrology, Taipei Veterans General Hospital, Taipei, Taiwan, [2]Department of Pediatrics, Faculty of Medicine, School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, [3]Institute of Emergency and Critical Care Medicine, School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, [4]Department of Nursing, Taipei Veterans General Hospital, Taipei, Taiwan, [5]Faculty of Medicine, Cardenal Herrera CEU University, Valencia, Spain, [6]Department of Pediatrics, Keelung Hospital, Ministry of Health and Welfare, New Taipei City, Taiwan

Background: Shared decision-making (SDM) is gaining increasing prominence in health care. It requires engagement, education, and empowerment of patients. Patients with end-stage renal disease (ESRD) experience a complex decision on dialysis modality performed either in hospital by hemodialysis or at home by peritoneal dialysis. Children are not a reduced version of adults. Taking care of such children should have a multidisciplinary team. SDM in the choice of dialysis modality in children with ESRD is more complex than adult. In addition to involving parents, how to establish a personalized SDM with family- and child-centered choice of dialysis modality is still not been performed.

Methods: Personalized SDM was designed for ESRD children and parents facing a choice of dialysis modality. The available modalities were hemodialysis and peritoneal dialysis. The aims of SDM is providing information and supporting the decision making process. We help ESRD children and their parents participate by providing high quality information. Many tools have been designed to help achieve this goal, including different video for adult and child, questionnaires for individual placing different importance on the outcomes associated with different options of dialysis, and structured interviews. The intervention will further adjust to patients' age and underlying disease categories with congenital anomalies of the kidney and urinary tract (CAKUT), glomerulonephritis (GN) and genetic disease.

Results: Patient-oriented outcomes and patient-reported experience are central to person-centered care in the decision-making in the choice of dialysis modality. Measuring decision quality by the concordance between knowledge, decision and preference was satisfied in both ESRD children and parents. Following the personalized SDM intervention, ESRD children had become more involved in their treatment.

Conclusion: Children with ESRD due to different causes have the different consideration in choice of dialysis modality. The dialysis options have different levels of impact on children and parents' physical and psychological condition and social life. A SDM intervention for dialysis choice has to be adapted to the needs of individual child and parents. We establish a personalized SDM for child and parents using the value clarification tool, including age and disease oriented video and questionnaire, in the decision aid and were helpful on informed preferences. Personalized SDM in dialysis choice has potential to improve self-management in child with ESRD. High-quality decision can increase the dialysis satisfying and success rate.

ACPN210330O09 EXAMINATION OF RELATIONSHIP BETWEEN MULTICYSTIC DYSPLASTIC KIDNEY AND INTRA-RENAL RENIN-ANGIOTENSIN SYSTEM: A PILOT STUDY OF NEW BIOMARKER

Mr. Shingo Ishimori[1], Mr. Junya Fujimura[2], Ms Tomoko Horinouchi[3], Mr Tomohiko Yamamura[3], Ms Nana Sakakibara[3], Ms China Nagano[3], Mr. Kousuke Nishida[3], Mr. Kazumichi Fujioka[3], Mr Takeshi Ninchoji[3], Mr Kandai Nozu[3], Mr Kazumoto Iijima[3]

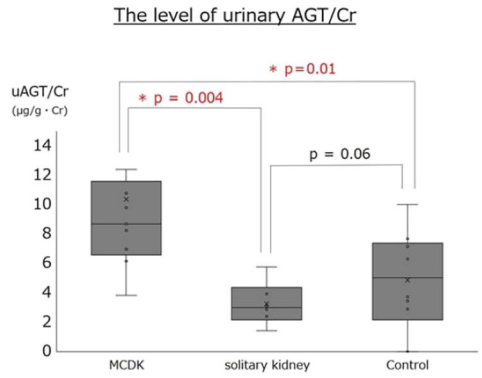
[1]Department of Pediatrics, Takatsuki General Hospital, Takatsuki City, Japan, [2]Department of Pediatrics, Kakogawa Central City Hospital, Kakogawa city, Japan, [3]Department of Pediatrics, Kobe University Graduate School of Medicine, Kobe city, Japan

Objectives: Multicystic dysplastic kidney (MCDK) is a disease of congenital anomaly of kidney and urinary tract. The kidney with multicyst has no renal function, decline spontaneously. Patients with MCDK often complicate hypertension. However, no data are available regarding these morphological and clinical progress. Here, we conducted a study evaluating the relationship between MCDK and renin-angiotensin system (RAS), with a focus on a urinary biomarker of the intra-renal RAS.

Methods: This study enrolled children with unilateral MCDK and solitary kidney who were diagnosed in our institutions between 2010 and 2020, and healthy children as control. We excluded children with decreased renal function, renal scarring related with past history of febrile urinary tract infection, low birth weight and preterm. We measured urinary angiotensinogen (AGT) as intra-renal RAS and serum AGT as systemic RAS, using the human total angiotensinogen kit. Renal function was evaluated with serum creatinine (Cr)- or cystatin C-based estimated glomerular filtration rate (eGFR). Hypertension was defined according to the criteria of international pediatric hypertension association. Renal length was recorded as the longest sonographic length (opposite side of kidney in MCDK group and solitary kidney), and expressed as standard deviation (SD) according to the normal renal length for each age.

Results: Nine children with unilateral MCDK, 6 with solitary kidney and 17 with control were included in this study. There were no significant differences in sex ratio, median age, gestational week and birth weight between MCDK, solitary kidney and control group. Urinary AGT/Cr levels of MCDK group (median: 8.7 μg/ng·Cr) was significantly higher compared with solitary kidney and control group (3.0 μg/ng·Cr, p= 0.023, 5.9 μg/ng·Cr, p= 0.01). Serum AGT level, urinary N-acetyl-β-D-glucosaminidase/Cr level, eGFR, renal length did not differ significantly between MCDK and solitary kidney group. Each renal length of opposite side in MCDK group was normal range (-0.31 to 1.79 SD) and those of solitary kidney also normal range (-0.14 to 1.76 SD). In MCDK group compared with solitary kidney group, the proportion of children with hypertension was not significant high (7/9, 88% vs 2/6, 33 %, p= 0.09), but the level of systolic blood pressure was significantly higher (111 vs 101 mmHg, p= 0.004).

Conclusions: Our results showed that MCDK might associated with intra-renal RAS, neither systemic RAS nor renal enlargement.



ACPN210330O10 INTRAUTERINE LOW-PROTEIN DIET EXACERBATES ABNORMAL DEVELOPMENT OF THE URINARY SYSTEM IN GEN1-MUTANT MICE

Ms. Minghui Yu, Ms. Yi Hui Zhai[1], Yaxin Li[1], Lihong Tan[1], Hong Xu[1], Qian Shen[1]

[1]Children's Hospital Of Fudan University, Shanghai, China

Objective: Gen1 mutation can cause various phenotypes of congenital anomaly of the kidney and urinary tract (CAKUT). An intrauterine low-protein-isocaloric diet can also cause CAKUT phenotypes in offspring. However, single factors such as gene mutation or abnormal environmental factor during pregnancy can only explain part of the pathogenesis of CAKUT.

Methods: There were four groups: normal (22%)-protein diet (ND) + wild-type mice (CON group), ND + Gen1 PB/+ mice (Gen1 PB/+ group), low (6%)-protein diet (LD) + wild-type mice (LD Group), and LD + Gen1 PB/+ group. The experimental design included: observing the proportion of CAKUT phenotypes of neonatal mice; evaluating the number of ureteric buds (UBs), location of UBs, and length of common nephric duct (CND) on embryonic day (E) 11.5; culturing embryonic kidneys from Gen1 PB/+ group in medium containing 10% or serum-free condition to observe branching of UBs; detecting the levels of p-PLCγ, p-Akt, and p-ERK1/2, as well as the apoptosis and proliferation in UBs and CND on E11.5.

Results: 1. We successfully constructed Gen1-mutant mice model fed with an intrauterine low-protein diet (LD + Gen1 PB/+). The neonatal mice in the LD + Gen1 PB/+ group weighed less than the Gen1 PB/+ group (0.9526 ± 0.1174 vs 1.277 ± 0.121 g, P < 0.0001).

2. Comparison of the proportion of CAKUT phenotypes in neonatal mice:

(1) LD + Gen1 PB/+ group had CAKUT significantly more often than the Gen1 PB/+ group (37.74% vs 25.69%, P = 0.0620). The proportion of duplicated collecting systems was also significantly greater (28.30% vs 13.76%, P = 0.0300).

(2) LD + Gen1 PB/+ group had CAKUT significantly more often than LD mice (37.74% vs 18.03%, P = 0.0180). They also had duplicated collecting systems significantly more often (28.30% vs 11.48%, P = 0.0170).

3. The rate of duplicated protrusion on E11.5 was significantly more in the LD + Gen1 PB/+ group than the other groups (39.13% vs 19. 70%, P = 0.0240; 39.13% vs 5.41%, P < 0.0001; 39.13% vs 0.91%, P < 0.0001). In the LD + Gen1 PB/+ group, location of the UB protrusions was lower, and length of CND was longer than in the other groups (293.9 ± 85.29 vs 185.6 ± 81.29 um, P = 0.0004; 293.9 ± 85.29 vs 227.6 ± 52.84 um, P = 0.0046; 293.9 ± 85.29 vs 205 ± 40.14 um, P < 0.0001).

4. After culturing the E11.5 embryonic kidneys of the Gen1 PB/+ group in vitro, the number of UB branches was significantly decreased in the serum-free medium.

5. p-PLCγ expression level in LD + Gen1 PB/group was significantly lower than that in the Gen1 PB/+ and LD groups (UB: P = 0.0385, P <0.0001; CND: P = 0.0482, P = 0.0064). The levels of p-ERK1/2 and p-Akt had no differences. Immunofluorescence was used to detect the apoptosis and proliferation of UB and CND, showing that the apoptosis of UBs in the LD + Gen1 PB/+ group was greater than in the Gen1 PB/+ group (P = 0.0377), CND apoptosis in the LD + Gen1 PB/+ group was greater than in the Gen1 PB/+ and LD groups (P = 0.0037; P = 0.0040), and there were no significant changes in proliferation.

Conclusion: The above findings suggest that an intrauterine low-protein-isocaloric diet can aggravate the occurrence of CAKUT in Gen1-mutant mice, which can mainly affect key steps in the metanephric development, such as the protrusion of UBs, which can mainly mediate UBs and CND apoptosis through p-PLCγ signaling.

ACPN210331O11 INDICATION OF VOIDING CYSTOURETHROGRAPHY FOR CHILDREN WITH FIRST FEBRILE URINARY TRACT INFECTION BASED ON RISK FACTORS FOR THERAPEUTIC INTERVENTION

Mr. Tomohiro Inoguchi[1,2], Mr. Riku Hamada[1], Ms. Yooka Num[1], Ms. Atsuko Anno[1], Mr. Wataru Shimabukuro[1], Mr. Shoichiro Shirane[1], Mr. Kouki Tomari[1], Mr. Keiji Akamine[1], Ms. Chikako Terano[1], Ms. Ryoko Harada[1], Ms. Yuko Hamasaki[1,3], Mr. Kenji Ishikura[4], Mr. Masataka Honda[4]

[1]Department of Nephrology, Tokyo Metropolitan Children's Medical Center, Tokyo, Japan, [2]Department of Pediatrics, Keio University School of Medicine, Tokyo, Japan, [3]Department of Nephrology, Toho University Faculty of Medicine, Tokyo, Japan, [4]Department of Pediatrics, Kitasato University School of Medicine, Kanagawa, Japan

Objectives: Vesicoureteral reflux (VUR) is associated with 30%–50% of pediatric febrile urinary tract infections (f-UTIs). Voiding cystourethrography (VCUG) is a gold standard to detect VUR. However, VCUG causes excessive discomfort, the risk of f-UTI, and radiation exposure for patients. Therefore, new recommendations in the guidelines from the National Institute for Health and Care Excellence (NICE) and the American Academy for Pediatrics (AAP) have been suggested to reduce the number of cases. These guidelines recommended that VCUG was not routinely indicated and should only be performed in cases requiring therapeutic intervention. However, several publications showed that NICE and AAP guidelines had low sensitivity and specificity to diagnose significant abnormalities in children with f-UTI. Moreover, these guidelines were created for children in Western countries, but the medical systems and backgrounds differ from region to region, for example, the customary practice of circumcision. The aim of this study was to determine the cases in which VCUG should be performed in Asian countries.

Methods: The study patients were treated for initial f-UTI at Tokyo Metropolitan Children's Medical Center of Japan from May 2010 to April 2018. VCUG was performed in all f-UTI cases. Febrile UTI was defined as the growth of more than 104 colony-forming units/mL of organism in urine collected by catheterization. The patients who should undergo VCUG were defined as the following patients with VUR grade ≥III patients with f-UTI relapse, and patients who require urological surgery, and the clinical characteristics of these patients were explored.

Results: There were 302 patients with f-UTI and subsequent VCUG. Of the patients, 205 (68%) were boys. The median age at onset of f-UTI was 4 months (IQR 2–8 months), and the follow-up period was 37 months (IQR 21–62 months). The causative organisms on urine culture were Escherichia coli in 259 cases (86%) and non-E. coli in 43 cases (14%). Abnormal findings on renal-bladder ultrasound (hydronephrosis, obstruction, scarring, or signs of high-grade VUR) were observed in 103 cases (34%). VCUG showed VUR in 84 cases (28%). VUR grade ≥III was found in 63 cases (21%), f-UTI relapsed in 37 cases (12%) and required urological surgery in 57 cases (19%). The number of patients requiring intervention (patients who should undergo VCUG) was 94 (31%). In multivariate logistic regression analysis, age 1 year or older (odds ratio 2.8, p = 0.006), non-E. coli infection (odds ratio 3.07, p = 0.003), and abnormal findings on renal-bladder ultrasound (odds ratio 3.04, p = 0.00007) were significant risk factors for therapeutic intervention. The sensitivity of the therapeutic intervention risk factors, which met at least one of previous three risk factors, was 70%, the specificity was 58% If we had performed VCUG for only patients having risk factors, VCUG could have been limited to 154 cases (51%). On the other hand, 28 patients (9.2%) would have been missed.

Conclusions: VCUG is recommended for patients having first-onset f-UTI with one or more of the following three characteristics: age 1 year or older; abnormal findings on renal-bladder ultrasound; and non-E. coli infection.

ACPN210331O12 THE ASSOCIATION OF 25 HYDROXY VITAMIN D AND FIRST EPISODE OF CULTURE POSITIVE URINARY TRACT INFECTION IN CHILDREN BETWEEN 1 TO 5 YEARS OF AGE – A CASE CONTROL STUDY

Ms. Divya Ravindran[1], Mrs. Sathya Chidambaram[1], Mr. Umapathy Pasupathy[1], Mrs. G Sangeetha[1]

[1]Sri Ramachandra Institute Of Higher Education and Research, Chennai, India

Objective: Urinary tract infection is one of the common bacterial infections in infants and young children. The incidence varies with age, with male: female ratio being 3-5:1 during infancy. Beyond 1 year, there is female preponderance with male to female ratio of 1:10. Vitamin D has antibacterial and immunomodulatory property besides the role on calcium and phosphorus homeostasis. Vitamin D plays a cardinal role in immune regulation by induction of human gene for cathelicidin cAMP. Considering the importance of identifying the risk factors associated with UTI and for prevention of complications, we did a study to determine the association of serum vitamin D levels and urinary tract infection in children. The main objective of the study is to determine whether vitamin D deficiency is one of the risk factors for first episode of urinary tract infection in children.

Methods: 60 children with first episode of culture positive UTI were taken as cases, 63 age and sex matched healthy children admitted for elective surgery without any obvious signs of rickets or genitourinary abnormalities were taken as controls (n -master software with power 80% and alpha error 5%). IEC approval and parent's consent obtained for cases and controls.25 hydroxy vitamin D levels in cases and controls were assessed by unicel dxl chemiluminescent immunoassay system. Vitamin D levels less than 12 ng/mL was considered deficient, levels between 12-20 ng/mL as insufficient and >20 ng/mL as sufficient (IAP Guidelines). Statistical analysis done with Chi square test and Pearson's correlation test.

Results: On analysing Vitamin D levels between the cases and controls, mean value of Vitamin D was 21.6+8.89 in cases and 31.31+10.77 in controls with a p value of 0.01 being statistically significant. In the study group, 6 were vitamin D deficient (10%), 27 insufficient (45%) and 27 had sufficient levels (45%). In the control group,10 had insufficiency (15.9%),53 had sufficient levels (84.1%). Out of 60 cases, 39 were in the age group 1-3years (65%) and 21 were between 4-5years (35%). Among 1-3 years, 23 cases were boys (38.3%). E. coli was the most common organism isolated among the culture positive cases accounting to 57 cases (95%). One of each proteus, Acinetobacter and Morganella were isolated. The most common symptomatology was fever (91.1%) seen in 55 cases whereas 27 had crying micturition (45%), 19 had vomiting (31.6%) and 17 had increased frequency of micturition (28.3%). Among the cases ,14 showed pyuria (23.3%) and 7 showed nitrate positivity (11.6%) in urine analysis. Leucocytosis was seen in 50% cases(n=30). In 58.4% cases with abnormal ultrasonography, the most common finding was cystitis. Pearson's correlation showed there was a negative correlation between serum vitamin D levels with WBC counts (-0.07) and polymorphs (-0.15).

Conclusion: Vitamin D levels were significantly lower in cases compared to controls. Since Vitamin D deficiency influences bladder wall immunity, it is postulated that Vitamin D deficiency could be a risk factor for UTI. Vitamin D supplementation could be a simple intervention of immune defence against UTI.

Table 1 COMPARISON OF VARIABLES IN CASES AND CONTROLS

	Case	Control	P value
Age (years)	2.3±1.3	2.5±1.2	0.23 T test
Sex(1/2)	30/30	37/26	0.42 Chisquare test
Serum 25 Hydroxy D level (ng/ml)	21.6±8.89	31.31±10.77	0.01 T test

Table 2 COMPARISON OF SERUM 25 HYDROXY D LEVELS IN CASES AND CONTROLS

Serum 25 Hydroxy D ng/ml	Case n (%)	Control n (%)	P value
< 12	6(10)	0	0.01 Fischer exact test
12-20	27(45)	10 (15.9)	
> 20	27(45)	53(84.1)	

ACPN210331O13 SECULAR TRENDS IN THE INCIDENCE AND PREVALENCE OF DIALYSIS THERAPY AMONG CHILDREN AND YOUNG ADULTS IN JAPAN COMPARED WITH THE USA, EUROPE AND OCEANIA

Mr. Yusuke Okuda[1], Ryoko Harada[2], Riku Hamada[2], Yuko Hamasaki[3], Kenji Ishikura[1]

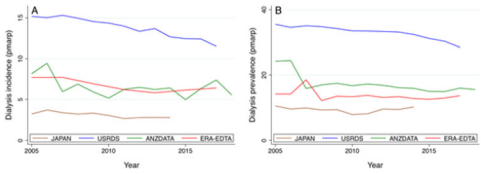
[1]Department of Pediatrics, Kitasato University School Of Medicine, Sagamihara, JAPAN, [2]Department of Nephrology, Tokyo Metropolitan Children's Medical Center, Fuchu, JAPAN, [3]Department of Nephrology, Toho University Faculty of Medicine, Ota, JAPAN

Objectives: Secular trends in the incidence and prevalence of dialysis therapy among Japanese children and young adults are unclear epically in comparison with other countries or regions. The aim of this study is to compare the incidence and prevalence rates of dialysis therapy and their secular trends in Japan with those in the US, European and Oceanian countries over a decade.

Methods: We calculated the incidence and prevalence rate among children and young adults <25 years old using populations and numbers of dialysis patients provided by Bureaus of Statistics and databases for kidney failure in Japan, the US, Europe and Oceania (JRDR, USRDS, ERA-EDTA and ANZDATA). We extracted age-stratified data between 2005 and 2018, and summarized secular trends of incidence/prevalence per million age related population (pmarp).

Results: The incidence and prevalence of dialysis therapy in Japan were lower than other three regions, where the incidence/prevalence rates were 3.1/9.3 pmarp in Japan and 6.3-13.8/12.9-33.1 pmarp in other three regions. The lower incidence and prevalence rates were consistent in each age stratum, i.e., <5, 5–<15 and ≥15 years. The dialysis incidence rate has been slowly declining in Japan, which is consistent particularly with the trend in the US (Figure A). On the other hand, the prevalence rate has remained constant in contrast with the decreasing trend in the US. (Figure B).

Conclusions: The incidence and prevalence rates of dialysis therapy in Japanese children and young adults were lower compared with the US, European and Oceanian countries. Secular trends in the incidence and prevalence in Japan were decreasing and stable, respectively. The trends vary across regions, and the variation is potentially due to mortality after transitioning to dialysis, transplant access and several other factors including race/ethnicity, socioeconomic backgrounds and insurance system.



ACPN210331O14 COMPARISON OF ESTIMATED GLOMERULAR FILTRATION RATE BY SERUM CREATININE AND SERUM CYSTATIN-C BASED EQUATIONS IN CHILDREN AND ADOLESCENTS WITH CHRONIC KIDNEY DISEASE

Vagata Ram, Mukta Mantan, Swarnim Swarnim, Sangita Yadav, *Bhawna Mahajan.

Department of Pediatrics, Maulana Azad Medical College and Lok Nayak Hospital, and *Department of Biochemistry, GIPMER, New Delhi, India

Mr. Vagata Ram[1], dr. Mukta Mantan[1], dr. Sangita Yadav[1], dr. Swarnim Swarnim[1], dr. Bhawna mahajan[2]

[1]Department of Pediatrics, Maulana Azad Medical College and Lok Nayak Hospital, New Delhi, India, [2]Department of Biochemistry, GIPMER, New Delhi, India

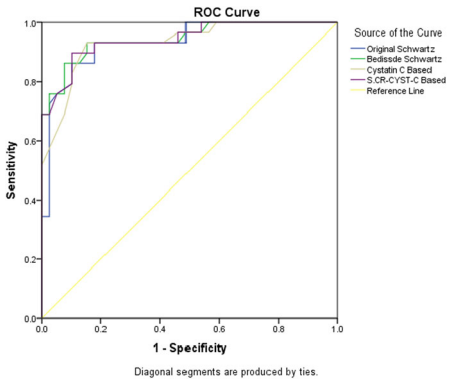
Introduction: GFR is best measured by clearance studies of exogenous markers, like inulin, iohexol, iothalamate, and Cr51-EDTA and plasma 99mTc-DTPA clearance. These procedures are costly and time-consuming hence not used in clinical practice. Clearance of endogenous substances like creatinine requires both serum and an accurately timed urine sample. With changing methods of estimating serum creatinine (modified Jaffe's and enzymatic method) newer equations have been developed for estimating GFR. Serum creatinine-based equations tend to overestimate GFR in children with malnutrition; Cystatin-C based equation correlates better to measured GFR.

Objectives: The primary objective of the study was to estimate GFR by serum creatinine and cystatin-C based equations in children and adolescents (2-19 years) with CKD and its comparison with measured GFR by 24 hours creatinine clearance. The secondary objective was to compare eGFR by serum creatinine and cystatin-C based equations in different stages of CKD with measured GFR.

Methods: This cross-sectional study conducted from March 2019 to March 2020 at a tertiary care teaching institution. Children of ages 2-19 years with all stages of CKD were enrolled. Patients presently with AKI, any bacterial infections, on immunosuppressants or on hemodialysis were excluded from the study. The serum creatinine was estimated by modified Jaffe's method. Serum cystatin-C was measured by PETIA (particle enhanced immunoturbidimetric immunoassay) method. The GFR was estimated using serum creatinine and cystatin-C based equations (Original Schwartz, Bedside Schwartz, CKiD- eGFR- cysC and CKiD- eGFR- Scr- cysC) and their performance of was assessed by the bias, precision, and P30, P10 accuracy against measured GFR by creatinine clearance.

Results: Of the 74 children enrolled in our study, 63 (85.1%) were boys; the median (IQR) age of the study population was 9 (5; 11) years. The median weight SDS was -1.20 and height SDS was -1.06; normal growth was observed in 70.3% while remaining were undernourished. Fifty-nine (79.7%) patients were in the early stages of CKD (1-3) and 15 (20.3%) were in stage 4 and 5 at the time of enrollment. The median value of serum creatinine was 0.70 (0.5; 1.4) mg/dL and of Cystatin C was 1.30 (1; 2.32) mg/L. The median value of measured GFR by 24 hours creatinine clearance was 67 (34.5; 127) ml/min/1.73 m^2. The median estimated GFR by Original Schwartz was 93.50 ml/min/1.73m^2, with bedside Schwartz was 65.50 ml/min/1.73m2, with cystatin-C Based CKiD equation was 52 ml/min/1.73m^2, and Combined Scr-cysC based CKiD equation was 59.50 ml/min/1.73m^2. The maximum precision in advanced stages of CKD was for Bedside Schwartz equation, but in the early stages of CKD, the serum creatinine and cystatin-C based combined equation was more precise than bedside Schwartz equation. The P30 accuracy for original Schwartz equation was 23%, bedside Schwartz equation was 72%, cystatin-C based equation was 64% and for the combined equation was 74.4% while The P10 accuracy values were 14.7%, 26.5%, 13.2%, and 16.2 % respectively. A Bland-Altman analysis showed that the mean bias was less for Bedside Schwartz equation than the combined and cystatin-C based equations.

Conclusions: Modified Schwartz equation is a reasonable equation to estimate GFR in Indian children with CKD; maximum precision in advanced stages of CKD was for modified Schwartz equation while for early stages the serum creatinine and cystatin-C based combined equation was more precise.



ACPN210331O15 COMPARISON OF CLINICOPATHOLOGICAL FINDINGS BETWEEN CHILDHOOD IGA NEPHROPATHY AND IGA VASCULITIS NEPHRITIS USING OXFORD CLASSIFICATION

Mrs. YUKO SHIMA[1], Mr. Koichi Nakanishi[2], Mr. Hironobu Mukaiyama[1], Mr. Yu Tanaka[1], Mr. Takuzo Wada[1], Mr. Kandai Nozu[3], Mr. Ryojiro Tanaka[4], Mr. Kazumoto Iijima[3], Mr. Norishige Yoshikawa[5]

[1]Pediatrics, Wakayama Medical University, Wakayama City, Japan, [2]Pediatrics, Graduate School of Medicine, University of the Ryukyus, Nakagami Gun Nishihara Cho, Japan, [3]Pediatrics, Graduate School of Medicine, Kobe University, Kobe, Japan, [4]Pediatric Nephrology, Hyogo Prefectural Kobe Children's Hospital, Kobe, Japan, [5]Clinical Research Center, Takatsuki General Hospital, Takatsuki, Japan

Background: IgA nephropathy (IgAN) and IgA vasculitis nephritis (IgAVN) are nephritis with a common pathological feature of significant mesangial IgA deposition, but it remains controversial whether they are the same disease.

Methods: We compared clinical and pathological findings between 148 patients with IgAN and 100 patients with IgAVN who underwent renal biopsy from April 2000 to April 2019 to clarify the differences.

Results: Clinical findings showed significant differences in onset age (IgAVN vs IgAN, 7.4 vs 10.7 years, p<0.0001), episode of gross hematuria (8.0 vs 24.3%, p=0.0007), duration from onset to renal biopsy (1.7 vs 6.6 months, p<0.0001), and amount of proteinuria (1.8 vs 0.5 g/gCr, p<0.0001). Pathological findings by Oxford classification showed significant differences in the frequency of M1 (94.0 vs 59.2%, p<0.0001), S1 (21.0 vs 42.2%, p=0.0004), T present (28.0 vs 46.1%, p=0.004), C present (72.0 vs 58.1%, p=0.03) and G present (8.0 vs 19.1%, p=0.01), but no difference in that of E1 (52.8 vs 55.0%, p=0.75). Fluorescence findings showed significant difference in the frequency of fibrinogen deposition (93.3 vs 74.6%, p=0.0004) but not in that of glomerular peripheral capillary IgA deposition (9.5 vs 3.5%, p=0.10). Electron microscopic findings showed significant difference in the frequency of GBM lysis (35.2 vs 12.0%, p=0.0001). Degree of proteinuria is positively correlated with the frequency of M1 in IgAVN.

Conclusion: IgAVN has a higher frequency of M1 lesion regardless of the degree of proteinuria, lower frequency of chronic lesions such as S, T, and G, and higher frequency of acute lesions such as M and C compared with IgAN. Although IgAVN had some pathological similarities to that of IgAN, there seems to be differences that cannot be explained by the timing of renal biopsy.

ACPN210331O16 RISK FACTORS AND MULTIPLE EFFECTS ON EGFR DETERIORATION AND THE TIME PROGRESSION PATTERNS IN PEDIATRIC CHRONIC KIDNEY DISEASE: A REPORT FROM THE TAIWAN PEDIATRIC RENAL COLLABORATIVE STUDY

Mr. Yi Hsuan Tang[1,2,3], Ms. Yu-Min Huang Huang[4], Ms. Hsin-Hui Wang*[1,2,3], Mr. Yuan-Yow Chiou[5], Mr. Yee-Hsuan Chiou[6], Mr. You-Lin Tain[7], Mr. Hsin-Hsu Chou[8], Ms. I-Fan Wang[9], Mr. Ching-Yuang Lin[10]

[1]Department of Pediatrics, Division of Pediatric Immunology and Nephrology, Taipei Veterans General Hospital, Taipei, Taiwan, [2]Department of Pediatrics, Faculty of Medicine, School of Medicine, National Yang Ming Chiao Tung University, Taipei , Taiwan, [3]Institute of Emergency and Critical Care Medicine, School of Medicine, National Yang Ming Chiao Tung University, Taipei , Taiwan, [4] Department of Statistics, Tunghai University, Taichung, Taiwan, [5]Division of Pediatric Nephrology, National Cheng Kung University Hospital, Tainan, Taiwan, [6]Department of Pediatrics, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan, [7]Division of Pediatric Nephrology, Kaohsiung Chang Gung Memorial Hospital and University, Kaohsiung, Taiwan, [8]Division of Pediatric Nephrology, Department of Pediatrics, Ditmanson Medical Foundation ChiaYi Christian Hospital, Chiayi, Taiwan, [9]Division of Pediatric Nephrology, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan, [10]Clinical Immunological Center, Medical College and Hospital, China Medical University, Taichung, Taiwan

Objectives: Chronic kidney disease (CKD) in children is a significant public health problem and may progress to end stage renal disease. Delay renal progression and maintaining renal function is the treatment goal in these children. Identifying the risk factors and together related multiple effects of renal function deterioration is then important. Further, recent years have growing interests in better understanding the time progression and how these patterns may be driven by different groups owning different disease

backgrounds or risk factors. This study investigated the potential marginal effects and joint effects of risk factors on renal function deterioration in children with CKD, and further aimed to evaluate the significant causal differences of the deterioration due to the risk factors. Along the disease stages, time progression function is analyzed and patterns of progression are clustered with respect to related risk factors.

Methods: Using data on the Taiwan Pediatric Renal Collaborative Study that followed Taiwanese children with CKD across multiple clinical centers, we first analyze the eGFR annual change and the longitudinal changes on the patients who had records on their first follow ups within a threshold of time since their entries. Regression analysis was used to identify the key features of diagnosis variables, comorbidities and family history regarding to the eGFR change from the baseline values. Second, using each follow ups data on eGFR, the functional time progression is built for each patient, and with principle components analysis, the patterns are clustered then the risk factors characterizing the groups are summarized.

Results: From the regression analysis and investigation of the multiple effects, among the non-GN CKD group, male patients and initial presentations with proteinuria, high blood pressure, proteinuria, past UTI history and family history with ischemic heart disease tend to have higher annual deterioration of eGFR from the time of diagnosis to the first follow-up taken within 3 years. Family history of hypertension associated with more rapid eGFR deterioration on the later follow-up. For the GN CKD group, initial presentations with edema and past history with UTI or blood transfusion may tend to have higher annual deterioration of eGFR from the time of diagnosis to the first follow-up. With functional time progression and principle component analysis, it is found that these aforementioned risk factors are associated with the patterns of the time progression under the development of the disease stages.

Conclusions: The risk factors and multiple effects on eGFR deterioration in children with CKD were identified in this study. We demonstrate the different time progression function in non-GN and GN group. We found that the risk factors associated with eGFR deterioration are different in the two groups. These observations can provide factors to predict renal function deterioration. Treatments focus on decreasing risk can be provided to delay renal progression, maintaining renal function and improving long term renal outcome.

ACPN210331O17 RISK FACTORS FOR ACUTE KIDNEY INJURY IN CRITICALLY ILL NEONATES-A SYSTEMATIC REVIEW AND META-ANALYSIS

Ms. Qian Hu, Mrs. Hua Ying Xiong[1], Mr. Shao Jun Li[2], Ms. Qian Ling Chen[3], Mr. Han Chen[1], Mrs. Qiu Li[1], Mrs. Mo Wang[1]

[1]Department of Nephrology; Ministry of Education Key Laboratory of Child Development and Disorders; National Clinical Research Center for Child Health and Disorders; China International Science and Technology Cooperation base of Child development and Critical Disorders; Children's Hospital of Chongqing Medical University, Chongqing, China, [2]Department of Emergency Department; Children's Hospital of Chongqing Medical University, Chongqing, China, [3]Department of Nephrology and Rheumatism; Hainan Women and Children's Medical Center, , Hainan, China

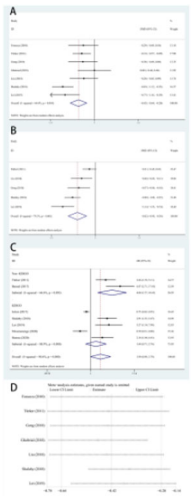
Abstract

Objective: To identify the risk factors for AKI in critically ill neonates to provide an important basis for follow-up research and early detection.

Methods: The PubMed, Embase, Web of Science, Cochrane Library, China National Knowledge Infrastructure, WanFang Med, SinoMed, and VIP Data were searched for studies of risk factors in critically ill neonates. Studies published from the initiation of the database to November 19th, 2020 were included. The quality of case-control and cohort studies was assessed by the Newcastle-Ottawa Scale. Heterogeneity was tested using the I2 test, with I2> 50% or P-value < 0.1 was considered significant. If there was significant heterogeneity, a random-effects model was used, or else a fixed-effects model. Sensitivity analyses were conducted by removing each individual study from the overall analysis. Heterogeneity was assessed by subgroup analyses based on the definition of AKI (KDIGO or non-KDIGO) and subgroup analyses based on the research method (case-control or cohort). Publication bias was estimated via Egger's test. The meta-analysis was conducted with STATA 15 and drafted according to the PRISMA guidelines.

Results: 12 studies (8 case-control and 4 cohort studies) were included in meta-analysis, with 1433 cases in the case group and 4753 cases in the control group. The incidence of AKI fluctuated from 8.4% to 63.3%. 14 risk factors were included, 10 of which were significantly associated with an increased risk of AKI in critically ill neonates: gestational age (SMD=-0.42, 95%CI=(-0.64, -0.20), P=0.000), birth weight (SMD=-0.62, 95%CI=(-0.95,-0.30), P=0.000), 1-minute Apgar score (SMD=-0.62, 95%CI=(-0.81,-0.42), P=0.000), 5-minute Apgar score (SMD=0.72, 95%CI=(-1.06, -0.38), P=0.000), congenital heart disease (OR=3.07, 95%CI=(2.15,4.38), P=0.000), hyperbilirubinemia (OR=2.26, 95%CI=(1.40,3.65), P=0.001), neonatal necrotizing enterocolitis (OR=6.07, 95%CI=2.72,13.54), P=0.000), umbilical artery intubation (OR=5.19, 95%CI=(3.25,8.31), P=0.000) , umbilical vein intubation (OR=3.71, 95%CI=(2.83,4.86), P=0.000), mechanical ventilation (OR=2.57, 95%CI=(1.57,4.19), P=0.000). Five of them have nothing to do with AKI in critically ill neonates: males (OR=1.17, 95%CI=(0.92,1.48), P=0.200), cesarean section (OR=1.52, 95%CI(0.77,3.01), P=0.234), prenatal hemorrhage (OR=1.41, 95%CI=(0.86,2.33), P=0.171), sepsis (OR=1.90, 95%CI=(0.98,3.70), P=0.058).

Conclusion: This meta-analysis provides a preliminary exploration of risk factors in critically ill neonatal AKI, which may be useful for the prediction of AKI.



ACPN210331O18 INCIDENCE AND RISK FACTORS FOR AMINOGLYCOSIDE-RELATED NEPHROTOXICITY IN HOSPITALIZED CHILDREN: A PROSPECTIVE OBSERVATIONAL STUDY

Ms. Madhileti Sravani[1], Mr. Sriram Krishnamurthy[1], Mr. Narayanan Parameswaran[1], Mrs. Medha Rajappa[1], Mr. Pediredla Karunakar[1]

[1]*Jawaharlal Institute Of Postgraduate Medical Education And Research (jipmer), Pondicherry-605006, India, Pondicherry-605006, India, India*

Introduction: There is a paucity of information regarding the incidence of aminoglycoside nephrotoxicity and underlying risk factors directly contributing to this entity, especially in children. Moreover, such information is mostly retrospective.

Objectives: The primary objective of this study was to determine the incidence of aminoglycoside-related nephrotoxicity. The secondary objectives were to determine the predictive risk factors for the aminoglycoside-induced nephrotoxicity and to determine the incidence of renal tubular nephrotoxicity in inpatient children.

Material and methods: In this prospective observational study, 110 study participants aged 1 month to 12 years, receiving aminoglycosides for at least 4 days were observed during the course of therapy. Serum creatinine and tubular markers including urine KIM-1 (Kidney Injury Molecule) were analyzed and outcome variables (incidence and risk factors) were measured using a pre-designed data proforma. Criteria for admission to the pediatric intensive care unit (PICU) included impaired level of consciousness (Glasgow Coma Scale score <7), raised intracranial pressure, hypotension, requirement of mechanical ventilation, requirement of renal replacement therapy, uncontrolled seizures, fulminant hepatic failure and congestive cardiac failure.

Results: Among the 110 recruited children, amikacin was the most commonly used aminoglycoside (109 received amikacin; 1 received streptomycin). The median (IQR) age group of the enrolled subjects were 8.5 (3, 48) months. Forty (36.4%) children were critically ill and required admission to the PICU. The clinical diagnosis of these children included pneumonia [49 (44.5%)], urinary tract infection (UTI) [36 (32.7%)], meningitis [10 (9.1%)], sepsis [6 (5.5%)], abscess [4 (3.6%)], post-cardiac surgery [3 (2.7%)], neonatal hepatitis [1 (0.9%)] and necrotizing enterocolitis [1 (0.9%)]. All children received aminoglycoside therapy for a mean (SD) duration of 6.75 (1.6) days. Among the 110 children, 16 (14.5%) had associated congenital anomalies of kidney and urinary tract (CAKUT), 10 (9.1%) had heart diseases, 21 (19.1%) had shock, 2 (1.8%) had Type 1 diabetes mellitus and 4 (3.6%) had acute liver failure. Forty-two (38.2%) of the 110 children developed acute kidney injury (AKI) based on the KDIGO classification. Fifteen (13.7%) of the 42 children with AKI had AKI stage 1, 14 (12.7%) had stage 2, and 13 (11.8%) had stage 3 AKI. Tubular toxicity in form of new-onset hypokalemia, hypophosphatemia, hypomagnesemia, hypocalcemia and metabolic acidosis were found in 57 (51.8%) children. When composite nephrotoxicity (combination of AKI and/ or tubular toxicity) was evaluated, 64.5% of the 110 enrolled children (n=71) had nephrotoxicity. Liverpool analysis was done to define causality of aminoglycoside nephrotoxicity, which showed that 15.5% (n=17) of all the enrolled subjects (n=110) had AKI definitively attributable to aminoglycosides. Multivariate logistic regression analysis revealed hypotension [OR 0.016 (95% CI 0.01-0.71), p value 0.03], critically ill children requiring admission to PICU [OR 4.11 (95% CI 0.9-18.86), p value 0.069], PRISM III score between 20-29% [OR 55.48 (95% CI 3.66-840.53), p value 0.004] and requirement of surgical intervention [OR 3.2 (95% CI 1.01-10.1), p value 0.047] to be independent predictors of AKI (R2 34.7%; Hosmer-Lemeshow goodness of fit p value 0.520). Urine KIM-1 values [median (IQR)] showed a significant increase on day 4 [58.82 (35.49, 99.9) pg/ml], as compared to day 1 [1.32 (1.11, 28.96) pg/ml] and day 7 [22.3 (16.72, 36.67) pg/ml] (p value <0.001). Seven out of 42 children with AKI died (16.7%).

Conclusion: About one-sixth of hospitalized children had AKI definitively attributable to aminoglycosides in this study. The requirement of admission to the PICU, hypotension, medium-risk PRISM III score and requirement of surgical interventions were independent risk factors for AKI in our study population. Identification of these predictive risk factors may help in planning appropriate interventions for preventing and managing AKI in developing countries.

ACPN210331O19 THE COMBINATION THERAPY FOR PATHOLOGICALLY MILD CHILDHOOD IGA NEPHROPATHY

Mr. Yuya Aoto[1], Mr. Kazumono Iijima, Mr. Kandai Iijima, Mr. Hiroshi Kaito, Mr. Yosuke Inaguma, Mr. Norishige Yoshikawa, Mr. Atsushi Kondo, Mr. Sadayuki Nagai, Mr. Tomohiko Yamamura, Ms. Tomoko Horinouchi, Ms. China Nagano, Ms. Nana Sakakibara, Mr. Shinya Ishiki, Mr. Shogo Minamikawa, Mr. Koichi Nakanishi, Ms. Yuko Shima, Mr. Shingo Ishimori, Mr. Naohiro Kamiyoshi, Mr. Junya Fujimura, Mr. Takeshi ninchoji

[1]*1.Department of Pediatrics, Kobe University Graduate School of Medicine, Kobe, Japan*

Immunoglobulin A nephropathy (IgAN) is the most common primary glomerulonephritis in children. Since the heterogeneous severity, there is no widely accepted consensus on how to treat this disease. According to Japanese unique evidence-based guideline, pediatric patients with IgAN will be treated which strategy will be decided by pathological severity; focal mesangial proliferation (focal IgAN) and diffuse mesangial proliferation (diffuse IgAN). Focal IgAN cases will be treated with renin-angiotensin system inhibitors (RASi) as the initial treatment and diffuse IgAN cases received 2 years multiple combination therapy including corticosteroids and immunosuppressants. Focal IgAN cases are expected to have good prognosis under RAS-i therapy alone. However, there are some complicated focal IgAN cases who show resistance to RAS-i therapy or nephrotic range proteinuria, and multiple combination therapy is often used in such cases. However, there is no study about the efficacy of multiple combination therapy for those focal IgAN cases. The aim of this study is to clarify the efficacy of multiple combination therapy for complicated focal IgAN cases compared to diffuse IgAN cases.

Methods: We conducted a multicenter retrospective study including 6 Japanese medical hospitals and analyzed 88 children and adolescents who underwent 2 years combination therapy between January 2000 and December 2018. Clinical and pathological data from medical records were collected and analyzed. The participants were classified pathologically into two groups of focal IgAN defined by mesangial proliferative glomerulus less than 80% and diffuse IgAN defined by mesangial proliferative glomerulus equal or more than 80%. Proteinuria and hematuria were defined as uP/Cr $\geq$ 0.2 (g/g) and more than five red blood cells under a high-power field, respectively. We determined primary endpoint as the duration between the beginning of combination therapy and proteinuria disappearance. P values under 0.05 was considered as significant.

Results: Twenty-six (29.5%) patients belonged to the focal IgAN group. They received combination therapy due to resistance to initial therapy (n=6), nephrotic range of proteinuria (n=12, including 7 nephrotic syndrome patients), or histologically close to the definition for the diffuse IgAN (n=8). There were no differences in clinical characteristics.

All 26 patients (100%) in the focal IgAN group and 52 out of 62 patients (83.9%) in diffuse IgAN group reached primary endpoint within 2 years. Kaplan-Meier analysis revealed that the duration until proteinuria disappearance was significantly earlier in focal IgAN cases than in diffuse IgAN cases (2.9 vs 4.2 months, Wilcoxon test: P=0.01). Additionally, proteinuria of all cases in focal IgAN group was eliminated within 8-month. Relapsed or refractory proteinuria cases in focal IgAN group were significantly lower than those of diffuse IgAN group (Pearson's test: P=0.04). On the other hand, there was no significant difference in duration until hematuria disappearance. Kidney dysfunction was found only in diffuse IgAN group (n=2). Severe

adverse events were shown 1 case [cataract (n=1)] in focal IgAN group, and 6 cases [hyperuricemia requiring discontinuation of mizoribine (n=2), pancytopenia (n=1), drug-induced pancreatitis (n=1), psychosis (n=1), and drug-induced kidney dysfunction (n=1)] in diffuse IgAN group, which was no significant difference.

Conclusions: In the case of complicated focal IgAN, multiple combination therapy was remarkably effective. Moreover, the prognosis at the last observation was good, and adverse effects were also acceptable. Since the period to the proteinuria disappearance is significantly shorter compared to diffuse IgAN cases, there is a room to reconsider the duration of combination therapy shorter than two years.

ACPN210331O20 THE PATHOLOGICAL SPECTRUM OF PEDIATRIC KIDNEY DISEASE: AN ANALYSIS OF 339 BIOPSY-PROVEN CASES FROM 2002-2020 IN NORTHERN TAIWAN

Mr. Chen Wei Yen[1], Mr. Teddy Chen[1], Ms. Mei-Ching Yu[1]

[1]*Linkou Chang Gung Memorial Hospital, Taoyuan City, Taiwan, Taiwan*

Background: Glomerular diseases remain the leading cause of chronic kidney disease and end-stage renal failure in children, particularly in many Asia-Pacific countries. This study aimed to evaluate the changes in the spectrum of biopsy proven pediatric kidney disease over time in Taiwan.

Methods: This is a retrospective chart review of 339 patients less than the age of 18 years undergoing percutaneous renal biopsy (PRB) of native kidneys between January 2002 to July 2020 in Pediatric Tertiary Care Center in northern Taiwan.

Results: A total of 339 pediatric native renal biopsies were analyzed in this study. The mean age of the participants was 13.7±7.0 years (184 girls and 155 boys). The most frequent indications of PRBs included nephritic syndrome (166/339, 49%), nephrotic syndrome (77/339, 22.7%), persistent asymptomatic microscopic hematuria accompanying with any degree of proteinuria (57/339, 16.8%), asymptomatic hematuria alone (13/339, 3.8%) and others (26/339, 7.7%). Lupus nephritis (LN), minimal change disease (MCD) and IgA nephropathy (IgAN) have been the most commonest kidney disease among Taiwanese children and adolescents. Furthermore, LN was more common in older children > 12 years old. Besides, we also found post-streptococcal glomerulonephritis appeared to be no longer recognized in Taiwan after 2010.

Conclusions: Apart from genetic and racial difference, environmental agents and conditions such as toxins and infections are associated with kidney disease. Along with the introduction of antibiotic restriction policy for acute respiratory tract infection and comprehensive immunization program in Taiwan, streptococcus progenies infection declined from 53.1 (1988-2000) to 10.7% (2006-2010), and vaccine-preventable diseases have declined significantly. These are helpful for reducing the burden of infection-associated glomerular disease including PGSN. Although the changing patterns of kidney disease were reported in some countries in Asia and Pacific regions such as China, MCD, IgAN and LN continue to be the most common pathophysiological findings of children with kidney disease in Taiwan.

ACPN210331O21 A NATIONWIDE SURVEY OF THE TIMING AND OCCASION OF DIAGNOSIS OF RARE AND INTRACTABLE PEDIATRIC KIDNEY DISEASES IN JAPAN

Mr. Riku Hamada[1], Dr. Yuko Hamasaki[2], Dr. Osamu Uemura[3], Dr. Motoshi Hattori[4], Dr. Koichi Nakanishi[5], Dr. Shoichi Maruyama[6], Dr. Shuichi Ito[7], Dr. Naoya Morisada[8], Dr. Kandai Nozu[9], Dr. Yutaka Harita[10], Dr. Ryoko Harada[1], Dr. Tetsuji Kaneko[11], Dr. Masataka Honda[1], Dr. Kenji Ishikura[12]

[1]*Department of Nephrology, Tokyo Metropolitan Children's Medical Center, Fuchu-shi, Japan,* [2]*Department of Nephrology, Toho University Faculty of Medicine, , Japan,* [3]*Department of Pediatrics, Ichinomiya Medical Treatment & Habilitation Center, , Japan,* [4]*Department of Pediatric Nephrology, Tokyo Women's Medical University, , Japan,* [5]*Department of Pediatrics, University of the Ryukyus, , Japan,* [6]*Department of Nephrology, Nagoya University Graduate School of Medicine, , Japan,* [7]*Department of Pediatrics, Yokohama City University Graduate School of Medicine, , Japan,* [8]*Department of Clinical Genetics, Hyogo Prefectural Kobe Children's Hospital, , Japan,* [9]*Department of Pediatrics, Kobe University Graduate School of Medicine, , Japan,* [10]*Department of Pediatrics, Graduate School of Medicine, , Japan,* [11]*Division of Clinical Research Support Center, Tokyo Metropolitan Children's Medical Center, , Japan,* [12]*Department of Pediatrics, Kitasato University School of Medicine, , Japan*

Objectives: To improve the management of rare kidney diseases in children through understanding the timing of their diagnosis, reasons leading to their detection, and their prognosis. We herein investigated how seven, rare, intractable diseases, including Galloway-Mowat syndrome (GM), Epstein syndrome (EP), Lowe syndrome (LO), Nephronophthisis (NP), Branchio-oto-renal syndrome (BOR), Bartter and Gitelman syndromes (BG), and Nail-Patella syndrome (NL) are detected in the pediatric nephrology setting. In Japan, regular annual urinalysis is performed at age 3 and after school, and we also focused on how these tests contribute to the detection of these diseases.

Methods: A nationwide survey of hospitals was conducted to determine the timing of the diagnosis, reasons for the detection, and the outcomes of the seven diseases mentioned above. A questionnaire was sent to 296 hospitals in Japan providing care for intractable pediatric kidney diseases according to a previous survey in 2017. Patients with any of the target diseases who were managed at January 2019 were reviewed for data on the timing of the diagnosis, reasons for detection, kidney function, and extra-renal comorbidities. The present study was funded by a Research on rare and intractable diseases, Health, Labour and Welfare Sciences Research Grants from the Ministry of Health, Labour and Welfare of Japan (H26-nanchitou(nan)-ippan-036 and H29-nanchitou(nan)-ippan-039).

Results: Responses were received from 229 facilities (77%), and data were collected from 325 patients (GM: 10, EP: 17, LO: 61, NP: 90, BOR: 45, BG: 78, and NL 24).

The median age at diagnosis was 3.0 years (GM: 3.1 years, EP: 6.0 years, LO: 0.3 years, NP: 7.0 years, BOR: 0.2 years, BG: 4.5 years, NL: 3.0 years), and on average 77% of the cases (GM: 80%, EP: 53%, LO: 74%, NP: 71%, BOR: 73%, BG: 94%, NL: 71%) were detected outside regular health checkups, for instance at infant health examinations, urine screenings for 3-year-olds, school urine screening, etc. The median estimated glomerular filtration rate at the time of diagnosis was GM: 130, EP: 115, LO: 110, NP: 28, BOR: 76, BG: 113, and NL: 122 mL/min/1.73m^2. The percentage of patients with stage 3-5 CKD at the time of diagnosis was GM: 0%, EP: 0%, LO: 12%, NP: 88%, BOR: 43%, BG: 6%, and NL: 8%. The percentage of patients with extra-kidney symptoms at the time of diagnosis was GM: 100%, EP: 100%, LO: 95%, NP: 74%, BOR: 93%, BG: 50%, and NL: 96%. The percentage of patients with pathogenic genetic variants was GM: 0%, EP: 100%, LO: 58%, NP: 38%, BOR: 42%, BG: 76%, and NL: 29%.

At the time of the survey (the median observation period for each disease is as follows: GM: 3.5 years, EP: 11 years, LO: 9 years, NP 7 years, BOR: 8years, BG: 5 years, NL 7.5 years), the percentage of patients with stage 3-5 CKD was GM: 33%, EP: 40%, LO: 18%, NP: 96%, BOR: 63%, BG: 4%, and NL: 18%, and the kidney failure rate was 30% overall (GM: 20%, EP: 35%, LO: 3%, NP: 76%, BOR: 38%, BG: 0%, NL: 4%).

Conclusions: The majority of these intractable diseases were detected by characteristic clinical symptoms or incidental examinations other than regular checkups.

Diseases lacking distinctive, extra-kidney symptoms, especially in NP was detected only when kidney dysfunction deteriorated, suggesting that the general physician needs to be aware of the characteristics of such diseases to be able to assess kidney function and implement treatment in a timely fashion. All the diseases studied except BG included cases of kidney failure, indicating the potentially serious nature of this group of diseases.

ACPN210331O22 OBSTRUCTIVE SLEEP APNEA AND AMBULATORY BLOOD PRESSURE ABNORMALITIES IN CHILDREN WITH CHRONIC KIDNEY DISEASES

Mr. Suryendru Kumar, Mr. Girish Chandra Bhatt[1], Mr. Abhishek Goyal[1], Mr Mahendra Atlani[1], Mr Shikha Malik[1], Mr Mahesh Maheshwari[1], Mr Girish Chandra Bhatt[1]

[1]*All India Institute Of Medical Sciences (AIIMS), Bhopal, M.P, India*

Background: Obstructive sleep apnea and hypertension are very common and important complications involved in children with chronic kidney disease (CKD). Progression of CKD can aggravate OSA and hypertension whereas worsening sleep apnea can make hypertension difficult to treat in CKD patients. However, most of these interpretations are derived from adult studies and only one study has been conducted in pediatric CKD patients. Thus, our aim is to determine the association of obstructive sleep apnea (OSA) with the help of overnight polysomnography (PSG) using AHI and OAHI, and ambulatory blood pressure abnormalities by using 24-hour Ambulatory blood pressure monitoring (ABPM).

Method: In this cross-sectional study with an estimated sample size of 30 children, overnight Polysomnography (PSG) was conducted in sleep laboratory in children with CKD stage 3-5 (Non-dialysis dependent). 24-hour ABPM was also performed on the same population.

Results: In this ongoing study, 13 children completed overnight polysomnography and 12 children completed 24-hr ambulatory BP monitoring. The mean (SD) age were 11.36 (4.4) years. Of thirteen participants, four (31%) had CKD stage-3, six (46%) had CKD stage-4 and three (23%) had CKD stage-5. Overnight polysomnography showed OSA in 12/13 (92%) participants [mild in 5(38%), moderate 3(23%) and severe 4(31%)]. Ambulatory hypertension was recorded in 7 participants with 1 participant having masked hypertension. All children with ambulatory hypertension had OSA, three had mild, two had moderate and two had severe OSA. Three children had uncontrolled hypertension on drugs and 2 of them had severe OSA and one child with masked hypertension had moderate OSA. Eight children had impaired dipping, in which 87.5% had obstructive sleep apnea.

Conclusion: Our preliminary findings suggests that ambulatory blood pressure abnormalities and OSA are highly common in children with CKD. Patients with CKD stage 3 to 5 should be screened for presence of OSA, more commonly if the blood pressure remains uncontrolled despite antihypertensive medications. Thus, OSA, ambulatory blood pressure abnormalities and CKD, though are different entities the presence of this triad altogether can have a negative impact on cardiovascular health and worsening OSA can result in hypertension difficult to treat.

ACPN210331O23 THE IMPACT OF SAMPLE COLLECTION TIME ON URINARY BIOMARKERS IN CHILDREN WITH CHRONIC KIDNEY DISEASE

Ms. Jianmei Zhou[1], Xuhui Zhong[1], Ke Xu[1], Huijie Xiao[1], Jie Ding

[1]*Peking University First Hospital, Beijing,*

Objectives: Previous studies have reported that protein: creatinine ratio in spot urine can be a surrogate of 24-hour urinary protein. However, the impact of collection time on levels of different urinary biomarkers is not fully known. This study aimed to investigate the impact of various collection time on urinary biomarkers in children with chronic kidney disease.

Methods: Hospitalized children with chronic kidney disease were enrolled in this study (14 boys and 6 girls, mean age 11.3 years), from August 2019 to November 2019. Urine samples were collected during 21:00 (bedtime)–07:00 (waking up), 07:00–12:00, 12:00–16:00, 16:00–21:00, and again during 21:00–07:00. Urinary total protein, albumin, N-acetyl-beta-D-glucosaminidase (NAG), epidermal growth factor (EGF), collagen type I alpha 1 chain [α1(I)], and creatinine were measured for each time interval.

Results: The results showed that within-day variations of the urinary protein/creatinine ratio (PCR), albumin/creatinine ratio (ACR), NAG/creatinine ratio (NAG/Cr), and α1(I)/creatinine ratio (α1(I)/Cr) were significantly higher than the day-to-day variations. There was a circadian rhythm in urinary PCR, ACR, NAG/Cr, and α1(I)/Cr ($P < 0.05$), with a peak in the daytime (07:00–21:00) and a trough in the nighttime (21:00–7:00). No significant difference was observed in levels of urinary EGF/Cr during 24 hours. When patients were divided into subgroups according to diuretic use, gender, age, and obesity, the circadian trends in urinary PCR, ACR, NAG/Cr, and α1(I)/Cr were consistent with those observed across all patients. However, urine samples from the 07:00–12:00 and 12:00–16:00 time intervals overestimated the level of the 24-hour urinary α1(I). Urinary PCR and ACR measurements of the 16:00–21:00 samples overestimated these levels in the 24-hour urine. Additionally, urinary EGF/Cr and α1(I)/Cr were not significantly affected by the application of additives, sample centrifugation, delayed processing or storage temperature.

Conclusions: Our findings indicate that considering the circadian rhythm observed for urinary biomarkers, urine samples should be collected during the same time interval in clinical practice and clinical studies when monitoring daily changes in urinary biomarkers. Urinary EGF/Cr and α1(I)/Cr were unaffected by the additives, sample centrifugation, delayed processing or storage temperature of urine samples.

ACPN210331O24 ALTERATIONS IN THE GUT MICROBIOTA AND METABOLITES BY MATERNAL RESVERATROL SUPPLEMENTATION ARE ASSOCIATED WITH PROTECTION AGAINST HYPERTENSION PROGRAMMED BY PRENATAL EXPOSURE TO ASYMMETRIC DIMETHYLARGININE AND TRIMETHYLAMINE-N-OXIDE

Mrs. Wei-Ling Chen[1], Dr. Chien-Ning Hsu[2], Prof. You-Lin Tain[1]

[1]*Division of Pediatric Nephrology, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan,* [2]*Department of Pharmacy, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan*

Objectives: Resveratrol, a phytochemical, has shown antioxidant properties and potential benefits in hypertension. Asymmetric dimethylarginine (ADMA)-related nitric oxide (NO) deficiency and gut microbiota-derived metabolite trimethylamine-N-oxide (TMAO) have been linked to hypertension. We aimed to test whether maternal resveratrol therapy would protect adult offspring against hypertension programmed by prenatal exposure to ADMA and TMAO.

Methods: Pregnant Sprague-Dawley rats received ADMA 10 mg/kg/day (A), TMAO 0.65 mg/hr (T), ADMA+TMAO (AT), or vesicle (CV). One group of ADMA+TMAO-exposed rats received 50 mg/L of resveratrol in drinking water during pregnancy and lactation periods (ATR). Male offspring (n=8/group) were assigned to five groups: CV, A, T, AT, and ATR. Rats were killed at 12 weeks of age.

Results: ADMA exposure caused the elevation of blood pressure in 12-week-old male offspring, which was exacerbated by TMAO exposure. Treatment with resveratrol rescued hypertension programmed by combined ADMA and TMAO exposure. This was accompanied by

alterations in the compositions of gut microbiota and increased fecal butyrate levels. Both the abundance of the butyrate-producing genera Lachnospiraceae and Ruminococcaceae were augmented by resveratrol. Meanwhile, resveratrol therapy significantly increased the abundance of the Cyanobiaceae and Erysipelotrichaceae families. Moreover, the protective effects of resveratrol were related to the mediation of the renin-angiotensin system (RAS).

Conclusions: Our data provide new insights into the protective mechanisms of resveratrol against hypertension programmed by ADMA and TMAO, including regulation of gut microbiota and their metabolites, the RAS, and NO pathway. Resveratrol might be a potential reprogramming strategy to protect against the hypertension of developmental origins.

Table 2. Morphological and biochemical values in different experimental groups.

Groups	CV	A	T	AT	ATR
Mortality	0%	0%	0%	0%	0%
Body weight (BW) (g)	344±8	306±5*#	337±14#	302±17*#	326±9#$
Left kidney weight (g)	1.51±0.03	1.48±0.03	1.59±0.1#$	1.39±0.04*#$	1.61±0.03$
Left kidney weight/ 100g BW	0.44±0.01	0.48±0.01#	0.47±0.02#	0.47±0.03#	0.49±0.03*#
Systolic BP (mmHg)	134±2	152±3*#	150±3*#	162±2*#$	141±2*#$
Diastolic BP (mmHg)	75±5	67±5*#	67±5*#	71±6	63±3*$
MAP (mmHg)	95±4	95±4	95±3	101±4*#$	89±2$
Creatinine (g/dl)	14.7±1.4	11.4±1.3	19.8±1.8*#$	18.1±1.2*#$	17.4±1.2*#$

N=8/group; MAP= mean arterial pressure; *P<0.05 vs. CV; #P<0.05 vs. A; †P<0.05 vs. T; ‡P<0.05 vs. AT

ACPN210331O25 REPROGRAMMING HYPERTENSION PROGRAMMED BY HIGH-FAT DIET: THE ROLE OF GARLIC OIL

Ms. Wei Ting Liao[1], Dr. Chien Ning Hsu[2], Prof. You Lin Tain[1]

[1]*Division of Pediatric Nephrology, Kaohsung Chang Gung Memorial Hospital, Kaohsiung, Taiwan,* [2]*Department of Pharmacy, Kaohsiung chang gung Memorial Hospital, Kaohsiung, Taiwan*

Objectives: Perinatal high-fat (HF) diet programs high blood pressure (BP) in adult offspring. Hydrogen sulfide (H2S) has shown benefits in hypertension by restoration of nitric oxide (NO) bioavailability and alterations of gut microbiota. Garlic, a naturally dietary source of H2S donors, supplementation has shown benefits in hypertension. We examined whether maternal garlic oil supplementation can prevent hypertension programmed by HF diet and elucidated its protective effects.

Methods: Pregnant rats received either a normal diet (ND) or HF diet (D12331, Research Diets, Inc.) Garlic oil (GO) or vesicle was administered daily by oral gavage at 100 mg/kg/day during pregnancy and lactation. Male offspring were weaned at 3 weeks of age, and onto either ND or HF diet to 16 weeks of age. Male offspring were assigned to four groups (n=8/group): ND, HF, ND+GO, and HF+GO.

Results: Garlic supplementation during pregnancy and lactation protected against programmed hypertension in adult male offspring fed with HF diet. The beneficial effects of garlic oil were associated with increased renal mRNA expression and activity of H2S-generating enzymes, increased NO bioavailability, increased plasma short chain fatty acid levels, and alterations of gut microbiota composition. Garlic oil supplementation increased abundance of genus Lactobacillus, but decreased genera Turicibacter and Staphylococcus.

Conclusions: Our data revealed associations between H2S-generating pathway in the gut and kidneys, NO system, gut microbiota, and microbiota-derived metabolites in hypertension programmed by HF intake and provided insight to garlic oil as a hypertension reprogramming strategy for further translational research.

ACPN210331O26 ANTI-FACTOR B ANTIBODIES IN ATYPICAL HEMOLYTIC UREMIC SYNDROME, C3 GLOMERULOPATHY AND IMMUNE-COMPLEX GLOMERULOPATHY

Mrs. Priyanka Khandelwal[1], Shreesha Nambiar[1], Dr. Aditi Sinha[1], Prof. Pankaj Hari[1], Prof. Arvind Bagga[1]

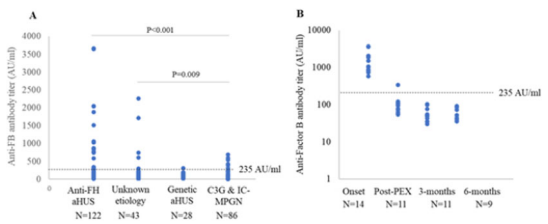
[1]*Division of Pediatric Nephrology, Department of Pediatrics, All India Institute Of Medical Sciences, New Delhi, India*

Introduction: Autoantibodies causing overactivation of the alternate complement pathway are often found in patients with atypical hemolytic uremic syndrome (aHUS), C3 glomerulopathy (C3G) and immune-complex membranoproliferative glomerulopathy (IC-MPGN). Anti-factor B (FB) antibodies enhance C3 convertase activity both in the fluid phase and cell surface in vitro. While a small proportion of patients with C3G and IC-MPGN have FB antibodies, these are not reported in patients with aHUS.

Methods: We screened for anti-FB antibodies in 306 patients (<18 years) including 220 with aHUS (from a nationwide database), 66 C3G (41 dense deposit disease & 25 C3 glomerulonephritis) and 20 patients with IC-MPGN. Anti-FB antibodies were measured by enzyme linked immosorbent assay (ELISA). Antibody titer was expressed as arbitrary units (AU)/ml 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). Following screening for anti-FB antibody in plasma from 103 healthy donors, the positive threshold was established at 235 AU/ml (mean±SD 93.1 ±71.3 AU/ml; 95th centile: 256.8AU/ml).

Results: Of 220 patients with aHUS, anti-FH antibodies were present in 122 (55.5%), complement genetics was abnormal in 28 (12.7%) and no etiology could be found in 43 (19.5%); sequencing was unavailable in another 27 patients. We identified 19 (8.6%) patients with anti-FB antibodies in aHUS, including 14 (11.5%) in patients with concomitant anti-FH antibodies (mean anti-FH titer 13856 AU/ml) and 4 (9.3%) in patients with unknown etiology (Fig. A). No patient with abnormal genetic variations in CD46 (n=10), CFH (n=6), CFI (n=3), DGKE (n=2), C3 (n=2), CFB (n=1) and CFHR1/3 duplication (n=4) had anti-FB antibodies. Following plasma exchange, anti-FB antibodies declined to mean 110 AU/ml (P<0.001) and remained low during 3- and 6-month follow up (Fig. B). There was no significant correlation between level of anti-FB antibodies, anti-FH antibodies (median 9837 AU/ml) and serum C3 (median 60 mg/dl; P>0.5 for both). After mean 24 months, 2 of 15 (13%) anti-FB positive patients had developed ESRD or died and 4 (26%) relapsed. We detected anti-FB antibodies in 5 (7.6%) patients with C3G and one patient with IC-MPGN, none of whom were positive for anti-FH antibodies. Antibody titers were higher in patients with aHUS (mean±SEM 1464.5±215.8 versus 492.5±56.9 AU/ml; P<0.001).

Conclusion: A small proportion of patients with aHUS and C3G have anti-FB antibodies; titers are significantly higher in aHUS. Presence of high titers of anti-FB and anti-FH antibodies shows propensity for autoantibody generation and co-existence of multiple concurrent risk factors for aHUS. There may be a therapeutic implication of detection of anti-FB antibodies in ~10% aHUS patients without any other obvious genetic/autoimmune etiology.



ACPN210331O27 GENOTYPE-PHENOTYPE CORRELATION ANALYSIS AND FUNCTIONAL ANALYSIS TO DETERMINE SEVERITY IN CASES WITH MISSENSE VARIANTS IN WT1 EXON 8 TO 9

Ms. China Nagano[1], Atsushi Kondo[1], Sadayuki Nagai[1], Yuya Aoto[1], Shinya Ishiko[1], Rini Rossanti[1], Nana Sakakibara[1], Eri Okada[1], Tomoko Horinouchi[1], Tomohiko Yamamura[1], Takeshi Ninchoji[1], Kazumoto Iijima[1], Kandai Nozu[1]

[1]*Kobe University Graduate School Of Medicine, Kobe, Japan*

Objectives: WT1 missense mutation in exon 8 or 9 causes infantile nephrotic syndrome with early progression to end-stage kidney disease (ESKD), Wilms' tumor and 46XY female (known as Denys-Drash syndrome). However, some patients with these variants progress to ESKD in their teens or later. Therefore, we conducted a systematic review and functional analysis of transcriptional activities to clarify the relation between genotypes, transcriptional activities and clinical severities.

Methods: We conducted systematic review for in total, 174 cases with WT1 exon 8 or 9 missense variants from our cohort (n=13) and previous reports (n=161). We calculated median age of developing ESKD and extracted the information about phenotypes including extra-renal symptoms and onset of Wilms' tumor. Of these cases, mild and severe genotypes were picked up for further in vitro functional analysis using luciferase assay.

Results: The median age of developing ESKD was at 1.5 years. A comparative study was conducted among three genotypes: mutations of the DNA binding sites (DBS group), mutations out of DNA binding sites but important for the formation of zinc finger structure by two cysteines and two histidines (C2H2 group), or mutations lead to other amino acids changes (Others group). As a result, cases in DBS group showed the severest, C2H2 group showed middle and Others group showed the mildest phenotype (0.9, 2, or 3 years, respectively at the age of reaching ESKD with significant differences).

In vitro functional analysis results showed the DBS mutation showed significantly lower transcriptional activity in comparison with other mutations. In addition, it showed the clear evidence of dominant negative effects in all missense variants.

Conclusions: Even among patients with missense mutations of the WT1 gene exon 8 to 9, we found two novel findings. 1) There were clear genotype-phenotype correlation which confirmed by functional transcriptional activity data. 2) We showed that not only the DNA binding sites but sites at C2H2 zinc finger structure sites are important in maintaining transcriptional activities and cause severe clinical symptoms.

ACPN210331O28 The Adjusted Renal Damage by Ages and Covariates in Patients with Classical Fabry Disease and the Late Onset Subtype with IVS4+919G>A Mutation under Enzyme Replacement Therapy

Mr. Chao Ting Teng[1], Mr. Yen-Wen Tseng, Mr. Yi-Hsuan Tang, Mrs. Hui-Lan Chen, Mr. Chien-Hung Lin, Mrs. Hsin-Hui Wang, Mrs. Chia-Feng Yang, Mr. Dau-Ming Niu, Mrs. Yu-Min Huang

[1]*Taipei Veterans General Hospital, New Taipei City, Taiwan*

The Adjusted Renal Damage by Ages and Covariates in Patients with Classical Fabry Disease and the Late Onset Subtype with IVS4+919G>A Mutation under Enzyme Replacement Therapy

Authors:Chao-Ting Teng1、Yen-Wen Tseng1、Yu-Min Huang2、Yi-Hsuan Tang1,3.4, Hui-Lan Chen1,4,5, Chien-Hung Lin 1,3, Hsin-Hui Wang*1,3,4、Chia-Feng Yang2,6、Dau-Ming Niu6,7

Department and institutional affiliation:

Department of Pediatrics, Division of Pediatric Immunology and Nephrology, Taipei Veterans General Hospital, Taipei, Taiwan{1}. Department of Statistics, Tunghai University {2}. Department of Pediatrics, Faculty of Medicine, School of Medicine {3}, and Institute of Emergency and Critical Care Medicine, School of Medicine, National Yang-Ming University{4}, Taipei, Taiwan. Department of Pediatrics, Keelung Hospital, Ministry of Health and Welfare, Taiwan {5}. Department of Pediatrics, Division of Pediatric Genetics and Endocrinology, Taipei Veterans General Hospital, Taipei, Taiwan{6}. Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan{7}

Objectives: Patients with the late onset IVS4+919 G>A (IVS4) Fabry disease are known to have cardiac involvements. However, the effects on renal manifestations adjusted for age and other related factors have been little to be reported. This study compares the renal damage in patients, with adequate adjustment of age and other variables, with the IVS4 mutation and classical Fabry mutation who are under enzyme replacement therapy (ERT).

Methods: This was a retrospective analysis of renal function from Taiwanese patients treated in Taipei Veterans General Hospital, IVS4 patients and classical Fabry patients who are under ERT are eligible for inclusion. Patients with diabetes are excluded from this study. We examine the demographics, baseline data, renal damage markers and renal function among these patients. Renal damage markers are evaluated by proteinuria, hematuria and renal function is evaluated by eGFR. The propensity score model is built for assessing the causal difference. With similar propensity scores and inverse probability weighting methods, the nonparametric causal inference is performed to assess the difference.

Results: 25 classical (11 males) and 38 IVS4 (31males) patients underwent ERT at the median (interquartile range) age of 43.0 (37-63.5) and 62.5 (57.0-67.0) years, with ERT treatment duration of 5.0 (1.540-8.250) and 3.875 (2.540-7.210) years, respectively. The median age of starting ERT was significantly younger in classical Fabry patients versus IVS4 patients ($p<0.001$). The median level of microalbuminuria was significant higher in classical Fabry patients versus IVS4 patients ($p=0.002$). The median (interquartile range) level of serum BUN, serum creatinine and eGFR were 12.0 (10.0-16.0), 0.790 (0.650-0.925) and 97.400 (73.900-121.250) in classical Fabry patients while 14.500 (12.000-19.250), 0.875 (0.810-1.040) and 76.200 (66.475-93.950) in IVS4 patients. A causal analysis with Mann-Whitney U test is used to compare differences between classical and IVS4 subtype patients. With controlling the age and confounders, the comparisons between the two groups remains to be significant for those major factors of interests.

Conclusions: Fabry disease with IVS4+919G>A mutation was previously reported as a cardiac variant, the natural history of renal involvement is not clear. In this study, we found that there are significant IVS4 subtype patients have renal damage. Regular follow up renal damage markers, such as microalbuminuria and hematuria, and renal function are suggested in both classical and IVS4 subtype patients of Fabry disease. Control blood pressure and proteinuria are important in both groups to prevent renal function deterioration and improve long term renal outcome.

ACPN210331O29 PAX2 MUTATION-RELATED RENAL DYSPLASIA IN THREE PATIENTS: CASE SERIES AND LITERATURE REVIEW

Mr. Yu Ming Chang[1], Mr. Chih Chia Chen[1], Mr. Yuan Yow Chiou[1,2]

[1]*Department of Pediatrics, National Cheng Kung University Hospital, Tainan, Taiwan,* [2]*Institute of Clinical Medicine, National Cheng Kung University Hospital, College of Medicine, Tainan, Taiwan*

Objectives: PAX2-related disorder is an autosomal dominant disorder associated with renal and eye abnormalities. The disorder was originally referred to as renal coloboma syndrome and characterized by renal

hypodysplasia and abnormalities of the optic nerve. Although registry data showed low incidence of PAX2 mutations, some other investigation revealed that the PAX2 related disorder might be underestimated. We here will present three cases with PAX2 mutations noted in recent one year and the literature reviews.

Case presentations: The first case was a boy with proteinuria when he was 5 years old. Impaired renal function (Serum creatinine 3.1 mg/ dL) was noted when presented, and renal sonography revealed bilateral renal atrophy and cystic lesion over the left kidney. The serial examination showed bilateral vesicoureteral reflux. He was found with optic nerve dysplasia on ophthalmic examination. He developed end stage renal disease and received dialysis since he was 9 years old and received kidney transplantation at 13 years old. Whole exome sequence revealed PAX2 mutation. The second case was a 7-day-old preterm girl born at gestational age of 34 weeks. Antenatal examination showed oligohydramnios. After birth, she had fluid overload and impaired renal function. Bilateral small kidney, right dysplastic kidney with moderate hydronephrosis and hydroureter, and left ectopic hypodysplastic kidney were found on renal sonography and magnetic resonance urography. Ophthalmic exam revealed right eye coloboma. She received dialysis due to end stage renal disease. Genetic investigations revealed that she has inherited a mutated PAX2 gene from his father, who is the third case of this presentation. He had proteinuria at a young age, and developed chronic kidney disease stage 2 later in life. Renal sonography revealed one cyst at left kidney. Focal segmental glomerulosclerosis was noted on renal biopsy.

Conclusions: Although some data showed low incidence of PAX mutations, we found three cases from two family in recent one year incidentally. The prevalence of PAX2 mutation may be underestimated. We may need more alert for the mutation when facing patients with congenital anomalies of the kidney and urinary tract with bilateral kidney involved or advanced kidney diseases.

ACPN210331O30 ELUCIDATION OF MOLECULAR PATHOGENESIS OF LOWE SYNDROME AND DENT DISEASE-2.

Ms. Nana Sakakibara[1], Dr Kandai Nozu[1], Dr Atsushi Kondo[1], Dr Sadayuki Nagai[1], Dr Shinya Ishiko[1], Dr Yuya Aoto[1], Dr Rini Rossanti[1], Dr China Nagano[1], Dr Tomoko Horinouchi[1], Dr Tomohiko Yamamura[1], Dr Takeshi Ninchoji[1], Dr Kazumoto Iijima[1]

[1]*Kobe University Graduate School of Medicine, Kobe City, Japan*

Objectives: Lowe syndrome and Dent disease-2 are both X-linked kidney diseases caused by OCRL gene abnormalities. However, the severity of these two diseases are quite different. Previous genetic studies have shown that patients with truncating mutation in exon 1-7 of OCRL gene were diagnosed with Dent disease-2, and those with truncating mutations in exon 8-24 were diagnosed with Lowe syndrome. OCRL protein encodes 5-phosphatase that acts on phosphatidylinositol 4,5-bisphosphate and is related to various cellular functions by the regulation of inositol phospholipids. It is suspected that an 'isoform' consisting of exon 8-24 exists and this 'isoform' works partially as a 5-phosphatase in Dent disease-2. However, the molecular mechanism of the phenotypic differences in Lowe syndrome and Dent disease-2 have not been clarified yet. The purpose of this study is to elucidate the pathogenesis of these two diseases by detecting the existence of this 'isoform'.

Methods: We extracted mRNA from cultured urine derived cells of healthy control and Dent disease-2 patient with truncating mutation in Exon4 of OCRL gene and then examined 5 'end of mRNA of these cells by using rapid amplification of cDNA ends (5' RACE) method. We prepared three types of OCRL protein expression vectors: wild type model, five Dent disease-2 models harboring truncating mutation in exon 3, 4, 5 and exon 7, and three Lowe syndrome models harboring truncating mutation in exon 13, 16 and exon 22. We also prepared the protein expression vectors of 'isoform' which contains the alternative transcript of OCRL gene detected by 5 'RACE. These vectors were transfected into Hela cells and analyzed the protein expression and 5-phosphatase activity.

Results: As a result of 5' RACE, the 5' end of alternative transcript were beginning of OCRL exon 6 in both cells of healthy control and Dent disease-2 patient. In immunofluorescent staining of transfected Hela cells, strong protein expression was observed in the wild type model, 'isoform' models, and Dent disease-2 models. No expression was observed in Lowe syndrome models. Western blotting detected two bands of 105kDa and 80kDa in the wild type model, single band of 80kDa in isoform models and Dent disease-2 models, and no band in Lowe syndrome models. 5-phosphatase activity of isoform models and Dent disease-2 models retained above 50% of that of wild type model, whereas that of Lowe syndrome models was less than 20% of that of wild type model.

Conclusions: The 'isoform' OCRL protein with 5-phosphatase activity is synthesized by the alternative transcription of OCRL gene. This 'isoform' contributes to the mild clinical phenotype in Dent disease-2.

ACPN210331O31 STATUS OF PEDIATRIC CHRONIC KIDNEY DISEASE STAGE 5D PATIENTS ON PERITONEAL DIALYSIS IN A RESOURCE LIMITED SETTING

Ms. MELISSA DATOR[1], Dr. Lourdes Paula Resontoc[1]

[1]*University Of The Philippines - Philippine General Hospital, Manila City, Philippines*

BACKGROUND: Peritoneal dialysis (PD) is the preferred kidney replacement modality for pediatric patients with chronic kidney disease stage 5D (CKD 5D) in resource limited countries that do not have the facilities to manage pediatric patients on maintenance hemodialysis. At present, there is no existing registry on the status of these patients in the Philippines.

OBJECTIVE: To determine the patient status and overall survival of Filipino children with CKD 5D on PD.

METHODS: Retrospective review of medical data of all pediatric CKD 5D patients initiated on PD at the Philippine General Hospital from 2017 to 2019. Descriptive analysis was used to describe the general data and Kaplan Meier method was used for survival analysis. Paired sample t-test and Wilcoxon signed ranks test determined if there was a significant difference in baseline and follow up data.

RESULTS: There were 17 patients included (mean age 11.4+3.2 years) in the study, chronic glomerulonephritis (70.6%) being the most common cause of chronic kidney failure. All patients were enrolled to the Philippine Health Insurance PD First Z-Benefit program which provides 3-4 2-liter bags of dialysate fluid per day to be used for CAPD. Only 10 patients were able to undergo the peritoneal equilibrium test, 6 (60%) revealed to be high average transporters requiring more than 3-4 exchanges per day.

The mean patient survival was at 475.9+289 days with a 1-year survival rate at 65% and 2-year survival at 41%. Among the 17 patients, 4 (23.5%) expired and 3 (17%) patients required transfer to hemodialysis with peritonitis as the most common cause of death or peritoneal dialysis failure. 9 (53%) patients had a total of 14 episodes of peritonitis, 42% (6) caused by Gram negative bacteria. The peritonitis rate is at 0.53 episodes per year.

Biochemical status showed metabolic acidosis, uremia and hyperuricemia upon initiation on PD with follow up average data showing statistically significant improvement of serum bicarbonate and urea levels. Cardiovascular status showed normal cardiac function but with left ventricular hypertrophy/enlargement in 14 patients (87.5%) and mean blood pressure trends above the 90th percentile. Growth and nutritional profiles revealed moderate to severe stunting and wasting, anemia, secondary

hyperparathyroidism and Vitamin D insufficiency with no statistical differences noted on follow up.

CONCLUSION: Peritoneal dialysis can still be a viable option for pediatric patients with CKD 5D in resource limited settings. It is recommended to strengthen existing programs to improve training with emphasis on infection control and patient follow up. It is also recommended to establish a national registry that can monitor a larger sample of pediatric CKD 5D patients on PD to be able to formulate recommendations to improve coverage of the PD First Z-Benefit program.

ACPN210331O32 LONG-TERM CHANGE AND CLINICAL OUTCOME OF PERITONEAL MEMBRANE FUNCTION IN CHILDREN ON CHRONIC PERITONEAL DIALYSIS

Mr. Yi Hsuan Tang[1,2,3], Ms. Hui Lan Chen[1,3,4], Mr. Chien Hung Lin[1,2,3], Ms. Hsin Hui Wang*[1,2,3]

[1]*Department of Pediatrics, Division of Pediatric Immunology and Nephrology, Taipei Veterans General Hospital, Taipei, Taiwan,* [2]*Department of Pediatrics, Faculty of Medicine, School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan,* [3]*Institute of Emergency and Critical Care Medicine, School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan,* [4]*Department of Pediatric, Keelung Hospital, Ministry of Health and Welfare, Keelung, Taiwan*

Objectives: Peritoneal dialysis (PD) is an established treatment in pediatric patients with end-stage renal disease. Some patients treated with PD gradually lose peritoneal membrane function, compromise the efficiency of dialysis and lead to treatment failure. Successful long-term PD treatment depends on the preserved functional integrity of the peritoneal membrane. In order to monitor peritoneal membrane function and the efficiency of PD, serial peritoneal equilibration test (PET) was performed in PD patients. This study is to investigate the long-term change of peritoneal membrane function by PET results in children undergoing PD. The clinical outcomes and prognosis was analyzed also.

Methods: A retrospectively study of the medical records of the patients who undergo PD and follow up in Pediatric Chronic Kidney Disease Center of Taipei Veterans General Hospital during 1995 to 2020. Demographic clinical characteristics, modality with continuous ambulatory peritoneal dialysis (CAPD) or automated peritoneal dialysis (APD), morbidity with peritonitis or encapsulating peritoneal sclerosis (EPS), serial PET results and mortality were collected. The exclusive criteria were lack of serial PET results. We divided all patients into 3 group by change in serial PET results (categories with high(H), high average(HA), low average(LA) and low(L)) with group A (change to higher category), group B (no change of category), and group C (change to lower category). We then analyzed of PET results, duration of PD, times of peritonitis and clinical outcome of these patients.

Results: Total of 34 patients were included in this study, and 3 were excluded due to lack serial PET results. Male was 16 (47%). Their age at PD beginning was 14.8 years old (IQR= 10.7-29.9). Duration in PD was 4.5 years old (IQR= 2.18-8.23). 22 patients (65%) perform CAPD and 12 (35%) perform APD. 19 patients (56%) had ever suffered from peritonitis and 4 (12%) had EPS development. The clinical outcomes revealed that 8 (24%) still undergo PD, 7 (21%) shifted to HD, 8 (24%) did renal transplantation, 6 (18%) referred to other hospital, and 5 (15%) died. According to the long-term peritoneal membrane function change, number of 3 groups (A, B, C) were 11 (32%), 15 (44%), and 8 (24%), respectively. The patients in latest PET categories in group A were 6 of H and 5 of HA; in group B were 2 of H, 9 of HA and 4 of LA; in group C were 4 of LA and 4 of L ($p < 0.05$). Duration of PD in A, B, C groups were 7.53 (IQR=4.46-10.75), 2.54 (IQR=1.55-4.53) and 5.95 (IQR=3.61-7.68) years old, respectively ($p < 0.05$). The peritonitis rates in A, B, C groups revealed no significantly difference. To correlate the clinical outcome and peritoneal membrane function, we found 7 patients shifting to HD, 6/7 (86%) of H and HA group and 1/7 (14%) of LA and L group ($p < 0.05$). There were 5 patients mortality, 3 patients with H or HA PET results and 2 patients are L or LA.

Conclusions: In our 25 years cohort study, we found that the duration of PD therapy correlate with change of peritoneal membrane function. Long duration of PD therapy may cause PET results move toward to H or HA peritoneal function. Patients with H or HA peritoneal function tend to shift to HD therapy. The long-term peritoneal function in pediatric patients undergoing PD therapy is important to clinical outcome. Maintain peritoneal membrane function will promote long-term successful PD treatment.

ACPN210331O33 ALTERNATIVE SURGICAL MANAGEMENT OF PERITONEAL DIALYSIS CATHETER IN REFRACTORY EXITSITE AND TUNNEL INFECTION

Ms. Ts Ting Wang[1], Mr. Hsin-Hsu Chou[1,2]

[1]*Department of Pediatrics, Ditmanson Medical Foundation Chia-Yi Hospital, Chiayi, Taiwan, Chiayi, Taiwan,* [2]*Department of Bioinformatics and Medical Engineering, Asia University, Taichung, Taiwan, Taichung, Taiwan*

Alternative Surgical Management of Peritoneal Dialysis Catheter in Refractory Exit-site and Tunnel Infection

Ts-Ting Wang1, Hsin-Hsu Chou1,2

1. Department of Pediatrics, Ditmanson Medical Foundation Chia-Yi Hospital, Chiayi, Taiwan

2. Department of Bioinformatics and Medical Engineering, Asia University, Taichung, Taiwan

Objectives: Refractory exit-site infection and tunnel infection of the peritoneal dialysis (PD) catheter are significant causes of catheter loss or even PD dropout as well as patient morbidity. The removal and replacement of the catheter often needs to be followed by switching temporarily to hemodialysis, whereas the difficulty of vascular access and unstable hemodynamic status of the patient during hemodialysis could potentially increase the mortality and morbidity in pediatric patients.

Methods: We described our experience of the management of refractory exit-site and tunnel infection of Tenckhoff catheter in a 10-year-old girl on chronic PD. Temporary hemodialysis while waiting for surgical wounds to heal sufficiently to prevent dialysate leak was not possible after failure of central venous catheter insertion due to central vein stenosis of the patient was noted. Simultaneous removal and replacement of PD catheter was performed, and PD was not interrupted. Published studies regarding the alternative surgical management of PD catheter related infection was also reviewed and discussed.

Results: Surgical salvage consisting of unroofing the tunnel tract and shaving of the superficial catheter cuff, partial replantation, and simultaneous removal and reinsertion of the PD catheter had been reported in the literature. These alternative surgical procedures allow significant prolongation of the catheter survival without major complications or interruption of PD.

Conclusions: Several surgical managements appear to be an appropriate alternative to catheter removal for the management of refractory exit-site and tunnel infection. Further controlled studies are needed to prospectively compare these surgical procedures with the traditional catheter removal and latent replacement of the catheter.

ACPN210331O34 PEDIATRIC PERITONEAL DIALYSIS PERITONITIS IN CHINA.

Ms. Yi Hui Zhai[1], Qian Shen[1], Hong Xu[1]
[1]*Children's Hospital Of Fudan University, Shanghai, China*

Methods: Data of 283 pediatric PD patients from the year 2001 to 2018 were retrospectively reviewed and analyzed. The criteria of diagnosis of PD peritonitis was according to the ISPD guidelines.

Results: During the 18 years, the number of PD patients treated in each year has increased from 1 case in 2001 to 113 cases in 2018, which made us the largest pediatric PD center in China. The median PD duration was 13 months (range 1~116 months). The death rate was 40 /1,000 patient-years. In all, 105 episodes of peritonitis were diagnosed in 62 (22%) PD patients. The total rate of PD peritonitis was 0.26 episodes/patient-year, with the lowest level of 0.12 in 2018. Among the 62 patients with PD peritonitis, 25 (40%) had more than one episode. Among 105 episodes, two were recurrent and five were relapsing peritonitis. The positive culture rate of peritonitis had been significant increased from 25% (before 2012) to 84% (2012-2018) ($p<0.05$). Bacteria peritonitis accounted for 92% of infection and the remaining 8% was fungi infection. As to the outcome, none patients died of peritonitis, but 9 (8.6%) patients discontinue PD permanently and convert to HD. Among the 9 cases, 6 were culture positive for fungi.

Conclusion: We reported a low rate of PD peritonitis in pediatric patients from the largest pediatric PD center in a developing country. Following the ISPD guideline and establishing CQI program including retraining and regular in-patient evaluation might be the reasons for the low and decreasing rate of PD peritonitis. PD peritonitis caused by fungi infection had the worst PD outcome, thus required the most attention and concern.

ACPN210331O35 RISK FACTORS AND OUTCOME OF ACUTE KIDNEY INJURY AMONG CRITICALLY ILL CHILDREN IN THE PAEDIATRIC INTENSIVE CARE UNIT

Mr. Wun Fung Hui[1], Mrs Vivian Pui Ying Chan[2], Dr Kam Lun Hon[1], Mr Freddie Poon[2]
[1]*Department of Paediatrics and Adolescent Medicine, Hong Kong Children's Hospital, Hong Kong, Hong Kong,* [2]*Department of Pharmacy, Hong Kong Children's Hospital, Hong Kong, Hong Kong*

Objectives: It is now recognized that acute kidney injury (AKI) contributes significantly to morbidity and mortality among critically ill children. However, the number of studies on its epidemiology in Asia remained limited. We presented the result of the interim analysis of an ongoing prospective cohort study on the epidemiology of acute kidney injury and electrolytes disturbances (E-AKI-Drug Study) in the paediatric intensive care unit (PICU) of a newly established children's hospital.

Method: All children aged 1 month to 18 years old admitted to the PICU of our hospital after 15/06/2020 would be enrolled. Those with pre-existing chronic kidney disease, impaired renal function for ≥3 months, immediate post-renal transplant and short stay in PICU <1 day with no blood taking would be excluded. Children without a urinary catheter would be excluded from urine output calculation. Demographic data, laboratory results of renal function and electrolytes profiles, as well as outcome data would be collected. Acute kidney injury would be defined using the KDIGO criteria. The results of the data collected from 6/2020 to 10/2020 would be presented.

Results: Altogether 62 patients with 63 episodes of admission were enrolled for the analysis. 58.7% were male and the median (25th, 75th percentile) age was 6.1 (1.6, 12.7) years old. 49.2% of patients had an underlying diagnosis of malignancy and 9.5% of them were recipient of bone marrow transplantation. 31.7% of patients were admitted after an operation. The prevalence of AKI on admission to PICU was 40.3% (stage 1: 17.7%, stage 2: 14.5%; stage 3: 8.1%). The overall incidence of AKI during PICU stay was 55.6% using either the creatinine-based or urine output-based criteria (stage 1: 20.6%, stage 2: 15.9% and stage 3: 19.0%). Most patients experienced AKI on Day 1 of PICU admission and most of them fulfilled the creatine-based criteria (Figure 1). Those with AKI had a more types of electrolytes disturbances (5 types vs 3 types, $p<0.01$). Urine output and fluid overload on Day 1 of PICU admission were not significantly different between those with and without AKI. Recipient of bone marrow transplantation (relative risk [RR with 95% confidence interval]: 1.58 [1.03, 2.44]), requirement of inotropic support (RR: 1.74 [1.17, 2.59]) and non-invasive ventilation (RR: 1.76 [1.22, 2.55]), and a higher number of nephrotoxic medication exposure (RR: 1.20 [1.04, 1.38]) were associated with higher risk of AKI during PICU admission (Table 1). Concerning the outcome, the overall mortality was 4.8% and 6.3% of patients required continuous renal replacement therapy. Comparing with children without AKI, patients with AKI had a longer PICU length of stay (4 days vs 3 days, $p=0.004$) and hospitalization period (11 days vs 23 days, $p=0.036$) and a lower estimated glomerular filtration rate (eGFR) (136.1 vs 174.1 ml/min/1.73m2, $p=0.012$) upon PICU discharge. Altogether 7.9% of patient were discharged from PICU with impaired renal function and 3.2% of them were dialysis-dependent.

Conclusion: AKI was commonly encountered among critically ill children with an incidence of 55.6% during PICU admission. History of bone marrow transplantation, requirement of inotropic and non-invasive ventilatory support, and nephrotoxic medications exposure were significant predictors for AKI development. Those who had AKI were associated with a higher mortality, longer PICU and hospital stay and a lower eGFR on PICU discharge. A significant proportion of children with AKI were discharged with impaired renal function and long term follow-up is required.

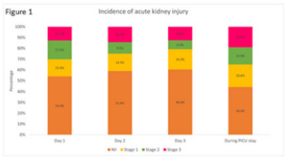


Table 1: Risk factors for development acute kidney injury during PICU admission

Clinical variable	With AKI	No AKI	p-value	Unadjusted relative risk (95% CI)
Male sex	24 (68.6%)	13 (46.4%)	0.076	1.53 (0.92, 2.55)
Age (year)	5.3 (1.3, 13.0)	7.4 (4.5, 11.8)	0.740	1.000 (0.996, 1.004)
Post-operative monitoring as indication of PICU admission	7 (20.0%)	13 (46.4%)	**0.025**	0.53 (0.28, 1.01)
Past medical history				
History of malignancy	21 (60.0%)	10 (35.7%)	0.055	1.55 (0.98, 2.46)
BMT recipient	5 (14.3%)	1 (3.6%)	0.214	**1.58 (1.03, 2.44)**
Shock index on admission	1.1 (0.9, 1.4)	1.1 (0.9, 1.2)	0.698	1.31 (0.61, 2.83)
PIM3 predicted mortality (%)	1.9 (1.2, 5.9)	1.2 (0.2, 1.5)	**0.018**	1.03 (0.99, 1.07)
Required inotropes support	15 (42.9%)	4 (14.3%)	**0.026**	**1.74 (1.17, 2.59)**
Required mechanical ventilation	11 (31.4%)	5 (17.9%)	0.257	1.35 (0.87, 2.08)
Required non-invasive ventilation	11 (31.4%)	2 (7.1%)	**0.027**	**1.76 (1.22, 2.55)**
Medication risk				
Total number of nephrotoxic medications	3.0 (1.0, 4.0)	1.0 (0.0, 1.5)	**<0.01**	**1.20 (1.04, 1.38)**
Total number of doses of nephrotoxic medications	25.0 (6.0, 55.0)	1.0 (0.0, 13.5)	**<0.01**	1.00 (1.00, 1.01)

*Expressed as either number (percentage) or median (25th, 75th percentile)
AKI: acute kidney injury; BMT: bone marrow transplantation; CI: confidence interval; PIM: Pediatric Index of Mortality

ACPN210331O36 CLINICAL USE OF URINARY-LIVER FATTY ACID BINDING PROTEIN (U-LFABP) IN VERY PRETERM NEONATES

Mrs. Henny Adriani Puspitasari[1], Dr Retno Palupi Baroto[1], Dr Eka Laksmi Hidayati[1]
[1]*Medical Faculty Of Universitas Indonesia, Cipto Mangunkusumo General Hospital, Jakarta, Indonesia*

Background: Very preterm neonates were born with lower amount of functional nephrons and immature tubular function. Hemodynamic stressors and nephrotoxic medications use poses risk to develop acute kidney injury (AKI). Acute kidney injury is related to longer hospitalization and higher mortality rate. Traditionally, AKI is diagnosed by measuring serum creatinine and urine output, which are not reliable markers in neonates due to maternal influence and non-oliguric type of AKI. Thus, more reliable and non-invasive markers are needed for early diagnosis and evaluation of AKI in this special population. Urinary excretion of LFABP which reflects proximal tubular epithelial cells injury is one of the proposed biomarker.

Objectives: This study aimed to describe the clinical profiles of very preterm neonates with high u-LFABP and clinical usefulness of u-LFB as a predictor of AKI and disease outcome.

Methods: A prospective cohort study was conducted in neonatal units of tertiary hospital, Cipto Mangunkusumo hospital, Jakarta, Indonesia. Participants were neonates born at 28-32 weeks gestational admitted to neonatal intensive care unit. The exclusion criteria were intrauterine growth retardation (IUGR), major congenital anomalies and those without parental consents. Particpiants were managed according to local NICU guidelines by neonatologist. Urine samples were taken 3 times at age 0-48 hours (T1), 72 hours (T2), and 21 days (T3) for u-LFABP examination. Urinary-LFABP was tested with immunochromatography methods semiquantitavely using human FLABP POC kit (CMIC, Tokyo, Japan); and categorized into normal (<12.5 ng/mL) and abnormal (□12.5 ng/mL). Data of anthropometry, sepsis, necrotizing enterocolitis (NEC), patent ductus arteriosus (PDA), the use of nephrotoxic medications and serum creatinine level were recorded from medical records when available.

Results: Twenty eight very preterm neonates were recruited, comprised of 57.1% males with median gestational age of 30 weeks (range 28-32) and mean birth weight of 1277.82 g (SD 237.43). Urinary LFABP level was found abnormal in 69.2% neonates at 0-48 hours, 83.3% neonates at 72 hours, and 65% neonates at day 21. Gestational age was significantly associated with level of u-LFABP on 0-48 hours (median 29 weeks (range 28-30) vs 31 weeks (range 30-31), p=0.03). Participants with lower birth weight had abnormal level of u-LFABP at 0-48 hours (1220 (SD □241.67) vs 1449.25 (SD □159.83), p= 0.022) and 72 hours (1234.70 (SD □203.29) vs 1548.75 (SD □259.92), p= 0.013). The use of nephrotoxic agents was substantially associated with abnormal u-LFABP at 0-48 hours (p= 0.02). During 3 weeks of follow up, we did not find any significant association between u-LFABP and mortality as well as length of stay. Abnormal u-LFABP was found in neonates with NEC compare to neonates without NEC at 0-48 hours (77.8% vs 22.2%, p=0.667), 72 hours (87.5% vs 12.5%. p=1.0), and day 21 (66.7% vs 33.3%, p=1.0). In PDA group, abnormal u-LFABP was also found compare to non-PDA group at 0-48 hours (90.9% vs 9.1%; p= 0.149), 72 hours (80% vs 20%; p= 1.0) and 21 days (66.7% vs 33.3%; p= 1.0). Abnormal u-LFABP level was similar in sepsis vs non-sepsis group. Serum creatinine levels were recorded in 7 of 28 patients. Of these patients, 4 (57.14%) was diagnosed with AKI. Three (100%) patients with AKI had abnormal u-LFABP at 0-48 hours.

Conclusions: The proportion of very preterm neonates with abnormal u-LFABP was found largest at 72 hours of age. Urinary LFABP was associated with gestational age, birthweight, and the nephrotoxic agents exposure. Further studies with larger sample size are warranted to investigate the clinical use of u-LFABP as a novel biomarker for detecting early tubular injury in very preterm neonates.

ACPN210331O37 GENETIC BACKGROUND OF INFANTS WITH URINARY TRACT INFECTION AND TRANSIENT PSEUDOHYPOALDOSTERONISM TYPE 1

Mr. Jhao-Jhuang Ding[1,2], MD, PhD Min-Hua Tseng[1], MD Shih-Hua Lin[3]

[1]Division of Nephrology, Department of Pediatrics, Chang Gung Memorial Hospital and Chang Gung University, Taoyuan, Taiwan, [2]Department of Pediatrics, Tri-Service General Hospital, National Defence Medical Center, Taipei, Taiwan, [3]Division of Nephrology, Department of Medicine, Tri-Service General Hospital, National Defence Medical Center, Taipei, Taiwan

Objectives: Transient pseudohypoaldosteronism type 1 (PHA1) is a severe complication of urinary tract infection (UTI) in infants. A detailed clinical and molecular analysis for this patient cohort is still lacking. This study aims to determine the genetic influences of infants with UTI and transient PHA1.

Methods: Infants with UTI who exhibited features of transient PHA1 were prospectively enrolled. Clinical characteristics, laboratory studies, and renal images were determined with follow-up. Direct sequencing of genes responsible for genetic PHA1 was performed.

Results: They included twelve infants (9 male) with an age of 1-8 months. All exhibited hypovolemic hyponatremia, hyperkalemia, metabolic acidosis, low TTKG, and relatively elevated FENa, high plasma renin and aldosterone levels. Seven had hyperkalemia-related arrhythmia and two of them developed life-threatening ventricular tachycardia. With prompt therapy for PHA1 and UTI, clinical manifestations and biochemical abnormalities were all resolved. Five patients had normal urinary tract, and 3 of them carried genetic variants on NR3C2. Three variants on NR3C2, including c.1645T>G (S549A), c.538G>A (V180I), andc.1-2C>G, were identified in 4 patients. During follow-up, none of them had recurrence of PHA1 and 4 of them developed renal scarring.

Conclusion: Besides the well-known urinary tract anomalies, genetic mutations on NR3C2 may contribute to PHA1 in UTI infants without identifiable risk factors.

ACPN210331O38 CYSTIC FIBROSIS IN A TAIWANESE INFANT WITH TWO HETEROZYGOUS MUTATIONS: A CASE REPORT

Mr. Yung-Chieh Huang[1], Dr. Lin-Shien Fu[1]

[1]Taichung Veterans General Hospital, Taichung, Taiwan

Objectives: Cystic Fibrosis (CF) is an extremely rare disease in Asia. The disease's clinical manifestations vary, mostly as gastrointestinal, respiratory and/or genitourinary. We present a four-month-old male infant with initial presentation with poor oral intake and dehydration, along with hyponatremia, hypokalemia, hypochloremia and metabolic alkalosis. After two episodes of hospitalization, and patient was confirmed as CF via genetic analysis.

Methods: We present the patient's medical history, including physical examination, serum and urine electrolyte profiles, and the result of genetic analysis.

We also reviewed current literatures about cystic fibrosis in Asian-Pacific area, with special attention on their electrolyte imbalance and genetic analysis.

Results: This infant had FENa as low as 0.24% and TTKG was 22.4 when his serum K was 3.0mEq/L. Two heterozygous mutations of CFTR gene were found in this patient, c.1766+5G>T and c.3883_3886delATTT. Both mutations have been reported previously as pathogenic, but no report about these two heterozygous mutations present in one patient. He received Na 1.5-1.8mEq/Kg/day supplement by NaCl tablets since 7 months old. His hypokalemia and metabolic alkalosis were corrected and he had fair physical growth.

Conclusions: Despite advanced genetic analysis, CF is still difficult to diagnose with varied clinical presentations and low incidence in Asian population. We hope this case presentation can raise the awareness of CF in daily clinical practices.

ACPN210331O39 THE IMPACT OF ELECTROLYTES AND ACID-BASE DISTURBANCES AND THEIR RELATIONSHIP WITH TUBULAR DYSFUNCTION AMONG CRITICALLY ILL CHILDREN

Mr. Wun Fung Hui[1], Dr Kam Lun Hon[1]

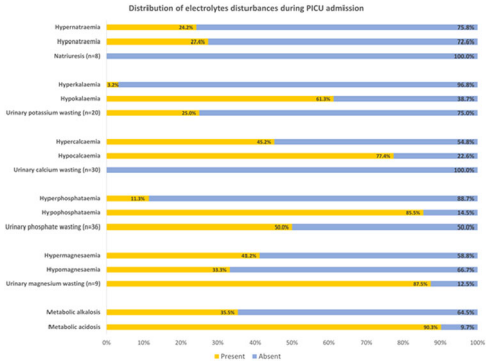
[1]Department of Paediatrics and Adolescent Medicine, Hong Kong Children's Hospital, Hong Kong, Hong Kong

Objectives: Electrolytes and acid-base disturbances are common yet largely ignored problems in critical care. Moreover, the relationship between electrolytes disturbance and acute kidney injury has not been extensively studied among critically children. We presented the results of the interim analysis of an ongoing prospective cohort study on the epidemiology of acute kidney injury and electrolytes disturbances (E-AKI-Drug Study) in the paediatric intensive care unit (PICU) of a newly established children's hospital.

Method: All children aged 1 month to 18 years old admitted to the PICU of our hospital after 15/06/2020 would be enrolled. Those with pre-existing chronic kidney disease, impaired renal function for ≥3 months, immediate post-renal transplant and short stay in PICU <1 day with no blood sampling would be excluded. Demographic data, laboratory results and outcome data would be collected. Appropriate urinary investigations would be carried out if there were electrolytes disturbances. For children with more than two types of electrolytes disturbances, urine beta-2-microglobulin and amino acid would also be determined. The degree of aminoaciduria is expressed as (number of amino acid with its urinary level > upper limit of normal range / total number of amino acids measured) *100%. Acute kidney injury would be defined using the KDIGO criteria. The results of the data collected from 6/2020 to 10/2020 would be presented.

Results: There were 63 episodes of admission identified for the interim analysis. Male patients accounted for 58.7% and the median (25th, 75th percentile) age was 6.1 (1.6, 12.7) years old. 49.2% of patients had an oncological diagnosis and 9.5% of them had received bone marrow transplantation. The overall incidence of AKI during PICU stay was 55.6% (stage 1: 20.6%, stage 2: 15.9% and stage 3: 19.0%). The median number of types of electrolyte disturbance was 4 (2, 5) types. The incidence of the three most common types of electrolytes disturbances were hypophosphataemia (85.5%), hypocalacemia (77.4%) and hypokalaemia (61.3%) respectively. The incidence of metabolic acidosis and alkalosis (determined by either the serum bicarbonate or base excess level) were 90.3% and 35.5% respectively. Figure 1 showed that urinary wasting of potassium, phosphate and magnesium were found in 25% of children with hypokalaemia, 50% of children with hypophosphataemia and 87.5% of children with hypomagnesaemia respectively. Among children with more than two types of electrolytes disturbances, abnormal urinary beta-2-microglobulin level occurred in 64.7% of patient (median level of 0.9 (0.2, 5.2) μg/ml). The median percentage of aminoaciduria was 23.1 (9.5, 47.6) %. The following conditions were associated with more types of electrolytes disturbances: children requiring inotropic (5.0 vs 3.0 types p<0.01) and ventilatory support (5.5 vs 4.0 types, p=0.008) and children with AKI (5.0 vs 3.0 types, p<0.01). Besides, children with AKI had more hypernatraemia (35.3% vs 10.7%, p=0.036) and hypokalaemia (73.5% vs 46.4%, p=0.029). Those with stage 3 AKI also had the highest proportion of hyperphosphataemia compared to those with less severe or no AKI (p=0.002). The number of types of electrolytes disturbances was associated with increased duration of ventilation (p=0.011) and PICU length of stay (p<0.001), and an increased risk of PICU mortality (relative risk 4.3 [95% confidence interval 1.4, 12.7]).

Conclusion: Electrolytes and acid-base disturbances were commonly encountered among critically ill children, especially for hypophosphataemia, hypocalacemia, hypokalaemia and metabolic acidosis. A significant proportion of hypo-electrolytes disturbance may be attributed to urinary wasting of the respective electrolytes, and proximal tubular dysfunction were commonly observed among children with multiple electrolytes disturbances. The occurrence of electrolytes disturbances was more frequently seen in children requiring inotropes and ventilatory support and those with AKI. The degree of electrolytes disturbances would contribute to longer ventilator days, PICU stay and even mortality.



ACPN210331O40 MULTIPLE ELECTROLYTE IMBALANCE RESPONSIVE TO CYCLOOXYGENASE-2 SELECTIVE INHIBITOR IN A FREQUENTLY RELAPSING NEPHROTIC SYNDROME PATIENT : A CASE REPORT

Ms. Budyarini Prima Sari[1], Mr Kristia Hermawan[1], Mrs Madarina Julia[2]

[1]Division of Nephrology, Department of Child Health, Faculty of Medicine, Nursing And Public Health, Universitas Gadjah Mada, Yogyakarta, Indonesia, [2]Division of Endocrinology, Department of Child Health, Faculty of Medicine, Nursing And Public Health, Universitas Gadjah Mada, Yogyakarta, Indonesia

Objectives: We aim to report a frequently relapsing nephrotic syndrome case complicated by severe multiple electrolyte imbalance, i.e. very low level of sodium, potassium, chloride, calcium and magnesium suggesting a tubular defect similar to those observed in Bartter or Gitelman syndrome and its treatment.

Methods: We conducted retrospective review of the medical record of the case. Informed consent was obtained from the child's parents.

Results: The case, an 8 year old boy diagnosed as frequently relapsing nephrotic syndrome since the age of 4 years was admitted due to profuse vomiting for three days. He received alternating dose of prednison (0.5 mg/kgBW/day), lisinopril, calcium and vitamin D. History of medication showed this patient had received several kind of immunosupressive agent before i.e cyclophosphamide, levamisole and cyclosporine during the nephrotic syndrome treatment. In the present admission, beside the usual symptoms of relapse such as oedema and proteinuria (+3), he also suffered from profuse vomiting. The laboratory finding showed severe hyponatremia (113 mmol/L), hypochloremia (71 mmol/L), hypophosphatemia (2.8 mmol/L) and hypoalbuminemia (2.16 g/dL). He had normal urine output, with normal creatinine level (0.27 mg/dL) . Gromerular filtration rate (GFR) was also normal (117 ml/min/1.73m2).

We increased the dose of prednisone into the fulldose of 2 mg/kgBW/day and corrected the hyponatremia intravenously. Although the vomiting resolved and the oedema improved, the patient still suffered from severe hyponatremia, severe hypokalemia, hypochloremia, hypophosphatemia and hypomagnesemia. We repeatedly tried to correct the electrolyte imbalance intravenously. After three attempts, his sodium level was 110 mmol/L, potassium 2.19 mmol/L, chloride 67 mmol/L, calcium 1.76 mmol/L and magnesium 1.35 mmol/L. Blood gas analysis showed metabolic alkalosis (pH 7.67, PCO2 48.1, BE 20, 6 HCO 41.3), while 24-

hours urine revealed normal excretion of sodium and potassium but low excretion of calcium.

The combination of the clinical signs, i.e. persistent severe multiple electrolyte imbalance, metabolic alkalosis and hypocalciuria at onset of more than 6 years old without polyuria and polydipsia and normal blood pressure, suggested a tubular defect similar to those observed in Gitelman syndrome.

We gave cyclooxygenase-2 selective inhibitor celecoxib, spironolactone and potassium supplementation. The clinical signs and the electrolyte imbalances improved. Apart from slight hypomagnesemia, the electrolyte level normalized after 12 weeks of treatment.

Conclusion: In nephrotic syndrome with multiple electrolyte imbalance that did not improve after electrolyte and albumin correction, a possibility of tubular defect responsive to cyclooxygenase-2 selective inhibitor should be considered.

ACPN210331O41 THE IMPACT OF INTERSTITIAL INFLAMMATION ON PEDIATRIC LUPUS NEPHRITIS CLASS III/ IV

Mr. Yung-Chieh Huang[1], Dr. Lin-Shien Fu[1]

[1]*Taichung Veterans General Hospital, Taichung, Taiwan*

Objectives: Lupus nephritis (LN) is one of the most severe clinical manifestations among systemic lupus erythematosus (SLE) patients, especially in children. Renal biopsy is indicted in suspicion of LN in order to determine treatment plans and prognosis. International Society of Nephrology/Renal Pathology Society (ISN/RPS) class III and IV LNs require aggressive immunosuppresion treatment to preserve the patient's renal function. In recent literatures, interstitial inflammation was demonstrated to be an indicator for focal inflammation in lupus nephritis, in contrast to the glomerulonephritis, which reflects systemic autoimmunity. This study, we evaluate the impact of interstitial inflammation on the proteinuria and renal survival in pediatric lupus nephritis.

Methods: We retrospectively reviewed the medical profiles of SLE patients who received renal biopsy when less than or equal to 18 years old at our hospital, a medical center. The pathology findings were reported or reviewed by the same pathologist. ISN/RPS class III and IV LN patients were included for analysis.

Results: Thirty-six pediatric patients who received renal biopsy from 2006 to 2018 were included in our study. Twenty-two patients had interstitial inflammation. Among these 22 patients, the number of score 3, 2, 1 were 7, 5 and 10 respectively.

Patients with interstitial inflammation noted in renal biopsy had higher activity than those without interstitial inflammation (9.59±5.14 vs 4.96 ±3.02, p=0.0017). There was no difference in chronicity in these two groups (1±2.09 vs 0.31±0.63,p=0.128).

The patients with interstitial inflammation score >=2 had higher chronicity scores(1.5±2.64 vs 0.35±0.78, p=0.029) than those with interstitial inflammation score 0 or 1. Besides, patients with interstitial inflammation score >=2 had higher probability of renal failure in 5 years (4/12 vs 1/24, p=0.017). Two patients with interstitial inflammation score >=2 had renal failure despite that their initial biopsy showed chronicity 2 and 0, respectively. The only one renal failure patient without interstitial inflammation had significant thrombotic microangiopathy in her renal biopsy. The existence of interstitial inflammation had no influence on the response of proteinuria to partial or complete remission (urine protein/creatinine <1 or 0.5).

Conclusions: From our study, we found interstitial inflammation, though a component of activity in lupus nephritis, has its own impact on chronicity and renal survival, especially among patients with score >=2.

ACPN210401O43 CLINICAL CHARACTERISTICS, TRIGGERING ETIOLOGIES, AND RESPONSE OF PLASMAPHERESIS IN THROMBOTIC MICROANGIOPATHY IN TAIWAN

Mr. Ching Hu Chung[1], Ms. I-Jung Tsai[2], Mr. Min-Hua Tseng[3], Mr. Hsin-Hsu Chou[4], Mr. You-Lin Tain[5], Mr. Jeng-Daw Tsai[6], Mr. Yuan-Yow Chiou[7], Mr. Yee-Hsuan Chiou[8], Mr. Ching-Yuang Lin[9]

[1]*Department of Medicine, Mackay Medical College, New Taipei, Taiwan,* [2]*Division of Nephrology, Department of Pediatrics, National Taiwan University Children Hospital, Taipei, Taiwan,* [3]*Division of Nephrology, Department of Pediatrics, Chang Gung Memorial Hospital, , Taiwan,* [4]*Department of Pediatrics, Ditmanson Medical Foundation Chia-Yi Christian Hospital, , Taiwan,* [5]*Division of Pediatric Nephrology, Chang Gung Memorial Hospital-Kaohsiung Medical Center, Kaohsiung, Taiwan,* [6]*Division of Nephrology, Department of Pediatrics, MacKay Children's Hospital, Taipei, Taiwan,* [7]*Departments of Pediatrics, Institute of Clinical Medicine, National Cheng Kung University Medical College and Hospital, Tainan, Taiwan,* [8]*Department of Pediatrics, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan,* [9]*Clinical Immunological Center, China Medical University Medical College and Hospital, Taichung, Taiwan*

Background: Thrombotic microangiopathy (TMA) syndromes are extraordinarily diverse in clinical presentations and aetiologies. However, there are still a limited number of large cohort studies focusing on the underlying causes, outcomes and response to plasmapheresis.

Methods: A retrospective study was designed to understand trigger aetiologies, organ dysfunctions, clinical outcomes and efficacy of plasmapheresis in patients with TMA. The whole population of Taiwan was set up into 2 cohorts: 875 patients with TMA in the 2006 cohort (2006–2010) and 1352 patients with TMA in the 2011 cohort (2011–2015). 195 patients in the 2006 cohort and 272 patients in the 2011 cohort were under plasmapheresis treatment.

Results: The common underlying aetiologies were pregnancy, followed by systemic lupus erythematosus, rheumatoid arthritis, transplantation and drugs, which were significantly higher than the control group. Stroke, seizure, arterial thrombosis, vascular stenosis, hypertension, myocardial infarction and pancreatitis were the main clinical signs and extra-renal involvements. In the multivariate regression analysis, stroke, arterial thrombosis, peripheral arterial disease and uraemia were significantly higher compared with the control group. The mortality rate in TMA under plasmapheresis was significantly higher than all TMA cases (39.33% vs 15.39% in the 2006 cohort and 39.27% vs 15.06% in the 2011 cohort).

Conclusions: This study indicated the spectrum of underlying causes, extra-renal characteristics and the response to plasmapheresis of patients with TMA in Taiwan. Of note, the poor clinical outcomes of plasmapheresis in patients with TMA might highlight the masked underlying aetiology or worse disease condition that should be noticed.

ACPN210401O44 MEMBRANOUS NEPHROPATHY IN A BOY WITH POMPE DISEASE UNDERGOING ENZYME REPLACEMENT THERAPY

Mr. Keigo Sasaki[1,2], Shuichi Ito[1,2], Toru Uchimura[2], Aya Inaba[2], Kenichi Ohashi[3], Mai Matsumura[3], Masako Otani[4], Junko Hanakawa[5], Koji Muroya[5]

[1]*Department of Pediatrics , Yokohama City University Medical Center, Yokohama, Japan,* [2] *Department of Pediatrics , Yokohama City University Hospital, Japan , Yokohama, Japan,* [3]*Department of Pathology , Yokohama City University Hospital, Japan, Yokohama, Japan,* [4]*Department of Pathology , Yokohama City University Medical Center, Japan, Yokohama, Japan,* [5]*Department of Endocrinology and Metabolism, Kanagawa Children's Medical Center, Japan, Yokohama, Japan*

Backgroud: In glycogen storage disease type II (Pompe disease), glycogen is accumulated in lysosomes due to deficiency or decrease in acid α-glucosidase (GAA) activity, and various organ involvements are exhibited. Early initiation of enzyme replacement therapy (ERT) using recombinant a-glucosidase (rhGAA) can improve the outcome. Patients producing some GAA are labeled as cross-reactive immunologic material (CRIM)-positive. A few patients are unable to synthesize any GAA and are labeled "CRIM-negative". CRIM-negative patients have been known to have poor outcome from ERT due to the development of anti-rhGAA antibodies that neutralize the rhGAA. Additionally, some patients develop immune-complex mediated glomerulonephritis due to the production of anti-rhGAA IgG.

Case: The case is a boy with late-onset Pompe disease. At 3 years-of-age, he was found to have motor developmental delay, Gowers' sign, muscle hypertrophy of the lower limbs, and elevated serum creatine kinase and aldolase. At 4 years and 7 months, he was diagnosed with Pompe disease based on the results of muscle biopsy and decreased GAA activity. Treatment was started with rhGAA once every 2 weeks, but an allergic reaction appeared from the third infusion, and anaphylaxis was often exhibited. As the patient was positive for anti-rhGAA antibody,so steroids, rituximab, and methotrexate were used, but the antibody titer remained high. At the age of 14 years, proteinuria was detected by urinalysis and the patient was referred to our institute for further evaluation. Renal biopsy revealed stage II membrane nephropathy. Anti-rhGAA antibody-specific immunostaining showed diffuse positive staining along the glomerular loop, suggesting that the cause was an anti-rhGAA/rhGAA immune complex. Thereafter, aggressive combined immunotherapy with bortezomib and rituximab targeting antibody-producing cells was initiated. Serum levels of anti-GAA antibody significantly decreased following this treatment and the proteinuria resolved.

Conclusions: There have been few reports of membranous nephropathy associated with ERT for Pompe disease. Routine urinary screening in patients undergoing ERT should be considered. We successfully clarified the cause in our patient by immunostaining. Suppression of anti-rhGAA antibody production by bortezomib and rituximab was effective both in improving proteinuria and preserving the efficacy of ERT. In groups with high anti-rhGAA antibody titers, aggressive B lymphocyte and plasma cell-targeted therapy could be a good option. However, the optimal therapeutic regimen and its indications have not yet been established. It is also necessary to develop therapies to increase tolerance to ERT.

ACPN210401O45 EARLY RECOGNITION AND MANAGEMENT OF CYSTINURIA: MEDICAL TREATMENT OF RARE KIDNEY STONE DISORDER

Mr. Yen Wen Tseng[1], Mr. Chao-Ting Teng[1], Mr. Yi-Hsuan Tang[1,2,3], Ms. Hui-Lan Chen[1,3,4], Mr. Chien-Hung Lin[1,2], Ms. Hsin-Hui Wang*[1,2,3], Ms. Chia-Feng Yang[2,5], Mr. Dau-Ming Niu[5,6]

[1]*Department of Pediatrics, Division of Pediatric Immunology and Nephrology, Taipei Veterans General Hospital, Taipei, Taiwan,* [2]*Department of Pediatrics, Faculty of Medicine, School of Medicine, Taipei, Taiwan,* [3]*Institute of Emergency and Critical Care Medicine, School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan,* [4]*Department of Pediatrics, Keelung Hospital, Ministry of Health and Welfare, Keelung, Taiwan,* [5]*Department of Pediatrics, Division of Pediatric Genetics and Endocrinology, Taipei Veterans General Hospital, Taipei, Taiwan,* [6]*Institute of Clinical Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan*

Objectives: Cystinuria is an inherited disorder of the dibasic amino acid transport system in the proximal tubule and the small intestine. It is also a relatively uncommon cause of pediatric stone disease, but has significant morbidity if not properly controlled because of its significant stone recurrence rate. The inability of renal tubules to reabsorb cystine and the relative insolubility of cystine at physiological urine pH lead to stone formation, which typically manifests in the first two decades of life. Approximately 50% of cystinuric patients develop their first stone in the first decade of life and 25% to 40% during their teenage years. Most patients will require surgical intervention for stone removal, although compliance with prevention strategies reduces the need for intervention.

Up to 70% of patients with cystinuria may develop some form of chronic kidney disease, which may lead to end stage renal disease. Compared with calcium oxalate stone formers, patients with cystinuria are more likely to have abnormal serum creatinine levels and are at higher risk for nephrectomy. Given the severity and chronicity of these conditions, as well as the associated risk of progressive renal injury, the importance of early diagnosis and appropriate management cannot be overemphasized.

Methods: We demonstrated the clinical course of cystinuria with recurrent hematuria, abdominal pain and recurrent renal stone. The effect of medical treatment and regular long-term follow up was evaluated.

A 19-year-old girl experienced episodes of cramping flank pain with hematuria since 15-year-old. There was no family history of nephrolithiasis. She visited emergency room several times due to cramping pain and underwent extracorporeal shock wave lithotripsy for renal stone removal. Due to repeated renal stone formation, she visited our hospital for further evaluation and treatment. No hypercalciuria was noted. The urine amino acid analysis revealed elevated cystine level.

Results: We initiated treatment of urine alkalization over pH 7.0 with potassium citrate, high diuresis, over 3.5 liters per day, well distributed throughout the day and night, and restriction of sodium intake, less than 2 grams per day. Dietitian also educated the patient about the restriction of protein intake, 0.8 to 1.0 gram per kilogram per day. In subsequent ultrasonography follow-up, no new stone formation was noted. There was no more episodes of emergency department visit due to abdominal pain with stone obstruction. During the long-term follow up period, occasional small stone formation was noticed by renal sonogram, which was correlated to the patient's not achieving our treatment plan of fluid intake or medication. Under well patient education, the patient understood the importance of high diuresis and urine alkalization, and better compliance can achieve. Overall benefits of medical treatment included decreasing renal stone formation, preserved renal function and less emergency department visits, which was associated with decreased risk of radiation exposure, such as x-ray and CT scan.

Conclusions: Although many advances have been made in the understanding of the genetic and physiological basis of cystinuria, the cornerstones of treatment still involve stone prevention with high diuresis, urinary alkalization, pharmacologic therapy, coupled with surgical interventions for stone removal. Poor control of recurrent renal stone will have renal function damage. It also increases risks of radiation exposure and surgical interventions. Considering reduced complications and preserved renal function, the importance of early diagnosis and management cannot be overemphasized. High diuresis, urine alkalization, sodium and protein restriction are effective in stone formation prevention. Patient education and long-term follow up are very important for good patient compliance and treatment outcome.

ACPN210401O46 A MULTICENTER PROSPECTIVE COHORT STUDY TO COMPARE THE EFFICACY OF STANDARD PRACTICE THERAPIES FOR CHILDHOOD IGA NEPHROPATHY IN CHINA

Mrs. Xuhui Zhong[1], Jie DING[1], Zhihui LI[2], Jianhua ZHOU[3], Yan GAO[4], Xiaoyun JIANG[5], Zhengkun XIA[6], Shuzhen SUN[7], Shipin FENG[8], Li YU[9], Xiqiang DANG[10], Chaoying CHEN[11], Jianhua MAO[12], Dongfeng ZHANG[13], Qiu LI[14], Zihua YU[15], Wenyan HUANG[16], Yan Liu[17], Jiangwei LUAN[18], Ying BAO[19], Xiaorong LIU[20], Aihua ZHANG[21], Fang DENG[22], Qingshan MA[23], Qing YANG[24], Bili ZHANG[25], Ruifeng ZHANG[26], Rui FU[27]

[1]Peking University First Hospital, No. 1, Xi An Men Da Jie, Beijing, China, [2]Hunan Children's Hospital, Changsha, China, [3]Tongji Hospital, Wuhan, China, [4]Guangzhou Women and Children's Medical Center, Guangzhou, China, [5]First Affiliated Hospital, Sun Yat-Sen University, Guangzhou, China, [6]Nanjing PLA General Hospital, Nanjing, China, [7]Shandong Provincial Hospital, Jinan, China, [8]Chengdu Women's and Children's Central Hospital, Chendu, China, [9]Guangzhou First People's Hospital, Guangzhou, China, [10]The Second Xiangya Hospital of Central South University, Changsha, China, [11]Capital Institute of Pediatrics, Beijing, China, [12]The Children's Hospital of Zhejiang University School of Medicine, Hangzhou, China, [13]Children's Hospital of Hebei Province, Shijiangzhuang, China, [14]Children's Hospital of Chongqing Medical University, Chongqing, China, [15]Fuzhou General Hospital, Fuzhou, China, [16]Shanghai Children's Hospital, Shanghai, China, [17]The First People's Hospital of Yunnan, Kunming, China, [18]Wuhan Women and Children's Medical Center, Wuhan, China, [19]Xi'an Children's Hospital, Xi'an, China, [20]Beijing Children's Hospital, Beijing, China, [21]Nanjing Children's Hospital, Nanjing, China, [22]The First Affiliated Hospital of Anhui Medical University, Hefei, China, [23]First Hospital of Jilin University, Changchun, China, [24]Second Affiliated Hospital of Wenzhou Medical University, Wenzhou, China, [25]Tianjin Children's Hospital, Tianjin, China, [26]Xuzhou Children's Hospital, Xuzhou, China, [27]Jiangxi Province Children's Hospital, Nanchang, China

Objective: This study aims to define treatment patterns for childhood IgA nephropathy in China, and to compare the effectiveness of standard practice therapies in cases with nephrotic proteinuria.

Method: A multicenter Registry of IgA Nephropathy in Chinese Children, entitled "Registry of IgA Nephropathy in Chinese Children" (Clinical Trials.gov NCT03015974), has been established since Jan. 2016. Children diagnosed as IgA nephropathy were enrolled from 30 centers, across China. Demographic, phenotypic, treatment, outcome data and bio specimens were collected, prospectively (http://www.igaregister.com/).

Results: At present, a total of 830 patients was included, with 572 boys and 258 girls. The mean age was 8.9 years old. The proportions of macroscopic hematuria, hypertension and nephrotic proteinuria were 71%, 9% and 52.7%, respectively. The most prevalent immunosuppressive medication prescribed was steroid (69.1%), followed by cyclophosphamide (39.7%), mycophenolate mofetil (13.5%), calcineurin inhibitor (12.1%), etc. According to the medications prescribed, children with nephrotic proteinuria were classified into treatment subgroups of steroids (group A), steroids with CTX (group B) and steroids with MMF (group C). No significant difference was found in the demographic and clinicopathological characteristics among the three subgroups. As for MEST-C score, the percentage of C1/2 in group A (25.4%) was

Conclusion: No significant difference has been found in the efficacy of steroids with or without immunosuppressive agents, in childhood IgA nephropathy with nephrotic proteinuria. Further randomized control study is still needed to identify both effective and safe immunosuppressive regimen.

ACPN210330P01 MORE THAN MEETS THE EYE: A CASE OF INTERNAL JUGULAR VEIN THROMBOSIS AND NECK CYSTIC HYGROMA IN A TEENAGER WITH NEPHROTIC SYNDROME

Ms. Caroline ENG[1], Sangeeta Arumugam[2], Malini Krishnalingam[2], Saraiza Abu Bakar[3], Khairul Azlan Shahril Abu Dahari[4], Shir Fong Tan[1], Joanne Pereira[1], Ming Lee Lee[1], SL Yap[1]

[1] Department of Paediatrics Hospital Tuanku Ja'afar , Seremban , Malaysia, [2]Department of Radiology Hospital Tuanku Ja'afar , Seremban , Malaysia, [3]Department of Orthorhinolaryngology Hospital Serdang, Serdang, Malaysia, [4]Department of Orthorhinolaryngology Hospital Tuanku Ja'afar , Seremban , Malaysia

Introduction: Although thrombosis is a known complication in nephrotic syndrome, internal jugular vein thrombosis is rare. We aim to highlight the unusual presentation of thrombosis and the importance of adequate evaluation.

Case presentation: We herein report a 15 years old adolescent with Steroid Dependent Nephrotic Syndrome who became Steroid Resistant after a relapsing remitting course for over 13 years. We incidentally noted a thrombosis over the left internal jugular vein while attempting central venous cannulation. An MRI thorax subsequently showed a left multilobulated, supraclavicular cystic mass with carotid artery encasement and internal jugular vein compression. Enoxaparin therapy was initiated and the child was planned for a sclerotherapy for the incidentally diagnosed cystic hygroma in the neck.

Conclusion: Internal jugular vein thrombosis is by itself, a rare condition. In a child with a predilection to thrombosis, it is challenging to unravel the underlying contributory factor. A throrough evaluation is necessary to decide on long term thrombolytic therapy.

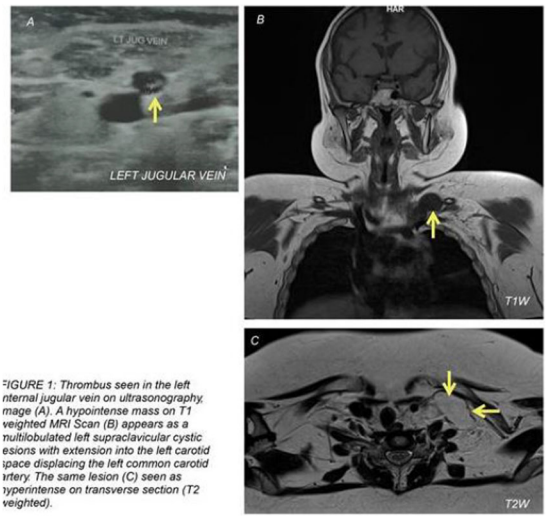


FIGURE 1: Thrombus seen in the left internal jugular vein on ultrasonography image (A). A hypointense mass on T1 weighted MRI Scan (B) appears as a multilobulated left supraclavicular cystic lesions with extension into the left carotid space displacing the left common carotid artery. The same lesion (C) seen as hyperintense on transverse section (T2 weighted).

ACPN210330P02 THE ASSOCIATION BETWEEN THE PREMATURITY AND THE NEPHROTIC SYNDROME

Mr. Chih Chia Chen[1], Mr. Tsung Yu[2], Mr. Hsin-Hsu Chou[3], Mr. Yuan-Yow Chiou[1], Mr. Pao-Lin Kuo[4]

[1]Department of Pediatrics, Division of Pediatric Nephrology, National Cheng Kung University Hospital, Tainan City, Taiwan, [2]Department of Public Health, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan City, Taiwan, [3]Department of Pediatrics, Ditmanson Medical Foundation Chiayi Christian Hospital, ChiaYi City, Taiwan, [4]Department of Obstetrics and Gynecology, National Cheng Kung University Hospital, , College of Medicine, National Cheng Kung University, Tainan City, Taiwan

Background: Idiopathic nephrotic syndrome (INS) may progress to chronic kidney diseases in the pediatric population. However, the data

regarding the risk factors of the INS is sparse and we did not know the relationship between INS and preterm births. We hypothesized that preterm births may predispose subsequent INS development and conduct current population-based study to reveal these association.

Method: By using the nationwide-population-based Taiwan Maternal and Child Health Database (TMCHD), we identified preterm births born between 2004 to 2009 and matched them with term baby by sex and birth year in the 1:10 ratio. The primary outcome is INS incidence. The secondary outcome is associated complications, including the hypertension, end stage renal disease (ESRD), and secondary immunosuppressants usage. Besides univariable analysis, we also perform multivariable analysis adjusting maternal and paternal age at delivery, family income, urbanization and maternal comorbidities because these factors may also influence offspring immune system development.

Results: A total of 78,651 preterm and matched 786,510 term infants were enrolled. Fifty in the preterm (6 per 10,000 population) and 285 in the term cohorts (4 per 10,000 population) had INS development. Preterm infants had a higher incidence than term infants (OR, 1.70 [95% CI: 1.23~2.35]). The INS development risk increased as the gestational age decreased from moderate to late preterm to extremely preterm births after adjustments (Gestational age 32~36 weeks: OR, 1.48 [95% CI: 1.04~2.10]; 29~31 weeks: OR, 3.86 [95% CI: 1.58~9.42]; ≤ 28 weeks: OR, 5.69 [95% CI: 2.11~15.34] , p for trend < 0.001). As the continuous variable, increased gestational ages were associated with decreased INS development (OR, 0.90 [95% CI: 0.85~0.96]). Maternal diabetes also predisposed the offspring to INS (OR, 2.31 [95% CI: 1.15~4.66]). Among the INS population, we found that the preterm birth did not result in a higher rate of complications. (Hypertension: OR, 2.54, [95% CI: 0.63~10.15]; ESRD: OR: 1.43, [95% CI: 0.16~13.10]; Secondary immunosuppressants usage: OR: 0.84, [95% CI: 0.43~1.64]).

Conclusion: In this nationwide-population-based cohort study, the preterm infants have an increased risk of INS but may not be associated with complicated clinical INS courses. Maternal DM will be the risk factor and the underlying mechanisms require further investigations to elucidate their causal relationship.

ACPN210330P03 EFFICACY AND SAFETY OF RITUXIMAB VERSUS TACROLIMUS IN FREQUENTLY RELAPSING NEPHROTIC SYNDROME: AN OPEN LABEL RANDOMIZED CONTROLLED TRIAL WITH NON-INFERIORITY DESIGN

Mr. Georgie Mathew[1], Dr Aditi Sinha[1], Mrs Neetu Grewal[1], Mr Aijaz Ahmed[1], Dr Pankaj Hari[1], Dr Arvind Bagga[1]

[1]*All India Institute of Medical Sciences, New Delhi, India*

Rituximab and tacrolimus effectively prevent relapses in children with frequently relapsing or steroid dependent nephrotic syndrome who have failed multiple steroid-sparing therapies (difficult-to-treat disease). Information on the relative safety and efficacy of these therapies is limited.

Objectives: The primary objective was to compare, in patients with difficult-to-treat steroid sensitive nephrotic syndrome administered intravenous rituximab or oral tacrolimus, the proportions of patients in sustained remission at 1-year follow up. Secondary objectives included comparisons, at 6 and 12-months follow up, of the proportion of patients with frequent relapses and treatment failure [frequent relapses, steroid resistance, significant toxicity related to corticosteroids or intervention necessitating discontinuation of intervention; ≥2 serious adverse events (AE)], frequency of relapses, cumulative prednisolone requirement, the time to first relapse, AE related to intervention and prednisolone use, and changes in body mass index, height and blood pressure standard deviation (SD) scores.

Methods: This single-center open-label randomized clinical trial (RCT) examined the non-inferiority of rituximab (2 doses at 375 mg/m2 one week apart) as compared to oral tacrolimus (0.1-0.2 mg/kg in two divided doses for one year) in patients, 1-18 years-old with difficult-to-treat steroid sensitive nephrotic syndrome (failure of ≥2 therapies). Patients were allocated 1:1 to the two groups using computer-generated random sequences stratified for disease severity and age while ensuring allocation concealment [CTRI/2018/11/016342].

Results: Of 108 patients screened, 41 patients were randomized and 40 included in modified intention-to-treat analysis; one patient allocated rituximab did not return for the infusion. Baseline characteristics were comparable (not shown). Outcomes, tabulated in Table, indicate that non-inferiority of rituximab in sustaining remission for one year was not demonstrated (pre-defined non-inferiority margin, 20%). Frequent relapses were significantly more often in patients administered rituximab versus tacrolimus. Both groups showed considerable and comparable reduction in relapse rates and prednisolone usage (85% and 70%, respectively). Changes in anthropometry were similar between groups and improved significantly from baseline. Serious AE were few and comparable in proportion between groups; chief AE were infusion-related with rituximab and gastrointestinal AE with tacrolimus.

Conclusions: In children with frequently relapsing nephrotic syndrome failing multiple steroid-sparing therapies, rituximab was not non-inferior to tacrolimus in maintaining sustained remission. Compared to tacrolimus, rituximab was associated with increased risk of frequent relapses.

Table. Outcomes at 12 months or at end of study

Outcome	Rituximab (n=20)	Tacrolimus (n=20)	Relative risk or risk ratio	Risk or mean difference	*P*
Primary					
Sustained remission, n (%)	11 (55)	11 (55)	1.0 (0.57, 1.75)	0 (-30,30) %	0.99
Secoadary					
Frequent relapses, n (%)	7 (35)	1 (5)	7 (0.95, 51.8)	30 (7.0, 53.0) %	0.01
Treatment failure, n (%)	7 (35)	1 (5)	7 (0.95, 51.8)	30 (7.0, 53.0) %	0.01
Incident relapse rates, per person year	0.84 (0.48, 1.46)	0.51 (0.24, 0.93)	1.66 (0.75, 3.65)	0.33 (-0.21, 0.85)	0.25
Cumulative prednisolone, mg/kg/day	0.11 (0.05, 0.24)	0.11 (0.04, 0.20)	-	-0.08 (-0.19, 0.03) of	0.15

ACPN210330P04 SPECTRUM OF MAJOR INFECTIONS IN CHILDREN ADMITTED WITH NEPHROTIC SYNDROME-FINDING THE FOCUS

Mrs. Gopika Nair[1], Mr. Mahantesh Patil

[1]*Jawaharlal Nehru Medical College,kaher, Belagavi, India*

Introduction: Infections in Nephrotic syndrome have remained a challenge to pediatricians in reducing morbidity and mortality. Infections trigger the onset of disease or relapse and hence identification and prompt treatment are first line concerns in hospitalised children of nephrotic syndrome who are susceptible to wide spectrum of organisms.

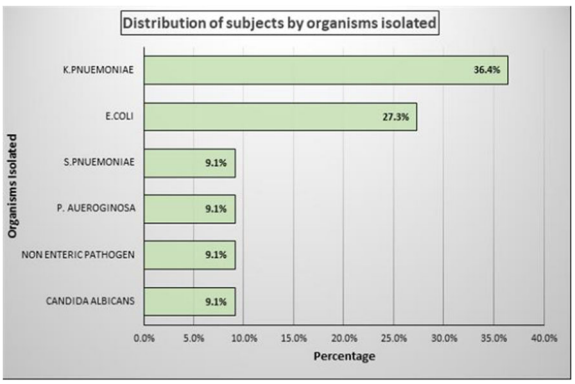
Objectives: In our study we aim at determining the type of infection, causative organism and risk factors causing infections in admitted cases of Nephrotic syndrome over a period of 6 months.

Methods: A Hospital based cross sectional study was conducted in our tertiary care centre, among children between 1- 18 years with nephrotic syndrome satisfying the International Study of Kidney diseases in Children(ISKDC) criteria, from January 2020 to August 2020.Major infections were defined as infections affecting deep organs and tissues which warrant hospitalisation. Suspicion of focus of infection and appropriate diagnostic methods were employed to confirm the diagnosis and an empirical antibiotic therapy based on the antibiogram was started. Complete hemogram, Blood culture and HS-CRP values

were mandatorily evaluated for all patients and based on the focus of infection relevant investigations like ascitic fluid analysis, urine analysis and pus culture were done. Demographic data, anthropometry and clinical examination was recorded in pre designed proforma by bedside clinical history and examination. Collected data was analysed using R software version 4.0.2.Categorical variables represented in frequency table. Frequency of serious bacterial infections and organisms isolated were tabulated.

RESULTS: A total of 40 children were admitted with nephrotic syndrome during this pandemic period of whom 15(40%) developed episodes of major infections.14 out of 15 were relapse cases. Peritonitis was the commonest infection(5),followed by urinary tract infection and septicaemia. Acute gastroenteritis, cellulitis and LRTI were the other infections. Klebsiella Pneumonia and Streptococcus pneumonia which have been rarely reported in association with pediatric nephrotic syndrome were also isolated. Appropriate antibiotic sensitive regimen was followed based on the antibiogram with MIC provided by the microbiology lab. All patients responded to treatment well except for one death owing to severe renal failure, morbid obesity and candidial sepsis.

CONCLUSION: Infections can be serious and life threatening in Nephrotic syndrome, focus targetted and specific antibiotic coverage should be introduced as soon as possible for improving outcome. In concordance with literature we found hypoalbuminemia as risk factor in our study. HS-CRP level was found to be a reliable inflammatory marker. The fewer deaths in our study in contrast to previous Indian studies can be attributed to the early presentation, high index of suspicion and prompt institution of treatment.



ACPN210330P05 BONE MINERAL DENSITY OF CHILDREN WITH NEPHROTIC SYNDROME ADMITTED TO YANGON CHILDREN HOSPITAL

Ms. Htike Zin Zin[1]

[1]*Cho Cho San, Yangon, Myanmar,* [2]*Khin Lei Lei Shein, Yangon, Myanmar*

Introduction: Nephrotic syndrome is one of the most common causes of childhood chronic kidney disease and long term steroid treatment is inevitable. By finding out correlation between bone mineral density and cumulative dose of corticosteroid and correlation between height and cumulative dose of corticosteroid, early and prompt treatment for osteoporosis can be given.

Methods: This cross-sectional descriptive study was done from January to December 2018 in Renal Unit of Yangon Children Hospital. The medical records of patients were reviewed and all doses of prednisolone were converted to prednisolone equivalents (mg/kg/day).They were scanned by Dual-energy X-ray absorptiometry at radiology department, Yangon General Hospital.

Results: Among 33 cases, 45 % of cases were steroid dependent nephrotic syndrome (SDNS), 30% were frequent relapse nephrotic syndrome (FRNS) and 24% were late resistant nephrotic syndrome (LRNS). Most children with SDNS and FRNS were above age of 10 year. Children with LRNS were mostly between 5 to 10 years. Twenty three children (69%) were boys and ten children (31%) were girls. Patients were treated with steroid dose ranging from 0.7 to 3.7 mg/kg/day for duration ranging from 18 to 62 months respectively.

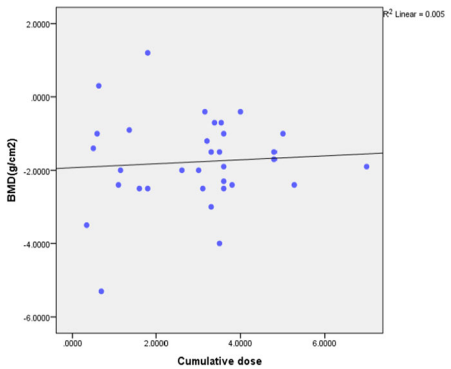
13.3% were osteopenic and 86.7% were osteoporotic in SDNS. 100 % of FRNS and LRNS were osteoporotic. Osteopenia was documented in 2 patients (13.3%) (2 patients of SDNS) and osteoporosis in 31 patients (13 in SDNS, 6.7%), (10 in FRNS, 100%), (8 in LRNS, 100%).

Osteopenia was found at cumulative dose of 1.2 +/- 0.8 mg/kg/day and osteoporosis was documented at cumulative dose of 3.0 +/- 1.6 mg/kg/day. Osteopenia was observed at 30 +/-11 months of steroid duration and osteoporosis was occurred at 38 +/- 17 months of steroid duration.

Conclusion: Prolonged use of corticosteroid can cause osteoporosis and osteopenia and can affect height of children. Osteopenia and osteoporosis can be detected by using DEXA scan. Early detection can prompt early treatment and reduction in steroid dose can affect height of patient. Thus children with nephrotic syndrome should be scanned with DEXA and adjust steroid dose for bone health.

Declaration

I have no potential conflict of interest to disclose.



Correlation between bone mineral density and cumulative dose of corticosteroid

ACPN210330P06 RECOVERY OF HYPOTHALAMIC-PITUITARY-ADRENAL AXIS POST WITHDRAWAL OF CORTICOSTEROIDS IN CHILDREN WITH NEPHROTIC SYNDROME

Mr. Jaiganesh M[3]

[1]*Dr. Jaiganesh. M, post graduate student, chacha Nehru bal chikitsalaya, New Delhi, India,* [2]*Dr. Kirtisudha mishra, associate professor, chacha Nehru bal chikitsalaya, New Delhi, India,* [3]*Dr. Manishkumar, associate professor, chacha Nehru bal chikitsalaya, New Delhi, India*

Objective: Administration of multiple or prolonged courses of exogenous glucocorticoids makes children with nephrotic syndrome (NS) at risk of adrenal insufficiency due to Hypothalamic-Pituitary-Adrenal

(HPA) axis suppression. Considering the insufficient evidence regarding this aspect in nephrotic syndrome, this study aimed to assess the status of HPA axis, three to six months following discontinuation of prednisolone, in children with nephrotic syndrome, and also to evaluate the factors associated with recovery of HPA axis.

Methods: A cross-sectional study, including children with NS, aged 1-12 years, in remission, were enrolled at different durations post discontinuation of steroids. Serum cortisol was measured at baseline (8.00 A.M.) and 1-hour post- ACTH stimulation. The stimulation test was done using long-acting intramuscular ACTH, with cortisol levels being interpreted as per the recently validated study for this ACTH preparation for diagnosing secondary adrenal insufficiency. Accordingly, 'Low baseline cortisol' was considered as a value <138nmol/l or 5□g/dl. An 'optimal response to ACTH' or HPA axis recovery was considered as a value >500nmol/l or 18 □g/dl.

Results: A total of 80 children (60 males), with a median age of 64(IQR 43, 91.8) months, were evaluated. Most children (42.5%) were infrequent relapsers or were enrolled after their first episode of nephrotic syndrome (43.8%), with a small proportion having been frequent relapsers (6.3%) or steroid dependent (7.5%) in the past. While 28.8% of children had discontinued steroids for a period 1month, 43.8% had discontinued for 3 months and 27.5% were off steroids for a period of 6 months.

The mean basal serum cortisol of the children was 266.58 + 112.88 nmol/l, with only 8/80 (10%) of children having low basal cortisol levels. After stimulation with ACTH, the mean serum cortisol level of all the children, was 563 +152.4 nmol/l, with 54/80 (67%) children demonstrated optimal response to ACTH, while 32.5% had HPA axis suppression. Even among the 72 children who had normal basal cortisol levels, 20 (27.8%) could not mount an optimal response post ACTH.

Among the factors analyzed (Table1), female gender and increasing duration since discontinuation of prednisolone was found to be independently associated with post-ACTH cortisol levels. It was deduced from our study that, with every increasing month since discontinuation of prednisolone, the probability of showing a stress response increased by 1.6-fold. Also, low basal cortisol levels below138nmol/l independently predicted sub-optimal post-ACTH response.

Conclusion: The present study thus shows that nearly two-third of children with nephrotic syndrome demonstrate HPA axis recovery between 1 to 6 months post cessation of steroids. Rather than the cumulative dose of prednisolone received, it is the duration since discontinuation of steroids, which independently decides the HPA axis recovery.

Table 1: Multivariate linear regression analysis to assess the adjusted effect of various parameters on post-ACTH mean cortisol levels

Parameters	Co-efficient	95% CI	p-value
Female gender	84.55	12.37 to 156.76	**0.02**
Age(months)	-0.67	-2.56 to 1.22	0.48
Age of onset(months)	0.32	-1.63 to 2.28	0.74
Duration since withdrawal of steroids	17.52	0.04 to 34.99	**0.04**
12 months cumulative dose(mg/kg)	0.37	-0.56 to 1.3	0.43
Basal cortisol <138nmol/l	-190.7	-297.95 to 83.62	**0.001**

ACPN210330P07 FINNISH TYPE CONGENITAL NEPHROTIC SYNDROME WITH EXON SEQUENCING CONFIRMATION IN TAIWAN: A CASE REPORT

Mr. Jien-Wen Chien[1]

[1]*1, Changhua city, Taiwan*

Congenital nephrotic syndrome Finnish type (CNF) is a rare and severe kidney disorder starting soon after birth, characterized by premature birth, a small size for gestational age, and an enlarged placenta. Early-onset nephrosis with heavy proteinuria, hyperlipidemia, hypercoagulopathy, and an immunocompromised status often causes poor growth and early mortality if not treated promptly. The current treatment strategy of parenteral albumin supplementation, a hyper-caloric and protein-abundant diet, and medications to prevent and treat complications has improved patient outcomes by making curative renal transplantation possible. This report describes a female newborn diagnosed with CNF incidentally before the onset of symptoms. To the best of our knowledge, she was the first CNF case with a diagnosis confirmed by genetic testing (whole-exon sequencing) in Taiwan.

ACPN210330P08 RESPONSE TO STEROID AND IMMUNOSUPPRESSIVE THERAPIES MAY PREDICT POST-TRANSPLANT RECURRENCE OF FOCAL SEGMENTAL GLOMERULOSCLEROSIS

Mr. Kenichiro Miura[1], Taro Ando[1], Shoichiro Kanda[1,2], Taeko Hashimoto[1,3], Naoto Kaneko[1], Kiyonobu Ishizuka[1], Riku Hamada[4], Hiroshi Hataya[4], Kiyohiko Hotta[5], Yoshimitsu Gotoh[6], Kei Nishiyama[7], Yuko Hamasaki[8], Seiichiro Shishido[8], Naoya Fujita[9], Motoshi Hattori[1]

[1]*Pediatric Nephrology, Tokyo Women's Medical University, Tokyo, Japan,* [2]*Pediatrics, the University of Tokyo, Tokyo, Japan,* [3]*Pediatrics, Yamagata University School of Medicine, Yamagata, Japan,* [4]*Nephrology, Tokyo Metropolitan Children's Medical Center, Fuchu, Japan,* [5]*Urology, Hokkaido University Graduate School of Medicine, Sapporo, Japan,* [6]*Pediatric Nephrology, Japanese Red Cross Nagoya Daini Hospital, Nagoya, Japan,* [7]*Pediatrics, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan,* [8]*Nephrology, Toho University, Faculty of Medicine, Tokyo, Japan,* [9]*Nephrology, Aichi Children's Health and Medical Center, Aichi, Japan*

Background: Recurrence of focal segmental glomerulosclerosis (FSGS) is a major challenge in kidney transplantation. Several clinical factors, including initial steroid sensitivity, have been associated with increased post-transplant FSGS recurrence risk. However, conflicting data have been reported, possibly due to the heterogeneous pathophysiology of FSGS and the lack of genetic testing of FSGS patients. Further, the response to immunosuppressive therapies have not been evaluated.

Objectives: This study aimed to assess the risk factors for post-transplant recurrence in stringently selected patients based on a comprehensive clinicopathological evaluation and genetic testing.

Methods: Fifty-nine patients aged 1–25 years at FSGS onset who underwent kidney transplantation between 2002 and 2018 in 7 tertiary centers in Japan were enrolled. Patients with secondary, familial, syndromic, and genetic FSGS and those who did not undergo genetic testing were excluded.

Results: Data from 15 kidney transplant recipients were analyzed. None of the patients had pathogenic mutations in the genes known to cause FSGS. Nine patients experienced post-transplant FSGS recurrence, while six patients did not. The proportion of patients who achieved complete or partial remission with initial steroid and/or additional therapies with immunosuppressive agents and/or plasmapheresis was significantly higher in the FSGS recurrence group (all nine patients) than the group without FSGS recurrence (three of seven patients) (P=0.04).

Conclusions: This study suggests that the response to steroid treatment, other immunosuppressive agents, and/or plasmapheresis may predict post-transplant FSGS recurrence. Further studies that examine a larger number of genetic-testing-negative FSGS patients will be needed to validate present findings.

ACPN210330P09 A DISTINCT IMMUNOLOGICAL SUBGROUP IN MINIMAL CHANGE NEPHROTIC SYNDROME WITH EARLY RELAPSE FOLLOWING RITUXIMAB THERAPY

Mr. David Liangjian Lu[1], Dr. Sharon Teo[2], **Dr. Liangjian Lu**[2], Dr. Yiong-Huak Chan[3], Dr. Perry Yew-Weng Lau[1,2], Dr. Mya Than[1,2], Prof. Stanley C Jordan[4], Prof. Kong-Peng Lam[1,5,6,7], Prof. Kar-Hui Ng[1,2], Prof. Hui-Kim Yap[1,2]

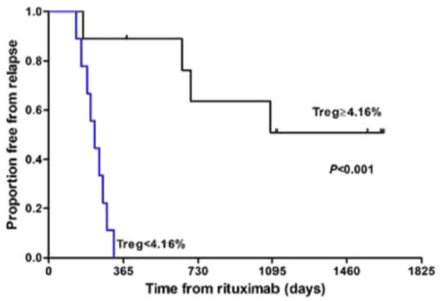
[1]Department of Paediatrics, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore, [2]Khoo Teck Puat-National University Children's Medical Institute, National University Health System, Singapore, Singapore, [3]Biostatistics Unit, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore, [4]Cedars Sinai Medical Center, Los Angeles, United States of America, [5]Bioprocessing Technology Institute, Agency for Science, Technology and Research (A*STAR), Singapore, Singapore, [6]Singapore Immunology Network (SIgN), Agency for Science, Technology and Research (A*STAR), Singapore, Singapore, [7]Department of Microbiology and Immunology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore

Objectives: Rituximab is an important second line therapy in difficult nephrotic syndrome (NS), especially given the toxicity of long-term steroid or calcineurin inhibitor (CNI) use. However, clinical response to Rituximab is heterogenous. We hypothesized that this was underpinned by immunological differences amongst patients with NS.

Methods: We recruited a cohort of 18 patients with steroid-dependent or steroid-resistant childhood-onset minimal change NS who received Rituximab either due to CNI nephrotoxicity, or due to persistent steroid toxicity with inadequate response to cyclophosphamide or CNIs. Immunological subsets, T-cell activation assays and plasma cytokines were measured at baseline and 6-months following Rituximab.

Results: Time to relapse was bifurcated: 56% relapsed within one year ("early relapse"), while the other 44% entered remission mainly lasting ≥3 years ("sustained remission"). At baseline, early relapse compared to sustained remission group had lower regulatory T-cells (Tregs) (2.90±0.28% vs 6.20±0.37%, P<0.001), and lower stimulated IL-2 (0.93±0.5% vs 5.43±1.7%, P=0.014) and IFNγ expression levels (3.79±1.4% vs 10.4±2.7%, P=0.035). Low Tregs strongly predicted early relapse (ROC-AUC 0.99, 95% CI 0.97-1.00, P<0.001, Figure). There were no differences in plasma cytokine levels. Following Rituximab, there was significant downregulation of Th2 cytokines in patients entering sustained remission (P=0.038). In particular, IL-13 showed a highly significant decrease in these patients (0.49±0.1pg/ml, P=0.007), but not in the early relapse group.

Conclusions: In conclusion, early relapse following Rituximab is associated with baseline reductions in Tregs and T-cell hyporesponsiveness, which suggest chronic T-cell activation and may be useful predictive biomarkers. Sustained remission, on the other hand, is associated with downregulation of Th2 cytokines following Rituximab.



ACPN210330P10 SELENIUM LEVEL AS PREDICTOR FACTOR OF REMISSION IN PEDIATRIC NEPHROTIC SYNDROME

Mr. Reza Fahlevi[1], Mrs. Henny Adriani Puspitasari[1], Mrs. Andini Striratnaputri[1], Mr. Sudung O Pardede[1]

[1]Child Health Departement of Cipto Mangunkusumo Hospital - Faculty of Medicine Universitas Indonesia, , Indonesia

Background: The pathogenesis of steroid-resistant nephrotic syndrome (SRNS) and steroid-sensitive nephrotic syndrome (SSNS) has not yet been fully known. Antioxidants such as glutathione peroxidase enzyme (GPx) and its cofactor, selenium, are thought to have an effect of slowing down the progress of nephrotic syndrome (NS). The purpose of this research is to find the possibility of the baseline selenium levels in pediatric patients with nephrotic syndrome to predict the remission status after 3 and 6 months of therapy.

Methods: This research was conducted on 58 SNRS and SNSS patients ages 2 to 18, who visited pediatric nephrology outpatient clinic in our hospital from November 2019 to July 2020, using a consecutive sampling method. Baseline blood selenium level was examined and other data were obtained from the patients. The patients received treatment based on our protocol therapy for SNRS and SNSS. We recorded the urinalysis data after 3- and 6-month therapy to determine the remission status.

Result: Out of 58 patients, 56 complete the follow up until 6 months, 2 other complete only 3 months follow up. Based on the nephrotic syndrome category, 20 (35%) patients were SSNS and 38 (65%) were SNRS. We obtained that blood selenium level of □ 97.5 μg/L best predicted 3 months remission (p=0.011, AUC=0.696), while for 6 months follow up, selenium level of □ 92.5 μg/L was not significantly predict the remission (p=0.23, AUC=0.399).

Conclusion: Selenium level can moderately predict the short term remission of pediatric patients with nephrotic syndrome.

ACPN210330P11 CLINICAL SIGNIFICANCE OF PROBIOTICS FOR CHILDREN WITH IDIOPATHIC NEPHROTIC SYNDROME

Mr. Shoji Tsuji[1], Dr. Tadashi Yamaguchi[1], Dr. Shohei Akagawa[1], Dr. Yuko Akagawa[1], Dr. Jiro Kino[1], Dr. Sohsaku Yamanouchi[1], Dr. Takahisa Kimata[1], Prof. Kazunari Kaneko[1]

[1]Department of pediatrics, Kansai Medical University, Hirakata-shi,, Japan

Objectives: We previously reported that a decrease in butyrate-producing bacteria in the gut is a possible cause of regulatory T cell (Treg) abnormality in children with idiopathic nephrotic syndrome (INS) (Tsuji S, et al. Am J Nephrol. 2018). Therefore, we hypothesized that oral administration of preparation of butyric-acid-producing bacteria might reduce INS relapse and the need for immunosuppressants.

Methods: Twenty patients (median age 5.3 years, 15 male and 5 female) in remission from INS were enrolled in the study and assigned to receive either daily oral treatment with a preparation of 3 g Clostridium butyricum MIYAIRI (CBM) (n=10; median age 6.4 years) or no probiotic treatment (n=10; median age 4.7 years). The number of relapses as a primary endpoint and requirement for immunosuppressive agents as a secondary endpoint were compared between the two groups. In the probiotic treatment group, the analysis of gut microbiota in conjunction with the measurement of Tregs were also performed before and after probiotic treatment.

The $\chi 2$, Wilcoxon signed-rank, and Mann–Whitney U tests were used for statistical analysis.

Results: The probiotic treatment group experienced less frequent INS relapses per year than the non-probiotic-treated group (median numbers of relapse per year: 1.0 vs. 1.8, p=0.016). Further, the requirement for rituximab in the probiotic treatment group was significantly lower than that in the non-probiotic-treated group (2 vs. 7, p=0.025). The percentage of butyrate-producing bacteria was significantly lower before probiotic treatment (2.2% at INS onset) compared with that in healthy children (6.7%; p=0.024). However, it increased significantly after probiotic treatment (4.7%; p=0.017).

The number of Tregs at onset of INS was not different between the probiotic-treated group (median 57.0 /μl) and the non-probiotic-treated group (median 78.1 /μl) (p=0016). Oral CBM was started after INS remission in the probiotic-treated group and Tregs were measured at least twice before and after the start of CBM administration (n=8). Median interval between twice blood sampling was 1.5 months (range: 1.2 months - 2. 6months). Peripheral blood Treg counts were significantly increased after the start of CBM administration (median before: 53.3 cells/μl, median after: 90.6 cells/μl; p = 0.012).

Conclusion: We suggest that the administration of CBM as a probiotic to INS patients effectively reduces INS relapse and the frequency of immunosuppressive drug use. This probiotic can improve dysbiosis at the onset of INS, and increase intestinal butyrate-producing bacteria and Tregs.

ACPN210330P12 HETEROGENEOUS PHENOTYPES OF CONGENITAL NEPHROTIC SYNDROME RELATED TO NPHS1 MUTATION

Mr. Sze Wa Wong[1], Dr. Eugene Yu Yin Chan[1], Dr. Alison Lap Tak Ma[1], Dr. Liz Yuet Ping Yuen[2], Dr. Wai Ming Lai[1]

[1]*Paediatric Nephrology Centre, Hong Kong Children's Hospital, Hong Kong, ,* [2]*Department of Pathology, Hong Kong Children's Hospital, Hong Kong,*

Objective: To review underlying genetic mutations, clinical courses and outcomes in patients with NPHS1-related congenital nephrotic syndrome (CNS).

Method: We retrospectively reviewed all children with genetically confirmed NPHS1-related CNS who presented between 2000 and 2020 at the tertiary paediatric nephrology centre in Hong Kong.

Results: Four patients were identified (Pakistani, 12/F; Pakistani, 20/M; Pakistani, 5/F; Thai/Chinese, 9/M). They all presented with generalized oedema or poor weight gain at a mean age of 1.5 months. All patients required medical therapies to reduce proteinuria and oedema, including regular albumin infusions, indomethacin, ACE-inhibitor and diuretics. Two patients required nephrectomies for proteinuria control. Three patients progressed to end-stage kidney disease (ESKD) and required renal replacement therapy. Time to ESKD ranged from 2.1 to 10 years (mean time to ESRD 5 years). The remaining one patient (patient 2) improved with treatments and only developed stage II chronic kidney disease by early adulthood. Details of clinical characteristics, genetic findings, treatments and outcomes are presented in table 1.

Patient 1 was a girl born to a consanguineous Pakistani couple, with a history of three stillbirths and one neonatal death. She presented on day 18 of life for poor weight gain and symptomatic oedema, together with heavy proteinuria and hypoalbuminemia. Despite initial response to medical therapies, her renal function continued to deteriorate over the years. By 10 years old, she reached ESKD and maintenance haemodialysis was initiated.

Patient 2, born to a non-consanguineous Pakistani family, was an elder cousin of patient 1 with similar presentation at 2.5 months. Although both children inherited the same NPHS1 mutation, he experienced different disease course. Patient 2 attained spontaneous complete remission following supportive medical therapies alone. He developed steroid resistant nephrotic syndrome in later childhood but was able to achieve partial remission with cyclosporine A. He slowly progressed to stage III CKD without major relapse by early adulthood. At the last follow-up, his estimated GFR was 49ml/1.73m2/min.

Patient 3 was the only child of a consanguineous Pakistani couple without significant family and antenatal history. Due to persistent massive proteinuria and poor growth, unilateral nephrectomy was performed at 13 months. Together with institution of gastrostomy feeding, she demonstrated satisfactory catch up growth. She went into ESKD at 25 months of age and is currently awaiting kidney transplantation.

Patient 4 was the first-born of a non-consanguineous Thai and Chinese couple with unremarkable family and antenatal history. He required unilateral nephrectomy and gastrostomy placement at 9 months and was put on automated peritoneal dialysis since 3 years old. He had nephrectomy of the remaining kidney prior to deceased donor kidney transplantation at the age of 7. At the last follow-up, his graft function was satisfactory.

Conclusion: CNS due to NPHS1 mutation can be a heterogeneous group of disease with a wide spectrum of clinical manifestations and outcomes. There is poor genotype and phenotype correlation which highlights the importance of individualized patient care.

Table 1. Clinical characteristics of the 4 patients with NPHS1-related Congenital Nephrotic Syndrome (CNS)

Case	Sex	Age at diagnosis (m)	Mutation			Treatment	Outcomes		
			Site	Nature	Nucleotide change	Conservative	Nephrectomy		Age at ESRD (years)
1	F	0.6	Homozygous exon 27	Nonsense	c.3478C>T p.(Arg1160*)	Albumin infusions	No	HD	10
2	M	2.5	Homozygous exon 27	Nonsense	c.3478C>T p.(Arg1160*)	Diuretics	No	SRNS/ CKD III	N/A
3	F	1	Homozygous exon 22	Frame shift	c.2944dupA p.(Thr982Asnfs*36)	ACEI	Unilateral	HD	2.1
4	M	2	Heterozygous intron 6 exon 7	Splice site frame shift	c.712+2T>A c.809dupG	Indomethacin	Bilateral, sequential	PD followed by KTX	3

ACEI: ACE inhibitor; CKD: chronic kidney disease; ESRD: end stage renal disease; SRNS: steroid resistant nephrotic syndrome; PD: peritoneal dialysis; KTX: kidney transplant

ACPN210330P13 COMPARATIVE PROTEOMIC ANALYSIS OF FSGS FFPE TISSUES FROM CHILDREN USING LABEL-FREE LC-MS/MS QUANTITATIVE PROTEOMICS

Ms. Yi Hui Zhai[1], Jialu Liu[1], Jia Rao[1], Qian Shen[1], Hong Xu[1]

[1]*Children's Hospital Of Fudan University, Shanghai, China*

Objectives Focal segmental glomerulosclerosis (FSGS) is the main cause of SRNS in children. Here, we analysed FFPE protein profiles, aiming to discover disease-specific candidates and the mechanism underlying steroid resistance in FSGS patients.

Methods We utilized liquid chromatography tandem mass spectrometry with an Orbitrap mass analyser to quantify the global protein abundances of clinically well-annotated formalin-fixed paraffin embedded (FFPE) renal biopsies of patients with steroid-sensitive (n=7) and steroid-resistant (n=11) FSGS.

Results Proteomic analysis demonstrated specific signatures between FSGS-SR and FSGS-SS. In total, we quantified 1795 differentially expressed proteins between the two groups. Clustering analysis highlighted distinct proteomic (302 up-regulated proteins, 23 down-regulated proteins) and pathway-level (lysosome, terminal pathway of complement) differences between the FSGS-SR and FSGS-SS groups. One specific lysosome pathway gene, LAMP1, was elevated in FSGS-SR kidneys compared to FSGS-SR kidneys and controls validated by immunofluorescence.

Conclusions Our proteomic study demonstrates that FSGS patients with different steroid sensitivities present distinct proteomic profiles. These proteomic variations are potentially helpful for better predicting patient outcomes and nominating novel therapeutic targets for personalized care. In addition, our data suggest that LAMP1 is associated with proteinuria and can be used as a molecular target for the detection of steroid-resistant FSGS.

ACPN210330P14 ANTI-ANGPTL3-FLD MONOCLONAL ANTIBODY PROTECT PODOCYTE FROM INJURY

Ms. Yi Hui Zhai[1], Xinli Han[1], Qian Shen[1], Jia Rao[1], Hong Xu[1]
[1]*Children's Hospital Of Fudan University, Shanghai, China*

Objective: Podocyte damage has been recognized as a crucial factor in the development of multiple variants of kidney disease, the mechanisms remain largely unknown. Our previous study found that the deletion of Angiopoietin-like protein 3 (ANGPTL3) greatly attenuates proteinuria and podocyte injury in Adriamycin-injected mice. The fibrinogen-like domain (FLD) of ANGPTL3 plays a key role in the process of podocyte damage caused by ANGPTL3. In the present study, our group developed a monoclonal antibody against ANGPTL3-FLD to explore whether this antibody can alleviate podocyte injury in vivo and in vitro.

Methods: We developed a mouse monoclonal antibody against human ANGPTL3-FLD (anti-ANGPTL3-FLD monoclonal antibody, anti-FLD mAb). Adriamycin nephropathy mice model was established by injecting Adriamycin (10.5mg/kg) once through the tail vein. Then, the anti-FLD mAb group was given intraperitoneally for 4 to 8 weeks. Urinary protein, serum total cholesterol, and serum creatinine were detected. Morphological change of renal pathology, podocyte foot processes, and mitochondrial were observed. Before treated with PAN, human conditional immortalized podocytes were pretreated with (or without) anti-FLD antibody mAb. Then, the morphological character of the podocyte was observed by confocal microscopy. The viability of the podocyte was measured by MTT assay. Flow cytometry was used to assess podocyte apoptosis (Annexin-V/7-AAD). Activated Integrin β3 and mitochondrial change were detected by immunofluorescence. The expression of ANGPTL3, Rac1, PGC1a, and other related molecules such as BAX, Bcl2 were measured by western blot.

Results: Compared with mice in the control group, the levels of urinary albumin excretion were increased in mice of the ADR nephropathy group. And the urinary protein levels were significantly decreased in the anti-FLD mAb treatment group than that in the ADR nephropathy group. ADR nephropathy mice developed more severe morphological injuries as evidenced by a tuft adhesion (TA) forms between PECs and the uncovered GBM. Transmission electron microscopy (TEM) further revealed podocyte injury in ADR nephropathy mice as demonstrated by loss of foot processes along the glomerular basement membrane (GBM), podocyte foot process broadening and effacement, and the foot processes were clear and intact without fusion and no electron-dense deposits in anti-FLD treatment mice. By TEM, we also observed the mitochondrial damages in podocytes from ADR nephropathy mice which were alleviated by anti-FLD mAb treatment as evidenced by changes of mitochondrial shape, size, and organization of cristae. In vitro, PAN upregulated ANGPTL3 expression in a time-dependent and dose-dependent manner. Notably, podocyte F-actin rearrangement and apoptosis occurred. The viability of podocyte decreased. And activated integrin αvβ3 on the podocyte surface increased. Pretreatment with anti-ANGPTL3-FLD antibody can reduce the activation of integrin αvβ3 on the surface of podocytes, enhance the survival rate of the podocyte, ameliorate podocyte apoptosis and podocyte F-actin cytoskeleton rearrangement induced by PAN. Under PAN treatment higher percentages of fragmented mitochondria were observed in podocytes, anti-FLD mAb treatment significantly prevented PAN-induced mitochondrial fission.

Conclusion: Our results indicate that anti-ANGPTL3-FLD monoclonal antibody can reduce proteinuria and ameliorated podocyte injury induced by ADR and PAN probably through alleviating damage in mitochondrial in vivo and in vitro. In summary, our study may suggest a new method for protecting podocytes in proteinuric kidney diseases.

ACPN210330P15 A CASE OF PLCE1 MUTATION AND DIFFUSE MESANGIAL SCLEROSIS WITH RAPID PROGRESSION TO END-STAGE KIDNEY DISEASE

Ms. Yoko Takagi[1], Ms. Yasuko Kobayashi[1], Ms. Mariko Takei[1], Ms. Yuka Ikeuchi[1], Ms. Chikage Yajima[1], Mr. Kandai Nozu[2], Mr. Kazumoto Iijima[2], Mr. Takumi Takizawa[1]

[1]*Department of Pediatrics, Gunma University Graduate School of Medicine, Gunma, Japan, 3-39-15, Showa-cho, Maebashi-shi, Gunma 371-8511, Japan,* [2]*Department of Pediatrics, Kobe University Graduate School of Medicine, Japan, 7-5-1, Kusunoki-cho, Chuo-ku, Kobe 650-0017, Japan*

Objective: PLCE1 encodes phospholipase Cε-1 and is known to be one of the causative genes of steroid-resistant nephrotic syndrome (SRNS), which exhibits both diffuse mesangial sclerosis (DMS) and focal segmental glomerulosclerosis (FSGS) in renal pathological findings. There are racial differences in the incidence rate of mutation in PLCE1, as there are many patient reports from the Middle Eastern and Western countries but few from Japan. Most patients with PLCE1 mutations progress to end-stage kidney disease (ESKD) by 5 years of age; however, some reports have shown that renal prognosis differs even among siblings sharing the same mutations. We report a Japanese case of DMS with a PLCE1 compound heterozygous mutation, which rapidly progressed to ESKD.

Patient and Methods:A 3-year-old girl was transferred to our hospital for renal biopsy and further treatment because she had not responded to prednisolone treatment for 4 weeks. Therefore, she was diagnosed with SRNS. We performed renal biopsy and podocyte-related gene screening using genomic DNA obtained from the patient and her parents. PLCE1 and other podocyte-related gene sequences were determined using targeted sequencing with a next-generation sequencer. Sanger sequencing was used to confirm the PLCE1 mutations detected by next-generation sequencing analysis using an automated DNA sequencer.

Results: Histopathological findings showed diffuse mesangial sclerosis, with 30% of glomeruli showing hypercellularity of podocytes. Genetic analysis revealed that the patient had a compound heterozygous mutation in PLCE1: a splice site variant of c.3279+1 G>T in intron 9 on the paternal allele, and a deletion mutation of c.6141_6144 del AAAT in exon 29 of the maternal allele. Although a single course of methylprednisolone pulse therapy was started, aimed at reducing the amount of urine protein of 10 g/day, 58.0 g/g•Cre, the steroid was tapered and stopped after we obtained pathological findings and genetic test results. Estimated glomerular filtration rate calculated from serum creatinine dropped rapidly from 58.8 ml/min/1.73 m2 on admission to the previous hospital to the level associated with ESKD within 6 weeks, accompanied by a decrease in urinary volume. Peritoneal dialysis was eventually introduced. The patient was registered for deceased donor kidney transplant.

Conclusions: We report a case of a Japanese girl who suffered from rapidly progressing ESKD due to DMS with a PLCE1 compound heterozygous mutation. The truncating mutations in PLCE1 resulted in poor renal prognosis.

ACPN210330P16 HYPERTENSION IN CHILDREN WITH INFREQUENTLY RELAPSING NEPHROTIC SYNDROME: A LONGITUDINAL OBSERVATIONAL STUDY.

Mrs. Thottathil Muhsina Fathima[1], Mr Dr Abhijeet saha[1], Ms Dr Sanya Chopra[1], Mr Dr Ajay Raj[2], Mr Dr Dhiraj Bhatt[3], Ms Dr. Aditi Das[1]

[1]. Division of Pediatric Nephrology, Department of Pediatrics, Lady Hardinge Medical College & Kalawati Saran Children's Hospital, New Delhi. , New Delhi, India, [2]Department of Cardiology, ABVIMS & Dr RML hospital, New Delhi., New Delhi, India, [3]Division of Pediatric Cardiology, Department of Pediatrics, ABVIMS, & Dr RML hospital, New Delhi., New Delhi, India

Objectives: Primary: To identify the proportion of IRNS (infrequently relapsing nephrotic syndrome) children developing hypertension during relapse.

Secondary: To study the association of hypertension with dyslipidemia and hypertensive retinopathy during relapse, and left ventricular mass index (LVMI) at 4 weeks of steroid therapy.

Methods: Inclusion Criteria:

Children with IRNS, between 1-12 years of age were included at the time of relapse (off steroid and antihypertensive medications for minimum of 3months).

Sample size With an estimated prevalence of hypertension in IRNS (P) of 25%, alpha error of 5% and an acceptable absolute precision (e) of 10 %, 95% CI, the sample size was estimated as 73. Assuming a 10% attrition, a total of 83 patients were recruited.

Methodology: All the subjects underwent blood pressure measurement, fundus examination, blood and urine investigations at the time of relapse and then at 4 weeks of steroid therapy during remission. In addition to 2017 AAP guideline, hypertension was classified and compared using the 4th report and ESC-ESH guidelines. This study used a linear method of LVM estimation using Devereux and Reichek "cube" formula, LVM =0.8x 1.04 x [(IVSd +LVIDd+PWTd)^3- LVIDd^3]+0.6. Relative wall thickness (RWT) was measured for concentric geometry (CG) at end diastole as RWT= IVSd +PWTd/ LVIDd at 4 weeks of treatment. Blood pressure of parents was classified using the 2017 AHA guidelines. Dyslipidemia in parents was diagnosed using AACE 2017 Guidelines.

Results: Out of the 83 cases enrolled, 32.5% patients developed hypertension during relapse [25.3% stage I and 7.2 % stage II]. The presence of hypertension in the first episode [63.0% vs 19.6 % p=<0.001] and previous relapses [87.5% vs 37.8%; p=<0.001] was significantly associated with the development of hypertension in the current episode. History of hypertension among parents was present in 36.7 % of the patients, of which 29.6% patients were hypertensive and 7.1% were normotensive [p=0.016]. At 4 weeks of follow up, 7.4% had hypertension of which 5.0% had a new onset and 2.3% had persistent hypertension [p= <0.001]. Hypertensive retinopathy was present in 11.1% of patients [p= 0.032] in the hypertensive group. Hypertension at relapse was seen more in persistent dyslipidemia at 4 weeks (48.4%) as compared to non-dyslipidemia group (15.2%) [p=<0.001]. Thirty percent of the patients with hypertension at relapse and 31.5% with persistent dyslipidemia at 4 weeks of therapy had a positive family history of hypertension and dyslipidemia respectively. CG on echocardiography was present in 28.0 % of the hypertensive and 5.5% of the non-hypertensive group. The presence of CG in the non-hypertensive group may be because of masked hypertension. Near perfect agreement was observed in the classification of hypertension between AAP 2017 and 4th report [k=0.963; p <0.001]and also between AAP 2017 and ESC-ESH guideline [k=0.973; p <0.001] in our study. CG had a significant association with a lower serum albumin at the time of relapse [1.36 ± 0.30 vs 1.58 ± 0.31; p=0.045]. Logistic regression analysis showed a higher spot Up: Uc [OR 1.61 (1.09-2.37); p=0.01] at relapse as a risk factor for hypertension.

Conclusion: One third of children with IRNS developed hypertension at the time of relapse. Even though the proportion of patients diagnosed with hypertension decreased after treatment, a few patients showed persistent or new onset hypertension in the absence of proteinuria on follow up. The familial role of hyperlipidemia and hypertension at the time of relapse showed a significant correlation with the persistence of dyslipidemia in patients even after steroid therapy. The higher proportion of hypertensive patients with concentric geometry pattern on an echocardiography indicates the importance of echocardiography to prevent cardiac morbidity in children with IRNS.

ACPN210330P17 THE PREVALENCE OF HYPERTENSION IN CHILDREN OF NEPHROTIC SYNDROME DIAGNOSED AS FREQUENTLY RELAPSING NEPHROTIC SYNDROME AND STEROID DEPENDENT NEPHROTIC SYNDROME IN A TERTIARY CARE HOSPITAL IN SOUTH INDIA

Mr. Ritesh B R[1], Dr Mahantesh V Patil[1]

[1]KAHER,JNMC, Belagavi, India

Objectives: This study was undertaken to find the prevalence of hypertension in patients diagnosed with Frequently Relapsing nephrotic syndrome (FRNS) and Steroid Dependent nephrotic syndrome (SDNS) using Ambulatory blood pressure monitor (ABPM) and its association with cardiovascular morbidity.

Methods: Children between the age group of 1 to 18 years who visited the hospital between June 2019 to June 2020 who were diagnosed to have FRNS and SDNS were enrolled for the study. It was a cross sectional study. Sample size was 49 which was calculated by the Cochran formula. Each patient was monitored for blood pressure via ambulatory blood pressure monitor which is approved by Association for the Advancement of Medical instrumentation, British hypertension society and European society of hypertension for children. Appropriate cuff sizes were used for each patient. The children who were detected to have hypertension were further evaluated with ECHO to look for left ventricular hypertrophy by Devereux formula. These children were also assessed for growth retardation. Data was analyzed using R software version 3.6.1 and Chi square test.

Results: Totally 49 children were included in our study with the mean age being 8.15±3.85 years with a male to female ratio of 1.72: 1. Among the study subjects, 59.2% cases belonged to the category of Steroid Dependent nephrotic syndrome and 40.8% cases belonged to the category of Frequently Relapsing nephrotic syndrome. Prevalence of hypertension measured by the Ambulatory Blood Pressure Monitor in nephrotic syndrome is 61.22%. It includes both categories of patients who have masked as well as ambulatory hypertension as recent studies proved that both these categories were associated with cardiovascular morbidity. Prevalence of hypertension among the groups SDNS and FRNS are 55.17% and 70% respectively. Many hypertensive patients (60%) were detected to have left ventricular hypertrophy. Association of left ventricular hypertrophy with hypertension at a risk for end organ damage (BP load >50%) was separately looked for in SDNS and FRNS cases and it was proven that it was significantly associated with each other. The chances of developing ventricular hypertrophy for hypertensive subjects with a risk for end organ damage in SDNS is 40 times higher than hypertensive subjects without a risk for end organ damage and chances of developing ventricular hypertrophy for hypertensive subjects with a risk for end organ damage in FRNS is 15 times higher than hypertensive subjects without a risk for end organ damage. Growth retardation were seen in 15 (33%) patients. 11(37.93%) of 29 SDNS cases and 4(20%) of 20 FRNS cases had Growth retardation. Among the patients with Steroid Dependent nephrotic syndrome, the mean steroid dependent dosage of the patients with growth retardation was higher (0.21 mg/kg/day) in

contrast to the patients without growth retardation in whom the mean steroid dependent dosage was 0.17 mg/kg/day.

Conclusions: The prevalence of hypertension in children diagnosed as SDNS and FRNS was 61.22% using ABPM. Children with hypertension at a risk for end organ damage (BP load >50%) were significantly associated with development of left ventricular hypertrophy in both FRNS and SDNS.

Association of ventricular hypertrophy with hypertension at a risk for end organ damage among the patients with SDNS and FRNS

Factors	Sub-category	SDNS			FRNS		
		Ventricular hypertrophy					
		Yes	No	P-value	Yes	No	P-value
Hypertension at a risk for end organ damage	Yes	10 (90.91%)	1 (9.09%)		5 (83.33%)	1 (16.67%)	**0.0475**
	No	1 (20%)	4 (80%)	**0.0175**	2 (25%)	6 (75%)	

ACPN2101 ASSOCIATION BETWEEN GASEOUS AIR POLLUTANTS AND IDIOPATHIC NEPHROTIC SYNDROME IN CHILDREN: A 12-YEAR POPULATION-BASED COHORT STUDY

MS. Chieh Wang, Ms. Changching Wei
[1]*China Medical University Hospital, Taichung, Taiwan*

Objectives: To date, there is insufficient knowledge about the association of air pollution and childhood nephrotic syndrome in the real world. This study aimed to evaluate the effects of the three common gaseous air pollutants, including sulfur dioxide, total hydrocarbon, and methane, on the risk of idiopathic nephrotic syndrome in children. **Methods**: We collected data from the Taiwan National Health Insurance Research Database and Taiwan Air Quality-Monitoring Database. Children younger than 18 years old, identified from January 1, 2000, were followed up until the first diagnosis of idiopathic nephrotic syndrome was established or until December 31, 2012. We measured the incidence rates and hazard ratios for idiopathic nephrotic syndrome stratified based on the quartiles (Q1–Q4) of air pollutant concentration. Multivariate Cox proportional hazards models were also applied by adjusting age, sex, monthly income, and urbanization. Results: Compared with participants exposed to Q1 concentrations, the adjusted hazard ratios for idiopathic nephrotic syndrome increased with the sulfur dioxide, total hydrocarbon, and methane exposure concentrations from 0.89 (Q2) to 1.78 (Q4), 2.09 (Q2) to 3.49 (Q4) and 1.21 (Q2) to 7.83 (Q4), respectively. **Conclusions**: Our study revealed that children with exposure to higher concentrations of sulfur dioxide, total hydrocarbon, and methane was associated with an increased risk of idiopathic nephrotic syndrome.

ACPN2102 TREATMENT OPTIONS AND CLINICAL OUTCOMES IN ADOLESCENCE PRIMARY NEPHROTIC SYNDROME

Mr. Chien Hung Lin[1,2], Fellow Yi-Hsuan Tang[1,2,3], Fellow Hui-Lan Chen[1,3,4], Chief Hsin-Hui Wang*[1,2,3]

[1]Department of Pediatrics, Division of Pediatric Immunology and Nephrology, Taipei Veterans General Hospital, Taipei, Taiwan, [2]Department of Pediatrics, Faculty of Medicine, School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, [3]Institute of Emergency and Critical Care Medicine, School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, [4]Department of Pediatrics, Keelung Hospital, Ministry of Health and Welfare, Keelung, Taiwan

Chien-Hung Lin 1,2, Yi-Hsuan Tang1,2,3, Hui-Lan Chen1,3,4, Hsin-Hui Wang*1,2.3

Department of Pediatrics, Division of Pediatric Immunology and Nephrology, Taipei Veterans General Hospital, Taipei, Taiwan{1} Department of Pediatrics, Faculty of Medicine, School of Medicine {2}, and Institute of Emergency and Critical Care Medicine, School of Medicine, National Yang-Ming University{3}, Taipei, Taiwan. Department of Pediatrics, Keelung Hospital, Ministry of Health and Welfare, Taiwan {4}

Objectives: Adolescence primary nephrotic syndrome appear to demonstrate a variety of histopathologic lesions that are not typical for young children and in being less responsive to corticosteroids. Few studies have examined the efficacy of current treatment for adolescence nephrotic syndrome. This study evaluated the relationship between medications and clinical outcomes in patients who had nephrotic syndrome with onset in adolescence.

Methods: We retrospectively studied 9 patients who had nephrotic syndrome with onset in adolescence. Histologic diagnosis, response to initial corticosteroid treatment, immunosuppressive treatment, with or without rituximab as second-line therapy, and relapse patterns were studied. The genetic tests associated with adolescence nephrotic syndrome and drug response were also analyzed.

Results: >Minimal change disease(MCD) was diagnosed in 5 of 9 patients. One was IgA nephropathy, one was focal segmental glomerulosclerosis, another two did not receive biopsy. 8 patients showed response to the treatment of initial corticosteroid treatment, however, clinical relapses were found among 7 patients. One patient has frequent relapse. All 9 patients received at least one immunosuppressive drugs included CsA, MMF and prograft. Rituximab was prescribed in one MCD patient with steroid-dependence and frequent relapse. His genetic testing was done which showed mutation at MUCIN 1 and he was suggested to follow-up for the possibility of medullary cystic kidney disease. All these nephrotic patients with adolescence onset showed normal renal function during study period and free of proteinuria during remission.

Conclusions: Renal outcomes may be improved with early aggressive treatment by additional immunosuppressant and rituximab in adolescence-onset nephrotic syndrome, further follow-up is needed to determine the long-term results of these treatment options. Genetic profiling should be considered in those response of initial therapy are not compatible with the pathology of MCD result. Personalized precision medicine should be considered in adolescence onset primary nephrotic syndrome to improve the treatment and prognosis.

ACPN210330P01 PROGNOSTIC FACTORS AND OUTCOME IN CRITICAL CHILDREN WITH ACUTE KIDNEY INJURY REQUIRING CONTINUOUS RENAL REPLACEMENT THERAPY

Mr. Jhao-Jhuang Ding1,2, MD, PhD Min-Hua Tseng1, MD Shih-Hua Lin3

1Division of Nephrology, Department of Pediatrics, Chang Gung Memorial Hospital and Chang Gung University, Taoyuan, Taiwan, 2Department of Pediatrics, Tri-Service General Hospital, National Defence Medical Center, Taipei, Taiwan, 3Division of Nephrology, Department of Medicine, Tri-Service General Hospital, National Defence Medical Center, , Taiwan

Objectives: Continuous renal replacement therapy (CRRT) had become the preferred device for hemodynamically unstable adults and pediatric

patients. However, the study focused on the impact of CRRT on clinical outcomes in critical pediatric remains limited. This study aims to identify prognostic factors of mortality and the development of advanced chronic kidney disease (CKD) in pediatric patients undergoing CRRT.

Methods: Pediatric patients who underwent CRRT between 2011 and 2018 were retrospectively enrolled. Patients with non-renal indications of CRRT, including inborn error of metabolism, hepatic failure, drug overdose, were excluded. The demographic and clinical characteristics, laboratory data, dose, duration, and efficacy of CRRT dosing, and outcomes were analyzed.

Results: Seventy-five patients with male predominance (M: F=39: 36) were enrolled. The mean age was 8.8±7.15 years old, of which, the youngest patient was 3 days old. Indications for CRRT were acute kidney injury with complicated acid-base imbalance, electrolytes imbalance, and/or fluid overload. The mean duration and replacement dosing of CVVH were 10.0±12.3 days and 37.9±11.0 ml/kg/hr, respectively. The overall survival rate and renal survival rate were 46.67% and 71.42%, respectively. High pediatric risk of mortality score, high pediatric sequential organ failure assessment (pSOFA) score, bone marrow transplantation (BMT), fluid overload >15%, and respiratory failure were significantly correlated with 90-day mortality. Multivariate Cox proportional model revealed that BMT (hazard ratio 3.53, 95% CI 1.43~8.72, p-value=0.006) and pSOFA (hazard ratio 1.14, 95% CI 1.02~1.27, p-value=0.019) were independently associated with 90-day mortality. Among survivors, 10 of 35 had advanced chronic renal disease. High serum fibrinogen on CVVH was independently associated with advanced CKD after AKI (OR 1.01; 95% CI 1.01~1.02). No benefit evidence of high replacement rate was found in this study.

Conclusion: In critical children with AKI requiring CVVH, the underlying BMT and high pSOFA score are the independent risk factors of 90-day mortality and high serum fibrinogen related to the development of advanced CKD.

ACPN210330P02 EARLY INITIATION OF CONTINUOUS RENAL REPLACEMENT THERAPY (CRRT) IN CHILDREN WITH SEVERE DENGUE – A NOVEL TREATMENT APPROACH

Ms. Jana Priya Sugumar[1], Dr. Kalaivani Ganesan[1], Dr. Sasidaran Kandasamy[1]

[1]*Mehta Multispecialty Hospital India Pvt Ltd, Chennai, India*

Objective: We aimed to report our experience in hemodynamically unstable children suffering from severe dengue who were initiated on CRRT in our pediatric intensive care unit (PICU).

Methods: This is a case record review of children admitted with severe dengue who required CRRT over a period of 2 years from June 2017-December 2019.

Results: Seventeen children admitted with severe dengue required CRRT. All 17(100%) children were dialyzed on CVVHDF mode with a prescription for increased pre-dilution to combat hemoconcentration. Nil fluid removal for the initial 2 hours was advised for 6(35%) children. Internal Jugular Vein [15(88%)] was the most preferred mode of access compared to the femoral line [2(12%)]. Both children with femoral lines experienced catheter-related complications such as catheter kink and increased resistance. Heparin [13(77%)] was the standard anticoagulant and in children where saline flushes [4(23%)] were used two had filter clots. Three (18%) children performed well without intubation on high flow oxygen support and CRRT. The average fluid overload percentage on initiation was found to be 4.53% (±0.02). The mean Ejection fraction noted was 50%. The mean duration from PICU admission to CRRT initiation was 24.82 hours. The mean duration of CRRT was 65.94 hrs. Scope for the unrestricted volume of nutritional support in the form of multiple blood component transfusions was noted across the entire sample size (100%). Three (18%) out of seventeen children expired due to disease complications.

Conclusion: Children with severe dengue experience excessive capillary leak whereas adults are more prone to severe bleeding. Fluid overload is an undesirable event occurring in children with hypotensive shock requiring large volumes of fluids for shock reversal. Though no established guidelines are available on the timing of initiation of renal support therapy, the latest consensus is that earlier initiation allows for the quicker achievement of target treatment goals. CRRT is an excellent therapeutic modality as it helps stabilize the hemodynamic status by allowing gentle fluid removal while providing scope for nutritional support. As fluid overload is a major outcome determinant for critically ill children with severe dengue, early initiation of ultrafiltration combined with a target of negative fluid balance in the initial hours of CRRT may improve clinical outcomes. Early initiation of CRRT might also help circumvent invasive mechanical ventilation. Multicentric trials comparing cohorts of children with early and late initiation of CRRT and sub cohorts studying positive pressure ventilation and noninvasive ventilation are required to further understand the benefits of early initiation of renal support therapy.

Table 1. Properties of children with severe dengue who were initiated on CRRT

S.No	Age in months	Sex	Weight in Kgs	Filter Used	Access	MODE	F.O % on initiation	E.F on initiation	Time of initiation from PICU admission (hours)	Duration of CRRT (hours)	Mechanical Ventilation (hours)	Anticoagulant	Significant events related to dialysis	Disease Course	Outcome
1	84	M	25	M-60	IJV	CVVHDF	0.00%	35%	5	63	72	Saline flushes	Filter clot	**	Survived
2	8	F	6.5	HF20	IJV	CVVHDF	8.50%	39%	24	72	118	Heparin		*	Survived
3	108	M	37	M60	IJV	CVVHDF	6.43%	50%	48	120	144	Heparin	Filter clot	***	Expired
4	96	M	23	M60	IJV	CVVHDF	9.80%	50%	72	48	72	Heparin		***	Expired
5	108	F	31	M60	IJV	CVVHDF	5.40%	68%	10	48	0	Saline flushes		*	Survived
6	96	M	19	M60	IJV	CVVHDF	1.70%	75%	96	64	170	Heparin		*	Survived
7	72	F	20	M60	IJV	CVVHDF	4.70%	52%	48	48	140	Heparin		*	Survived
8	84	M	32	M60	FEMORAL	CVVHDF	0.20%	50%	24	48	144	Heparin	Catheter kink	**	Survived
9	132	M	34	M60	IJV	CVVHDF	4.00%	25%	16	39	48	Heparin	Terminated as child expired	#	Expired
10	48	F	18	M60	IJV	CVVHDF	9.30%	58%	10	60	0	Heparin		*	Survived
11	84	F	27	M60	IJV	CVVHDF	2.30%	48%	7	72	70	Heparin		*	Survived
12	144	M	52	M100	FEMORAL	CVVHDF	1.50%	52%	20	90	144	Saline flushes	Increased resistance, filter clot	**	Survived
13	144	F	10	M60	IJV	CVVHDF	4.10%	64%	6	54	0	Heparin		*	Survived
14	60	M	14	M60	IJV	CVVHDF	5.30%	56%	12	80	96	Heparin		**	Survived
15	88	M	20	M60	IJV	CVVHDF	4.21%	39%	10	75	120	Heparin		**	Survived
16	60	F	21	M60	IJV	CVVHDF	3.98%	47%	8	68	216	Saline flushes		**	Survived
17	84	M	31	M60	IJV	CVVHDF	4.91%	48%	6	72	48	Heparin		$	Survived

*-Multiple unit platelet transfusions, **-Multiple unit platelet and FFP Transfusions, ***-Acute Liver Failure, #-Significantly reduced LVEF, $-Developed Hypertension and hematuria (background – solitary kidney status), F.O % - Fluid overload, E.F - Ejection fraction

ACPN210330P03 FEASIBILITY AND EFFICACY OF SUSTAINED LOW-EFFICIENCY DIALYSIS IN CRITICALLY ILL CHILDREN WITH SEVERE ACUTE KIDNEY INJURY

Mrs. Menka Yadav[1], Dr. Aditi Sinha[1], Mr. Anand Tiwari[1], Dr. Rakesh Lodha[2], Dr. Jhuma Sankar[2], Dr. Pankaj Hari[1], Dr. Arvind Bagga[1]

[1]*Division of Nephrology, Department of Pediatrics, All India Institute of Medical Sciences, New Delhi, , India,* [2]*Division of Pulmonology, Intensive care, Tuberculosis, Department of Pediatrics, All India Institute of Medical Sciences, New Delhi, , India*

Objectives: To examine the feasibility, efficacy, and safety of sustained low-efficiency dialysis (SLED) in hemodynamically unstable critically ill patients, 1-18 years-old, requiring kidney replacement therapy (KRT) for conventional indications.

Methods: This prospective unicentric study enrolled critically ill patients, 1-18 yr-old and admitted to pediatric intensive care unit (ICU), with hemodynamic instability (≥1 inotrope) and severe acute kidney injury (AKI) requiring KRT. Patients weighing ≤8 kg or with mean arterial pressure <5th centile despite use of >3 vasopressors, were excluded. The primary outcome was the proportion of patients in whom the first session of SLED was performed within 12 hours of KRT indication without premature (<6-hr) termination. Efficacy estimates included net

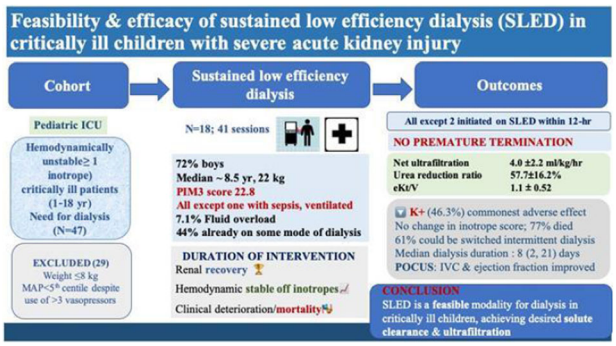
ultrafiltration, equilibrated Kt/V, and urea reduction ratio. Other outcomes included changes in hemodynamic scores; % sessions with circuit clotting; % with clinical and biochemical adverse events (AE); % requiring switch to alternative KRT modality; duration of ICU and hospital stay; and mortality. We also explored indices on point of care ultrasound and echocardiography.

Results: Over 18-months, 47 episodes of severe AKI merited KRT in 42 critically ill patients. Eighteen patients (72% boys; median age 104 months; weight 22 kg) were eligible for and underwent 41 sessions of SLED. These patients had high pediatric index of mortality 3 and vasopressor dependency indices (median 22.8 and 42.8, respectively). Except one, all patients were mechanically ventilated and/or had multiorgan dysfunction and sepsis. All eligible patients, except two, were initiated on SLED at <12-hr of indication (median 4.6 hr) for mean±standard deviation session length of 387±41 min. No session required premature termination. Therefore, SLED was feasible in 88.9% (95% CI, 67.2%-96.9%) patients. SLED sessions relied on temporary central venous catheters and pediatric hemodialysis tubings, usually primed with 5% albumin. Blood and dialysate flow rates were 3.7±0.6 mL/kg/min and 241±49.9 mL/min, respectively. No anticoagulation was required in 50% sessions; while circuit clotted in 3 sessions, all sessions were completed.

SLED enabled net ultrafiltration of 4.0±2.2 ml/kg/hr, urea reduction ratio of 57.7±16.2% and equilibrated Kt/V of 1.10±0.52. Inotrope score, vasoactive inotropic score, and vasopressor dependency index did not change significantly. The chief AE was asymptomatic hypokalemia (46% sessions). SLED sessions led to significant decrease in the inferior vena cava diameter and increase in its distensibility, along with improved left ventricular function. The changes were weakly to moderately correlated with ultrafiltration. Fourteen (77.8%) patients died. Survival was associated with dialysis adequacy, assessed by ultrafiltration ≥25 ml/kg and eKt/V ≥1.5

Conclusions: SLED is feasible, safe, and effective in enabling KRT in hemodynamically unstable pediatric patients with severe AKI. SLED enables adequate solute clearance and ultrafiltration. Large studies with more SLED sessions per patient should examine these associations prospectively.

Encl: Figure (visual abstract)



ACPN210330P04 RENAL GROWTH OF MULTICYSTIC DYSPLASTIC KIDNEY, A COMPARISON STUDY WITH THE RENAL GROWTH OF CONGENITAL SOLITARY KIDNEY

Ms. Lin Shien Fu[1], Dr. Sufei Chang[1], Dr. Yung Chieh Huang[1]

[1]*Taichung Veterans General Hospital, Taichung, Taiwan*

Background: Compensatory hypertrophy is a well-known phenomenon in patients with congenital solitary kidney. Functional congenital solitary kidney can be due to one side agenesis or multicystic dysplastic kidney (MCKD). Both have one functional kidney since birth. We have established a regression formula to estimated renal growth in unilateral agenesis as Renal length (mm) = 31.36 + 6.15 (if female) + 0.47 x Bw (kg) + 0.47 x Ht (cm), which has good prediction on real renal length (R square= 0.863, p<0.0001). This study is to use this formula to check if it is adequate for MCKD children.

Patients and Methods: We retrospectively studied 40 children with MCKD. After excluding those has associated anomalies–VUR (N=3), severe hydronephrosis (N=2), congenital heart disease (N=1) and Pompe's disease (N=1), we estimated renal length on sonography and their physical growth of 36 children with MCKD (aged from newborn to 15 years). We estimated the renal length by our established formula for one side renal agenesis. Then we compared the real and estimated length. Paired T test was used to measure their differences. Multiple linear regression analysis was performed on measured renal length and width adjusted for gender, body weight and height.

Results: There were total 178 measurements in these children with MCKD. The estimated and real renal length in these children were 95.41±23.03 vs 90.22±22.40mm, p=7.8x10-19). After we minus the 6.15mm in the female formula, the estimated renal length were 91.51 ±22.93mm, which is still longer than the real renal length (p=0.004). The differences were even more significant than those body length were higher than 100cm. Renal length in those higher than 100cm were 108.15 ±16.66 vs 106.21±16.3mm, p=0.0033. However, there was no difference between estimated and real renal length in those had body length lower than 100cm (71.12±8.55 vs 70.63±12.88mm, p=0.23)

Conclusion: Checking from the formula considering body weight, length and gender to estimated renal growth in children with single kidney, we found those simple MCKD children had shorter renal length than the patients with congenital one kidney agenesis. The difference was even significant as their body length increases.

ACPN210330P05 CLINICAL IMPLICATION OF GENOME DIAGNOSTICS FOR EARLY AND SEVERE POLYCYSTIC KIDNEYS DISEASES

Ms. Tzu-Ching Lin[1,2], Yi-Hsuan Tang[1,2,3], Hui-Lan Chen[1,3,4], Chien-Hung Lin[1,2], Hsin-Hui Wang*[1,2,3]

[1]*Department of Pediatrics, Division of Pediatric Immunology and Nephrology, Taipei Veterans General Hospital, Taipei, Taiwan,* [2]*Department of Pediatrics, Faculty of Medicine, School of Medicine, National Yang Ming Chiao Tung University , Taipei, Taiwan,* [3]*Institute of Emergency and Critical Care Medicine, School of Medicine, National Yang Ming Chiao Tung University, , Taiwan,* [4]*Department of Pediatrics, Keelung Hospital, Ministry of Health and Welfare, Keelung, Taiwan*

Objectives: Congenital anomalies of the kidney and urinary tract (CAKUT) is the most common cause of end stage renal disease (ESRD) and undergoing dialysis in children. Polycystic kidney disease (PKD) is one of the most severe diseases in CAKUT. Furthermore, rapid deterioration of renal function in severe PKD could result in dialysis in infancy and/or early childhood. The heterogeneity of the clinical presentations and extra-renal manifestations hampers physicians to reach an early and accurate diagnosis clinically. However, delayed diagnosed or undiagnosed diseases make it difficult in treatment, early intervention of possible complications, and improving prognosis. We present three patients with rapidly progressive early onset PKD but with diverse manifestations and prognoses.

Methods: We elucidate the clinical manifestations of patients with early and severe PKD. The renal and extra-renal manifestations, the time course of clinical symptoms, the renal function at initial presentation, the intervals between renal insufficiency to ESRD and dialysis condition and complications were analyzed. Whole exome sequencing (WES) was carried out in two patients and the results helped us making diagnosis.

Results: We present three patients with early and severe polycystic kidney diseases. They are all ciliopathy but with different clinical diagnoses and diverse manifestation and prognosis.

The first one is clinically diagnosed as Joubert syndrome. Multiple small renal cysts and ESRD was found at age 6 years and continuous ambulatory peritoneal dialysis (CAPD) was started. Accompanied presentations included polydactyly, molar-tooth sign of midbrain, Dandy-Walker malformation, and severe intellectual disability. The patient experienced events of PD catheter malposition, bilateral inguinal hernia, exit site and tunnel infections, and PD-associated peritonitis. Undergoing PD therapy for 15 years, PD was shifted to hemodialysis (HD) due to encapsulating peritoneal sclerosis. The patient was expired at age of 21 years because of choke.

The second one is diagnosed as infantile nephronophthisis (NPHP) presented with metabolic acidosis and impair renal function at 1 month old. There was no history of oligohydramnios. The renal sonogram showed normal kidney size and increasing parenchyma echogenecity initially, thereafter multiple bilateral renal cysts appeared. Fluctuation in the liver transaminases level was noted also and biopsy revealed cholestasis. We conducted WES and confirmed compound heterozygous mutations in the NPHP3 gene, c.1817G>A, p.Trp606Ter, and c.3402_3403delTG, p.Ala1135SerfsTer5. The genome profiling related to renal-hepatic-pancreatic dysplasia and infantile NPHP. CAPD was started at age 3 months and 24 days. Complications of PD including inguinal hernia, peritonitis, pleuroperitoneal leak, and chylous ascites had ever occurred. The patient is now 1-year and 2-month-old and undergoing regular PD therapy. Kidney and perhaps liver transplantation will be considered in the future.

The third one is a case of autosomal recessive polycystic kidney disease (ARPKD). The preterm girl came to our hospital at infancy, presented with oligohydramnios, CKD, enlarged kidneys and hepatomegaly. WES showed compound heterozygous mutations of the PKHD1 gene, c.2107G>A, p.Asp703Asn, and c.8863C>T, p.Arg2955Ter. After a respiratory syncytial virus infection, she experienced acute on chronic kidney injury and fluid overload with generalized edema. Emergent HD and continuous venovenous hemofiltration (CVVH) was performed. The patient was expired because of respiratory failure at age of 6 months and 2 days.

Conclusions: Early-onset and severe PKD contribute to morbidities and mortalities in pediatric population. The clinical features, disease course, and prognosis are diverse between these diseases. Therefore, an early and accurate diagnosis is meaningful in clinical practices. The advances in genetic testing such as new generation sequencing (NGS) may provide benefit in making definite diagnoses earlier, avoiding unnecessary diagnostic measures, early detecting comorbidities and potential complications, searching for possible family supports, genetic counselling, and researches of potential future treatment.

ACPN210330P06 ROBO2 AND GEN1 REGULATE BRANCHING MORPHOGENESIS AND INDUCE URINARY TRACT DEVELOPMENTAL ABNORMALITIES IN MICE

Ms. Yi Hui Zhai[1], Minghui Yu[1], Lihong Tan[1], Jing Chen[1], Hong Xu[1], Qian Shen

[1]*Children's Hospital Of Fudan University, Shanghai, China*

Objectives: Congenital anomalies of the kidney and urinary tract (CAKUT) are one of the most common developmental defects affecting 3-6/1000 pregnancies in human. To clarify the mutation of ROBO2 combined with GEN1 in CAKUT, and to further explore the relationship between the superposition effect of ROBO2 and GEN1 genes, we established a double knockout mouse model to identify the superposition effect on the development of metanephros in mice; and explore the underlying mechanism that these two genes may regulate the outgrowth and branching of ureteric bud (UB).

Methods: The PB transposon inserted into the intron of the Gen1 and Robo2 genome to reduce the expression of the target gene in mice. By real-time PCR, we identified the level of expression of Gen1 and Robo2 in the developing kidney of mice. We analyzed the characters of varied phenotype of CAKUT in all kinds of mutation (Gen1PB/+, Robo2PB/+ , Robo2PB/+Gen1PB/+) mice. Using novel Hoxb7/myr-Venus transgenic mice as a useful tool, we observed the budding and branching of UB of Gen1PB/+, Robo2PB/+ and Robo2PB/+Gen1PB/+ mice in vivo. By real-time PCR, we further investigate the different expression of related transcriptions after the disruption of Gen1 and Robo2 in Gen1PB/+, Robo2PB/+ , Robo2PB/+Gen1PB/+ and WT mice.

Results: 1) The incidence of CAKUT in Robo2PB/+Gen1PB/+ newborn pups was higher than those in Gen1PB/+ group (32.3% vs. 17.3%, P=0.038), and in Robo2PB/+ group (32.3% vs. 15.8%, P=0.01). The isolated duplex kidney were the most common anomalies in Robo2PB/+Gen1PB/+ newborn pups which account for 30.2%, and the remaining 2.1% presented hydronephrosis complicated with duplex kidney. 13.5% of Gen1PB/+ newborn mice showed duplex kidney and 3.8% of mice showed hydronephrosis. The incidence of duplex kidney, hydronephrosis and renal dysplasia were 5.2% respectively in Robo2PB/+ neonatal mice. There were no obvious morphological and structural abnormalities in the glomeruli, tubules and mesenchyme of the duplex kidney tissues of double knockout mice by HE staining. 2) Over 30% Robo2PB/+Gen1PB/+ mice grew supernumerary ectopic UB in E11.5d , which was more significant than Robo2PB/+ (10/31 vs 0/14, P=0.01) and Gen1PB/+ (10/31 vs 1/24, P=0.02) groups. 3) Real-time PCR of E11.5 ureteric bud in Robo2PB/+Gen1PB/+ mice revealed that the expressions of Gdnf (2.94±0.62, P = 0.01), Ret (1.31±0.11, P = 0.02), Gremlin1, (1.41±0.1, P = 0.004), Srgap1 (1.74±0.17, P = 0.005) and Six2 (1.82±0.18, P = 0.0038) were increased, while the expression of Pax2 (0.25±0.12, P = 0.007) was decreased.

Conclusions: Robo2 and Gen1 have a superposition effect on regulating branching morphogenesis and inducing urinary tract developmental abnormalities in mice, providing a model basis for the future study of CAKUT as a polygenic disease.

ACPN210330P07 OVEREXPRESSION OF LONG NONCODING RNA 4933425B07RIK CAUSES URINARY MALFORMATIONS IN MICE

Ms. Yi Hui Zhai[1], Minghui Yu[1], Yaxin Li[1], Hong Xu[1], Qian Shen[1]

[1]*Children's Hospital Of Fudan University, Shanghai, China*

Objective: Congenital anomalies of the kidney and urinary tract (CAKUT) is a common birth defect and leading cause of end-stage renal disease in children. The etiology of CAKUT includes mainly genetic and environmental factors. However, these factors cannot fully explain the etiological mechanism of CAKUT. Recently, participation of long noncoding RNAs (lncRNAs) in the development of circulatory and nervous systems was demonstrated; however, the role of lncRNAs in the development of urinary tract system is unclear.

Methods: We used the piggyBac (PB) transposon-based mutagenesis to construct a mouse with lncRNA 4933425B07Rik (Rik) PB insertion (RikPB/+, RikPB/PB). The experimental design included: detecting the spatiotemporal expression distribution and subcellular localization of Rik; observing the proportion of CAKUT phenotypes of neonatal mice; culturing embryonic kidneys from RikPB/PB mice to observe branching of ureteric buds (UBs); clarifying the expression of genes related to metanephric development by RNA-seq from embryonic day (E) 12.5 Rik+/+, RikPB/PB kidney tissues and validating those differentially expressed genes by RT-PCR.

Results: 1. Rik overexpression in RikPB/PB mice

① We detected the spatiotemporal expression distribution of Rik in wild-type (Rik+/+) and found the Rik expression level was high during E12.5-

E15.5, highest on E12.5 and then gradually decreased, and highly expressed in the urinary system at E14.5.

② PB was inserted into intron 3 of the mouse Rik gene, resulting in Rik overexpression. RT-PCR of whole embryos and embryonic kidneys of E12.5 RikPB/PB, RikPB/+ and Rik+/+ mice detected an increase in Rik expression level in RikPB/PB and RikPB/+ mice than Rik+/+ mice.

③ Using the nuclear and cytoplasmic protein extraction assay to detect the subcellular localization of Rik indicated that Rik is almost exclusively present in the nucleus.

2.RikPB/PB mice develop urinary malformations

Gross phenotypes of the urinary system of RikPB/PB, Rik+/+ newborn mice were examined, and indicated significantly higher incidence of CAKUT in RikPB/PB than Rik+/+ mice [66.7% (34/51) vs 9.3% (4/43), $P < 0.0001$]. The renal hypo/dysplasia was the most common phenotype (82.4%, 28/34). In vitro culturing the E11.5 embryonic kidneys of RikPB/PB and Rik+/+ mice and found the number of UBs branches were significantly lower in the RikPB/PB group than in Rik+/+ group ($P < 0.0001$).

3.Rik overexpression induces abnormal expression of metanephric development related genes in mice

① We extracted RNA from the kidneys of E12.5 Rik+/+ and RikPB/PB mice to perform RNA-seq and showed that the number of differentially expressed genes (DEGs) were 186 (150 upregulated, 36 downregulated). These 186 DEGs were classified and enriched, including the SMAD protein signal transduction pathway Bmp4, Trf, Gdf2, Gdf10, Gata4, Hnf4a, and Afp, which are related to the development of mice urinary system.

② Subsequent analysis of the molecules involved in regulation of the UBs branching: the upregulated genes (fold increase) included Foxc1 (1.20), Wnt9b (1.24), Foxc2 (1.18), and Gata3 (1.18), and downregulated genes (fold decrease) included Bmp4 (0.48).

③ RT-PCR was performed to validate the DEGs regulating UBs branching and found the expression of Bmp4 in the E12.5 and E14.5 RikPB/PB group were significantly decreased, while the expression of other genes were not significantly changed.

④ We identified the genes Bmp4, Cdkn3, Samd4, Cnih1, Gmfb, and Cgrrf1 located adjacent to Rik in the same region in kidney of E14.5 RikPB/PB and indicated that Bmp4 was also significantly downregulated.

Conclusions: These findings suggest that abnormal expression of Rik may cause a reduction in the UB branches by reducing the expression levels of the UB branching-related molecule Bmp4, thus leading to the de

ACPN210330P08 A MULTICENTER STUDY OF TC-99M DMSA RENAL SCINTIGRAPHY TO PREDICT VESICOURETERAL REFLUX IN CHILDREN WITH FEBRILE URINARY TRACT INFECTION

Ms. Yi Hui Zhai[1], Qian Shen[1], Hong Xu[1]
[1]*Children's Hospital Of Fudan University, Shanghai, China*

Objective: Vesicoureteral reflux (VUR) is a major risk factor for recurrent symptomatic urinary tract infection (UTI) in pediatric patients. Micturating cystourethrography (MCU) and Technetium-99m dimercaptosuccinic acid renal scintigraphy (DMSA) are widely used in the detection of VUR in the diagnosis of childhood febrile UTI. To evaluate the role of DMSA in predicting VUR in pediatric febrile UTI, and to explore the evaluation criteria aligned to DMSA.

Methods: A retrospective analysis that was conducted from January 2016 to December 2018 of children under the age of 24 months with febrile UTI who visited four pediatric clinics. The DMSA was first performed within 1 week after diagnosis, and the MCU was performed within 1 week after the infection was controlled in all children. We refined DMSA into three indicators: 1) acute pyelonephritis (APN); 2) difference in the relative uptake >10% (DRU>10%); 3) renal scar. We compared sensitivity and specificity of the different DMSA indicators in predicting VUR. According to the MCU results, they were divided into non-VUR and VUR group.

Results: We enrolled 447 patients (278 boys and 169 girls), of which 201 patients had VUR (44.9%) and 172 patients had high-grade VUR (grade III-V) (i.e., 85.6% of all VUR). In the VUR and the non-VUR groups, when the DMSA indicator for predicating VUR was a renal scar and/or when the DRU > 10%, this resulted in an optimal predictive performance with approximately 69.7% sensitivity, 81.7% specificity, a 79.3% positive predictive value, a 72.8% negative predictive value and a 0.757 AUC value.

Conclusion: Renal scar and/or DRU > 10% of the DMSA scan was an effective predictive indicator of VUR in children with febrile UTI under the age of 24 months.

ACPN210331P09 VAGINAL FOREIGN BODY WITH UROGENITAL DISCHARGE IN A CHILD - A CASE REPORT

Mr. Jien-wen Chien[1]
[1]*Changhua Christian Children's Hospital, Changhua city, Taiwan*

An 8-year-old girl presented with bloody urogenital discharge for 9 months. The patient had been diagnosed with recurrent urinary tract infection and received antibiotic treatment, which resulted in little improvement and frequent recurrence. Urogenital discharge with an odor was aggravated, and the patient was brought to our outpatient department by her father. A radiograph of the plain abdomen showed a 1.8-cm rounded foreign body superimposed within the suprapubic region. A urogenital examination performed by a gynecologist revealed an old hymenal laceration, and rectal examination suggested an intravaginal nature of the foreign body. A computed tomography scan of the pelvis revealed a 1.7 × 1.2 × 2.1 cm partially-radiodense foreign body in the proximal vaginal canal. The extraction of the foreign body from the genital tract was then performed by a gynecologist under general anesthesia.

ACPN210331P10 URINARY TRACT INFECTION IN KAWASAKI'S DISEASE, A CONDITION BEING UNDERESTIMATED

Ms. Lin Shien Fu[1], Dr. Lin Shien Fu[1], Dr. Yung Chieh Huang[1]
[1]*Taichung Veterans General Hospital, Taichung, Taiwan*

Background: Although Kawasaki disease (KD) often presents with sterile pyuria, bacterial pyuria (urinary tract infection [UTI]) occasionally occurs.

Methods: This was a retrospective cohort study of 216 children with KD diagnosed between Jan. 2010 and Dec. 2015. Among these patients, a total of 169 patients underwent routine urine tests and 52 children underwent urine culture tests. This study was conducted to investigate the incidence, clinical manifestations, management and outcome of KD with pyuria.

Results: The incidence of pyuria was 24.7% (66/266). Among the 52 children undergoing urine culture, 31 (60%) have received antibiotic treatment before urine sampling. Twenty-five had sterile pyuria (48.1%), 7 had bacterial pyuria (13.5%), 3 had UTI without pyuria (5.8%) and 17 had neither pyuria nor UTI (32.7%). The bacteriology included E.coli (9/10) and Citrobacter koseri (1/10). When pyuria was used as a predictor of KD with UTI, the positive and negative predictive values were 21.9% and 86.4%, respectively. Kawasaki patients younger than 1 year old carried higher risk to have bacterial pyuria (11.3% [7/62] vs 2.8% [3/108], p=0.023). There were no significant differences in other demographic data, clinical presentations, laboratory results, duration of fever, of ratio of resistant KD between both groups.

Conclusions: In our experience, the rate of UTI during acute Kawasaki's disease was 3.75%. In infant, the rate was as high as 11.3%. Pyuria was not always sterile in patients with KD. Although there was no different clinical phenotype or coronary outcome in KD patients with or without UTI, the care of UTI was not satisfactory when physicians pay their major attention to acute KD and its cardiac sequences.

ACPN210331P11 URINE NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN FOR DIFFERENTIATING PEDIATRIC URINARY TRACT INFECTION AND ROSEOLA INFANTUM.

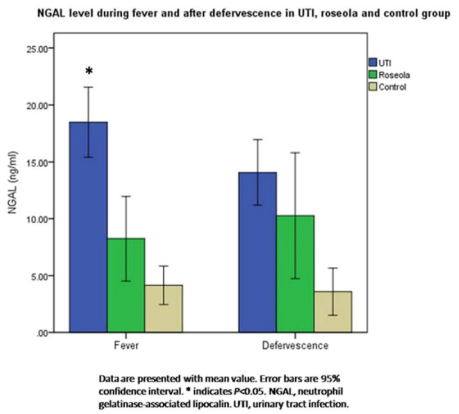
Mr. Naiwen Fang[1], Ms Yu-Shan Huang[1], Mr Yee-Hsuan Chiou[1]
[1]*Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan*

Introduction: Urinary tract infection(UTI) is the most common bacterial infection in children, diagnosing UTI requires pyuria(urine white blood cell> 5 per High power filed) and a positive urine culture. Clinically, physicians usually prescribe antibiotics when a febrile child has pyuria before urine culture report comes out; however, roseola infantum may present with pyuria and a negative urine culture, it leads to a clinical dilemma when treating a febrile children with pyuria. Neutrophil gelatinase-associated lipocalin(NGAL) is a protein expressed in α-intercalated cells in the collecting duct of the kidney. Our study aims to use urine NGAL as a biomarker in differentiating UTI and roseola infantum in early febrile stage.

Method: We prospectively enroll febrile children aged 4 month to 6 years-old, hospitalized during Jan/2019 to Dec/2020. Patients with pyuria and positive urine culture were classified as UTI group, patients with pyuria but negative urine culture, and developed trunk maculopapular rash when fever subsided were classified as roseola infantum group. Patients with fever were classified as control group. Urine NGAL were obtained during fever and after defervescence. Demographics and laboratory data of the patients were collected for comparison.

Result: Total 108 patients were enrolled, 62 patients were in UTI group, 13 in roseola group and 33 in control group. During fever stage, urine NGAL is significantly higher than that in roseola or control group (Mean(95% confidence interval): 18.5(15.4~21.6)ng/ml, 8.2(4.5~12.0)ng/ml and 4.2(2.5~5.9)ng/ml, respectively), and after defervescence, urine NGAL became similar in UTI and roseola group (14.1(11.2~17.0) and 10.3(4.7~15.8), respectively).

Conclusions: Urine NGAL may be a useful marker in differentiating UTI from roseola infantum in young children; however, further studies with larger number of patients should be performed for a more comprehensive result.



ACPN210331P12 URINARY TRACT INFECTION IN INFANTS YOUNGER THAN TWO MONTHS

Mr. Sze Wa Wong[1], Dr. Sik Nin Wong[1]
[1]*Tuen Mun Hospital, Hong Kong,*

Objective: Urinary tract infection (UTI) in infants younger than 2 months old can result in severe co-morbidities and long-term sequelae. A well-established imaging guideline for workup in this group of patients is lacking. We analyzed the characteristics of young infants less than 2 months of age with UTI to shed light on the feasibility of adopting a more selective imaging approach for investigation.

Method: This is a post-hoc analysis using data of the patient cohort collected between 2005 and 2006 for the study by Wong et al. in 2010. Patients of age 2 months or younger with no known urological abnormalities and presenting with first episode urinary tract infection were selected out for review. Number of significant abnormalities were noted in relation to presenting features. These abnormalities include high grade VUR (Grade IV to V), scarring with a decreased differential function <40% on DMSA scan, and other entities such as abscess, or obstructive uropathies. Those with bilateral VUR or defects on DMSA scan were classified according to the side with worse grading and greater extent of defect or impaired differential function.

Results: A total of 170 patients were reviewed. Median follow up duration after the first episode of UTI was 19.2 months (interquartile range 9.7-32.5 months).

Male predominance was observed. Significant urological abnormalities were found in 11 (6.5%) young infants. There were 7 patients with grade IV-V VUR, 3 with severe scarring in the absence of high grade VUR, and 1 with posterior urethral valve. All the 11 infants had at least one of the following characteristics: 1. atypical UTI features, 2. abnormal urinary USG findings, 3. UTI recurrence within the follow up period.

Conclusion: Following first occurrence of UTI, infants < 2 months old presenting with atypical features, abnormal USG of the urinary system, or recurrence of UTI may warrant more extensive investigations with micturating cystourethrogram (MCUG) and dimercaptosuccinic acid (DMSA) scans. For those with typical features at presentation, USG of the urinary system alone may be adequate as basic screening, unless UTI recurs. Further studies are required to establish a specific guideline for this group of patients.

ACPN210331P13 CLINICAL PARAMETERS IN DIAGNOSING PEDIATRIC ACUTE PYELONEPHRITIS

Ms. Yu shan Huang[1], Mr. Nai-Wen Fang[1], Mr. Yee-Hsuan Chiou[1]
[1]*Department of Pediatrics, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan*

Objects: Urinary tract infection (UTI) is the most common serious bacterial infection in children, its prevalence is approximately 7%. Those children with acute pyelonephritis (APN) are at risk of developing long-term sequelae. 99Tc-dimercaptosuccinic acid (DMSA) is currently the gold standard for diagnosing APN; however, performing DMSA requires specialized equipments and facility, and the child received an intravenous line insertion, possible sedation and radiation exposure. Our study aim to test multiple clinical parameters and biomarkers in diagnosing APN in pediatric UTI cases.

Method: We retrospectively reviewed pediatric UTI cases during 2016/8~2020/12, excluded those with recurrent UTI, congenital anormalies of kidney and urinary tract or other systemic diseases. Using DMSA as gold standard, we compared fever duration before antibiotics usage, defervescence days after adequate antibiotics administration, labs

(white blood counts, C-reactive protein and Procalcinotin) and urinalysis results in APN and non-APN groups.

Results: Total 125 cases were enrolled for analysis. We found that procalcitonin, C-reactive protein, white blood counts, neutrophil percentage, fever days before antibiotics administration, and fever days after adequate antibiotics treatment revealed a significant difference between APN and non-APN group. Using ROC curve, we found PCT had similar accuracy with CRP in diagnosing APN.

PCT had an AUC(area under curve) of 0.813(95% confidential interval (CI): 0.72~0.90), using 1.4mg/dL as cutoff value had sensitivity of 48% and specificity of 91%. CRP had an AUC of 0.810(95% confidential interval (CI): 0.71~0.89), using 6.3mg/dL had sensitivity of 40% and specificity of 94%.

Conclusions: Although PCT is more correlated with bacterial infection, we found PCT was equally effective as CRP for diagnosing APN. Fever duration before antibiotics usage and time to defervescence after adequate treatment are useful in diagnosing APN. It seems that there is no single reliable clinical parameter for diagnosing APN, further multiple regression model and normogram may be helpful.

Table1. Baseline demographic and laboratory data in APN and non-APN group.

	Overall (N=125)	APN (N=89)	Non-APN (N=36)	P-value
Age(month)	15.1±26.6	17.3±30.2	9.6±13.2	0.052
Gender-Male(%)	66(52.8)	40(45.0)	26(66.7)	0.006
BH	74.3±17.6	76.0±19.2	70.3±11.7	0.100
BW	10.0±7.1	10.6±8.2	8.6±3.0	0.142
BMI	17.2±2.5	17.2±2.6	17.1±2.3	0.789
Fever days before treatment (day)	1.9±1.6	2.1±1.8	1.5±0.9	0.045
Days before defervescence (day)	1.7±1.0	1.9±1.0	1.3±0.8	0.001
Serum				
Procalcitonin	2.76±4.9	3.51±5.5	0.89±2.6	<0.001
CRP	5.6±4.3	6.7±4.3	3.0±3.2	<0.001
WBC	16299±6493	17439±6425	13431±5814	0.002
Neutrophil	9671±5324	10576±5439	7398±4309	0.002
Band	270±506	307±526	176±440	0.194
Lymphocyte	4678±2282	4753±2347	4487±2131	0.562
Urine				
Positive nitrite(%)	46(37)	31(35)	15(42)	0.67
Leukocyte esterase				0.462
Negative	1	0	1	
1+	2	2	0	
2+	15	10	5	
3+	106	76	30	
WBC				0.120
5~49	33	20	13	
50~99	17	15	2	
>100	75	52	21	
Bacteruria				0.291
Negative	10	6	4	
Few	53	35	18	
Many	62	48	14	
RBC				0.022
<5	63	39	24	
5~49	55	46	9	
50~99	5	3	2	
>100	2	1	1	
Abnormal sonography	84	72	12	<0.001

ACPN210331P14 FRACTURE BURDEN IN PAEDIATRIC END STAGE KIDNEY DISEASE

Mr. Chung Sum Samuel Ho[1,2], Dr. Eugene Yu-hin Chan[1,2], Ms. Ellen Yu[3], Dr. Matthew Hon-lam Lee[1], Dr. Yuet-ling Tung[4], Dr. Alison Laptak Ma[1,2]

[1]Paediatric Nephrology Centre, Hong Kong Children's Hospital, Hong Kong, , [2]Department of Paediatrics and Adolescent Medicine, Princess Margaret Hospital, Hong Kong, , [3]Clinical Research Centre, Princess Margaret Hospital, Hong Kong, , [4]Endocrine Team, Department of Paediatrics, Hong Kong Children's Hospital, Hong Kong,

Objectives: Paediatric patients with chronic kidney disease are known to have an increased risk of fracture. However, data pertaining to children with end stage kidney disease (ESKD) receiving renal replacement therapy (RRT) is limited. The aim of this study is to determine the incidence of fracture and associated factors in this specific group of patients.

Methods: We conducted a retrospective review on all paediatric patients with ESKD at the tertiary Paediatric Nephrology Centre in Hong Kong. Children who presented before 18 years with active follow-ups for 12 or more months by November 2020 were included.

Results: RRT was initiated in 69 children (55% boys) at a mean age of 9.2 ±5.9 years. At the time of evaluation, 21 (30.4%), 10 (14.5%) and 38 (55.1%) patients received peritoneal dialysis (PD), haemodialysis (HD) and kidney transplant respectively. 3 patients (4.3%) had prior kidney graft loss and resumed on dialysis. One patient (1.5%) reported a fracture prior to RRT.

Over a median of 5.2 years (IQR 3.0-8.3) follow-up, 10 fracture episodes were observed in 7 patients (10.1%) at a mean duration of 7.8 ±8 years since RRT initiation, corresponding to a cumulative fracture incidence of 227.8 per 10000 patient year (95% CI, 86.6-369.0). This rate was 5-folds higher than published data from our local general paediatric population (45 per 10,000 person-years; 95% CI, 43.9-46.1; p=0.01). Of note, all patients experienced single fracture episode except one child who developed 4 fracture episodes. Details of the fracture episodes are presented in Table 1.

Children who sustained fractures were significantly younger at the time of RRT initiation (3.5 vs 10.4 years; p=0.02) and had a longer time on dialysis (12 vs 2.7 years; p<0.001). Other factors associated with fractures included metabolic bone disease (28.6% versus 1.6%; p=0.03), difficulty in walking (28.6% versus 3.2%; p=0.05), radiological evidence of renal osteodystrophy (85.7% vs 25.8%; p=0.003), parathyroid hyperplasia/ adenoma (100% vs 31.8%; p=0.01) and a higher parathyroid hormone level (pmol/L) (62.7 vs 30.3; p=0.02). Calcium, phosphate and ALP levels, as well as the proportion of patients with vitamin D deficiency were similar between the two groups. While the practice of native and active vitamin D and phosphate binders were not different, more patients with fracture received cinacalcet (57.1% versus 12.9%; p=0.02), which may suggest more severe hyperparathyroidism.

Conclusions: Children with ESKD receiving RRT are at a higher risk of fracture. Longer duration of dialysis and a higher average parathyroid hormone level were potential modifiable factors associated with fractures.

Table 1. Fracture episodes in children with ESKD receiving RRT

Patient	Primary kidney / metabolic disease	Immobility	Age of initiating RRT (year)	Age of fracture (year)	History of trauma	Location of fracture	Treatment
Patient 1	PH type 1	Yes	9.1	10.4	No	Left wrist	Conservative
				10.4	No	Right humerus	Conservative
				10.6	No	Bilateral femoral neck	Surgery
				21.3	Yes	Left fifth metatarsus	Conservative
Patient 2	Multicentric carpotarsal osteolysis syndrome	Yes	10	31.7	Yes	Left femur	Conservative
Patient 3	CAKUT	No	0.1	2.2	Yes	Left radius and ulna	Surgery
Patient 4	CAKUT	No	3.5	6.4	No	Left fibula	Conservative
Patient 5	Ischaemic nephropathy	No	1.4	15.2	Yes	Right big toe	Conservative
Patient 6	CAKUT	No	6.9	11.9	No	Right fibula	Conservative
Patient 7	Ischemic nephropathy	No	0.02	1.2	No	Left femur	Conservative

CAKUT, Congenital Anomalies of kidney and urinary tract; PH, Primary Hyperoxaluria

ACPN210331P15 THE INCIDENCE AND RISK FACTORS FOR CHRONIC KIDNEY DISEASE IN CONGENITAL HEART DISEASE PATIENTS.

Mr. Naiwen Fang[1], Mr Shih-Hsiang Ou[1], Mr Chun-Hao Yin[1], Mr Jin-Shuen Chen[1,2], Mr Yee-Hsuan Chiou[1]

[1]Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan, [2]National Defense Medicine, Taipei, Taiwan

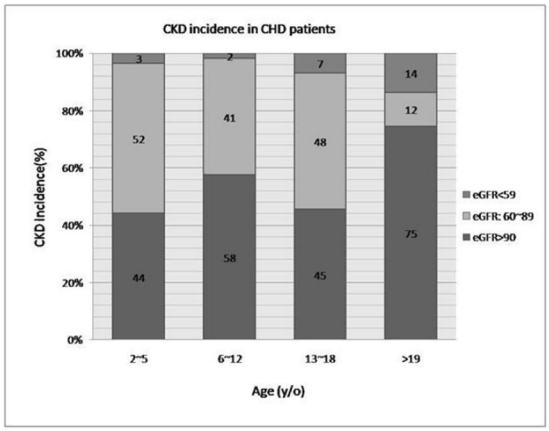
Objective: Chronic kidney disease(CKD) is prevalent in adult congenital heart disease(CHD); however, it is underdiagnosed in pediatric CHD

patients owing to insidious symptoms in early CKD. Our study aim to study the incidence of CKD in CHD patients, and identify risk factors for the development of CKD.

Methods: Patients with CHD diagnosis of by international classification of diseases of ninth or tenth were enrolled from Kaohsiung Veterans General Hospital database during 2010 to 2019. Age of enrollment was the date of their first visit at our hospital. The end of follow-up was the last checkup of creatinine, urine protein-to-creatinine ratio(UPCR) or urine microalbumin-to creatinine-ratio(UACR) after enrollment, and only patients have been tested for aforementioned tests in two separated years were collected. Demography data, medications, contrast related examinations and operations of patients were collected and compared.

Results: 359 CHD patients were included for analysis, and CKD was diagnosed in 167 CHD patients.18 patients with eGFR<60ml/min/1.73m2, UPCR>0.5 or UACR>30mg/g were classified as severe CKD(S-CKD), 149 patients were classified as non-severe CKD(NS-CKD). S-CKD was significantly higher in age of enrollment than NS-CKD. In fact, the incidence of S-CKD reached 7% in adolescence and became higher after adulthood. Furthermore, corrective operation may be a protective factor for CKD development. In addition, cyanotic heart disease, more or equal to 2 times of contrast exposure and diuretic prescription may be associated with CKD; however, they became insignificant in logistic stepwise regression analysis.

Conclusion: CHD patients has high CKD incidence, early detection of CKD in young age and prompt correction of CHD may be beneficial to further renal function.



ACPN210331P16 REPURPOSED ROLE OF PEDIATRIC NEPHROLOGIST DURING PANDEMIC: EXPERIENCE OF MANAGING ADULTS WITH CKD AND COVID19 INFECTION

Mr. Onkar Singh Bhinder[1], Dr. Swarnim Swarnim[1], Dr. Kumar Ratanjeet[1], Dr. Meyyan A[1], Dr. Mukta Mantan[1]

[1]*Maulana Azad Medical College, New Delhi, New Delhi, India*

Objectives: Coronavirus disease 2019 (COVID-19) is a novel viral disease caused by SARS-CoV-2 virus and has emerged as a deadly pandemic affecting countries all over the world. Patients with CKD are expected to be at a higher risk of severe disease since their rate of all-type infections and the prevalence of cardiovascular disease are higher than in the general population. Since the month of June the pediatric nephrology team has been taking care of adults with CKD on maintenance hemodialysis and diagnosed with COVID19 infection in our tertiary care Covid only facility. Here we share our experience of managing adults with CKD, on maintenance HD and concomitant Covid19 infection.

Methods: This retrospective study was done for admissions between 20th June- 30th November 2020. Data of all adults (>18 years) with previously diagnosed CKD and hospitalized with COVID 19 infection during this period was retrieved; data pertaining to the demographic details, exposure history, underlying co-morbidities, clinical presentation, medications, dialysis requirement, laboratory and radiological profile, complications and outcomes were collected. The hematological and biochemical parameters including hemogram, neutrophil/lymphocyte ratio, kidney function tests, liver function tests were recorded; inflammatory markers like CRP, IL-6, procalcitonin (PCT) and thrombosis marker like D-dimer were noted.

Results: A total of 295 adults (62.7% M) with CKD were admitted during this period with median age of 51 (18-88) years; 102(34.6%) had associated T2DM, 65.1% had hypertension, 9.2% had hypothyroidism and 7.5% coronary artery disease, HCV positivity was seen in 2.4% and HBV in 1.3%. A further analysis was done for 213 patients with complete records; 165 (77.5%) were on maintenance HD and 72.7% had AVF as vascular access at the time of admission. Most (84.5%) patients were symptomatic for Covid19; chief symptoms being fever in 60.6%, cough 41.8%, dyspnea 44.6%, fatigue 12.7%, sore throat 8.9% and 2.3% had diarrhea. Oxygen therapy was needed in 62.9% (42.5% by venturi and 57.5% by non-rebreathing mask) and median (IQR) duration of oxygen use was 5 (3;10) days. Medications used were HCQS in 84.5%, azithromycin in 21.6%, ivermectin in 82.6% and steroids in 63.8%. LMWH was used in 59% and inotropes in 9% of the patients. Radiological changes were present in 70% and were bilateral in 91.3%; lower zones were more commonly involved and diffuse ground glass opacities and scattered consolidation were seen frequently. The overall mortality was 16.3% and ICU transfers were done for 23.1% patients. The median time to attain RTPCR negativity was 15 (10;19) days and 27.2% became negative after 2 weeks while the duration of hospital stay was 13 (8;19) days.

Conclusions: Adults with CKD especially on HD are prone to more severe Covid infection and they take a longer time for viral clearance (> 2 weeks) and mortality (16.3%) is much higher. The challenge of managing these complicated renal patients during the pandemic also provided the pediatric nephrology team an opportunity to broaden their horizons and emphasizes the need for close coordination between pediatric and adult teams for better future preparedness.

Parameter	Median (IQR)
Creatinine (mg/dL)	8.8 (6.3; 11.9)
Haemoglobin (g/dL)	7.9 (7; 9.4)
Total leucocyte counts(/mm³)	6000 (4242.5; 9520)
Neutrophil/lymphocyte ratio	5.3 (3.3; 10)
Platelet Counts (X10⁵/mm³)	1.5 (1.1; 1.9)
Ddimer (ng/ml)	903 (373; 2050)
Serum albumin (g/dL)	3.3 (3.1; 3.6)
Radiological changes	70% (91.3% B/L, 10.7% pleural effusions)
39.4% had elevated Ddimer, 17% had leukopenia, 17.4% had thrombocytopenia	

ACPN210331P17 IDENTIFYING NONSPECIFIC CLINICAL MANIFESTATIONS OF DIGITALIS INTOXICATION: A CASE SERIES OF PEDIATRIC CHRONIC KIDNEY PATIENTS WITH CARDIOMYOPATHY

Mr. Radhian Amandito[1], Mr. Reza Fahlevi[1], Mrs. Retno Palupi-Baroto[1], Mr. Mulyadi M. Djer[1], Mrs. Henny Adriani Puspitasari[1]

[1]*Cipto Mangunkusumo Hospital, Central Jakarta, Indonesia*

Objectives: Cardiovascular (CV) complications remain the main etiology of mortality in pediatric chronic kidney disease (CKD) patients,

especially those who underwent chronic hemodialysis (HD). One of the most common CV complication is dilated cardiomiopathy. Digoxin, a long-standing drug used for cardiomyopathy, has also been used in pediatric CKD cases despite of the narrow margin of safety dose. Potential risk of digoxin intoxication is higher in pediatric CKD population, especially in middle to low income countries where the availability of serum digoxin concentration examination is lacking. Here we presented three cases of digoxin intoxication in pediatric CKD patients underwent HD, in order to identify and devise a practical approach for intoxication cases.

Methods: We reviewed the medical records of three pediatric patients with chronic HD who had their serum digoxin levels examined and were of levels greater than 2.4ng/mL within 1-year period. We studied their presenting symptoms, associated electrolyte abnormalities, electrocardiogram data, indication for digoxin use, digoxin usage, concurrent medications, and treatment of intoxication.

Results: All patients received digoxin at dose of equal to or more than 0.02 mg/kg/day as treatment for dilated cardiomyopathies. Gastrointestinal symptoms were the main features in all patients. All of them complained diarrhea, nausea, and vomiting, while 2 of 3 patients had epigastric pain. Arrythmia were evident in all patients, in the form of ST depression and junctional bradycardia. Two of 3 patients experienced fatigue and 1 of 3 patients had recurrent syncope, chest discomfort, and decrease consciousness. Laboratory investigations revealed severe hyperkalemia (range 6-7mg/dL) and elevated serum digitalis levels above 2.4 ng/mL (3.65 ng/mL – 5.04 ng/mL). One patient had to undergo a temporary pacemaker placement, and no patients received digoxin immune fab (DIF). Digoxin cessation and electrolyte correction were done. Hospitalization and close monitoring of vital signs, ECG, and electrolyte levels were performed. Patients received their HD sessions with high-flux dialysis and regular prescriptions according to the standard protocol. Patients were discharged after 1 week of monitoring.

Conclusions: Close monitoring of intoxication symptoms should be done for CKD children who underwent HD and receive digoxin therapy. Dose adjustments must be reconsidered for every CKD patients receiving digoxin. Digitalis intoxication should be suspected whenever gastrointestinal symptoms, cardiac arrythmia and bradycardia appear. If DIF is unavailable, correction of electrolyte imbalances and hemodialysis, along with close observation of clinical symptoms and ECG is an adequate alternative.

ACPN210331P18 CYANOTIC NEPHROPATHY IN A CHILD WITH COMPLEX CONGENITAL HEART DISEASE (CHD): THE ROLE OF PHLEBOTOMY

Ms. Retno Palupi[1,4], Dr Henny Adriani Puspitasari[1], Dr Cahyani Gita Ambarsari[1], Dr Riski Muhaimin[2], Professor Mulyadi M Djer[3], Dr Sudung O Pardede[1]

[1]Division of Nephrology, Department of Child Health, Faculty of Medicine Universitas Indonesia, , Indonesia, [2]Division of Hematology-oncology, Department of Child Health, Faculty of Medicine Universitas Indonesia, , Indonesia, [3]Division of Cardiology, Department of Child Health, Faculty of Medicine Universitas Indonesia, , Jakarta, [4]Division of Nephrology, Department of Child Health, Faculty of Medicine Nursing and Public Health, Universitas Gadjah Mada, , Indonesia

Introduction: Cyanotic nephropathy (CN) is a common complication in children with unoperated cyanotic congenital heart diseases (CCHDs). However, due to poor awareness of this problem, CN generally is left untreated leading to chronic kidney disease (CKD). As the long-term hypoxia and hyperviscocity continue to occur in the CCHDs, tubular and glomerular function are affected resulting in proteinuria and azotemia, which subsequently can progress to end-stage kidney disease.

Objective: We report a case of a 12-year old boy with complex cyanotic CHD who attended our pediatric nephrology outpatient clinic for the problems of proteinuria and decreased estimated glomerular filtration rate (eGFR).

Methods: We reviewed a medical record of a child with pulmonary atresia with ventricular septal defect (PA-VSD), no-native pulmonary atresia (PA), major aortopulmonary collateral arteries (MAPCAs) who had persistent proteinuria and decreased eGFR. Clinical features and interventions done were noted.

Results: The patient was referred to the pediatric cardiology clinic from a rural area in Bandar Lampung, Indonesia due to CCHD since 2 months of age. At 7 years old, he was diagnosed with PA-VSD, no-native PA and MAPCAS and treated conservatively. Three years later he developed persistent albuminuria and was consulted to pediatric nephrology clinic. He looked cyanosis with hemoglobin level of 20 g/dL and haematocrit level of 60%. At the first visit his ureum level was 23.4 mg/dL and creatinine level was 0.6 mg/dL. Proteinuria was found to be in a nephrotic range (>40 mg/m2/hour) based on the 24-hour urine protein test. Kidney function declined based on the result of serum creatinine from 0.6 mg/dL (eGFR 80 mL/min/1.73 m2) to 0.7 mg/dL (eGFR 69 mL/min/1.73 m2). Further investigations including possibilities of immunological causes of nephropathy such as C3, C4, ASTO were normal. The patient was treated with captopril and valsartan for 2 months, however albuminuria was not resolved. Phlebotomy was considered as an adjunctive treatment to reduce blood viscosity thereby improving kidney function. After phlebotomy, the patient was less cyanotic, creatinine level decreased to 0.6 mg/dL, and the 24-hour urin protein test decreased substantially to 10 mg/m2/hour.

Conclusion: In a patient with inoperable complex CCHD and cyanotic nephropathy, routine phlebotomy may have some favourable effects. Our case displayed remarkable improvements in some important CKD parameters following a phlebotomy procedure, those were the eGFR and protein urine excretion.

ACPN210331P19 DIAGNOSTIC AND CLINICAL UTILITY OF GENOMIC TESTING IN CHILDREN WITH END-STAGE KIDNEY DISEASE

Ms. Yi Hui Zhai[1], Doctor Fang Lin[1], MD, PhD Yihui Zhai[1], MD, PhD Qian Shen[1], MD, PhD Hong Xu[1]

[1]Department of Nephrology, Children's Hospital Of Fudan University, Shanghai, China

Background and Objectives: End-stage kidney disease (ESKD) can be caused by a wide variety of primary kidney disorders. Genetic kidney disease is increasingly recognized as an important cause of pediatric ESKD and genetic testing might increase the diagnostic accuracy while evidence is limited. This study was conducted to determine the diagnostic yield and clinical impact of genomic testing for ESKD children.

Design, setting, participants, and measurements

Patients who diagnosed with ESKD before 19 years of age at Children's Hospital of Fudan University from January 2009 to December 2018 and received next-generation sequencing (NGS) from 2014 were enrolled for this study. A three-pronged NGS approach including targeted exome sequencing (TES), singleton whole-exome sequencing (WES) or trio-WES was performed for genetic testing and we analyzed results for likely deleterious variants in genes known to cause chronic kidney disease (CKD).

Results: A molecular diagnosis was identified in 39.9% (75/188) children with ESKD, encompassing 30 mutant genes, one certain copy number variation (CNV), one chromosome abnormality and 93 diagnostic variants. When comparing the clinical diagnosis in the 75 patients with genetic diagnosis, 53 (70.6%) discerned specific subtype of clinical category, 8 (10.7%) reclassified the kidney disease, 5 (6.7%) with unknown ESKD origin had a molecular diagnosis, and the other 9 (12.0%) had their clinical diagnosis confirmed. In addition, genetic diagnosis was

considered to have contributed to the clinical management, including negating the need for kidney biopsy (26/75, 34.7%), avoiding immunosuppressive therapy (24/75, 32.0%), changing surveillance (48/75, 64.0%), guiding specific treatment (21/75, 28.0%), advising peritransplant management and options for kidney transplantation (12/75, 16.0%). Furthermore, cascade testing was subsequently offered to 34.7% (26/75) families.

Conclusions: Genetic testing identified a molecular diagnosis in nearly 40% of children with ESKD. Our results confirm that in a pragmatic pediatric cohort with ESKD, genetic testing was not only valuable for establishing a specific molecular diagnosis, but also demonstrated substantial quantifiable impacts on clinical management.

Key words: end-stage kidney diseasegenegenetic testingchildrenkidney transplantation

ACPN2103 TRANSITION FROM ADOLESCENCE TO YOUNG ADULTHOOD IN CHRONIC KIDNEY DISEASE CARE: FOCUS ON DISCREPANCY BETWEEN ESTIMATED GLOMERULAR FILTRATION RATE AND TRANSFERRED RATIO

Yee-Hsuan Chiou[1], MD Nai-Wen Fang[1], MD Shih-Hsiang Ou[2], MS Chun-Hao Yin[3], MD PhD Jin-Shuen Chen[3,4]

[1]*Division of Pediatric Nephrology, Department of Pediatrics, Kaohsiung Veterans General Hospital, Kaohsiung City, ROC,* [2]*Division of Nephrology, Department of Internal Medicine, Kaohsiung Veterans General Hospital, Kaohsiung City, ROC,* [3]*Department of Medical Education and Research, Kaohsiung Veterans General Hospital, Kaohsiung City, ROC,* [4]*School of Medicine, National Defense Medical Center, rg4nw, ROC*

Introduction: We studied estimated glomerular filtration rate (eGFR) discrepancies during transition to adulthood and transferred ratios of different pediatric chronic kidney disease (CKD) etiologies.

Methods: Twenty-five patients aged 15 to 21 years with at least 3 test results for normal serum creatinine level were enrolled from the big databank of Kaohsiung Veterans General Hospital. The Schwartz and Modification of Diet in Renal Disease (MDRD) formulas were used for eGFR calculations. The difference and ratio between the eGFRs calculated using these two formulas and clinical demographic data of the patients were analyzed. Additionally, 3066 pediatric CKD cases were extracted from the Longitudinal Health Insurance Database. Etiologies for pediatric CKD and their transferred ratios were studied.

Results: eGFRs calculated using MDRD were higher than those calculated using the Schwartz formula among patients aged 15 to 21 years. At age 18, the mean difference was 27.7±15.9 ml/min/1.73 m2 (range, 6.9 to 60.9). Overweight (body mass index>25) was related to high eGFR discrepancy and was an independent risk factor for eGFR (MDRD/Schwartz)>1.5. Congenital anomalies of the kidney and urinary tract was the main etiology of pediatric CKD; however, GN had the highest follow-up duration of up to 18 years (30%) and transferred ratio (24%).

Conclusion: Overweight is associated with high discrepancy in eGFR calculated by different formulas used by nephrologists. This should be recalled during transition to adulthood. GN had highest follow-up rate and transferred ratio, a specific transition guideline for such group is required.

ACPN2104 IMPROVED EQUATIONS TO ESTIMATE GFR IN CHINESE CHILDREN WITH CKD

Mrs. Ying Tang[1], Mrs Yue Du[1]

[1]*Shengjing Hospital of China Medical University, Shenyang, China*

Background: Current equations to estimate glomerular filtration rate in CKD are either underestimated for GFR>75 ml/min/1.73m2 or not developed in Asian children. We studied 751 children with chronic kidney disease in China and generate an estimation equation suitable for Chinese pediatric CKD patients.

Methods: 751 children in Shengjing hospital affiliated to China Medical University from January 2011 to October 2018 was divided into training group (501 children) and validation group (250 children). In the training group, univariate linear regression model was used to calculate the predictability of variable related to estimate GFR. Residuals were compared to determine the multivariate predictability of GFR in the equation (Scr, height/Scr, cystatin C and BUN). Standard regression techniques for Gaussian data were used to determine the coefficients of the GFR estimating equations after logarithmic transformation of the continuous variables. Validation of the equation was used in the remaining 1/3 of the patients.

Results: An equation of eGFR(ml/min/1.73m2)= 91.021 [height(m)/Scr/2.7]0.443 [1.2/Cystatin C(mg/L)]0.335 [13.7/BUN(mg/dl)]-0.095 [0.967male] [height(m)/1.4]0.275 was calculated, and the 30% and 10% of measured iGFR was 75.85% and 32.93%, respectively. The equation was tested in the validation group and the 30% and 10% of measured iGFR was 76.11% and 29.15%, which is the highest compare to the CKiD, CAPA and other well-known equations.

Conclusion: We generate an equation of eGFR based on blood Scr, BUN and cystatin C in Chinese CKD children. This equation might be more accurate in Asian children and CKD patients with mild decreased GFR. Further studies are needed to validate this equation and more equations should be generated for Asian children.

Key word: glomerular filtration ratechildren,chronic kidney disease

ACPN210331P20 THE CRRT EXPERIENCE IN A SINGLE TERTIARY REFERRAL MEDICAL CENTER

Mr. Chih Chia Chen[1,2], Mr. YuanYow Chiou[1,2]

[1]*Department of Pediatrics, Division of Pediatric Nephrology, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan City, Taiwan,* [2]*nstitute of Clinical Medicine, College of Medicine, National Cheng Kung University, Tainan City, Taiwan*

Objectives: Acute kidney injury (AKI) is common in critical-ill children admitted to intensive care units (ICU). Several publications in recent years have documented the poor prognosis of AKI, especially those with higher stages, including those requiring renal replacement therapy (RRT). However, little is known regarding the characteristics of different etiologies, vascular accesses, prescribed dose and long-term outcomes between children receiving continuous RRT (CRRT) in different age groups. We therefore conduct the current investigation to reveal the information of patients requiring CRRT. We also share our experiences in infants weighted less than 2000 gm and receiving CRRT.

Methods: Children admitted to our hospital, one referral tertiary hospital in southern Taiwan, and received CRRT between January 2014 and April 2019 were enrolled. The baseline demographic data, including disease severity scores, and vital signs was recorded. The diuretics usage, laboratory data, urine amount, and fluid status were extracted. We also identified the vascular access, and the detail of CRRT prescriptions. We characterized the primary diseases as sepsis on admission, oncology and hematology, cardiac, nephrology, renal, rheumatology, prematurity and neonates, metabolic and others. We further defined kidney injury etiologies according to possible mechanisms for AKI. We then compare these factors between patients requiring CRRT less (younger group) or

more (older group) than 120 days old. After discharged, we documented the long-term serum creatinine data, if available.

Results: Total 75 patients with 82 admissions were identified. The younger group receiving CRRT had cardiac diseases (35.3%) or premature births (41.2%) as the main underlying diseases while the older group had oncologic and hematologic (21.5%) and renal diseases (29.2%). Most etiologies for AKI were asphyxia (17.6%) or cardiogenic (41.2%) in the younger group and were infection (32.3%) or renal origin (23.1%) in the older group. Compared to the older group, the younger group was more prone to have ECMO (52.9% and 23.1% in the younger and older group, respectively, p= 0.033) or diuretics use (76.5% and 58.5% in the younger and older group, respectively, p= 0.029) prior to CRRT. The younger group also had more fluid overload when CRRT performed (16% and 2.64% in the younger and older group, p = 0.001). 72.3% of the older group used double lumen as the vascular access while 52.9% of the younger group use the ECMO. After children who cannot survive to discharge or had end stage of renal diseases (ESRD) when admitted, 32 admissions were identified. During the long-term follow-up, 25% had no serum creatinine measurements after discharged. Among 24 patients with long-term follow up, four patients progressed to ESRD and about 14% of patients had worsen renal functions,

Conclusions: Our data demonstrated that the etiologies, vascular accesses, and outcome difference in distinct age groups. Besides, we also showed the poor outcomes of children receiving CRRT. However, 25% may loss of follow up after discharged. We may pay more attention in these patients.

ACPN210331P21 IMPACT OF ACUTE KIDNEY INJURY ON OVERALL SURVIVAL IN CHILDREN AND YOUNG ADULTS UNDERGOING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

Mr. Daisuke Matsuoka[1], Koichi Hirabayashi[1], Tsubasa Murase[1], Shoji Saito[1], Yozo Nakazawa[1]

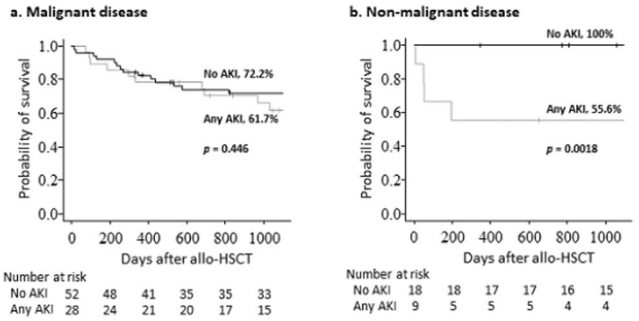
[1]*Shinshu University School of Medicine, Matsumoto, Japan*

Objectives: Acute kidney injury (AKI) is a common complication after allogeneic hematopoietic stem cell transplantation (allo-HSCT). Increasing severity and the early appearance of AKI have been reported to be associated with a stepwise increase in the risk of death and a decrease in overall survival (OS). However, previous reports in the literature were based on the data of entire population of patients who received allo-HSCT, without regard to primary disease; patients with malignant disease undergo chemotherapy and receive myeloablative conditioning, and patients with non-malignant disease undergo no chemotherapy and receive non-myeloablative conditioning. We thus hypothesized that the cumulative incidence of AKI and impact of AKI on survival outcomes differ between patients with malignant disease and those with non-malignant disease. In the present study, we investigated the cumulative incidence of AKI by severity within 100 days post-transplant, as well as the impact of AKI on overall survival (OS) at 3 years after allo-HSCT for all patients, according to the Acute Kidney Injury Network (AKIN) classification. We then performed the same analysis for patients with malignant and those with non-malignant disease.

Methods: This is a retrospective cohort study of consecutive pediatric and young adult patients, aged < 25 years, who received first allo-HSCT at Shinshu University Hospital, Matsumoto, Japan between January 2006 and December 2019. Data were collected retrospectively using electronic medical records at Shinshu University Hospital. AKI within the first 100 days after transplantation was graded into three grades according to the modified AKIN classification system. All participants were followed until either October 2020 or death.

Results: In our cohort, 107 patients were analyzed: 65 (60.7%) were male and 80 (74.8%) had a malignant disease. The median age at the time of transplant was 8.3 years (range, 0–24 years). The cumulative incidences of AKI stages 1–3, 2–3, and 3 at day 100 after allo-HSCT were 34.6%, 17.8%, and 3.7%, respectively. OS in the overall cohort was reduced for patients with AKI compared with patients without AKI (60.1% vs. 79.4%, p = 0.0377). Compared to patients without AKI, the OS in patients with stage 1 AKI was similar (80.8%, p = 0.7890), but patients with stage 2 and 3 AKI had significantly diminished OS (46.7% and 25.0%, p = 0.0266 and 0.0018, respectively). The cumulative incidences of all AKI at day 100 after allo-HSCT in patients with malignant disease and with non-malignant disease were 35.0% and 33.3%, respectively. Time at development of AKI in patients with non-malignant disease was significantly earlier than in those with malignant disease (21.0 days vs. 39.5 days, p = 0.0469). While there was no significant difference in OS between the non-AKI group and the AKI group in patients with malignant disease (72.2% vs. 61.7%, p = 0.446), the OS in the AKI group with non-malignant disease was significantly lower than that in the non-AKI group (100% vs. 55.6%, p = 0.0018).

Conclusions: AKI after allo-HSCT was not only a frequent event but also related to reduced OS. The incidences of AKI within 100 days post-transplant in patients with malignant disease and non-malignant disease were similar; however, the impact of AKI after allo-HSCT on OS in patients with non-malignant disease was stronger than in those with malignant disease. This highlights the need to closely monitor the development of AKI in patients receiving allo-HSCT, especially those who have non-malignant disease.



ACPN210331P22 STUDY OF PREVALENCE AND CLINICAL SPECTRUM OF SEPTIC ACUTE KIDNEY INJURY (SAKI) IN STEROID RESPONSIVE NEPHROTIC SYNDROME

Mr. Debanjan Sinha[1], Prof. (Dr.) Sanat Kumar Ghosh[2]

[1]*Dr. B C Roy PGIPS, Kolkata, India,* [2]*Dr. B C Roy PGIPS, Kolkata, India*

Nephrotic syndrome is known to be susceptible for moderate to severe grade of infection, leading to sepsis and AKI. Systemic inflammatory response syndrome (SIRS) insult in the nephrotic background initiates interplay between inflammation and oxidative stress, leading to adaptive response to the tubular epithelial cell in presence of microvascular dysfunction- explained as septic acute kidney injury (SAKI).

Objectives: The clinical spectrum and any association of SAKI in steroid responsive nephrotic syndrome is not well understood. The present study is aimed to determine -

i) Prevalence

ii) Clinical spectrum

iii) Contributory factors

iv) Short-term outcome

Methods: Study Area: department of paediatrics.

Study Population: Patients of steriod responsive Nephrotic Syndrome upto 12 years age. [As maximum age of admitted patients in this hospital is 12years].

Study period: One and half year

Sample size: Exact prevalence of SAKI is not found. Since it is a time-bound study, all the patients of steroid responsive nephrotic syndrome will be included.

Inclusion criteria: Up to 12 years.

Exclusion criteria: Congenital malformation of kidney, multiple congenital defects or dysmorphism or with known immune deficiency.

Study design: A prospective observational study.

Study tools:

a)Diagnosis of steroid responsive nephrotic syndrome

b)Glomerular filtration rate (GFR)- Schwartz formula

c)Diagnosing and staging of AKI- pRIFLE

d)Criteria of sepsis- SIRS criteria

Statistical analysis: SPSS (version 24.0; SPSS Inc., Chicago, IL, USA) and Graph Pad Prism version 5.

Results: In our prospective observational study

□Incidence of AKI among hospital admitted steroid responsive nephrotic syndrome patients – 27.23% (n=64), while incidence of SAKI – 25.10% (n=59)

□Proportion of SAKI among all AKI patients – 92.10% (59 out of 64)

Non-septic AKI - 7.8% (5 out of 64)

□Among 59 SAKI patients, 40 children- SEPSIS category (67.8%), 10-SEVERE SEPSIS (16.9%) and 9- SEPTIC SHOCK (15.3%).

□Among 59 SAKI patients, 38 children (64.4%) developed AKI: pRIFLE stage R, 12 (20.3%) in stage I, 8 (13.6%) in stage F and 1 child (1.7%) in stage L.

□Among 38 patients of STAGE 1 AKI- 34 patients due to sepsis (89.5%), 3 patients- severe sepsis (7.9%) and 1 patient- septic shock (2.7%). Among 12 patients of STAGE 2 AKI: sepsis (50%), severe sepsis (33.3%) and septic shock (16.7%). Among 9 patients of STAGE-3 AKI, severe sepsis (33.3%) and septic shock (66.7%).

□ 15.3% SAKI cases were positive for blood culture while 8.5% were positive for urine culture.

□most common presentation were Ascites (93.2%) followed by tachycardia (84.5%). 29 out of 59 patients (49.2%) developed hypertension while 23 of them developed congestive cardiac failure (39%).

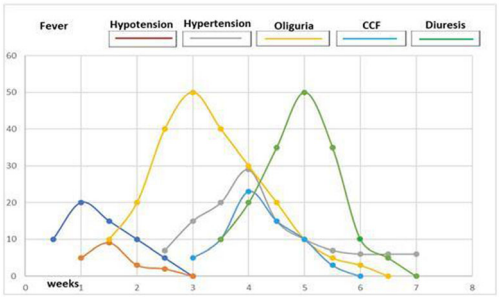
□Clinical features included features of peritonitis or sepsis or septic shock followed by prolongation of the oliguric phase, development of hypertension, azotemia and congestive heart failure in some cases. Diuresis followed with subsidence of edema, CCF, azotemia. Hypertension persisted for variable period.

□Among 59 SAKI cases, majority (n=14, 23.7%) was frequent relapse nephrotic syndrome (FRNS) followed by 1st relapse (18.7%), 2nd relapse (18.7%).

□Regarding contributory factors, 52.4 % patients (31 out of 59) had features of hypovolemia and among them 27 patients discharged and 4 patients died. 6 patients out of 59 SAKI patients (10.17%) had prior usage of nephrotoxic drugs and among them only 1 patient died.

□We found that 4 out of 55 patients (7.27%) had features of relapse after 6 months, while 6 patients (10.91%) remained hypertensive as well as 2 patients developed CKD (3.64%).

Conclusion: SAKI were the most important complications of steroid responsive nephrotic syndrome. Duration of hospitalisation, ICU requirement, Ventilatory-support and inotropes use are more among SAKI patients than nephrotic syndrome without SAKI.



ACPN210331P23 NEONATAL ACUTE KIDNEY INJURY FOLLOWING CONGENITAL HEART SURGERY

Mr. Gwo-Tsann Chuang[1], Dr. I-Jung Tsai[1], Dr. En-Ting Wu[1], Dr. Shu-Chien Huang[1], Dr. Yih-Sharng Chen[1], Dr. Chin Yee Ho[2]

[1]National Taiwan University Hospital, Taipei, Taiwan, [2]Taipei Tzu Chi Hospital, Xindian Dist., New Taipei City, Taiwan

Background: Acute kidney injury (AKI) is associated with increased morbidity and mortality in hospitalized adults and children. Post-cardiac surgery AKI is common, while few studies focused on neonatal population. We aim to identify the incidence and the risk factors of AKI in neonates after congenital heart surgery, as well as the impact on long-term outcome.

Methods: We enrolled 250 neonates retrospectively who received congenital heart surgery during year 2012-2016. AKI was defined based on the Neonatal AKI KDIGO classification. Statistical analyses were performed to detect factors and outcomes associated with postoperative AKI.

Results: AKI occurred in 124 neonates (49.6%) after surgery for congenital heart diseases. Preoperative serum lactate level, Risk Adjusted classification for Congenital Heart Surgery (RACHS-1) categorical score and perioperative extracorporeal membrane oxygenation (ECMO) use were independent risk factors for developing AKI. In neonates receiving cardiac surgery, in-hospital and 2-year mortality rate were both significantly associated with AKI stage and perioperative ECMO use.

Conclusions: Postoperative AKI is common among neonates receiving congenital heart surgery, and it predicts poor clinical outcome independently. Identifying modifiable risk factors for neonatal AKI after cardiac surgery is crucial in future studies.

Key words Neonatal AKIcongenital heart surgery

ACPN210331P24 RISK FACTORS FOR IN-HOSPTIAL MORTALITY AND ACUTE KIDNEY INJURY IN NEONATAL-PEDIATRIC PATIENTS RECEIVING EXTRACORPOREAL MEMBRANE OXYGENATION

Ms. I-Jung Tsai[1], **Dr. I-Jung Tsai[2]**, Mr. Fu-Huang Lin[3], Ms. Li-Jung Tseng Tseng[4], Dr. Shu-Chien Huang[4], Dr. Yih-Sharng Chen[4], Dr. En-Ting Wu[5], Dr. Yong-Kwei Tsau[3]

[1]Department of Pediatrics, Taoyuan Armed Forces General Hospital, Taoyuan, Taiwan, [2]Division of Nephrology, Department of Pediatrics, National Taiwan University Children's Hospital, Taipei, Taiwan, [3]School ofPublic Health, National Defense Medical Center, , Taiwan, [4]Departments of Surgery, National Taiwan University Hospital, National Taiwan University College of Medicine, , Taiwan, [5]Division of Critical Care, Department of Pediatrics, National Taiwan University Children's Hospital, , Taiwan

Background: Acute kidney injury (AKI) is the most frequent complication in critically ill neonatal and pediatric patients receiving extracorporeal membrane oxygenation (ECMO) support. This study analyzed risk factors for in-hospital mortality and the incidence of AKI in neonatal and pediatric patients received ECMO support.

Methods: We reviewed the medical records of 105 neonatal and 171 pediatric patients who received ECMO support at the intensive care unit (ICU) of a tertiary care university hospital between January 2008 and December 2015. Demographic, clinical, and laboratory data were retrospectively collected as survival and AKI predictors, utilizing the Kidney Disease Improving Global Outcome (KDIGO) consensus definition for AKI.

Results: In the 105 neonatal and 171 pediatric patients, the overall in-hospital mortality rate were 58% and 55% respectively. The incidence of AKI at post-ECMO 24 h were 64.8% and 61.4%. A greater KDIGO24-h severity was associated with a higher in-hospital mortality rate (chi-square test; $p<0.01$) and decreased survival rate (log-rank tests, $p<0.01$). In univariate logistic regression analysis of in-hospital mortality, the CVP level at post ECOMO 24-h increased odds ratio (OR) (OR=1.27 [1.10-1.46], p=0.001) of in-hospital mortality in neonatal group; as for pediatric group, elevated lactate (OR=1.12 [1.03-1.20], p=0.005) and PT (OR=1.86 [1.17-2.96], p=0.009) increased OR of in-hospital mortality. And the KDIGO24h stage 3 had the strongest association with in-hospital mortality in both neonatal (p=0.005) and pediatric (p=0.001) groups. In multivariate OR of neonatal and pediatric groups were 4.38 [1.46-13.16] (p=0.009) and 3.76 [1.70-8.33] (p=0.001), respectively.

Conclusions: AKI was a significant risk factor for in-hospital mortality in the neonatal and pediatric patients who received ECMO support. A greater KDIGO24-h severity was associated with higher mortality rates and decreased survival rate in both neonatal and pediatric groups. Of note, KDIGO24h can be an easy and early tool for the prognosis of AKI in the neonatal and pediatric patients.

ACPN210331P25 THE DIAGNOSTIC ACCURACY OF AKI ASSESSED BY TIMED URINE COLLECTIONS IN EXTREMELY PRETERM INFANTS

Mr. SOSAKU YYAMANOUCHI[1], Mr. Masato Hirabayashi[1], Mr. Shohei Akagawa[1], Mrs. Yuko Akagawa[1], Mr. Jiro Kino[1], Mr. Takahisa Kimata[1], Mr. Shoji Tsuji[1], Mr. Kazunari Kaneko[1]

[1]Department Of Pediatrics, Kansai Medical Unversity i, Hirakata, Japan

Objectives: Acute kidney injury (AKI) complications in extremely preterm infants born at gestational age less than 28 week are associated with increased mortality. Neonatal AKI is often assessed by the neonatal modified Kidney Disease: Improving Global Outcomes (KDIGO) classification using serum creatinine (Cr) levels.

However, this evaluation of AKI is limited because renal function is immature during the neonatal period, and serum Cr levels within the first week after birth reflect maternal serum Cr levels. As such, a new method for diagnosing AKI in neonates by timed urine collections has been proposed the neonatal Risk Injury Failure Loss End-stage kidney disease (nRIFLE), which has been shown to have a high diagnostic accuracy (Ricci et al., Nephrol Dial Transplant, 2013). However, no studies have been performed on extremely preterm infants. The purpose of our study was to clarify the relationship between the AKI complication rate and dead discharge rate using timed urine collections in extremely preterm infants.

Methods: Of the 170 extremely preterm infants (gestational age: 22–27 weeks) admitted to our hospital from 2006 to 2019, 11 died within 48 h after birth, and 76 that did not undergo catheter urine volume measurements were excluded. Thus, 83 subjects (43 boys) were included in this study. Urine volume was measured with an indwelling bladder catheter for accuracy. The AKI complications were assessed as described above for nRIFLE (R: urine volume <1.5 mL/kg/h; I: urine volume <1.0 mL/kg/h for 24 h; F: urine volume <0.7 mL/kg/h for 24 h or anuria for 12 h; L and E were omitted because there were no applicable subjects). The dead discharge rates were compared between patients with AKI (AKI group) and those without AKI (Non-AKI group).

Results: The AKI complication rate was 56.6% (47/83 cases), of which R was 34.0%, I was 8.5%, F was 57.5%, and L and E were 0%. The dead discharge rate was significantly higher ($p<0.05$) in the AKI group (25.5%; 12/47 cases) compared with the Non-AKI group (2.8%; 1/36 case).

Conclusions: Timed urine collections revealed a AKI complication rate of 56.6% in extremely preterm infants; this rate differed from the rate of a previous report (39.8%) that examined serum Cr levels (Carmody et al., Clin J Am Soc Nephrol, 2014). The dead discharge rate of the AKI group in this study (25%) was also higher than that previously reported (14%). Therefore, evaluating AKI using timed urine collections may improve the diagnostic accuracy in extremely preterm infants.

ACPN210331P26 ACUTE KIDNEY INJURY IN RELATION TO NEPHROTOXIC MEDICATION USE AMONG CRITICALLY ILL CHILDREN IN THE PAEDIATRIC INTENSIVE CARE UNIT (PICU)

Mr. Wun Fung Hui[1], **Dr Wun Fung HUI[2]**, Ms Veronica Ka Wai LOK[1], Mr Hei Kiu TSE[1], Mr Cheng WONG[1], Ms Sze Ming WONG[1], Dr Kam Lun HON[2], Mr Man Hong POON[1]

[1]Department of Pharmacy, Hong Kong Children's Hospital, Hong Kong, Hong Kong, [2]Department of Paediatrics and Adolescent Medicine, Hong Kong Children's Hospital, Hong Kong, Hong Kong

Objectives: Children in the Paediatric Intensive Care Unit (PICU) are vulnerable to acute kidney injury (AKI) and due to the complex nature of the disease, they are often exposed to multiple medications which may individually or in combination have the potential to cause addition risk for renal injury. Among hospitalized children, nephrotoxic medication exposure is one of the most common contributors to AKI. However, it is difficult to establish a causal link between medication exposure and the subsequent kidney damage as the development of AKI is often multi-factorial. We presented the result of the interim analysis of an ongoing prospective cohort study on the potential association between nephrotoxic medications and the risk of developing AKI in critically ill children in PICU of a newly established children's hospital.

Method: Patients were included if they were aged > 1month to ≤ 18 years of age and admitted to the PICU of Hong Kong Children's hospital since 6/2020. Patients were excluded if they had pre-existing chronic kidney disease or impaired renal function for ≥ 3 months prior to PICU admission or admitted for post-renal transplant. All data were retrieved from the hospital's electronic database. The initial list of nephrotoxic medications included was based upon the Hong Kong Children's Hospital (HKCH) formulary of approved medications and included any medications with reported nephrotoxicity (Table 1). The medication records from 14 days prior to PICU admission to PICU discharge would be retrieved and reviewed by an independent pharmacist to determine the number and doses of nephrotoxic medications exposure in relation to the development of AKI. AKI was diagnosed according to the KDIGO criteria. The results of the initial four months of data would be presented.

Results: A total of 62 patients with 63 admissions fulfilling the study criteria were identified. The prevalence of AKI on admission to PICU was 40.3% (stage 1: 17.7%, stage 2: 14.5%, stage 3: 8.1%). The overall incidence of AKI during PICU stay was

55.6% (stage 1: 20.6%, stage 2: 15.9% and stage 3: 19.0%). Of these, 68.6% were male and the median age (25th, 75th percentile) was 5 (1, 13) years old. 60% of patients had an underlying history of malignancy and 14.3% of them were recipient of bone marrow transplant. 75% of the patients was exposed to one or more of 43 nephrotoxic medications. The median number of nephrotoxic medication exposure was 2 (1, 3) with maximal number being 8 medications. The total medications doses received was 13 (1, 33) doses with the maximal doses being 334 doses. Patients with AKI received a significantly higher total number of nephrotoxic medications (3 vs 1 medication, $p<0.01$) and a higher total dose of nephrotoxic medications (25 vs 1 doses, $p<0.01$) than those without AKI. Vancomycin, piperacillin-tazobactam and furosemide were the three nephrotoxic medications with the highest total administered doses. Acyclovir, cyclosporine A, foscarnet, ganciclovir and gentamicin were only given to those who had developed AKI. Higher number of nephrotoxic medication exposure increased the risk of AKI during PICU admission (relative risk [95% confidence interval]: 1.2 [1.04, 1.38]).

Conclusion: AKI was commonly encountered among critically ill children in PICU. Critically ill children received a higher number and doses of nephrotoxic medications were at a higher risk of developing AKI. As nephrotoxic medications are one of the few potentially modifiable risk factors for AKI, critically ill children at risk for drug-associated AKI should be monitored frequently and judicious use of nephrotoxic medications should be encouraged.

Table 1: List of nephrotoxic medications

Medications associated with acute kidney injury			
Medication class	**Medication**	**Medication class**	**Medication**
Alkylating agent	Cyclophosphamide	Calcineurin inhibitors	Cyclosporine A
	Ifosfamide		Tacrolimus
	Melphalan	Diuretics	Amiloride
Aminoglycosides	Amikacin		Furosemide
	Gentamicin		Hydrochlorothiazide
Angiotensin-converting enzymes inhibitor	Captopril		Metolazone
	Enalapril / enalaprilat		Spironolactone
	Lisinopril	Glycopeptide antibiotics	Vancomycin
	Ramipril	m-TOR inhibitor	Everolimus
Angiotensin II receptor blocker	Losartan		Sirolimus
	Telmisartan	Monoclonal antibody	Nivolumab
Antifungal	Amphotericin	Non-steroidal anti-inflammatory drug	Ibuprofen
Antimetabolites	Cytarabine		Indomethacin
	Gemcitabine		Diclofenac sodium
	Methotrexate		Ketorolac
Antiviral	Acyclovir		Naproxen
	Cidofovir	Penicillin group	Tazocin
	Foscarnet	Plant alkaloids	Etoposide
	Ganciclovir	Platinum compound	Carboplatin
	Valganciclovir		Cisplatin
Bisphosphonates	Zoledronic acid	Salicylates	Aspirin
		Sulfonamides	Co-trimoxazole

ACPN210331P27 CLINICOPATHOLOGICAL FEATURES AND OUTCOME RESULTS OF PEDIATRIC IGA NEPHROPATHY IN TAIWAN: A SINGLE CENTER EXPERIENCE

Mr. Chia Hung Chu[1]

[1]*Chang Gung University, Taoyuan, Taiwan*

Chia-Hung Chu, MD1 , Mei-Ching Yu, MD, PhD1,2

1College of Medicine, Chang Gung University, Taoyuan,Taiwan

2Division of Pediatric Nephrology, Department of Pediatrics, Lin-Kou Chang Gung Memorial Hospital, Taoyuan, Taiwan

Objective: Immunoglobulin A nephropathy (IgAN) has been recognized as the most common form of primary glomerulonephritis in children and adolescents worldwide, particularly predominant in Asians. Long-term follow-up studies have shown that the disease will progress to end-stage renal failure among 20–50 % of adult patients within 20 years, particularly for those with nephrotic range proteinuria, hypertension and renal insufficiency. According to the recent Annual Report on Kidney Disease in Taiwan (2019), it showed IgAN accounted for 26.1% of primary glomerulonephritis. However, there are limited data concerning IgAN in Taiwanese pediatric patients. In this study, thus, our aim was to investigate the clinical and histopathological spectrum of pediatric IgAN in Northern Taiwan.

Methods: This is a retrospective study consisting of 26 pediatric patients with biopsy-proven IgAN (male/female: 17/9) from a Pediatric Tertiary Care Center at Northern Taiwan, Lin-Kou Chang Gung Memorial Hospital, during the period from September 2006 to February 2020. There were three patients who were lost to follow-up during the study period. Comprehensive medical histories, data on serial biochemical tests and urinalysis were obtained from the medical records. The pathohistological diagnosis of IgAN is determined by the Hass classification (2006~2014) and Oxford classification (2015~2020), respectively.

Results: There was a male predominance of biopsy-proven pediatric IgAN in the study (65.4% males vs. 34.6 % females). The age of the patients undergoing the first renal biopsy was 12.2 ± 4.1 years (mean ±SD). All of the pediatric IgAN patients presented persistent asymptomatic hematuria, and 11 cases (42.3 %) had severe hematuria and nephrotic range proteinuria. Furthermore, 10 (43.5%) cases were treated with prednisolone alone, while 13 (56.5%) cases received an immunosuppressive agent, such as cyclophosphamide, cyclosporine or mycophenolate mofetil combined with prednisolone. Remission of proteinuria was no statistically different between these two groups, steroid alone vs. combination immunosuppression. With respect to renal function and survival, there was only one IgAN patient who had initial presentations consisting of severe hematuria, moderate proteinuria and renal insufficiency developed chronic renal failure 7 years after diagnosis.

Conclusions: IgAN is the most common cause of primary glomerular disease for Taiwanese children and adolescents presenting persistent asymptomatic hematuria with/without proteinuria. Our findings revealed bout 50% of the pediatric IgAN patients required additional immunosuppressive medication, while complete or partial remission was not achieved after initial 3- to 6- month steroid treatment. Overall, the renal outcome of our pediatric IgAN is good, except the affected patient with persistent severe hematuria, mild proteinuria and renal function impairment.

ACPN210331P28 RISK FACTORS OF RENAL INVOLVEMENT IN HENOCH–SCHÖNLEIN PURPURA

Ms. Eun Mi Yang[1], Ms Woo Kyung Kim[1]

[1]*Chonnam National University, Gwangju, South Korea*

Background: Henoch–Schönlein purpura (HSP) is a systemic vasculitis that mainly occurs in children. Renal impairment is a major complication of HSP, however, there is no established predictive marker of renal involvement or progression of renal disease. The aim of this study is to investigate the predictive values of renal involvement in children with HSP.

Methods: The medical records of children with newly-diagnosed HSP from June 2005 to July 2020 were reviewed retrospectively. The selected laboratory data were recorded before starting the treatment and blood neutrophil-to-lymphocyte ratio (NLR) and blood platelet-to-lymphocyte ratio (PLR) were calculated using these results. Age at diagnosis, gender, arthritis and arthralgia, abdominal pain, GI involvement, renal involvement and presence of nephritis were investigated retrospectively.

Results: A total of 207 HSP patients were included in this study, 93 (44.9 %) of the patients had renal involvement. 48.3% of patients have

proteinuria and 20.4% have nephrotic range proteinuria during follow up. The mean age was older (7.20±2.77 vs. 6.21±2.96, p = 0.014) and female is predominant (p = 0.009) in HSP children with renal involvement than those without. The NLR (p = 0.018) and the PLR (p = 0.015) were significantly higher in HSP children with renal involvement than those without. No statistically significant difference was observed in the red cell distribution width (RDW), platelet, mean platelet volume (MPV), MPV-to-platelet ratio between HSP children with and without renal involvement. A NLR of 3.0 and a PLR of 126.4 were the cutoff values for predicting renal involvement (area under the curve, 0.59 and 0.60; sensitivity, 40.9% and 57%; specificity, 78.1% and 70.2%, respectively). Logistic regression analysis revealed that NLR (OR = 1.19, p = 0.018) and PLR (OR = 1.01, p = 0.017) were the risk factor for renal involvement.

Conclusion: NLR and PLR are a potential predictive marker of renal involvement in children with HSP.

ACPN210331P29 GENOMIC PROFILING-BASED PRECISION MEDICINE IN ACUTE GLOMERULONEPHRITIS

Mr. Yi Hsuan Tang[1,2,3], Ms. Hui Lan Chen[1,3,4], Mr. Chien Hung Lin[1,2,3], Ms. Hsin Hui Wang*[1,2,3]

[1]Department of Pediatrics, Division of Pediatric Immunology and Nephrology, Taipei Veterans General Hospital, Taipei, Taiwan, [2] Department of Pediatrics, Faculty of Medicine, School of Medicine, , National Yang Ming Chiao Tung University, Taipei, Taiwan, [3] Institute of Emergency and Critical Care Medicine, School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, [4]Department of Pediatrics, Keelung Hospital, Ministry of Health and Welfare, Keelung, Taiwan

Objectives: To date, precision medicine is not only a novel but considerable tool on disease management and individualized health care. As our current knowledge, there are many etiologies of acute glomerulonephritis in pediatric patients with multiple treatments. In some clinical practice, refractory glomerulonephritis courses with variant multi-organs presentation were difficult to treat and may affect severe morbidity and mortality. Therefore, the earlier to profile genomic characteristic by whole exon sequence (WES) or whole genome sequence (WGS), the earlier for physicians and caregivers to focus on personalized diseases' therapy and prevention policy is essential and important.

Methods: We retrospectively reviewed two medical charts of pediatric patients in Taipei Veterans' General Hospital in 2018/Jan. to 2020/Dec.. Both of them were admitted in our PICU due to critical condition of acute renal failure with hyperkalemia and pulmonary edema. After emergent dialysis therapy, end-stage renal disease (ESRD) was noticed in both of them. Thereafter, they have started to undergo peritoneal dialysis (PD) since then. Because of difficult clinical courses and refractory responses to pulse therapy of methylprednisolone, immunosuppressant (eg. mycophenolic acid), anti-CD-20 antibody (eg. Rituximab) and plasmapheresis, we arranged WES examination for them for further hints of their underlying disease.

Results: Patient A was a 6-year-old boy without other systemic past history or family history. His WES report showed WT1: c.1144A>G, p.T382A, heterozygous, Uncertain significance. After then, he was referred to pediatric cardiologist for heart ultrasound evaluation. He was regular followed up at both of pediatric nephrologist and cardiologist outpatient clinics. Early detection of dilated cardiomyopathy with pending decompensated heart failure was noticed, so he was admitted in PICU with inotropic agents and Levosimendan therapy. His heart failure was improved then.

Patient B was a 1 month-old male newborn without abnormal prenatal examination or any family history. His WES reports showed NPHP3: c.1817G>A,p.Trp606Ter, heterozygous, Pathogenic (Paternal gene) and NPHP3:c.3402_c.3403delTG, p.Ala1135SerfsTer5, heterozygous, Pathogenic (Maternal gene). He was diagnosed as renal-hepatic-pancreatic dysplasia type 1, heterozygous mutation in NPHP3. His liver enzyme and pancreatic enzyme were regular monitoring. During his admission, many episodes of acute liver injury with elevated alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were noticed. Drug toxicity, such as Nicardipine, Linezolid, and medium-chain triacylglycerol (MCT) oil were all suspected. We discontinuoused those medicine and then his liver enzymes decreased to upper limit of normal range.

Conclusions: In this era, precision medicine with genome variant expression in critical and difficult patients revealed advantages in providing much more clear and promising knowledge to predict and prevent further personalized disease. It also makes clinical nephrologist operators increase alertness in not only renal disease but also other organs disorder.

ACPN210331P30 FACIAL NERVE PALSY IN A CHILD ON DIALYSIS

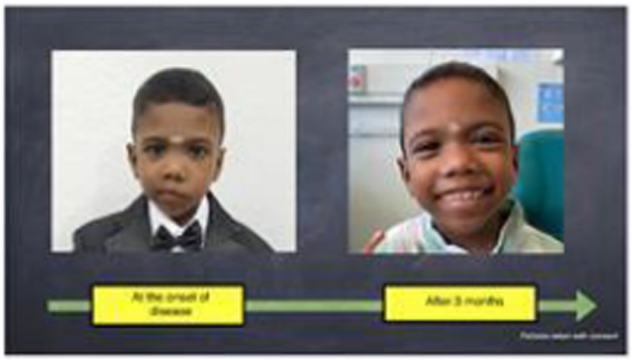
Ms. Caroline ENG[1], Dr Nurul Ain Mohamed Ashrudin[1], Dr Ming Lee Lee[1], Dr Yok Chin Yap[2], FF Wan Ahmad Nasir[1]

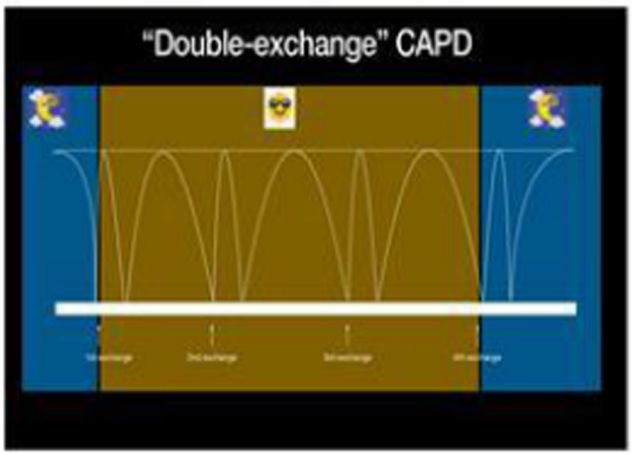
[1]Paediatric Department, Hospital Tuanku Jaafar, Jalan Rasah, Malaysia, [2]Paediatric Nephrology Unit, Hospital Tunku Azizah, Kuala Lumpur, Malaysia

Introduction: Acquired facial nerve palsy in children is uncommon. Aetiology in up to 90% of cases is idiopathic (Bell's palsy) followed by infection related (10%). Although evidence is unclear, steroids have been one of the treatments prescribed to many of these patients.

Case illustration: A 6 year old boy with end stage renal failure on chronic ambulatory peritoneal dialysis (CAPD) presented with sudden onset of unilateral facial asymmetry. Physical examination disclosed a left lower motor neuron facial nerve palsy. He was unable to close his left eyes fully and had slurring of speech. At presentation, his blood pressure was 255/150mmHg with other signs of fluid overload. An urgent computed tomography of the brain rule out intracranial bleed or hypodensity lesions to suggest Posterior Reversible Encephalopathy Syndrome (PRES). He had been struggling with volume management with reducing residual renal function in the recent weeks. Blood pressure was acutely controlled with four antihypertensives and intermittent peritoneal dialysis (IPD) over 72 hour via a cycler. He was discharged home once optimum blood pressure achieved. However, the left facial nerve paresis remained. Continuous cycling peritoneal dialysis could not be offered readily due to limited resource and hemodialysis was not a feasible option either. We had to resort to a "double-exchange" manual peritoneal dialysis (PD) to address volume managemen. Optimal volume and blood pressure control were achieved within 3 months enabling cessation of antihypertensive agents and complete resolution of the facial nerve paresis.

Conclusion: Peripheral facial nerve palsy associated with hypertension has been reported in children albeit being infrequent. The underlying mechanism remains inconclusive. Recovery correlates closely with time to achieving normal blood pressure. In a resource-limited environment, this could pose significant challenge and warrants manipulation of PD physiology.





ACPN210331P31 FIBROBLAST GROWTH FACTOR 23 (FGF23) AND DIASTOLIC DYSFUNCTION IN PAEDIATRIC CHRONIC KIDNEY DISEASE

Mr. Chee Teck Koh[1], Dr. Liangjian David Lu[1], Dr. Sher Leen Sharon Teo[1], Dr. Mya Than[2], Dr. Yew Weng Perry Lau[1], Prof. Swee Chye Quek[1,2], Prof. Lieng Hsi Ling[3,4], Ms. Lingli Gong[4], Dr. Ching Kit Chen[1,2], Dr. Kar Hui Ng[1,2], Dr. Desheng Isaac Liu[1], Prof. Hui Kim Yap[1,2]

[1]Department of Paediatrics, Khoo Teck Puat- National University Children's Medical Institute, National University Health System, Singapore, , [2]Department of Paediatrics, Yong Loo Lin School of Medicine, National University of Singapore , , , [3]National University Heart Center, National University of Singapore, , , [4]Yong Loo Lin School of Medicine, National University of Singapore, ,

Objectives: Cardiac dysfunction is a leading cause of mortality in paediatric patients with chronic kidney disease (CKD). Emerging evidence implicates Fibroblast Growth Factor 23 (Fgf23) in cardiovascular dysfunction beyond its established role in mineral and bone disorder. In this study, we examined the association between Fgf23 and early indices of cardiac diastolic dysfunction.

Methods: Paediatric patients with CKD (n=119, median age 16.9 (IQR 11.15) years) received a baseline echocardiogram. Diastolic dysfunction was assessed by M-mode indices, comprising peak early (E) and late (A) diastolic mitral inflow velocity and the E/A ratio, as well as Tissue Doppler imaging indices, comprising E', E'/A' ratio and Mitral E/Septal E'. Routine serum chemistries as well as Fgf23 were measured at the same time. Linear regression was used to evaluate the relationship between Fgf23 and indices of diastolic dysfunction.

Results: 119 patients (median age 16.9 (IQR 11.15) years) were recruited, comprising 48 (40.3%) with pre-dialysis CKD, 41 (34.5%) on chronic dialysis, and 30 (25.2%) post-renal transplantation. 40 (33.6%) patients had glomerular disease. Fgf23 was significantly associated with E/A ratio [-0.14 (95% CI: -0.26 to -0.02) per fg/ml increase, p= 0.022], septal E'/A' ratio [-0.25 (95% CI: -0.04 to -0.11) per fg/ml increase, p= 0.001], lateral E'/A' ratio [-0.13 (95% CI: -0.23 to -0.03) per fg/ml increase, p= 0.012], and mitral E/ septal E' [1.20 (95% CI: 0.60 to 1.80) per fg/ml increase, p< 0.001]. After adjusting for age, gender, eGFR, mean ambulatory systolic blood pressure z-score, haemoglobin level, serum calcium and phosphate concentrations, and serum parathyroid hormone level, Fgf23 remained independently associated with septal E'/A' ratio [-0.30 (95% CI: -0.54 to -0.06) per fg/ml increase, p= 0.016].

Conclusions: Enhanced Fgf23 levels are associated with multiple indices of progressive diastolic dysfunction in the pediatric population. Enhancing control of mineral and bone disorder, and the therapeutic repurposing of the Fgf23 antagonist Burosumab, may be viable strategies to ameliorate cardiac dysfunction in patients with CKD and improve survival.

ACPN210331P32 CALCIFIED KIDNEY IN A YOUNG INFANT WITH STEVEN JOHNSON SYNDROME AND RENAL FALIURE

Mrs. ALIZA MITTAL[1], Dr Amarpal Singh[1], Dr Vikarn Vishwajeet[2], Dr Taruna Yadav[3], Dr Pawan Kumar Garg[3], Dr Siyaram Didel[1]

[1]Department of Pediatrics, All India Institute Of Medical Sciences, Jodhpur. Rajasthan India, Jodhpur. Rajasthan, India, [2]Department of Pathology, All India Institute of Medical Sciences, Jodhpur, Jodhpur, India, [3]Department of Diagnostic and Interventional Radiology, All India Institute of Medical Sciences, Jodhpur, Rajasthan, Jodhpur, India

Objective: To study and describe causes of Nephrocalcinosis in a young infant presenting with renal failure in light of an interesting clinical presentation

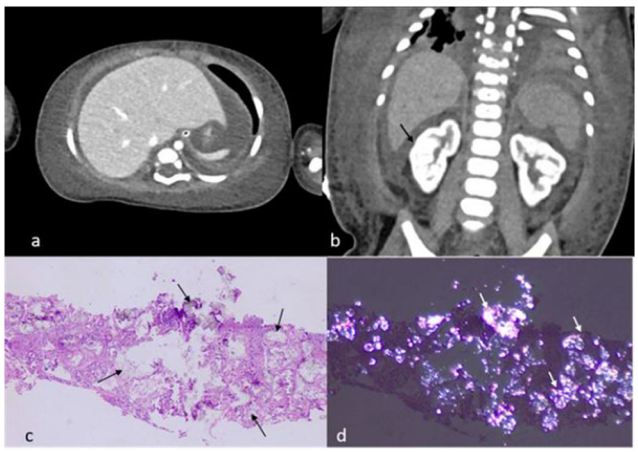
Methods: Clinical presentation:

A 3 month old male child born out of a third degree consanguineous marriage and death of a previous sibling at birth presented with acute gastroenteritis and lethargy. He was treated at another hospital initially where he also developed reduced urine output and AKI. During the course of illness, child developed respiratory failure with septic shock for which multiple antibiotics were administered. In view of worsening AKI an emergent Peritoneal dialysis was performed but as the child developed traumatic effluent along with hemodynamic instability and bullous skin lesions (features of Steven Johnson syndrome) he was then referred to us. As there was a leak at PD site and bullous lesions all over abdomen, PD could not be continued. CRRT was initiated followed by multiple sessions of hemodialysis were performed.IvIg was given for SJS, following which the skin lesions gradually resolved.With continued renal support, child gradually improved and inotropes tapered and he was off ventilator over next 2 weeks , however urine output remained nil and his renal faliure persisted beyond 4 weeks to renal loss. Ultrasound KUB showed increased echogenicity without any anatomical abnormality. On CT there appeared to be normal sized kidneys with well-preserved renal architecture with hyper-dense cortex. (Fig 1). Causes of infantile renal calcification such as excessive use of diuretics, corticosteroids, and vitamin D over dose were not plausible in the given scenario. Evaluation for pathological causes like Bartter syndrome, Dents disease, Hypercalciuria ,Cystinuria and other Renal tubular defects (Like Renal Tubular Acidosis) was attempted however in view of AKI stage 3, it was not conclusive. Also most of these defects do not cause renal failure at such a young age. Enzyme defects like, Tyrosinemia, Gordon's syndrome, Primary Hyperoxaluria and Hyper uricosuria were considered.

As child developed complete renal shutdown with no recovery, a biopsy to look for underlying renal pathology was done. Renal biopsy showed diffuse calcium oxalate crystals deposition suggestive of Crystalline Nephropathy (Figure 1). A Clinical exome sequencing confirmed a likely pathogenic mutation in AGXT gene [AGXT +, Exon 2 c.302T>C(p.Leu101Pro) Homozygous] and hence a diagnosis of Primary Hyperoxaluria was established.

Discussion and conclusion: Primary Hyperoxaluria type 1 (PH1) is a rarely encountered metabolic disorder due to hepatic alanine-glyoxylate-aminotransferease deficiency (AGT). Recurrent urolithiasis and nephrocalcinosis are hallmarks of the disease. Patients with this disorder are prone to develop ESRD at an early age. Since the enzyme defect lies in the liver, a combined liver kidney transplant is the modality of choice for treating these children. Presentation in Infancy though rare has been reported. However, one should be vigilant for uncommon causes of renal failure and increased cortical echogenicity while dealing with such catastrophic presentation of AKI at early age. Other causes that should be always evaluated with such a presentation include, congenital anomaly of kidney and urinary tract, atypical HUS due to inherited causes. The presence of calcification in the kidneys may point to metabolic abnormality one should not miss inherited tubular disorders, enzymatic defects and other causes of crystalline nephropathy.

Legends: Figure 1 a: Contrast enhanced CT axial section showing liver enhancement. b: Sagittal section of CECT abdomen showing hyper dense cortex (black arrow) of the kidney with well preserved renal architecture. C. Renal biopsy Kidney biopsy shows renal tubules containing crystalline oxalate crystals (Black arrows on H& E, 100X), which are (d) refractile and appears birefringent on polarizing microscopy (White arrows)



ACPN210331P33 COALESCENCE OF CANTU AND ALPORT SYNDROME IN A YOUNG GIRL

Ms. Chi San Wai[1], Dr. Wai Ling Lau[1], Dr. Alison Lap Tak Ma[2], Dr. Lai Ka Lee[2], Dr. Ho Ming Luk[3]

[1]Department of Paediatrics, Caritas Medical Centre, Hong Kong, Hong Kong, [2]Department of Paediatrics, The Hong Kong Children's Hospital, Hong Kong, Hong Kong, [3]Clinical Genetic Service, Department of Health, Hong Kong, Hong Kong

Background: Patients with dual molecular diagnosis are uncommon and the diagnosis is always challenging. We encountered a young girl who presented with proteinuria and dysmorphism and was diagnosed to have Cantu and Alport syndrome by whole exome sequencing.

Case presentation: 9-year-old girl presented with edema and physical examination showed dysmorphism including hypertrichosis, gum hypertrophy and short stature. Urinalysis showed nephrotic range of proteinuria and hematuria suggestive of nephritis. Laboratory investigations for the cause of nephritis were unremarkable. Renal biopsy showed features of Alport syndrome. Endocrine tests revealed growth hormone deficiency and adrenal insufficiency. Whole exome sequencing was then performed and found heterozygous mutation in ABCC9 (c.3746G>A) and COL4A5 (c.3203del) which is associated with Cantu and X-linked Alport syndrome respectively. The latter mutation was also found in her mother and younger brother. (Table 1) She was treated with Ramipril, hydrocortisone replacement and growth hormone injection.

Conclusion: Diagnosis of patients with two or more syndromes are challenging as they often present with overlapping features resulting in blended phenotypes. Whole exome sequencing serves as a useful tool in managing these patients.

Investigations for nephritis	
Serum creatinine (umol/L)	35 (33-59)
Complement level (g/L)	C3 1.15 (0.90-1.61) C4 0.22 (0.13-0.38)
Anti-nuclear antibodies, anti-nuclear cytoplasmic antibody	Negative
Ultrasound urinary system	Increased renal parenchymal echogenicity
Renal biopsy	Focal segmental glomerulosclerosis pattern with interstitial foamy cells and splitting of the basement membrane, suggestive of Alport syndrome
Investigations for dysmorphism and short stature	
Bone age	7 year and 10 months at chronological age of 9 year and 6 months
Skeletal survey	No abnormalities detected
Insulin-like growth factor 1 (ug/L)	42 (99-483)
Glucagon stimulation test	Low peak growth hormone at 2.7ug/L and cortisol level at 240nmol/L
Clonidine stimulation test	Low peak growth hormone level at 4ug/L
Low dose Synacthen stimulation test	Low peak cortisol at 356nmol/L (reference cut-off 440nmol/L)
Metabolic studies (lactate, ammonia, plasma amino acid and dried blood spot test)	Normal
MRI pituitary gland	Increased pituitary gland height of 8.4mm (reference 5.09+1.36mm for her age) without intraglandular defect or mass
MRI brain and pelvis	No arteriovenous malformation A T2 hyperintense non-enhancing lesion at lower mesorectum and rectal wall thickening suggestive of lymphatic malformation or lymphangiectasia of malformation
Echocardiogram	Normal chamber sizes with no evidence of congenital heart disease or pulmonary hypertension
Hearing and ophthalmological assessment	Normal
Genetic test (whole exome sequencing)	
Heterozygous mutation in ABCC9 (c.3746G>A), associated with Cantu syndrome Heterozygous mutation in COL4A5 (c.3203del), associated with Alport syndrome (present in patient's mother and younger brother also)	

ACPN210331P34 LMX1B- ASSOCIATED DISEASE PRESENTED WITH PROMINENT ASYMPTOMATIC PROTEINURIA

Ms. Fang Wang1, Baihong LI1, Xiaoyu LIU1, Huijie XIAO1, Yong YAO1, Suxia WANG2, Yanqin ZHANG1, Jie DING1

1Department Of Pediatrics, Peking University First Hospital, Beijing, CHINA, 2Departments of Electron Microscopy, Peking University First Hospital, BEIJING, CHINA

Objective: Glomerular proteinuria may result in nephrotic syndrome or may persist without symptoms. Mutations in about 50 genes lead to steroid-resistant nephrotic syndrome. However, there are a very few reports of asymptomatic glomerular proteinuria led by a genetic etiology. The aim of this retrospective study was to further improve the recognition of asymptomatic proteinuria with genetic causes.

Methods: Three girls with prominent asymptomatic proteinuria and LMX1B -associated disease diagnosed using targeted next generation

sequencing were included in this study. Comprehensive clinical data were collected and analyzed.

Results: The age at onset of nephropathy were 2 years, 1 year, and 4 years, and they were diagnosed at the age of 11 years, 5years and 6 years. All of them had glomerular proteinuria, and nephrotic-level proteinuria occurred in 1 patient. Microscopic hematuria was found in 2 females. All of them had normal renal function. Only one patient underwent renal biopsy. Electron microscopy revealed irregular thickening of the glomerular basement membrane with electron-lucent areas giving a mottled "moth-eaten" appearance and collagen fibrillar material deposition. No abnormalities of nails, limbs and joints were observed by physical examination. Two of three patients had a positive family history of renal disease, which indicates a dominant inherited trait.

Conclusions: Genetic factors should be considered in children with asymptomatic proteinuria. Genetic testing can help diagnose and guide treatment as early as possible.

ACPN210331P35 A RARE CASE OF DENYS-DRASH SYNDROME PRESENTING AS PNEUMOPERITONEUM

Mr. Gwo-Tsann Chuang[1]

[1]*National Taiwan University Hospital, Taipei, Taiwan*

We report a female patient suffering from nephrotic syndrome within one week of age which then rapidly progressed to end-stage renal disease and the patient was dialysis-dependent at one month of age. After ruling out secondary etiology of congenital nephrotic syndrome, whole exome sequencing was done. She carried a de novo germline heterozygous missense mutation of WT1 c.1316G > A, p.Arg439His (formerly R366H) in exon 8, which is common in Denys-Drash syndrome (DDS). DDS is a rare disorder with features consisting of early glomerulopathy, male pseudohermaphroditism and Wilms tumor. Most patients with this syndrome have heterozygous WT1 gene mutation within DNA binding region of exon 8 or 9. This is different from other primary congenital nephrotic syndrome, where homozygous or compound heterozygous mutation is required to cause nephropathy. WT1 encodes a transcription factor that plays an essential role in normal development of the urogenital system and the maintenance of normal podocyte function. From literature review, the median onset age of nephropathy due to missense mutation in DDS is 3-month-old. On the contrary, WT1 glomerulopathy due to truncating mutation in exon 8 or 9 and has a later onset with median age around 12-year-old; WAGR (Wilms tumor-aniridia-genitourinary anomalies-mental retardation) syndrome, with the complete deletion of one WT1 allele, may also suffer from renal insufficiency since early adolescence. Since the severity of nephropathy is more pronounced in missense mutation than truncating mutation or WAGR syndrome, a dominant-negative effect is presumed; in other words, the mutant WT1 protein from missense mutation must possess undesired effect thus being more deleterious than haploinsufficiency alone. Current murine models also supported the fact that missense mutation affecting DNA-binding region causes earlier onset of glomerulosclerosis than truncating mutation or deletion of Wt1. Here we propose possible dominant-negative mechanisms by summarizing the current evidences available from clinical and basic research.

ACPN210331P36 GENETIC ARCHITECTURE OF PEDIATRIC KIDNEY AND UROLOGICAL DISEASES IN CHINA

Ms. Yi Hui Zhai[1], Doctor Hua Shi[1], **MD, PhD Jia Rao**[1], MD, PhD Hong Xu[1], , CCGKDD

[1]*Department of Nephrology, Children's Hospital Of Fudan University, Shanghai, China*

Background: The kidney disease is subject to a wide range of phenotypes, many of which have a significant hereditable component. To delineate the genotype and phenotype spectrum of pediatric kidney disease, a multicenter registration system is currently being conducted based on Chinese Children Genetic Kidney Disease Database (CCGKDD).

Methods: All consecutive patients with kidney and urological disease were recruited from 2014 to 2020. Genetic analysis through exome sequencing was conducted for the families who had multiple affected individuals with nephropathy or clinical suspicion of a genetic kidney disease owing to early onset or extrarenal features.

Results: Genetic diagnosis was confirmed in 883 from 2256 (39.1%) patients from 23 provinces in China. The phenotypic profile showed the primary diagnosis including steroid resistant nephrotic syndrome (SRNS, 23.5%), glomerulonephritis (GN, 32.2%), congenital anomalies of the kidney and urinary tract (CAKUT, 21.2%), cystic renal disease (3.9%), renal calcinosis/stone (3.6%), tubulopathy (9.7%), and chronic kidney disease of unknown etiology (CKDu 5.8%). Pathogenic variants of 105 monogenetic disorders were identified. 10 distinct genomic disorders were established as pathogenic copy number variants (CNV) in 11 patients. The diagnostic yield differed by diagnostic subgroup, being highest in those with cystic renal disease (66.3%), followed by tubulopathy (58.4%), GN (57.7%), SRNS (29.2%), renal calcinosis /stone (29.3%), CAKUT (8.6%), and CKDu (43.5%). Reverse phenotyping permitted allowed correct identification in 40 cases with clinical reassessment and unexpected genetic findings.

Conclusion: Data sharing combined with genotype and phenotype based on national patient registry is pivotal in gaining knowledge on genetic kidney disease.

Keywords: chronic kidney disease (CKD)whole exome sequencing (WES)steroid-resistant nephrotic syndrome (SRNS)congenital anomalies of the kidney and urinary tract (CAKUT)Nephronophthisis (NPHP)polycystic kidney disease (PKD)

ACPN210331P37 SURVEY RESULTS ON THE CURRENT STATE OF DIAGNOSIS OF ALPORT SYNDROME IN ASIAN COUNTRIES-FROM ASPNA WORKING GROUP FOR PEDIATRIC TUBULAR AND INHERITED DISORDERS IN ASIA-

Mr. Kandai Nozu[1], Ms. Lourdes Resontoc, Ms. Jie Ding, Ms. Nakysa Hooman, Mr. Anil Vasudevan, Ms. Hee Gyung Kang

[1]*Kobe University Graduate School Of Medicine, Kobe, Japan*

Objectives: Alport syndrome is one of the most common inherited kidney diseases in the world. It shows progressive kidney disease and hearing loss and many patients develop end-stage kidney disease (ESKD). Recently, it has been reported that RAS inhibitors can significantly delay the development of ESKD. Therefore, early diagnosis is necessary to improve the kidney prognosis in patients with Alport syndrome. We aimed to survey the diagnostic state of Alport syndrome in Asian countries.

Methods: A web-based platform was used. A number of patients each physician cares per year for 28 tubular and inherited diseases including Alport syndrome were collected. Information on methods of diagnosis and availability or access to genetic tests was also included. This study was conducted from September to the end of October 2020 among the members of the Asian Society of Pediatric Nephrology. The patient number was counted as the following rule; when the answer was "1 to 5", it was counted as 1, "5 to 9" counted as 5, and more than 10, counted as 10. In addition, we collected additional information from working members about the current status of diagnosis in China, India, Iran, Philippine, South Korea, and Japan.

Results: A total of 299 pediatric nephrologists from 21 countries in Asia participated in the online survey. The total patient number of Alport syndrome was 764 patients, 328 from China, 213 from Japan, 54 from South Korea, 41 from Iran, and 40 from India. It was less than 30 in other countries. Physicians have good access to gene test in China (including Hong Kong), Japan, South Korea, India, and Philippine. The patient number per institute was 7.5 in Hong Kong, 6.3 in China, 4.1 in Japan, 3.7 in Pakistan, and 3.6 in South Korea. It was less than 3 patients in other countries. Additional information from 5 countries suggested that routine pathological assessment including electron microscopy and/or gene test enables the physicians to find more Alport syndrome patients.

Conclusions: The results showed that there was a big difference in diagnosed patient numbers in Alport syndrome between countries. It might be derived from the lack of awareness of this disease among pediatric nephrologists or lacking the system for definitive diagnosis of this disease. However, this disease can be suspected from the clinical symptoms such as hematuria, proteinuria, and hearing loss. In addition, family history with chronic kidney disease (CKD) and hearing loss can also suggest this disease. RAS inhibitors are not harmful but beneficial for all CKD cases. Especially, this kind of medicine is supposed to delay the development of ESKD more than 10 years on average in Alport syndrome. We hope that the results of this study will help pediatric nephrologists realize that patients with this disease need to be diagnosed early and started treatment in all Asian countries.

ACPN210331P38 POLYHYDRAMNIOS AS A SYMPTOM OF ANTENATAL BARTTER SYNDROME

Mr. Kohei Kawada[1], Mr. Yusuke OKUDA[1], Mr. Shinya KON[1], Mrs. Haruna SERIZAWA[1], Mr. Shuji ISHIDA[1], Mr. Kandai NOZU[2], Mr. Kenji ISHIKURA[1]

[1]Department Of Pediatrics, Kitasato University School Of Medicine, Sagamihara-shi, Japan, [2]Department of Pediatrics, Kobe University Graduate School of Medicine, Kobe-shi, Japan

Background: Antenatal Bartter syndrome (BS) is the most severe form of salt losing tubulopathies, characterized by polyhydramnios, premature birth and severe salt and water loss in addition to metabolic alkalosis and hypokalemia. Fetal polyuria owing to antenatal BS is one of the rare causes of polyhydramnios. However, antenatal BS is seldom listed as a differential diagnosis for polyhydramnios.

Case Presentation: A 16-month-old boy without gastrointestinal or other anomalies. His mother was diagnosed with polyhydramnios during pregnancy, and had amnioreduction twice (4,200 mL and 4,800 mL) at 27 and 31 weeks of gestation, respectively. However, the cause of polyhydramnios was unclear. He was born by emergency cesarean section at a gestation of 31 weeks with a birth weight of 1,482 g because of preterm prelabor rupture of membranes. He was admitted to the neonatal intensive care unit due to preterm birth, extremely low birth weight, and neonatal respiratory distress syndrome that required intubation and mechanical ventilation. Although respiratory status improved rapidly, he needed prolonged hospitalization owing to poor weight gain. Hypokalemia (K, 2.8 mmol/L) and metabolic alkalosis (pH, 7.408; HCO3-, 34.1 mmol/L) accompanied by hyperaldosteronemia (aldosterone, 3,780 pg/mL) were detected at 30 days old without diuretic use. Taking into account the history of polyhydramnios, we clinically diagnosed him with BS, and immediately started potassium and sodium supplement to stabilize serum potassium level and to promote weight gain. During the hospitalization and after discharge, he did not experience a critical event including arrythmia and severe dehydration though he had poor weight gain and mild developmental disorder. A compound heterozygote was detected by a genetic test and the diagnosis of BS was confirmed.

Conclusions: In this case, hypokalemia and metabolic alkalosis were detected at one month after birth and serum potassium levels were normal or slightly high during the first month, as commonly observed in antenatal BS, which may result in delayed diagnosis. If the diagnosis gets delayed, infants may present with poor feeding, dehydration, and severe electrolyte imbalance. Maternal history of polyhydramnios will help early diagnosis. Clinicians should carefully follow up electrolyte, body fluid and growth status in neonates born from mothers with polyhydramnios even if they have no symptoms soon after birth.

ACPN210331P39 PAEDIATRIC TUBULAR AND INHERITED DISORDERS IN ASIA: RESULTS OF PRELIMINARY SURVEY

Ms. Lourdes Paula Resontoc[1], Professor Hee Gyung Kang[2], Professor Jie Ding[3], Dr. Nakysa Hooman[4], AProf Kandai Nozu[5], AProf Anil Vaseduvan[6]

[1]Department of Pediatrics Division of Pediatric Nephrology University of the Philippines-Philippine General Hospital, Manila, Philippines, [2]Seoul National University Children's Hospital & College of Medicine Kidney Research Institute Medical Research Center Seoul National University Wide River Institute of Immunology, Seoul National University, Seoul, South Korea, [3]Peking University First Hospital , Beijing, China, [4]Iran University of Medical Sciences, Tehran, Iran, [5]Department of Internal Medicine Graduate School of Medicine, Kobe University, Kobe, Japan, [6]St. John's Medical College Hospital, Bangalore, India

Objective: Most paediatric kidney diseases including tubular and inherited disorders are not well characterized in Asia. We aimed to establish the prevalence of tubular and inherited disorders among Asian children.

Methods: A web-based platform was used. Demographics and number of patients each physician cares for per year with 28 tubular and inherited diseases were collected. Information on methods of diagnosis and availability or access to genetic tests was also included. A pilot test was conducted among selected participants to ensure the validity and reliability of the survey. This study was conducted from September to end of October 2020 among the members of the Asian Society of Pediatric Nephrology. Quantitative data was analysed with descriptive statistics while qualitative responses were interpreted and classified using thematic analysis.

Results: A total of 299 predominantly female (60%) paediatric nephrologists from 21 countries in Asia participated in the online survey. Median duration of practice was 12 years (range 1 – 50 years); mostly (66.6%) were affiliated with academic and research institutions. For each of the 28 diseases included in the questionnaire, less than 5 cases per year were seen by more than half (57.9%) of the respondents, 18.4% have seen an average of 5-10 cases per year and interestingly, 14% have not seen (n=0) a single case of tubular kidney diseases at all. The two common tubular disorders were distal renal tubular acidosis (dRTA) and Bartter syndrome followed by autosomal dominant polycystic kidney disease (ADPKD), Alport syndrome, and autosomal recessive kidney disease (ARPKD). Diseases with low prevalence were seen in more specialized centres. Clinical history, radiologic imaging, biochemical and genetic tests were employed by more than 70% of the respondents as methods of diagnosis. Percutaneous kidney biopsy was used by 43% as an aid in the diagnosis of some tubular and inherited kidney diseases. More than half (55.4%) of the institutions have access to genetic testing. For future collaborative projects, 88% expressed interest to participate.

Conclusions: The results highlight the diversity of the region in terms of disease prevalence, diagnostic practices, capability and access to genetic tests. Presence of nephrologists who did not see a single case can be attributed to the absence of the disease itself, low index of suspicion, or lack of awareness of these diseases. Therefore, promoting awareness by inclusion of tubular and inherited diseases in regular lectures or continuing medical education sessions is recommended. The data gathered from this preliminary survey can also be

utilized to set up patient registries, develop clinical practice guidelines for diagnosis and therapy, and improve the outcome of these diseases. To bridge the gaps in the knowledge of the disease, diagnostic practices and access to genetic tests, a network for broader collaborations is needed in undertaking prospective research studies.

ACPN210331P40 A NOVEL MUTATION IN TWO SIBLINGS WITH CYSTINOSIS

Mr. Milind Shinde[1], Mr Girish Bhatt[1]

[1]*All India Institute Of Medical Sciences, Bhopal, India, Bhopal, India, India*

Title : A novel mutation in two siblings with cystinosis

Milind Shinde1, Lalit Malviya1, Nagarjun Vijay2, Girish C Bhatt1, Amber Kumar1, Shikha Malik1

1-All India Institute of Medical Sciences, Bhopal, Madhya Pradesh India.

2-Indian Institute of Science Education & Research, Bhopal, India.

Introduction: Cystinosis is a rare autosomal recessive lysosomal storage disorder in which the amino acid cystine accumulates in the lysosomes of cells. The accumulation of cystine crystals in the body cells and tissues leads to kidney damage that causes nutrient imbalance due to excretion of important nutrients. It manifests as poor growth with bone abnormalities.

Case : A 5 year old male child born of second degree consanguineous marriage presented with complaints of failure to gain weight and height since 4 years, increased urine frequency and thirst since 1 year and respiratory distress since 4 days. On examination child had pallor, Harrison sulcus, rachitic rosary, wrist widening, lower limb deformity (wind swept), bilateral infra-scapular crepitations, wheeze and hepatosplenomegaly. Arterial blood gas analysis revealed a normal anion gap metabolic acidosis and urinalysis showed a pH of 5.2, positive urinary anion gap, aminoaciduria, proteinuria, ketonuria, glucosuria and increased β2microglobulins. Urine net charge was positive, fractional excretion of bicarbonate was 16 % and (U-B)Co2 was - 50 mm. Further evaluation revealed hypocalcemia, hypophosphatemia, hyperchloremia, hypothyroidism and raised iPTH . TmP/GFR was 1.4 & 2.2 on 2 consecutive occasions. Radiological imaging showed typical features suggestive of rickets. On ophthalmological evaluation cysteine crystals were observed in cornea suggesting a diagnosis of cystinosis. For confirmation genetic work up was done which detected a heterozygous 5' splice-site proximal variation in intron 9 in the CTNS gene (chr17:3560093A>G) that affects the position 4 nucleotides downstream of donor splice-site of exon 9 (c.681+4A>G) and a heterozygous missense variation in exon 11 of the CTNS gene (chr17:3563233A>C; c.934A>C). Younger male sibling had similar complaints and thus when screened was found to have generalized proximal tubular RTA. Genetic work up of this child also revealed the same heterozygous mutation in CTNS gene confirming the novelty and pathogenicity of this mutation. Proband analysis of mother showed mutation in intron 9 in the CTNS gene (chr17:3560093A>G).

Both the children were started on bicarbonate, phosphate, potassium and vitamin D supplementation along with cysteamine therapy. On follow up at 3 months, both the children's pH has normalized, but the requirement of bicarbonate remains high (10.2 meq/kg/day).

Discussion: More than a hundred pathogenic mutations in the CTNS gene have been reported in the literature. Patients with nephropathic infantile cystinosis are born without any complications. At the age of 6–12 months, Fanconi syndrome causes polyuria, thirst, failure to thrive, growth retardation, vomiting, dehydration, constipation, developmental delays, and rickets. Untreated infantile patients rapidly progress to ESRD in the first decade of life. Our cases had the clinical and biochemical findings favouring Fanconi's syndrome with corneal cysteine deposits. Both sibling had same mutation in CTNS gene with locus at exon 9 and exon 11. This can be explained on the basis of Compound heterozygosity, which is confirmed by mutation in mother at exon 9.

Conclusion :We found a novel mutation which was previously not reported in the literature. In case of similar case presentation the reported mutation also should be looked for as early diagnosis and treatment are essential for prevention of renal and extrarenal damage.

ACPN210331P41 RARE CAUSE OF KIDNEY STONE AND RENAL FAILURE IN JORDANIAN CHILD

Dr Reham Almardini

This patient is seventeen year old male, his symptoms started at the age of 6 years with renal colic, he passed stones in many occasions but unfortunately stone analysis was not done at that time, he continued to develop stone for which many interventions and surgical procedures were commenced and he had recurrent UTI.

Initial investigation reviled high 24 hour urinary oxalate, genetic testing was not done since it is not available and expensive, kidney function test was normal and abdominal X rays showed radio-opaque stones.

initially he had mild renal impairment as creatinine was 0.9 mg/dl, kidney function was stabilized for around seven years on high water intake, Pyridoxine and sodium bicarbonate.

At the age of 13.5 he developed acute gastroenteritis for few days, he was managed at home and did not seek medical care until he developed general weakness and decrease in urine output; he had sever renal impairment which was irreversible and started on hemodialysis

Parents are consanguineous, mother died with the diagnosis of Leukemia, father is 41 year old developed renal colic at the age of 29- it was small stone and he passed it out, he has metabolic syndrome-diabetes, hypertension and high uric acid. There is family history ESRF in far cousin from father side he received kidney transplant, the transplanted kidney failed kidney and he died- no documents regarding genetic testing or the etiology of graft failure.

At this time when he started on hemodialysis; the family were looking for renal transplantation, genetic diagnosis was needed.

Hyperoxaluria panel was done as part of research: 24 hour urine volume was 250 ml, Glycolate level was high (245 mg/g Cr) the normal ratio is less than 30mg/gm, Glycerate was normal 6 mg/g Cr, and Oxalate 6.2 mg/24 h (low urine volume)

last 25 hydroxycholecalciferol level is 26.33, PTH is 630,

Genetic testing was done as part IRB-approved research protocol entitled "Characterization of Monogenic Kidney Stone Disease" at Mayoclinic

genetic testing showed the presence of two mutations consistent with a diagnosis of 24-hydroxylase deficiency, in addition, this patient's genetic testing showed a single known pathogenic variant "carrier" of an AGXT mutation (carrier of primary Hyperoxaluria type 1).

Conclusion: genetic testing is mandatory in cases of kidney stone disease since many diseases can have same clinical phenotype but differ in the management and the long term outcome, in addition to the fact that as more genetic data we got as clinician will have more insight and knowledge about rare diseases.

ACPN210331P42 EVALUATION OF SYNONYMOUS VARIANTS OF COL4A3 AND COL4A4 IN SUSPECTED AUTOSOMAL ALPORT SYNDROME PATIENTS USING AN IN VITRO SPLICING ASSAY

Mrs. Rini Rossanti[1], Mrs. Tomoko Horinouchi[1], Mr. Tomohiko Yamamura[1], Mrs. China Nagano[1], Mrs. Nana Sakakibara[1], Mr. Shinya Ishiko[1], Mr. Yuya Aoto[1], Mr. Atshusi Kondo[1], Mr. Sadayuki Nagai[1], Ms.

Eri Okada[1], Mr. Shingo Ishimori[1], Mr. Hiroaki Nagase[1], Mr. Satoshi Matsui[2], Mr. Keiichi Tamagaki[3], Mr. Yoshifumi Ubara[4], Mr. Masahiko Nagahama[5], Mrs. Yuko Shima[6], Mr. Koichi Nakanishi[7], Mr. Masafumi Matsuo[8], Mr. Takeshi Ninchoji[1], Mr. Nozu Kandai[1], Mr. Kazumoto Iijima[1]

[1]Department of Pediatric,Kobe University Graduate School Of Medicine, Hyogo, Kobe, , [2]Department of Nephrology and Hypertension, Mitsubishi Kyoto Hospital, Kyoto, , [3]Department of Nephrology, Kyoto Prefectural University of Medicine, Kyoto, , [4]Nephrology Center, Okinaka Memorial Institute for Medical Research, Tokyo, , [5]Internal Medicine, St. Luke's International Hospital, Japan, Tokyo, , [6]Department of Pediatrics, Wakayama Medical University, Wakayama, Japan, Wakayama, , [7]Department of Child Health and Welfare (Pediatrics), Graduate School of Medicine, University of the Ryukyus, Nishihara, Japan, Ryuku, Nishihara, , [8]Research Center for Locomotion Biology, Kobe Gakuin University, Kobe, Japan, Kobe,

Objectives: Alport Syndrome is an inherited disorder characterized by progressive renal disease, variable sensorineural hearing loss, and ocular abnormalities. Although many pathogenic variants have been identified in COL4A3 and COL4A4 in autosomal Alport syndrome cases, synonymous mutations in those genes have been rarely identified.

Methods: We conducted in silico splicing analysis using Human Splicing Finder (HSF) to predict splicing domain strength and disruption of the sites. Furthermore, we performed in vitro splicing assays using minigene construction and mRNA analysis using patients' samples to determine the pathogenicity of the synonymous variants detected in 5 cases of unsolved Alport cases; COL4A3 (c.693G>A (p.Val231=) and c.4329 G>A (p.Thr1443=)) or COL4A4 (c.1353C>T (p.Gly451=), c.735G>A (p.Pro245=), and c.870G>A (p.Lys290=)) among 5 suspected Alport Syndrome patients.

Results: Both in vivo and in vitro splicing assays showed exon skipping in 2 out of 5 variants (c.735G>A and c.870G>A in COL4A4). Prediction analysis of wild-type and mutated COL4A4 sequences using the HSF suggested that these two mutations may lead to the loss of binding sites for several splicing factors, including acceptor site and exonic splicing enhancer by SF2/ASF motif. The other 3 variants did not show aberrant splicing.

Conclusions: This study highlights the pitfalls of classifying the functional consequences of disease mutations by a simple approach. Synonymous variants, although does not alter the amino acid sequence of the encoded protein, can sometimes dramatically affect pre-mRNA splicing as shown in 2 of our cases. Our findings indicate that transcript analysis should be carried out to evaluate synonymous variants detected in autosomal Alport Syndrome cases.

ACPN210331P43 A CASE OF POTTER SEQUENCE WITH WT1 GENE MUTATION

Mr. Wataru Shimabukuro[1], Mrs. Miwa Yoshino[2], Mrs. Mina Takeichi[2], Mr. Junya Omura[2], Mrs. Chie Yokota[2], Mrs. Junko Yamamoto[2], Mr. Yasuhiko Takahashi[2], Mr. Kandai Nozu[3], Mr. Naoya Morisada[4], Mr. Kazumoto Iijima[3], Mr. Koichi Nakanishi[1]

[1]Department Of Child Health And Welfare (pediatrics), Graduate School Of Medicine, University Of The Ryukyus., Nishihara-cho, Nakagami-gun, Japan, [2]Department of Pediatrics, Japan Community Healthcare Organization Kyusyu Hospital, Yahatanishi-Ku, Kitakyusyu-shi, Japan, [3]Department of Pediatrics, Kobe University Graduate School of Medicine, Kusunoki-cho, Chuo-ku, Kobe-shi, Japan, [4]Department of Nephrology, Hyogo Prefectural Kobe Children's Hospital, Minatojimaminami-machi, Chuo-ku, Kobe-shi, Japan

Objectives: Wilms tumor-1 (WT1) is the causative gene of Denys–Drash syndrome and Frasier syndrome, and in most cases, renal failure develops after birth. We report an unusual case of Potter sequence due to fetal nephropathy and end-stage renal failure with a WT1 gene mutation.

Methods: Oligohydramnios was observed at 32 weeks of gestation in a patient at our institution. Fetal magnetic resonance imaging at 33 weeks of gestation showed pulmonary hypoplasia, but the fetal kidney size was at the upper limit of normal and no renal cysts were observed. A male neonate was born at 37 weeks of gestation with a birthweight of 2558 g. There was no distinctive facial appearance or anomalies of the extremities. The external genitalia were ambiguous. There were penile-like structures or clitoral hypertrophy, the urethra opened at the base of the penis or clitoris, there was dysplasia of the scrotum or labial pudendi, and a non-palpable testis was found. On an ultrasonographic examination, the right and left renal lengths were 30 and 38 mm, respectively. No renal cysts were noted, but renal parenchymal luminosity was increased. After birth, the neonate required mechanical ventilation owing to severe retractive breathing, but lung compliance was low. Because he developed air leak syndrome, pleural space drainage was performed, but he died of poor oxygenation 60 hours after birth. He had oliguria and developed metabolic acidosis, but initiating renal replacement therapy was difficult because his respiratory status was not stable. This case of Potter sequence with increased renal parenchymal luminosity and no renal cysts on echocardiography, no family history of kidney disease, and a normal male karyotype with 46, XY, was initially suspected as having autosomal recessive polycystic kidney disease (ARPKD). Therefore, we extracted genetic DNA from a whole blood sample, and performed a congenital anomalies of the kidney and urinary tract (CAKUT) gene panel of 181 genes, including WT1 analysis, using next-generation sequencing.

Results: The CAKUT gene panel showed a heterozygous missense mutation in WT1 (NM_024426.5:exon9:c.1400G>A,p.R467Q). In WT1, missense mutations are associated with earlier onset of nephropathy than nonsense or splicing mutations. The median age of initiating renal replacement therapy is 1.1, 16.5, and 12.3 years for missense, nonsense, and splicing mutations, respectively. More severe cases of fetal onset and early neonatal death are rare, and only one case of the same missense mutation of WT1 was reported previously.

Conclusions: A WT1 gene mutation should be suspected in Potter sequences with external genital abnormalities. Missense mutation in WT1 (NM_024426.5:exon9:c.1400G>A,p.R467Q in our case) may indicate a severe case of fetal onset of nephropathy and end-stage renal failure.

ACPN210331P44 MUTATIONS OF IFT-A SUBUNITS IN CHILDREN WITH NEPHRONOPHTHISIS

Ms. Yi Hui Zhai[1], Ye Fang[1], Xiaoshan Tang[1], Jia Rao[1], Hong Xu[1]

[1]Children's Hospital Of Fudan University, Shanghai, China

Objectives: Nephronophthisis (NPHP) is an autosomal recessive cystic kidney disease, which is one of the common causes of end-stage renal disease (ESRD) in children and adolescents. NPHP is caused by defects in primary cilia which serves as cellular antennae by sensing the extracellular environment and transducing developmental signal. The IFT-A complex, comprised of 8 proteins, plays an important role in cilium transport. This study focuses on the 8 genes related to the IFT-A, aims to find novel pathogenic variants in children with NPHP.

Methods: Trio exome sequencing (Trio-ES) was performed to screen the pathogenic variants of IFT-A complex related genes in the cohort of Chinese children with NPHP from Chinese Children Genetic Kidney Disease Database(CCGKDD). Function study on human renal tubular epithelial cells (HK2) was underwent to elucidate the molecular mechanism of pathogenetic variants in IFT-A subunits.

Results: In the seven children with NPHP, biallelic pathogenic variants of IFT122, IFT140, IFT144 (WDR19) and IFTAP (C11ORF74) were detected respectively. In silico analysis for prediction of pathogenesis in the variants was performed. A total of 12 pathogenic variants were identified, including 2 homozygous mutations. And all of the pathogenic variants hadn't been reported before. Among these genes, IFTAP (C11ORF74) was a novel gene that could cause the occurrence of NPHP. The renal phenotypes included proteinuria, renal damage and renal cysts. We also found the extrarenal phenotypes including fundus retinitis pigmentosa, hearing loss, scoliosis, psychomotor retardation and submandibular rhabdomyosarcoma. In the experiments of HK2 cells in vitro, we observed that the length of primary cilia in cell with IFT122, IFT140, IFT144 or IFTAP knockdown was significantly shorter than that in the control group through immunofluorescence staining ($P < 0.05$, t test).

Conclusions: Screening pathogenic variants in IFT-A subunits such as IFT122, IFT140, IFT144 or IFTAP can establish the monogenetic cause of NPHP with the deficiency of cilium. Screening of IFT-A complex related mutations based on WES will speed up the precise diagnosis and typing of NPHP. Further genetic and functional studies will shed light on the mechanism of NPHP.

ACPN210331P45 GENOTYPE AND PHENOTYPE ANALYSIS IN PATIENTS WITH AUTOSOMAL RECESSIVE OR DOMINANT ALPORT SYNDROME

Mr. Yo Han Ahn[1], Mr. Peong Gang Park[2], Mrs. Seon Hee Lim[1], Mrs. Ji Hyun Kim[3], Mrs. Kyung Mi Jang[4], Mr. Seong Heon Kim[5], Mrs. Heeyeon Cho[6], Mr. Joo Hoon Lee[7], Mr. Young Seo Park[7], Mr Ki Soo Pai[8], Mrs. Hee Gyung Kang[1], Mr. Il-Soo Ha[1], Mr. Hae Il Cheong[1]

[1]Seoul National University Children's Hospital, Seoul, Republic of Korea, [2]Ministry of Health and Welfare, Sejong, Republic of Korea, [3]Seoul National University Bundang Hospital, Seongnam, Republic of Korea, [4]Yeungnam University College of Medicine, Yeungnam University Hospital, Daegu, Republic of Korea, [5]Pusan National University Children's Hospital, Yangsan, Republic of Korea, [6]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea, [7]Asan Medical Center, Seoul, Republic of Korea, [8]Ajou University Hospital, Suwon, Republic of Korea

Objectives: Alport syndrome (AS) is an inherited disease characterized by hematuria, progressive kidney failure, sensorineural hearing loss (SNHL), and ocular abnormalities. AS is genetically heterogeneous: X-linked inheritance due to COL4A5 mutations and autosomal recessive (AR) or dominant (AD) inheritance due to mutations in COL4A3 or COL4A4. Here, we evaluated genotype-phenotype correlations in patients with AR- or AD-AS.

Methods: From 2010 to 2020, pathogenic or likely pathogenic variants in COL4A3 or COL4A4 were detected in 34 patients (M:F=20:14) with AS.

Results: The median age at the onset with hematuria was 2.9 (interquartile range (IQR) 1.4–9.0) years. Kidney biopsy, obtained in 27 patients at the median age of 7.9 (IQR 3.9–9.8) years, revealed typical glomerular basement membrane (GBM) changes (n=15), diffuse GBM thinning (n=3), focal segmental glomerulosclerosis (n=4), and others (n=5). SNHL developed in 13 patients at the median age of 15.2 (IQR 13.1–21.0) years, while ocular involvement was noted in one patient. Seven patients progressed to kidney failure with replacement therapy (KFRT) at the median age of 17.0 (IQR 10.4–20.5) years. Most patients were treated with renin-angiotensin-aldosterone system inhibitors (88.2%). For genotype-phenotype analysis, the patients were divided into 2 groups based on their inheritance patterns: Group 1 including 25 patients with biallelic mutations in COL4A3 or COL4A4, and Group 2 including 9 patients with single heterozygous mutations in one of the genes. While kidney survival was not significantly different between the two groups, hematuria and SNHL developed earlier in group 1 than in group 2. Meanwhile, kidney and hearing survival were compared according to the presence of truncating mutations (TM) as well. There were no differences in kidney and hearing survival according to the presence of TM (Table 1).

Conclusions: This study showed that AD-AS has milder renal and extrarenal progression than AR-AS patients, as expected. Kidney and hearing survival were not different between genotypes in AR-AS. Further study with sufficient length of follow-up should be conducted to demonstrate a more comprehensive prognosis in AS patients with autosomal inheritance.

Table 1. Comparison of clinical manifestations according to genotypes and inheritance patterns.

	Group 1 (n=25)		*P*	Group 2	*P* between
	TM (n=14)	No TM (n=11)		(n=9)	groups 1 and 2
Onset age, years	1.9 (1.1-2.7)	4.1 (2.1-9.1)	0.080	12.4 (3.5-16.5)	0.030
Kidney biopsy, n (%)	n=13	n=10	0.895	n=4	0.079
Typical GBM changes	9 (69.2)	5 (50.0)		1 (25.0)	
Diffuse GBM thinning	1 (7.7)	1 (10.0)		1 (25.0)	
FSGS	1 (7.7)	1 (10.0)		2 (50.0)	
Others	2 (15.4)	3 (30.0)		0	
KFRT, n (%)	3 (21.4)	2 (27.3)	1.000	1 (11.1)	0.644
Kidney survival, years	24.0 (19.9-28.0)	18.6 (13.3-23.9)	0.369	41.6 (41.6-41.6)	0.097
SNHL, n (%)	8 (57.1)	3 (27.3)	0.227	2 (22.2)	0.427
Hearing survival, years	21.5 (16.9-26.2)	22.6 (16.9-28.3)	0.550	38.8 (36.2-41.4)	0.014
Ocular abnormalities, n (%)	1 (7.1)	0	1.000	0	1.000

Values are presented as median (interquartile range) and numbers (%). TM, truncating mutation; GBM, glomerular basement membrane; FSGS, focal segmental glomerulosclerosis; KFRT, kidney failure with replacement therapy; SNHL, sensorineural hearing loss.

ACPN210331P46 FRASIER SYNDROME: AN EXTREMELY RARE CAUSE OF NEPHROTIC SYNDROME

Mr. Yung-Chieh Huang[1], Dr. Lin-Shien Fu[1]

[1]Taichung Veterans General Hospital, Taichung, Taiwan

Objectives: Frasier syndrome is an extremely rare disease that affects the kidneys and genitalia. Patients with Frasier syndrome develop focal segmental glomerulosclerosis (FSGS) in early childhood, and male patients have gonadal dysgenesis since birth and possible cancer development during teenage.

Methods: We present a 14-year-old girl who had refractory nephrotic syndrome since she was 6 years old, and prolonged menstrual period for several months. We will present with the patient's medical history, including physical examination, image studies, treatment course and the result of genetic analysis.

Results: Physical examination revealed no edema. She had normal female exogenitalia. The patient was found to have an adnexal mass when she was 14 years old, and she underwent surgical resection and chemotherapy. Gynecologist noted normal uterus and right adnexa during operation. The pathology report of the tumor was gonadoblastoma, which was almost always associated with Y chromosome material. A mutation was found in the WT1 gene Intron 9, c.1447+4C>T. This mutation has been reported previously to be pathogenic as a transcript intron variant. We prescribed angiotensin convertase inhibitor and statin to decrease her urine protein loss and hyperlipidemia. Her urine output and blood pressure were stable, and her serum creatinine level were normal (0.85mg/dl) to date.

Conclusions: From this patient, we learned that for girls presented with FSGS, it is essential to check exogenitalia in physical examination and arrange sonogram of pelvic cavity. Chromosome study is indicated in refractory FSGS cases. Immunosuppressant are indicated in the treatment of refractory FSGS but contraindicated in Frasier syndrome. Since the first Frasier syndrome reported in 1963, only about 50 - 100 cases have been described in scientific literatures. We will review current knowledge of WT1 mutation and its consequential diseases.

ACPN210331P47 SEGMENTAL SCLEROSIS AND MESANGIAL PROLIFERATIVE GLOMERULONEPHRITIS IN A CHILD WITH BRANCHIO-OTO-RENAL SYNDROME

Mr. Zhilang Lin[1], Mrs. Yuxin Pei[1], Mrs. Lizhi Chen[1], Ms. Cheng Cheng[1], Mrs. Ying Mo[1], Mrs. Xiaoyun Jiang[1]

[1]*Pediatrics department, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China*

Objectives: To increase awareness of branchio-oto-renal (BOR) syndrome and its renal pathology in pediatrics.

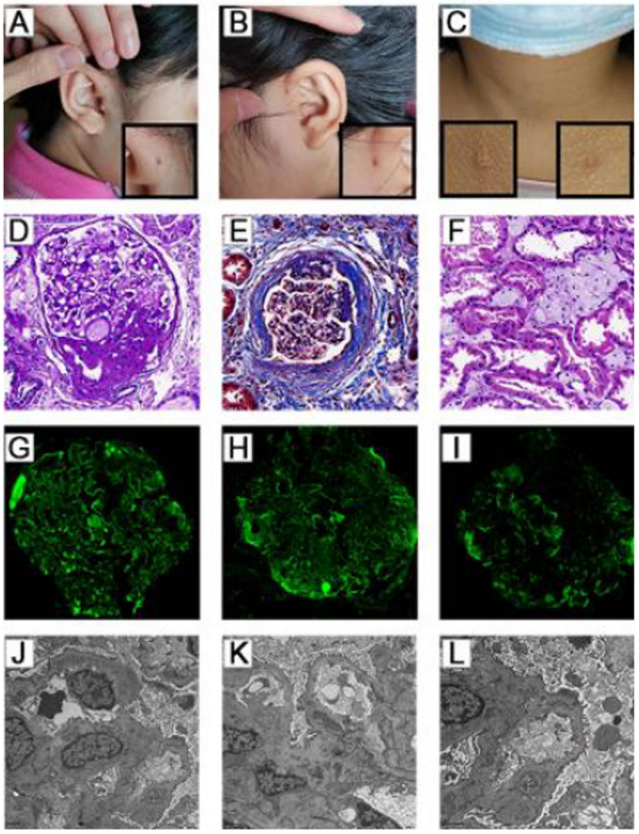
Methods: To report a BOR child, missed diagnosed for 1 year, with proteinuria and presenting as segmental glomerular sclerosis and mesangial proliferative glomerulonephritis (MsPGN) in renal pathology.

Results: Case: An 8-year old girl was found to have proteinuria (urine protein ++), hypoproteinemia (ALB 26.9g/L) and renal insufficiency (SCr 111μmol/L) during a health examination in local clinics. After traditional medicine treatment for a month, she was referred to a general hospital in which laboratory examination showed: urine protein ++(55.6mg/kg/24hr), BUN 15.8mmol/L, SCr 87μmol/L, Chol 6.4mmol/L, cystic changes in renal ultrasound. Renal biopsy was conducted and immune complex-mediated MsPGN with segmental sclerosis was diagnosed. Blood examinations for secondary factors causing immune diseases or secondary NS were all negative. WES examination showed no variation with sufficient pathogenic evidence; a doubtful PKHD1 variation with insufficient pathogenic evidence (PKHD1 c.4009G>A from father, PKHD1 c.7855G>T from mother); and some other variants without family verification. Autosomal recessive polycystic kidney disease (ARPKD) was also considered. Glucocorticoid (GC, Medrol 8mg Bid) and mycophenolate mofetil (MMF, 0.25g Qd) were given, which were irregularly adjusted during the following year without regular follow-up. One year later, proteinuria showed no significant relief (51.3mg/kg/24hr). She was then referred to our hospital and admitted with "MsPGN; ARPKD?" as outpatient diagnosis.

Interestingly, during physical examination, bilateral anterior auricular fistula was found (which appeared at birth but overlooked by her mother and not noticed by previous clinicians)(Fig. 1 A, B). There was also bilateral anterior cervical fistula (Fig. 1 C). WES report was reviewed carefully and a "likely pathogenic" variant (EYA1 c.1319G>A) was redefined as "pathogenic" with added family verification and clinical evidence. Examination showed proteinuria (39.0~68.9mg/kg/24hr), BUN 15.1~18.5mmol/L, SCr 102~119μmol/L, ALB 35g/L, Chol 10.2mmol/L. Test for C3, SLE, ANCA and etiology were negative. MMF-AUC was 47.6 μg.hr/ml. Ultrasound showed small kidneys (Left 5.9cm×2.7cm, right 4.6cm×2.2cm). MRI showed small renal cysts bilaterally. Renal biopsy samples were re-stained and taken reassessment with the formers: Segmental glomerular sclerosis, mild-to-moderate proliferation of mesangial cells with partial periglomerular fibrosis, multifocal tubular atrophy (~40%) with foam cells and interstitial fibrosis(Fig. 1 D, E, F); IF showed IgG+, IgM+, C3+, C1q+, depositing focally, segmentally and granularly along mesangial areas (Fig. 1 G, H, I); EM showed dense deposition in subendothelial area, mesangial area and GBM(Fig. 1 J, K, L). Pure tone audiometry test showed mild hearing loss in both ears. Diagnosis of BOR was clear. Weighing the pros and cons, MMF treatment was stopped and GC was reduced regularly. Monthly follow-up was advised while her long-term prognosis still need time to observe.

Conclusions: Careful physical examination is important in discovering those genetic diseases. Immunosuppressive therapy in BOR patients should be considered carefully as its disadvantages may overweigh the advantages. Moreover, we report the renal biopsy information of a BOR child, which is rare to date.

Fig.1



ACPN210331P48 APPLICATION OF 3D-PRINTED ARCHITECTURE SCALED-MODEL FOR PATIENT EDUCATION IN CONTINUOUS AMBULATORY PERITONEAL DIALYSIS

Ms. Julie Chen[1], Ms. Belinda Tedjokusumo[1], Ms. Hsin-Yi Kung[1], Ms. Jui Fang Hsu[1], Ms. Meei-Chyi Guo[2,3], Mr. Yi-Hsuan Tang[2,4,5], Ms. Hui-Lan Chen[2,5,6], Mr. Chien-Hung Lin[2,4], Ms. Hsin-Hui Wang*[2,4,5]

[1]*Department of Architecture, National Taiwan University of Science and Technology, Taipei, Taiwan,* [2]*Department of Pediatrics, Division of Pediatric Immunology and Nephrology, Taipei Veterans General Hospital, Taipei, Taiwan,* [3]*Department of Nursing, Taipei Veterans General Hospital, Taipei, Taiwan,* [4]*Department of Pediatrics, Faculty of Medicine, School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan,* [5]*Institute of Emergency and Critical Care Medicine, School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan,* [6]*Department of Pediatrics, Keelung Hospital, Ministry of Health and Welfare, Keelung, Taiwan*

Objective: High quality physical environment for Continuous Ambulatory Peritoneal Dialysis (CAPD) can help minimize infection during manual instillation. Space design considerations such as ergonomics, circulation, and environmental control are crucial to assure a hygienic and efficient physical environment. As manual instillation is often conducted outside the hospital, often in patients' home, patient education on the procedure along with proper physical environment is vital. Traditionally, patient education is conducted in a designated space in the hospital by an experienced nurse. Demonstration of manual instillation procedure is communicated verbally with teaching aids such as

videos or pamphlets. Proper physical environment is pointed out during these education sessions. With the advancement and feasibility of 3D printing technology, architectural scaled-models can be printed to serve as a teaching aid. This research is to evaluate the possibility of using 3D-printed architectural scaled-model in lieu of a full-size built space for patient education.

Method: A cross-professional collaboration team consist of architecture and medical practitioners and students are formed. Architectural space requirements will be developed from in-depth interviews with medical practitioners and visits to various hospital patient education spaces. First, computer models will be created based on the most optimal physical environment dictated by medical practitioners. Second, 3D-printed architectural scaled-models will be made to determine the scale and size for legibility, maneuverability, and mobility. Third, 3D-printed models will be tested on patients of different ages to evaluate the learning outcome.

Result: An architectural scaled-model suitable for CAPD patient education is developed using computer software, and is produced with a 3D printer. 3D-printing an architecture scaled-model is more cost-effective than building a physical space. Pediatric patients may associate architectural scaled-model to that of a toy doll house. This association may lessen anxiety toward patient education, and thus make the learning experience more enjoyable. Family members may also find it easier to understand the spatial sequence and environmental quality with architectural scaled-model as a visual aid.

Conclusion: In Continuous Ambulatory Peritoneal Dialysis (CAPD) patient education, 3D-printed architecture scaled-model is an innovative educational aid to enhance the learning experience, lower the cost, and regain the space allocated for patient education back to the hospital for other essential functions. Architectural scaled-model combines fun and learning for pediatric patients and their family members. Additionally, it is cost-efficient and adaptable because it is easy to modify and reprint to adhere to advancement in medical technology. Furthermore, architectural scaled-models are easy to transport and reconfigure. Patient education can be conducted anywhere and simultaneously, thus providing flexibility to much needed clinical spaces.

ACPN210331P49 FLUID OVERLOAD IN CRITICALLY ILL PATIENTS : CHALLENGING OUTCOMES.

Mrs. Gopika Nair[1], Mr. Mahantesh V Patil Patil[1]
[1]*Jawaharlal Nehru Medical College,kaher, Belagavi, INDIA*

Introduction: Parenteral fluids are the second most common intervention in acutely ill patients (after oxygen) in intensive care units. Fluid overload has been associated with severe morbidity in several pediatric studies which include Acute Kidney Injury (AKI) and Acute Lung Injury (ALI) .Chest radiography, ultrasonography, echocardiography and impedance cardiography are non-invasive methods that detect fluid overload in ICU setting but in a developing country like India their use becomes cumbersome, requires expertise and is economically burdening. Documenting the daily intake-output and serial body weight measurements becomes an ideal method in such settings.

Objectives: This study was designed to find incidence of fluid overload (FO) at 24 hours and 48 hours of admission in critically ill children admitted in pediatric intensive care unit (PICU) and to determine the outcome of fluid overload.

Materials & methods: This study was conducted from January 2016 to December 2016 in PICU under the Department of Pediatrics, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi. A total of 125 critically ill children admitted in PICU were studied.Fluid overload was calculated by the formula:

% FO = [(Total fluid in (L) – Total fluid out (L)) / admission weight (kg)] × 100.

Results: Most of the children (59.20%) were boys and the boy to girl ratio was 1.45:1. The most common age group was ≤ 3 years (36.80%) and the mean age was 6.21±4.85 years. Septicemia (44%) was the cause of admission in 44% of the children. At 24 hours, 83 patients (66.4%) were found to have FO of <10%. However, significant FO considering of >10% was noted in 6.4% of the children. At 48 hours, 69 (55.2%) children had some degree of FO. The incidence of significant fluid overload at 48 hours was 0.81%. Significantly higher number of children (25%) with FO were aged between 3 to 5 years (p=0.037). Outcome was significantly associated with fluid overload (p=0.027). Significantly higher number of children (76.92%) with FO at 48 hours had a longer duration of ICU stay (8 to 14 days) (p=0.020). Complications of AKI were noted in 16.8% of the children. No association was found between AKI and FO (p=0.416), mean oxygen support days and ventilator support days (p>0.05).

Conclusion: A considerable subset of children admitted to PICU are at risk of significant fluid overload (≥10%). Weight-based definitions of FO are useful in defining FO in a broad PICU patient population and provides evidence for a more practical weight-based definition of FO that can be used at the bedside especially in a developing country with resource limited setting.

ACPN210331P50 SEVERE HYPONATREMIA IN INFANTS WITH URINARY TRACT INFECTION

Mrs. Karmila Abubakar[1], Professor Muhammad Yazid Jalaludin[1], Dr Nur Amanda Zainal[1], Dr Sze Lyn Woon[1], Dr Nurwahida Mohd Zikre[1], Dr Nurshadia Samingan[1], Dr Syaza Zafirah Ab Rahman[1], Dr Caroline Siew Yin Eng[1]
[1]*University Of Malaya, Kuala Lumpur, Malaysia,* [2]*Hospital Tuanku Ja'afar, Seremban, Malaysia*

Abstract

Introduction: Infants with UTI are prone to electrolytes abnormalities related to poor feeding or following non-specific symptoms such as vomiting or diarrhoea. Secondary pseudohypoaldosteronism (PHA) is uncommon yet a known association. We aim to highlight these uncommon sequelae in UTI to avoid incorrect diagnosis and subject to unnecessary investigations.

Methods: Critical reviews of case note were carried out by members of the clinical team. All the patients were admitted and referred to paediatric nephrology unit at University Malaya Medical Center between May 2019 to October 2020.

Results: We herein report 3 infants with UTI who showed concomitant hyponatremia and hyperkalemia. All 3 infants presented before 1 year of age. Hyponatremia was severe (below 120mmol/L) in all cases. The electrolyte derangements were transient and they resolved within 48 to 72 hours after treatment with intravenous fluid and appropriate antibiotic therapy. One had a hormonal study which confirmed pseudohypoaldosteronism. Two infants had underlying posterior urethral valve (PUV) while the third infant was found to have a vesico-vaginal fistula during evaluation following the UTI.

Conclusion: Secondary pseudohypoaldosteronism should be considered in infants with severe UTI and deranged electrolytes. This is more evident among infants with urological abnormalities. As this is usually transient, not all infants require hormonal screening. Those who require prolonged salt replacement and demonstrate involvement of other organ systems warrant further endocrinological evaluation.

Table 1: Characteristics and laboratory data of infants with severe hyponatremia

Age	Na (mmol/L)	K (mmol/L)	Creatinine (umol/L)	Aldosterone (pmol/L)	17-OHP (nmol/L)	Structural abnormality	Organism
Case 1. 3 months	119	6.4	43	15428	3.8	Posterior urethral valve	*Klebsiella pneumonia* ESBL
Case 2. 2 months	116	7	40	-	-	Bladder vaginal fistula	*Pseudomonas aeuroginosa*
Case 3. 8 months	112	6.4	40	-	-	Posterior urethral valve	*Enterobacter cloacae*

ACPN210331P51 HEPARIN-INDUCED HYPERKALEMIA IN END-STAGE RENAL DISEASE INFANT UNDERGOING PERITONEAL DIALYSIS

Mr. Yi Hsuan Tang[1,2,3], Ms. Hui-Lan Chen[1,3,4], Mr. Chien-Hung Lin[1,2], Ms. Hsin-Hui Wang*[1,2,3]

[1]*Department of Pediatrics, Division of Pediatric Immunology and Nephrology, Taipei Veterans General Hospital, Taipei, Taiwan,* [2]*Department of Pediatrics, Faculty of Medicine, School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan,* [3]*Institute of Emergency and Critical Care Medicine, School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan,* [4]*Department of Pediatrics, Keelung Hospital, Ministry of Health and Welfare, Keelung, Taiwan*

Objectives: Hyperkalemia is a life-threatening complication in end-stage renal disease (ESRD) patients. There are many medications for decreasing plasma potassium level, by shifting potassium into cells, ion-exchange resin and dialysis. Refractory hyperkalemia is rare but troublesome for clinical physician. Heparin-induced hyperkalemia is a less-known etiology in pediatric intensive care unit (PICU). Hence, we presented the clinical presentation and management of an ESRD infant undergoing peritoneal dialysis (PD) with refractory hyperkalemia.

Methods: This is a 1.1-year-old and 9 kilogram infant with renal-hepatic-pancreatic dysplasia type 1, heterozygous mutation in NPHP3, and ESRD undergoing PD therapy for 9 months. He was admitted in PICU due to PD-related peritonitis. After emergent hemodialysis (HD) and completed antibiotics treatment for peritonitis. His serum potassium level ([K]) was 5.3mmol/L after last HD. We hold HD under improving PD function and clinical condition, and we increased his PD prescription. Arterial catheter (A-line) was then inserted for closely monitor blood pressure, serum electrolyte levels and blood gas analysis with 1U heparin per 1cc half saline. His [K] was up to 6.4mmol/L on 2nd day of A-line insertion. Blood gas analysis was not acidosis. Electrocardiogram showed mild elevated peak T wave. After several courses of Salbutamol nebulization, intravenous sodium bicarbonate and insulin with dextrose water infusion, his [K] was up to 6.9mmol/L on 3rd day of A-line insertion.

Results: After reviewing his intake content and medication, heparin was the only medication added in this period. Heparin-induced refractory hyperkalemia was then suspected. We immediately stopped heparin infusion and removed A-line. However, [K] was still 7.0mmol/L follow-up 12 hours after discontinuous heparin. Fludrocortisone 20mcg twice per day was then prescribed. Follow-up [K] 12 hours later was 5.9mmol/L. and 5.5mmol/L 18 hours later without Salbutamol nebulization, intravenous sodium bicarbonate and insulin with dextrose water infusion management. We then tapered and stopped fludrocortisone in 3-day-course. His electrolyte levels and blood gas analysis were within upper limit. PD dialysis was smoothly undergoing.

Conclusions: Etiology of refractory hyperkalemia is difficult to recognize but important for further appropriate treatment. Heparin-induced hyperkalemia is one of adverse effect of heparin use and it can be managed properly if clinical physicians notice.

ACPN210331P52 SHORT- TERM EXPERIENCE IN MANAGEMENT OF PEDIATRIC SLE IN WESTERN INDIAN ETHNIC POPULATION COMPARED WITH OTHER PARTS OF INDIA

Mrs. ALIZA MITTAL[1], Dr Harshita Bamnawat[1], Dr Aasma Nalwa[2], Dr Pravin Kumar[1], Dr Siyaram Didel[1], Prof Kuldeep Singh[1]

[1]*Department of Pediatrics All India Institute Of Medical Sciences, Jodhpur. Rajasthan India, Jodhpur. Rajasthan, India,* [2]*Department of Pathology, All India Institute of Medical Sciences, Jodhpur, Jodhpur, India*

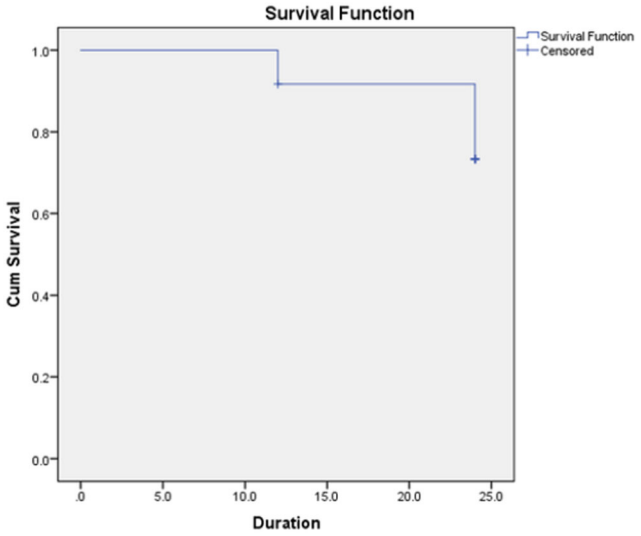
Aim: To determine the clinical, laboratory and biopsy characteristics and outcomes of children diagnosed with lupus nephritis in a tertiary level hospital in western Rajasthan and compare it with the data available from other parts of the country.

Material and methods: A retrospective review of children presenting to All India Institute of Medical sciences (AIIMS) Jodhpur, with a diagnosis of pediatric Systemic Lupus Erythematosus (p SLE), between July 2017 to July 2020 was done. Data was collected about clinical presentation at disease onset, other system involvement, biochemical parameters, biopsy findings, treatment received and outcome.

Results: 18 children were admitted during the study period with a diagnosis of SLE with Renal involvement and followed up. The mean age at presentation was 12.09 years, (range- 5 - 17 years) with female predilection (M: F-3:9). Fever, oral ulcers and rashes were most common clinical presentation at the time of disease onset while at the time of presentation the most common symptoms were proteinuria (83%), hypertension (65%) fever (100%) and rash (85%). 8/18 children presented with AKI of which 5/8 children presented as rapidly progressive renal failure. 13 biopsies were done in 18 children(1 had repeat biopsy).Six children did not undergo kidney biopsy. Out of those who did five patients (38%), had class III nephritis, five patients (38%) had class IV nephritis and three patients (25%) had class II nephritis. Four of those with class IV nephritis also had crescents. Eight patients (44%) had neurological involvement with six manifesting as seizures at disease onset. 7 patients (40%) developed hepatitis. One patient presented with autoimmune pancreatitis and subsequently developed shock and died within 24 hours. Cyclophosphamide was used in 7 out of 9 patients for induction of remission with class 3 and 4 nephritis and MMF in four children for induction therapy. Azathioprine was used for maintenance in patients with class 3 nephritis and for therapy in those with class 2 nephritis. Three patients had renal dysfunction requiring dialysis at the time of presentation.5/18 (27%) patients died (Of which 2 died following a relapse after attaining initial complete remission while 3 died following disease complications at initial admission itself, 3/18 (16%) patients developed end stage renal failure and 10/18 (55%) patients had complete remission after completing induction and 5 had partial remission, of which 3 relapsed during the follow up. 3 patients were lost to follow up. Figure 1 depicts the survival of our patients by Kaplan Meier analysis. All patients were positive for ANA of which only 1 was negative for Ds DNA. All except 1 had low C3 at presentation. Antiphospholipid antibodies were positive in 6/12 children which is much higher than a reported incidence of 30% in other Indian studies, DCT positive in 3/10 children.

Conclusion: An early renal involvement in pSLE was noted in our patients, with a much higher incidence of hypertension, at the time of presentation. Extra renal manifestations such as CNS Lupus and Hepatitis was reported in a much higher number of patients when compared to other parts of the country. Autoimmune pancreatitis and Digital Gangrene of lower limbs are some of the very rare manifestations of disease seen in the present study. The profile of our patients is similar to other descriptions of disease from North India and appears to be less severe than those reported from eastern India in terms of disease outcomes (death and ESRD) and much higher prevalence of extra renal manifestations were reported from the present study.

Legend: figure 1: Kaplan meier analysis of survival shows 90 % children survived at 10 months follow up which declined to 70% at 25 months.



ACPN210401P53 EXERCISE-INDUCED GROSS HAEMATURIA IN AN ADOLESCENT WITH CONCURRENT NUTCRACKER SYNDROME AND IGA NEPHROPATHY

Mr. Eugene Yu-hin Chan[1], Dr. Kevin Kin-Fen Fung[2], Dr. Tsz Wai Ho[1], Dr. Alison Lap-tak Ma[1], Dr. Elaine Yee-ling Kan[2]

[1]Paediatric Nephrology Centre, Hong Kong Children's Hospital, Hong Kong, Hong Kong, [2]Department of Radiology, Hong Kong Children's Hospital, Hong Kong, Hong Kong

Objective: Nutcracker syndrome with concomitant IgA nephropathy is infrequently reported in children with exercise-induced haematuria. The aim of this report is to describe the diagnostic challenge and approach in a patient presenting with exercise-induced haematuria in the presence of both conditions

Method: We report the case of a 17-year-old adolescent boy presented with recurrent, exercise-induced, whole stream painless gross haematuria and intermittent left loin pain for two months. The haematuria exacerbated following mild ambulation. There was no frothy urine, urinary symptoms or stone passage. There was no history of trauma and participation in contact sports. He had a thin body built and a BMI of 17. His blood pressure was normal at 100/53mmHg and physical examination was unremarkable.

Result: The patient had non-glomerular haematuria (RBC >50 cells/mm3) and persistent albuminuria (4.8mg/mmol) without crystals, casts or hypercalciuria. Urine culture was negative. His serum albumin (46g/L), creatinine (64umol/L) and clotting profile were normal. Other investigations including X-ray, Doppler ultrasound (DUS), infection and autoimmune workup were unremarkable. Computer tomography (CT) with contrast did not demonstrate evidence of left renal vein (LRV) compression. Both aortomesenteric angle and ratio of LRV diameter were normal and thus did not suggest nutcracker syndrome. Kidney biopsy showed IgA nephropathy (IgAN) (Oxford Classification, M1, E0, S0, T0, C0).

Since a diagnosis of IgAN could not fully explain the exercise-induced haematuria, renal venography with pressure measurement was performed and demonstrated an indentation upon mid portion of the LRV (figure 1a). The pressure gradient between the distal LRV and the inferior vena cava was 5mmHg, which was elevated (normal <3mmHg) (Figure 1b). These findings confirmed the presence of nutcracker syndrome. Interestingly, a second look ultrasound showed narrowed aortomesenteric angle at standing position but normal during deep inspiration (Figure 1c and d).

Conclusion: Nutcracker syndrome is an important differential diagnosis for exercise-induced gross haematuria. Although non-invasive modalities are often helpful, the diagnostic yield may be affected by patient's posture and respiratory effort. The widening of distance between superior mesenteric artery and aorta in this case could be related to deep inspiratory effort which the patient was instructed to take during scanning. This finding was reproduced in our second look ultrasound. Venography should be performed in cases with diagnostic difficulties.

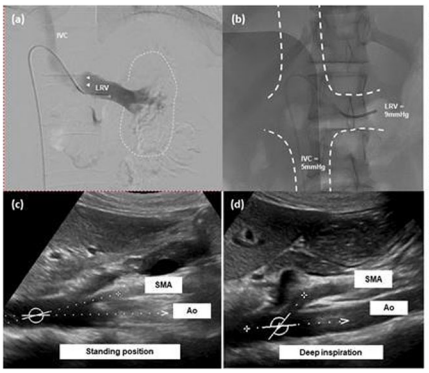


Figure 1 (a) Diagnostic venogram showed an abnormal indentation at the aorto-mesenteric portion of left renal vein (LRV) (white triangles) and slowing of contrast flow into more proximal portion of LRV (Left kidney outline annotated by white dash line). (b) Venous pressure at IVC was 4mmHg and that at distal LRV was 9mmHg. The pressure gradient between LRV and IVC was thus 5mmHg. (c) Dynamic ultrasound performed at standing position showed narrowed aortomesenteric angle (13.8°, normal = 38 – 65°) and (d) with deep inspiration showed normal aortomesenteric angle measuring 47.0°.

ACPN210401P54 PEDIATRIC C3 GLOMERULOPATHIES: EXPERIENCE IN A SINGLE MEDICAL CENTER

Ms. Lin Shien Fu[1], Dr. Yung Chieh Huang

[1]Taichung Veterans General Hospital, Taichung, Taiwan, [2]YangMing University, Taipei, Taiwan

Background: The C3 glomerulopathies are a group of rare kidney diseases characterized by prominent deposition of C3 in renal biopsy samples. We share our experience of 6 patients ever diagnosed in our hospital.

Methods: We followed 6 patients diagnosed as C3 glomerulopathy from histopathological findings in past 15 years. Their clinical, laboratory and pathological findings are recorded.

Results: There were 4 males and 2 females.

Case 1: Eighteen-year-old boy has residual ventricular septum defect (VSD) after operation in his early childhood. This time he presented as typical clinical acute glomerulonephritis (AGN). Besides gross hematuria, he had nephrotic syndrome, extremely C3 (8.01mg/dl) and normal C4 level at the time of renal biopsy. There were strong C3 depositions in mesangium and glomerular capillary wall. His condition was completely recovered after amoxicillin/clauvulanate acid and pentoxyphyllin treatment for 5 months.

Case 2: Four-year-old boy presented as steroid resistant nephrotic syndrome (SRNS). Otherwise, there was no hematuria, decreased C3/C4, or increased serum creatinine level. His renal pathology was mesangial nephropathy, electron microscope (EM) revealed mesangial deposition. He received regular methylprednisolone pulse therapy for 12 months and regular oral prednisolone for 18 months. There was complete remission of NS for 13 years up to now.

Case 3: Twelve-year-old boy presented as persistent proteinuria for 6 years. No other abnormality was noted. Renal pathology was similar to case 2, except additional C3 deposition in arterioles. His received angiotensin convertase inhibitor (ACEI) for 5 years and had daily urine protein 0.5-0.9gm. He has discontinued ACEI in past 8 years and spot urine protein/creatinine ratio was 0.2-0.3. He visited our emergency department due to palpitation. His echocardiogram showed mitral valve prolapse.

Case 4: Thirteen-year-old boy presented as intermittent gross hematuria for 5 years. Surgical pathology and EM revealed negative finding. Only C3 deposited in mesangium as 2+ was noted in the biopsy. Two years after biopsy, he had acute flank pain and gross hematuria, CT of kidney at that time showed a vessel cross his left ureteropelvic junction. There was no gross or microscopic hematuria noted as he grew up in past 5 years.

Case 5: Four-year-old girl presented as hematuria for 5 months. Renal biopsy revealed negative finding in surgical pathology and EM. Only 2+ C3 and 1+ IgM deposited mesangium and 2+ C3 in arterioles were noted. Initially, she received dipyridamole for 4 years. Then, we shifted ACE I due to proteinuria in past 9 years. Her proteinuria became heavy gradually in recent 4 years. During follow-up period, her mother and two aunts received chronic hemodialysis due to uremia of unknown reason. Another renal biopsy done in Oct.2020 revealed IgA nephropathy.

Case 6: Ten-year-old girl presented as hematuria for 3 years. Renal biopsy revealed mesangial nephropathy in surgical pathology and EM. There was C3 deposited in mesangium as one+. She had solely persistent microscopic hematuria in past 14 years and received no medical treatment.

Conclusion: There clinical spectrums of C3 glomerulopathies are diverse. It can be non-specific finding to AGN, SRNS. Patients in our series do not have persistent complement dysregulation and their prognoses were fair except one whose 2nd renal biopsy became IgA nephropathy.

ACPN21P55 PERCUTANEOUS ULTRASOUND GUIDED RENAL BIOPSY IN CHILDREN: EXPERIENCE AT A TERTIARY CARE CENTRE IN WESTERN INDIA

Mrs. ALIZA MITTAL[1], Dr Aasma Nalwa[2], Dr Amarpal Singh[1], Dr Vikarn Vishwajeet[2], Dr Pawan Kumar Garg[3]

[1]*Department of Pediatrics, All India Institute Of Medical Sciences, Jodhpur. Rajasthan India, Jodhpur, India,* [2]*Department of Pathology, All India Institute of Medical Sciences, Jodhpur, Jodhpur, India,* [3]*Department of Diagnostic and Interventional Radiology, Jodhpur, India*

Introduction: Percutaneous renal biopsy(PRB) is standard of care in the evaluation and management of renal diseases in pediatric population. Present study was conducted to evaluate the clinical indication for renal biopsy in native kidneys and spectrum of histopathological findings in a tertiary pediatric nephrology centre in western Rajasthan.

Objectives: to evaluate the indications for renal biopsy in native kidneys and spectrum of histopathological findings in a tertiary pediatric nephrology centre in western Rajasthan.

Methods: All children who underwent renal biopsy from 2017 to 2020 were included in this retrospective study. Light microscopy and immunofluorescent microscopy was performed on all renal tissue specimens with application of electron microscopy in specific cases.

Results: There were total 52 patients in the study group. Of which 57.6 % were female. The mean age was 10.5 years .The most common indication for PRB was nephrotic syndrome 48 %.Adequate renal tissue specimen was obtained in 72.5% cases. The most common histopathological diagnosis was minimal change disease(MCD)(17.5%) followed by FSGS(15%).MCD accounted for 36.8% of total nephrotic syndrome cases. Acute glomerulonephritis(AGN) was indication of PRB in 25 % cases. Poststreptococcal glomerulonephritis (38.4%) was the most common histopathological finding in cases of AGN followed by lupus nephritis(23%),mesangioproliferative glomerulonephritis(5.7%),IgA nephropathy(3.84%),Diffuse mesangial sclerosis(3.84%) and one case of primary hyperoxaluria. 30.7% patients with AGN had crescentic glomerulonephritis. Post biopsy 9.6% patients had minimal subclinical hematoma and one patient had seizure.

Conclusions: Percutaneous ultrasound guided renal biopsy was found to be safe ,effective and useful technique in the children in our study. It should be utilised to identify the disease early in course and to decide about the treatment.

ACPN21P56 BARRIERS TO KIDNEY TRANSPLANTATION IN PEDIATRICS PATIENTS: A SYSTEMIC REVIEW

Ms. GUOHUA HE[1], Mrs. Jie Ding[1], Mrs. Xuhui Zhong[1], Ms Fang Wang[1]

[1]*Peking University First Hospital, Beijing , China*

Introduction: Kidney transplantation is the treatment of choice for end-stage renal disease. However, there are great disparities between countries in children's access to kidney transplantation, suggesting that there may be some influencing factors that hinder children's access to kidney transplantation. There is currently a lack of an overview of the factors affecting children's access to kidney transplantation worldwide.

Methods: >A systematic literature search was conducted using PubMed, EMBASE, Cochrane library, Web of Science, clinicaltrials.gov, SinoMed, Chinese Biomedicine, China National Knowledge Infrastructure, Wangfang data and Chongqing VIP Information databases for original studies from inception to 8 July 2020.

Results: A total of 2168 articles were identified and extracted. The most common studied barriers affecting children's access to kidney transplantation were immunological factors (such as ABO mismatching, HLA mismatching, etc.), young age, female gender, non-white race, BMI out of normal range(BMI either too high or too low), remote geographic location, lower socio-economic status, late referral to transplant services and allocation policies.

Conclusion: There was a wide variation in the barriers to kidney transplantation in children worldwide. Some of the barriers could be the optimized via medical care system and social secure system so as to enhance children's access to kidney transplantation.

ACPN21P57 IMMUNOSUPPRESSIVE THERAPIES IN CHILDREN WITH BIOPSY-PROVEN IGA VASCULITIS NEPHRITIS: A TERTIARY CENTRE EXPERIENCE

Mr. Hon Lam Lee[1], Dr. Eugene Yu-hin Chan[1], Dr. Alison Lap-tak Ma[1], Dr. Wai-ming Lai[1]

[1]*Paediatric Nephrology Centre, Hong Kong Children Hospital, Hong Kong,*

Objective: IgA Vasculitis Nephritis (IgAVN) can lead to severe presentation including nephrotic syndrome. Data pertaining to the treatment outcomes of IgAVN with persistent moderate or nephrotic range proteinuria in children are, however, limited. The aim of this study is to determine the response to immunosuppressive therapies in this patient population.

Methods: We conducted a retrospective review on all children presenting with IgAV before 18 years between January 2009 and December 2019 in the Paediatric Nephrology Centre in Hong Kong. Patients with biopsy-proven IgAVN developing persistent moderate or severe nephrotic-range proteinuria despite ACE-inhibitor (ACEi), and followed for 24 months or more were included. Patient demographics, clinical and laboratory data, therapies received, and treatment outcomes were evaluated.

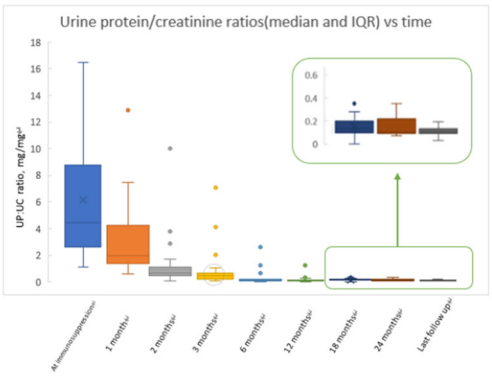
Results: Of the 177 patients with IgAV, 42 children developed proteinuria. 21 Chinese patients (76% boy) had persistent proteinuria despite ACEi and kidney biopsy confirmed IgAVN at a median age of 8.5 years (IQR 5.8-11.2). At baseline, 3 (14%), 14 (66%), 3 (14%) and 1 (4%) patients had moderate proteinuria, nephrotic-range proteinuria, nephrotic syndrome and nephritic-nephrotic syndrome, respectively. All patients had normal kidney function, except one child with an estimated GFR of 31ml/min/1.73m2. Median urine protein to urine creatinine ratio (UPCR) was 4.4mg/mg (IQR 2.4-9.0) and serum albumin was 32g/L (IQR 28-33.5). Histological findings were classified according to International Study of Kidney Diseases in Children (ISKDC): Class II (n=5, 24%), Class IIIa (n=9, 42%), Class IIIb (n=6, 29%), Class IV (n=1, 5%).

All patients received corticosteroid at a median time of 33 days (IQR 12-52) since kidney involvement. Whereas 7 children (33%) with severe disease received monthly intravenous cyclophosphamide as induction therapy, 12 patients (57%) and 2 patients (10%) received calcineurin inhibitors and azathioprine, respectively. The maintenance therapy consisted of corticosteroid and one additional immunosuppression, including calcineurin inhibitors (n=16, 76%), azathioprine (n=4, 19%) and mycophenolate mofetil (n=1, 5%).

Over a median follow-up period of 3.6 years (IQR 2.8-5.6), 18 patients (86%) attained complete remission at a median of 139.5 days (IQR 102-225) since immunosuppressants initiation. The other 3 patients achieved partial remission. Three patients (14%) relapsed in 7.5 months (IQR 1.2-16.2) following complete remission but resolved promptly with treatments. At last follow-up, all patients had normal kidney function and the median UPCR was 0.11mg/mg (IQR 0.10-0.16).

Conclusion: Immunosuppressive therapies were associated with favourable renal outcomes in children with biopsy-proven IgAVN presented with persistent moderate or nephrotic range proteinuria despite ACEi. Further studies are required to determine the optimal treatments in this patient population.

Fig 1.



The course of urine protein/creatinine ratio after the use of immunosuppressants during follow-up was depicted in Figs. 1. Whisker and box plot denote the median and interquartile range, respectively.

ACPN21P58 KIDNEY FUNCTION IN CHILDREN WITH TRANSFUSION-DEPENDENT THALASSEMIA

Mrs. Karmila Abubakar[1], Dr. Nurwahida Mohd Zikre[1], Dr. Nor Asiah Muhammad[3], Dr. Nur Emylia Zailanalhuddin[2], Dr. Charles De Kun Lai[1], Dr. Jen Chun Foo[1], Dr. Suet Li Yap[2], Professor Hany Ariffin[1], Dr. Caroline Siew Yin Eng[2]

[1]University Of Malaya, Kuala Lumpur, Malaysia, [2]Hospital Tuanku Ja'afar, Seremban, Malaysia, [3]National Institute of Health, Kuala Lumpur, Malaysia

Objectives: Thalassemia is a hemoglobinopathy commonly seen in the region of South East Asia. Kidney dysfunction, a high disease burden by itself, is an under-reported sequelae in this group of patients. We investigated the prevalence of this phenomenon and identify its potential predictors.

Methods: We conducted a retrospective study involving children with transfusion-dependent thalassemia. Abnormal kidney function is defined as children with glomerular filtration rate (GFR) of <90ml/min/1.73m2, declined in GFR of more than 20ml/min/1.73m2 within 3 years or presence of nephrotic range proteinuria. Data analyzed were age, age at diagnosis, number of years dependent on transfusion, chelation therapy, ferritin and pre-transfusion hemoglobin level.

Results: Eighty one children were recruited. Median age was 11.42 ±5.27years. Thirty out of 81 (37%) demonstrated abnormal kidney function. Age at diagnosis (RR, 0.858; 95% CI, 0.754–0.976; p = 0.02) and months of transfusion (RR, 1.03; 95% CI, 1.010–1.051; p = 0.003) were associated with increased risk of developing kidney dysfunction.

Conclusion: Abnormal kidney function in thalassemia may go unnoticed without screening. Children on regular transfusion require active surveillance of kidney function. This will allow early detection and active interventions to slow progression.

Table 1: Multivariate analysis of patients with transfusion-dependent thalassaemia.

	B	df	*p*-value	Adjusted RR	95% C.I.for EXP(B)	
					Lower	Upper
Age (year)	.153	1	**.020**	.858	.754	.976
Duration of transfusion (months)	.030	1	**.003**	1.030	1.010	1.051

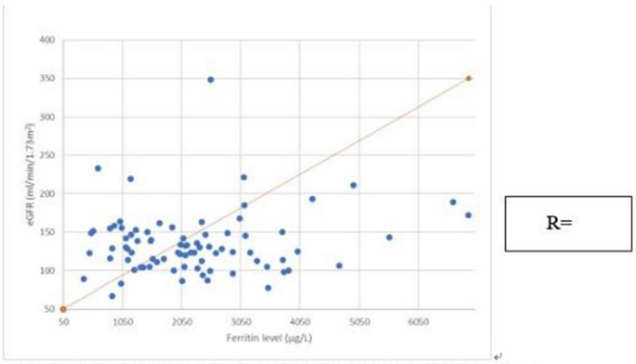


Figure 1: Scatter plot showing correlation of ferritin level and eGFR.

ACPN21P59 EFFECT OF BIRTH WEIGHT, GESTATION, CATCH-UP GROWTH ON ADULT EGFR: A CASE-CONTROL STUDY

Mr. David Liangjian Lu[1], Dr. Sandar Ko Saw[2], Ms. Ching Ching Seah[2], Ms. Nurul Jannah Binti Ahmad[2], Dr. Mya Than[2], Ms. Dion Lim[3], Dr. Chian Chau Lee[3], Dr. Krishnamoorthy Niduvaje[4], Prof. Jiun Lee[4], Prof. Kar-Hui Ng[1,2], Dr. Isaac Desheng Liu[1], Prof. Hui Kim Yap[1,2]

[1]Department of Paediatrics, Khoo Teck Puat-National University Children's Medical Institute, National University Health System, Singapore, Singapore, [2]Department of Paediatrics, Yong Loo Lin

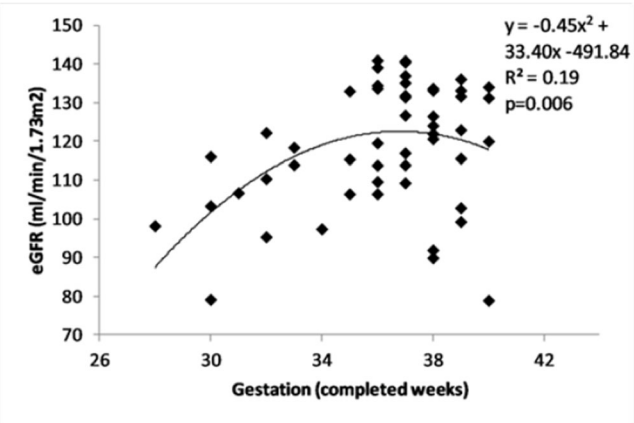
School of Medicine, National University of Singapore, Singapore, Singapore, [3]University Health Centre, National University of Singapore, Singapore, Singapore, [4]Department of Neonatology, Khoo Teck Puat-National University Children's Medical Institute, National University Health System, Singapore, Singapore

Objectives: Low birth weight (LBW) is associated with chronic kidney disease in later life. The relative contributions of growth restriction and prematurity, subsequent catch-up growth, as well as confounders such as neonatal acute kidney injury and concomitant metabolic syndrome, to reductions in adult eGFR remain uncertain.

Methods: 42 LBW individuals and 16 age- and sex- matched controls were recruited from healthy volunteers aged 18-25 years. Birth details as well as serial anthropometric measurements were obtained from their personal health record. Participants underwent 24-hour ambulatory blood pressure monitoring, and a serum creatinine measurement to determine their eGFR.

Results: There were no significant differences between LBW participants and controls in terms of Apgar scores, body mass index and 24-hour blood pressure. Instead, eGFR showed an inverse 'U' shaped relationship with gestation (Figure, p=0.006), but not with sex- and gestation- adjusted birth weight SDS (p=0.63). Within the LBW sub-group, gestation was related to eGFR [3.07 (95% CI: 1.35-4.80) ml/min/1.73m2 per additional week, p=0.001] independent of adjusted birth weight SDS (p=0.31). The effect of catch-up growth depended on gestation, with increasing catch-up growth only being associated with reductions in eGFR in participants born at 34 weeks or less [interaction between gestation and respectively change in weight SDS from birth to 6-12 months (p=0.05), daily weight gain from birth to 6-12 months (p=0.008), and change in height SDS from birth to adulthood (p=0.006)].

Conclusions: Prematurity underpins the association between low birth weight and reductions in adult eGFR, and modulates the deleterious effects of catch-up growth on eGFR.



ACPN21P60 CLINICAL OUTCOMES OF TMA IN KOREAN PEDIATRICS

Ms. Seon Hee Lim[1], Ms. Ji Hyun Kim[2], Mr. Yo Han Ahn[1], Mr. Il-Soo Ha[1], Mr. Hae Il Cheong[3], Ms. Hee Gyung Kang[1]

[1]Seoul National University Children's Hospital, Seoul, South Korea, [2]Seoul National University Bundang Hospital, Seongnam, South Korea, [3]Hallym University Sacred Heart Hospital, Anyang, South Korea

Objectives: Thrombotic microangiopathy (TMA) features thrombocytopenia, microangiopathic hemolytic anemia (MAHA) and the damage of organs and commonly causes acute kidney injury (AKI) or chronic kidney disease by invading kidney. It should be treated through early screening and diagnosis as its management and prognosis varies by its cause. TMA is classified into thrombotic thrombocytopenic purpura (TTP, when ADAMTS-13 activity < 10%), hemolytic uremic syndrome (HUS), and other TMA. The most common TMA in pediatrics is typical HUS which is related to shiga-toxin producing E. coli, and the other HUS, aHUS, occurs due to dysregulation of complement pathway in most cases. Recently, the importance of early diagnosis of aHUS has emerged as its medication (C5 inhibitor) has been developed. This study tries to understanding the clinical condition and prognosis of TMA occurred in pediatrics.

Methods: The study investigated medical records on children under 18 years old who were diagnosed with TMA or were treated for known TMA from 2003 to 30th May 2019 at SNUH children's hospital excluding typical HUS and TMA after SCT. First, TMA was defined as case with the evidence of MAHA, thrombocytopenia, and organ damage and case with histologically diagnosis of TMA. Next, TTP was defined as clinical diagnosis or ADAMTS-13 activity < 10%, and a HUS was defined as clinical diagnosis or related gene abnormality were found. Finally, other cases were defined as others. The clinical condition, cause, and prognosis of patients were investigated.

Results: A total 45 patients (5.3±4.0 years of mean age, 44.4% of male) were investigated during period. Among them, 93.3% of patients were diagnosed with clinical manifestations such as AKI (90.5%), neurologic problem (42.9%), MAHA and thrombocytopenia. And 6.7% were diagnosed with histological diagnosis. There were 15 patients of TTP (33.3%), 26 of aHUS (57.8%) and 4 of other TMA (8.9%), and there is no difference of age between three groups (P=0.71).

Neurological symptoms were more in TTP than aHUS (P =0.013), and AKI occurred even in 53.3% of TTP. Platelet was 20k in TTP and was lower than other groups (P =0.007). Plasmapheresis was conducted on more than 80% of TTP and aHUS, and it progressed to ESRD in 23% of aHUS. One patient died in aHUS.

Conclusions: The treatment and prognosis of TMA varies depending on its type, but it is not easy to distinguish TMA only by clinical manifestations. So, it is necessary to conduct a differential diagnosis based on the early implementation of ADAMTS13 and gene test as well as shiga-toxin for TMA

ACPN21P61 WHAT DO YOUNG PEOPLE THINK ARE THE FACTORS LEADING TO MEDICATION NONADHERENCE, AND HOW CAN THIS INFORMATION BE USED TO IMPROVE SERVICES?

Mr. Shouja Alam[1], Dr Elizabeth Farr[2], Mr Shaun Thomas[2], Dr Judith van der Voort[2]

[1]Birmingham Children's Hospital, Birmingham, United Kingdom, [2]University Hospital of Wales, Cardiff, United Kingdom

Objectives: Those who receive kidney transplants in adolescence and young adulthood have shorter graft survival than those receiving grafts earlier or later in life. Graft loss is multifactorial, but treatment nonadherence and transition from paediatric to adult services have been identified as contributors. The perspectives of young people (YP) regarding medication nonadherence were investigated in a qualitative service improvement project aiming to improve graft health and the experiences of YP transitioning from a tertiary paediatric nephrology service to adult services.

Methods: Institutional ethics approval was sought but deemed unnecessary and informed written consent was gained. Young people attending a renal patient summer camp were questioned in two semi-structured focus group discussions ran in parallel by two researchers. Transcribed responses were thematically analysed by two investigators independently, then agreed upon jointly.

Results: There were 11 participants (13-30y, average 21y, 36% female). Six themes emerged: 1) Staff approach, either positive or negative; 2)

Challenging life events; 3) Peer support; 4) Chances to talk; and 5) Patient-related factors. Patient-related factors subdivided into exercising autonomy, no perceived immediate consequences, and normalising & denial.

Conclusions: Healthcare services and consultations involving YP should incorporate their own suggestions to help guard against nonadherence. YP wanted staff to value and support them. Being scolded by staff when revealing nonadherence led to disengagement and threats about consequences were counterproductive. YP suggested a more appropriate response would be to work through reasons behind nonadherence. Given that YP reported that nnadherence can be a form of choice and control, ensuring that YP feel involved with decision making and can exercise autonomy in other ways may address this.

Participants also reported that they avoided treatment to feel normal, and that they thought it acceptable because they did not initially perceive any negative consequences from nonadherence. YP valued different members of their healthcare team taking an interest in their lives and giving them opportunities to talk about such thoughts and feelings. Robust staff support mechanisms should capture YP experiencing challenging life events. Additionally, peer support through peer mentorship or peer-group support was greatly valued and deemed protective against nonadherence.

ACPN21P62 WHAT DO YOUNG PEOPLE THINK CAN BE IMPROVED WITH THE TRANSITION TO ADULT SERVICES?

Mr. Shouja Alam[1], Dr Elizabeth Farr[2], Mr Shaun Thomas[2], Dr Judith van der Voort[2]

[1]*Birmingham Children's Hospital, Birmingham, United Kingdom,* [2]*University Hospital of Wales, Cardiff, United Kingdom*

Objectives: Local audit showed NICE Guidance regarding the transition of young people (YP) to adult services is not well implemented. This qualitative service improvement project investigated the perspectives of YP transitioning from a tertiary paediatric nephrology service to adult services. The aim was to identify key factors underpinning positive and negative experiences of transition and provide suggestions for change in practice to better support transition for YP.

Methods: Institutional ethics approval was sought but deemed unnecessary and informed written consent gained. Young people attending a renal patient summer camp were questioned through critical incident technique via both written questionnaire and semi-structured focus group discussion overseen by two researchers. Transcribed responses were thematically analysed by two investigators independently, then agreed upon jointly.

Results: Of 11 participants (13-30y, average 21y, 36% female), only 30% knew what ReadySteadyGo was, the locally employed transition tool. 15 themes were identified, organised into 5 key factors underpinning positive experiences of transition: 1) Preparation for adult services; 2) Approach adopted by staff; 3) Chances to talk; 4) Peer support; and 5) Environmental improvement.

Conclusion: Young people generated recommendations to improve the experience of transition. These included improving preparation through familiarisation with staff and places by being introduced to the new team sooner with more opportunities to interact, trips to the new unit and more information about the practicalities within adult services. YP wanted staff to be more like friends, ideally with some familiar faces on both sides of transition. They wanted staff to ease YP into transition gradually and tailor the process to each YP's individual needs, to be honest about pros and cons and provide truthful experiences from other patients, acknowledge YP's concerns by listening to how they feel and empower YP to take more involvement with learning to promote self-efficacy. Additionally, YP wanted the opportunity to talk about their life experiences, and particularly valued the support of peers. Through socialising with others their age with similar chronic conditions, YP were able to share experiences and feel normal. Finally, YP wanted adult services to invest in comfort and entertainment as provided in paediatric services.

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