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From the Editor's Pen

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On behalf of ISPN bulletin editorial board I extend greetings to all of you! The board is also thankful for the wonderful messages and words of appreciation from you on the new format of ISPN bulletin.

We wish that Covid 19 cases decline further and we all can meet soon in a physical ISPNCON soon. In this issue we bring for you interesting articles on peritoneal dialysis. ISPD has recently published the revised guidelines on peritoneal dialysis for acute kidney injury. We have two invited articles on important aspects of peritoneal dialysis in India from senior pediatric nephrologists. Interpretation of the genetic tests in children with kidney diseases is always a challenge. This puzzle has been simplified for the fellows in the educational review section. We have other interesting sections of Journal Scan, Clinical Quiz, Blog, ISPN Desk and Webinar links of you as usual. Hope you will find this issue interesting.

On academic front the ISPN published **guidelines** on **SSNS** and **SRNS** in Indian Pediatric which are widely read world over. Congratulations to the AIIMS team and the whole ISPN for bringing out the guidelines. We eagerly await the revised UTI guidelines for children.

At the end, I thank all the members of the editorial board who have worked hard to bring the issue, and also to all the members of ISPN for writing articles for this issue, all what matters the most is that we work as a **TEAM.**

Call for Article

We invite articles for the Category of Educational Review, Clinical Quiz, Blog and Journal Club from ISPN Members

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Peritoneal Dialysis in Children

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Keywords

Peritoneal Dialysis, AKI, CKD

Peritoneal Dialysis (PD) was first introduced in early 1920s as a modality for replacement of kidney function by George Ganter. It was in 1940s that it was first described to save the life of a patient with Acute Kidney Injury (AKI) [1]

The early PD solutions led to adverse events like post instillation pain due to low pH, higher concentration of sodium and chloride causing hyperchloremic metabolic acidosis, volume overload, and hypertension [2]

Later modifications made these solutions more physiological as well as promoted sodium removal by diffusion [3]

Successful adaptation of the technique for use in infants and children with AKI was first reported in 1961[4] Peritoneal dialysis is being used regularly for management of AKI and chronic kidney failure (CKF) since 1970s [5] Over the decades the PD technique and technology has made huge progress and PD still remains the preferred modality in developing world.

PD as Modality of Kidney Replacement Therapy in AKI

Acute kidney injury is common in hospitalised children especially in critically ill. It contributes significantly to mortality, morbidity and prolonged hospital stay, especially in those with multi- organ failure. Peritoneal dialysis (PD) is the preferred and convenient treatment modality for AKI in children especially in the resource limited settings due to its feasibility, simplicity, requirement of minimal infrastructure, cost effectiveness, safety and efficiency in correcting correct metabolic, electrolyte, acid – base abnormalities and volume overload [6] In recent years, the technologically advanced newer extra corporal therapies including hemofiltration and hemodiafiltration are being increasingly utilised in the developed world. There are standard treatment regimen for these modalities and the dose delivered can be objectively measured while these are lacking in PD. However acute PD is still the preferred modality for managing Paediatric AKI in most of the centres in Asia and Africa. Acute PD is the preferred RRT modality in neonates, infants and post cardiac surgery AKI. Recently, there has been a renewed interest to manage AKI with acute peritoneal dialysis even in developed countries [7]

The age and size of the child seems to be the most important factor influencing the decision on the choice of dialysis modality. PD is still the most common modality used in small children especially those younger than 6 years. Technical simplicity, no need for anticoagulation or placement of central venous catheters, and excellent tolerance in hemodynamically unstable patients are among major advantages of PD [8]

PD requires only single access to peritoneal cavity unlike CRRT requires vascular access with risk of septicaemia. Fluid removal can be modulated by altering the dialysate fluid composition. The glucose absorption from PD fluid provides nutritional benefits to critically ill. In paediatric AKI, PD is preferred the option as it is an intra-corporeal modality without need for vascular access. Vascular access is the Achilles heel in paediatric extracorporeal therapies especially in neonates and infants. PD is the preferred option in critically ill children with coagulopathy and those with increased risk of intracranial pressure. There is gradual and continuous removal of solutes with less risk of rapid fluid shifts and hypotension as in extracorporeal therapies. PD is more physiologic with better preservation of renal hemodynamic that could contribute to earlier renal recovery. There is no inflammatory injury from exposure of blood to synthetic membranes as in HD or CRRT. The pores in the peritoneal membrane also allows removal of toxic cytokines [9]

The 0 by 25 initiative by the International Society of Nephrology's AKI to prevent all avoidable deaths from AKI by 2025 also supports the role of PD in AKI in developing countries as CRRT is available in only very few centres located mostly in metro cities. Availability of qualified paediatrics haemodialysis staff and appropriate equipment is often limited or almost non-existent in most of the centres across the country while PD offers effective, affordable lifesaving treatment for children with AKI especially in PICU. The recent additions to paediatrics continuous RRT including CARPIDIEM, NIDUS and AQUADEX are not available to children with AKI in the developing world. At the same time, automated peritoneal dialysis using cyclers have made continuous high volume PD therapies possible.

However there are several concerns regarding acute PD in AKI. Unpredictable fluid removal rates, inadequate solute clearance especially in hyper catabolic AKI in critically ill children on vasopressors, hyper glycemia, excessive protein loss through peritoneal membrane and risk of peritonitis are the important ones. Diaphragmatic impediment affecting ventilation is yet another concern especially in children on ventilator. In such situations, appropriate reduction in the dwell volume is required for good patient outcome.

The kidney replacement therapy (KRT) options for AKI in children include PD, HD, CRRT and hybrid modalities. The choice of modality in paediatric AKI still remains an open challenge. The decision about dialysis modality should be based on local expertise, resources available, and the patient's clinical status. Results of surveys of RRT options available for children in India showed that PD was the most preferred dialysis in children and was available in almost 100% of centres surveyed [10] Similar surveys in developed world showed CRRT as the preferred and most practised modality for AKI in children [11,12]

Lack of good data on acute PD in children remains a limiting factor in comparing the outcome of PD with CRRT in paediatrics AKI. There are no prospective randomised controlled trials comparing the impact and outcome of PD, HD and CRRT in paediatric AKI [8]

A randomized study in critically ill adults with AKI comparing continuous venovenous hemodiafiltration with continuous PD showed that although hemodiafiltration provided higher urea and creatinine clearances, with faster correction of fluid overload, there were no differences in mortality or hemodynamic stability between the two modalities [13]

The outcome following institution of high volume continuous PD with a flexible PD catheter and an automated PD cycler was comparable to six times weekly HD as per the randomized, controlled trial by Gabriel et al [9]

A comparative study on the three dialysis modalities in children with AKI showed that the underlying clinical diagnosis, hemodynamic stability and use of pressor agents are the key predictors of mortality rather than the RRT modality [14]

In the absence of evidence indicating better survival with any modality, the most appropriate dialysis choice for children with AKI is based on the patient's characteristics, institutional resources, efficiency and local practice [15]

Chronic Peritoneal Dialysis in Children

End-stage kidney disease (ESKD) is a rare condition in childhood with an annual incidence ranging from 4 to 14 and a prevalence from 18 to 100 per million age-related population. [16,17]

The definitive management of children with chronic kidney failure is transplantation and pre-emptive transplantation is the best option. However it is most often not possible and (KRT) is required for sustenance of life as a bridge to kidney transplantation.Continuous peritoneal dialysis is the initial modality of choice in younger children given its almost universal applicability, cost-effectiveness and the possibility of a home-based treatment [18,19].

Most often these children are dependent on KRT throughout their life and various dialysis modalities complement each other. Every attempt should be made to preserve the peritoneum and vascular access as these are the life lines.

There are no studies in children with chronic kidney failure comparing the outcome or quality of life on continuous PD or HD. The decision to start one or the other is based on the feasibility and suitability for the child at a given point of time. PD will be the modality of choice in infants, toddlers and school going children given the ease of home based treatment, universal applicability, absence of pricks, needles and need for vascular access. Preservation thus residual kidney function and urine output is yet another advantage of PD. The dietary restrictions are not as rigorous as while on intermittent HD and this makes continuous PD more child friendly.

The financial commitment required and sophisticated technical needs are the major constraints for running an efficient dialysis program for children with chronic kidney failure in many countries in developing world. Automated cycler assisted peritoneal dialysis is also not feasible due to cost constraints and technical problems [18] The advantage of CAPD is ease of use and limited cost of equipment. However the neat and clean environment required for CAPD, sterile precautions needed at home and care giver burn out in home based modalities should be taken into account especially in a developing country like ours. A multi-disciplinary team effort coupled with family support is absolutely essential for sustaining dialysis treatment in our country. Yet another issue is the finances required for KRT. In a country like ours the allocation for health is below 1.5% while the WHO guideline is at least 5%. RRT remains unaffordable for the majority of families in view of catastrophic health expenditure and lack of Governmental support or insurance schemes.

In Kerala with a percapita income of 2600 USD, cost of dialysis and transplantation is unbearable for most families. Access to care is also limited. Pediatric Nephrologist often faces the ethical dilemma of whether to start RRT in a child who will most probably discontinue therapy and die after depleting all the family's resources. In Kerala, a unique state funded program "Thalolam" started in 2010 for treatment of kidney diseases in children below 18 years.

A retrospective chart analysis was done in children up to 18 years initiated on dialysis between January 2007 and September 2019 in Pediatric Nephrology at SAT Hospital. Demographic features, etiology, modality and duration on dialysis and outcome were assessed.

Finances needed per child for dialysis, transplantation and post-transplant care were also analyzed. Improved utilization of services is assessed by comparing the number of children initiated on RRT between 2007-2010 and 2010- 2019. Study population comprised 97 children on RRT. Mean age was 10.52 ± 4.02 years with a male: female ratio of 1.48:1. Basic disease was CAKUT in 31.9% (31). PUV comprised 58 % of CAKUT (18). CAPD was the initial KRT modality in 25 (25.7 %) and hemodialysis in in 72 (74.2%). 8 Babies were initiated on PD in infancy. Automated cycler assisted PD was done in one infant who got transplanted at 2 years. Switch from PD to HD was needed in 12 children due to resistant peritonitis or ultrafiltration failure or mechanical issues. 38 children got transplanted. Initiation of dialysis prior to and after start of 'Thalolam' was 3.07 child per year and 9.9 child per year respectively. Expenses per child per year on dialysis was 2800 USD. This was inclusive of dialysis consumables, erythropoietin and supportive medications [20] The cost of maintaining children on dialysis is prohibitive and without financial support, the care will not be a sustained one.

Development of a National PD Registry

Development of a national PD registry for children is the need of the hour for a country like ours so that we can improve our knowledge regarding the PD practices in different centers across the country, complications and outcome. Now end-stage kidney disease (ESKD) data is available only from Europe and North America. Lack of data from developing countries is the major hurdle for planning and implementing strategies for improving the ESKD treatment for children from developing world. The International Pediatric Peritoneal Dialysis Network (IPPN) was established in 2007 in order to improve the dialysis care in children worldwide, and to provide standard guidelines on dialysis care and assign useful tools and management algorithms based on evidence-based medicine [21]

We hope to collaborate with IPNA in this endeavor most efficiently and effectively so that children with ESKD from our country will get benefitted ultimately.

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‘PD first’ in India- the way forward!

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Keywords

CAPD, ESRD, Peritoneal dialysis

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The importance of Continuous Ambulatory Peritoneal Dialysis (CAPD), as the lifeline for children with End stage renal disease (ESRD) awaiting kidney transplantation cannot be emphasized enough, especially in a low resource country like ours and more so with the raging pandemic. Maintenance hemodialysis for children require manpower resources that are hard to come by. Centers with pediatric nephrology trained personnel, experts in vascular access, adequate technical and nursing staff and with the ability to give the required time and attention to run a good quality hemodialysis unit is extremely scarce and practically non-existent outside major metropolitan cities.

CAPD is also better suited for the pediatric population in terms of maintaining good residual renal function as well as a better quality of life with better growth and development with continued schooling and near normal activities. Many studies have found a positive correlation of receiving PD in the initial years of dialysis to survival advantage in patients [1–4] Notable advantages are the wide age range (infancy to adolescence) that it can cater to, while being more “environmentally responsible” and a “cheaper” modality with reduced burden on the health care systems and resources. CAPD has been quoted as the “ideal” mode of dialysis especially for the middle and lower-income countries[5,6]

The Economic Divide

The economic condition of the nation and the government expenditure on public health are the key determinants of access to equitable health care. In developed countries, like Europe, North America and Japan, every child with ESRD is offered Renal replacement therapy (RRT) [7] In spite of this, CAPD accounts for only 20-30% of the total children dialyzed [8] This is partly because of the reimbursement policies which tend to favor incentre Hemodialysis (HD), and partly because the waiting period for the renal transplantation is short. On the other hand, developing nations like most African and Asian countries, dialysis is offered only to a fraction of the patients, of which CAPD accounts for <10%.

PD – First Policy!

Hong Kong, Mexico and Thailand, belonging to the middle and low-income countries, have been the only countries that have successfully adopted the CAPD-first policy.[9, 10] Hong Kong initiated this policy more than 25 years ago in 1985, which stated that all ESRD patients will be treated with CAPD unless contraindicated. Supported both by the government and charitable organizations, today those who do not opt for PD need to pay for the dialysis sessions from their own pocket. This has made Hong Kong a Centre with the highest number of CAPD patients in the world (75.6% as of 2010 data) [11]

In Thailand, PD first policy was introduced in 2007 and introduced various changes in the health policies to enable this [10] Prior to 2007, only hemodialysis was getting reimbursed in the public hospitals and gradually in some private centers. After 2007, to implement the peritoneal dialysis (PD) preference, reimbursements were given for CAPD in public hospitals along with incentives to the health care professionals and the public hospitals for every patient started on CAPD, by the National Health Security Office until 2014. The Central purchasing by the Government Pharmaceutical Organization has been important in cost containment hence avoiding price clashes. This strategy improved the PD usage, more in the public hospitals, though the private hospitals still needed utilization of HD machines. New PD centres were established under three nationwide main PD training centers, in collaboration with the Nephrology Society of Thailand, Thai nephrology nursing association and the Thai Red Cross Nursing College. Along with this, the PD nurses training programs training about 70-80 PD nurses per year were introduced. The scarcity of nurses was appropriately utilized in PD where 30-50 CAPD patients were attended to against the 15 HD patients per nurse. The public health care system also takes care of the transportation for routine visits and emergencies of patients to the PD centers and various philanthropic communities are helping the patients set up a clean and suitable area in their houses[12]

PD Scenario in India

The availability of resources adequate for safe implementation and continuation of CAPD is hampered by several resource limitations

Manpower: Pediatric nephrologists, trained nurses, trained clinical coordinators and field healthcare workers are needed for implementing the program successfully for children all over India.

Pediatric nephrologists are not more than 150 to 200 in the country who are mostly located in big cities. There is no training program for nurses or technicians in CAPD although several nurses are trained in hemodialysis. Clinical coordinators are provided by the company manufacturing CAPD fluid. This number (coordinators) are few and services not available in any of the smaller cities. An additional setback is the lack of nephrology-oriented pediatricians and hence inability to recognize and treat emergencies leading to preventable deaths.

Government Support for Dialysis

Central Government. Up until recently the Pradhan Mantri National Dialysis Program was fully-funding the hemodialysis services for all Below poverty line (BPL) patients and offering a subsidized rate to all non-BPL patients[13] Only recently, influenced by CAPD first approach, there has been the addition of CAPD in the program but this has not yet been implemented at ground level.

State Government supports. A few states have incorporated certain health programs to provide free of cost CAPD to the children. Barring Tamil Nadu, in other states only select hospitals are supported in this free CAPD program

Economic Burden

As many of our patients are self-payees the cost of CAPD becomes prohibitive

Cost of CAPD disposables in India (catheter insertion and one year of PD)

Type of CAPD	No. of bags (2L) in a month	Cost of catheter (one time cost)	Cost of minicaps + transfer set	Total cost/year
True CAPD: <15 kg	4 x 365 =1460 1460 X 225 = 3,28,500	12,000	30 X 365 =10,950 2200 x 4 =8800	3,60,250
>15kg	4 x 365 =1460 1460 X 225 = 3,28,500	12,000	30 X 365 = 10,950 2200 x 4 = 8800	3,60,250
Modified CAPD	2 x 365 = 730	12,000	30 X 360 = 10,950	1,96,000
CpAPD <15 kg	730 X 225= 1,64,250		2200x 4 = 8800	

The modified CAPD practiced by many Indian paediatric nephrologists utilizes the 2 litre CAPD bag for 2 cycles where the patient remains attached to the bag for the first cycle and is only ambulatory in the second cycle. This reduces the monthly expenditure by using half the number of bags but makes the PD partially ambulatory PD or CpAPD.

Lessons from COVID-19

The importance of CAPD has increased manifolds in this COVID-era, where avoiding hospital visits for dialysis was ideal and travel during lockdowns has been difficult and risky for the patients who had to spend ridiculous amounts for private transport.

The risk is also for the hospital staff who have been already burdened with the COVID duties. At this time, for patients with ESRD, the option of CAPD is life-saving.

The COVID-era has already introduced the importance of hand washing and mask wearing to the whole world, and it might make the task of aseptic care easier for patients to understand and follow.

COVID has made us realize that physical meetings are not necessary for learning. Learning on the virtual platform is a big boon.

ISPN has so far not taken up any public health program for implementation. It is time we lead the way with PD First.

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Educational Review

In this issue we have published Part I of the educational review on Genetics from St John's Medical College, Bangalore.

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Making Sense of Genomic terminology, Genetic testing methods and Genetic report: Part I

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Keywords

Genomics, Paediatric Nephrology

Introduction

A substantial proportion of pediatric kidney disease cases are due to genetic cause. Genetic testing is emerging as a powerful diagnostic tool as establishing a genetic diagnosis can have many potential benefits in children with kidney diseases, such as guiding treatment, informing prognosis, familial testing, and providing deeper understanding of pathobiology of kidney diseases. The increasing utilization of genetic testing in nephrology care is chiefly due to expanded accessibility of genetic sequencing technologies, such as massively parallel sequencing (formerly next generation sequencing), chromosomal microarray along with traditional genetic testing approaches like Sanger sequencing and karyotyping. In addition, completion of human genome project that provided a reference genomic sequence and helped in discovery of genes and novel pathological genetic variation in human disease phenotypes improved the yield of genetic testing in the clinical setting.

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Today, with wider clinical use of genetic testing as part of the diagnostic evaluation, pediatric nephrologists have the challenging task of selecting the most suitable genetic test for each patient, and then applying the results into appropriate clinical contexts. This review in two parts is intended to familiarize with various aspects of genetic testing in children with kidney diseases. The first part familiarizes clinicians with genomic terminology, various genetic testing methods and ordering a genetic test. The second part will deal with analysis of sequencing data and interpretation of report.

Genomic terminology

Gene: Gene is made up of DNA and is the basic physical and functional unit of heredity. Genes vary in size from a few hundred DNA bases to more than 2 million bases. It is estimated that human genome contains 20,000 -25,000 genes.

Base pair (bp): BP are 2 complementary nucleotides paired in double-stranded DNA. Adenosine (A) pairs with thymine (T), and guanine (G) pairs with cytosine (C). A bp is also used as a physical distance of length of a sequence of nucleotides, eg, 20 bp is a chain of DNA composed of 20 nucleotides

Codon: Three bases in a DNA or RNA sequence that specify a single amino acid.

Central Dogma of Biology: The DNA is transcribed into an mRNA (by a process known as transcription), which is in essence, converted into a protein (by a process known as translation), the ultimate effector of the action of the specific gene.

Genetic variation: It is the difference in DNA sequences between individuals within a population. Variation occurs in germ cells i.e. sperm and egg, and also in somatic (all other) cells. Only variation that arises in germ cells can be inherited from one individual to another.

Variant: The term variant is used to refer to a specific region of the genome which differs between two genomes.

Types of genetic variation:

a) **Small genetic variations-** Variation the involves 1 base pair to 1,000 base pairs Single base substitution (point mutation): Transition [interchange of the purine (Adenine/Guanine) or pyrimidine (Cytosine/Thymine) nucleic acids]; Transversion [interchange of a purine and pyrimidine nucleic acid]

   Insertions or deletions (indel): Insertion or deletion of bases in the genome of an organism is classified among small genetic variations (Indel can involve 1 -1000 base pairs).

b) **Large genetic variations -** Variations occurs over a larger DNA sequence and includes both copy number variation and Copy number variations: Stretches of genomic sequence of roughly 1000 base pairs (1kb) to 3 million base pairs (3 Mb) in size that are deleted or are duplicated in varying numbers

   Chromosomal rearrangement event: such as inversion, deletions, duplications and deletions

Effect of variant on protein (Fig.1):

a) **Synonymous/silent -** Due to redundancies in the genetic code, many nucleotide changes will not change the amino acid sequence, (eg: GCT to GCC change would still encode an alanine).

b) **Nonsense (Stop variant) -** These turn a coding codon to a stop codon (e.g. GGA to TGA – Glycine to stop) resulting in a truncated protein, which may or may not be subject to nonsense-mediated decay depending on where in the peptide it occurs (see frameshift for more explanation).

c) **Missense -** This change results in a change in amino acid, for example ACC threonine to AAC asparagine.

d) **Frameshift -** Insertion or deletion of base pairs and length is not divisible by three, will cause a frameshift where all codons downstream of the insertion or deletion are shifted. This often results in a malformed protein or nonsense-mediated decay (stop in the first ~90% of the coding region, leads to no protein being translated at all). Stop in the last ~10% of the coding region are expected to typically escape nonsense-mediated decay of mRNA and result in truly truncated protein products. Indel refers to insertion and deletion occurring in the same sequence and region.

e) **Inframe or non-frameshift -** Indels with a length divisible by three (i.e. whole codon indels) in coding regions will cause insertions or deletions of whole amino acids into the protein.

f) **Stop-Loss variant -** A sequence variant where at least one base of the stop codon is changed, resulting in an elongated transcript.

g) **Splice site variant -** A genetic alteration in the DNA sequence that occurs at the boundary of an exon and an intron (splice site). The change usually disrupts RNA splicing resulting in the loss of exons or the inclusion of introns and an altered protein-coding sequence.

Haploinsufficiency: The situation that occurs when one copy of a gene is inactivated or deleted and the remaining functional copy of the gene is not adequate to produce the needed gene product to preserve normal function (such as with frameshift or non-sense variants or deletion of whole gene).

Novel variant: A newly discovered, distinct genetic alteration; NOT the same as new or de novo mutation.

De Novo variant (mutation): Causal variant in index case, when both the parents do not harbor any germline mutations i.e not inherited

Single-nucleotide polymorphism (SNP): DNA sequence variations that occur when a *single nucleotide* (A, T, C, or G) in the genome sequence is altered. SNPs are the most abundant variant in the human genome and most common source of genetic variation. More than 10 million SNPs are present in the human genome, i.e 1 SNP for approximately every 100 bases (Human genome consists of 3 billion base pairs). Not all SNPs are benign (eg: HFE c.845G>A variant, causing amino acid substitution, p.Cys282Tyr, is a SNP in the European Ancestry population, as the allele frequency is ~ 4%; it is pathogenic for hemochromatosis).

Mutation: Originally, "mutation" meant any deviation from a standard sequence, independent of the phenotypic impact. It is now replaced by more neutral term such as pathogenic variant, risk variant, disease-causing variant or de novo variant.

Inheritance: It is phenotype or trait that exhibits a given inheritance pattern, not the pathogenic variant (variant is associated with an autosomal recessive (or dominant) pattern of inheritance).

Autosomal dominant, autosomal recessive, X-linked dominant, X-linked recessive, multifactorial, and mitochondrial inheritance are examples. Each mode of inheritance results in a characteristic pattern of affected and unaffected family members.

Locus (*plural is* loci): The physical site on a chromosome occupied by a particular gene or other identifiable DNA sequence.

Allele: One of two, or more, forms or versions of a particular gene that are located at the same position or genetic locus on a chromosome. Variations in clinical traits and phenotypes are allelic if they arise from the same gene sequence or locus (eg: Cystinosis) and nonallelic (eg: Steroid resistant nephrotic syndrome) if they arise from different gene sequences of different loci.

Allele Frequency: It represents the prevalence of a genetic variant in a population. Allele frequency can be calculated by the number of occurrences of an allele of interest divided by the total number of copies of the allele in the entire population. It can be expressed as fraction or percentage

Zygosity: It refers to extent to which both copies of a chromosome or gene have the same genetic sequence. Individual inherits two alleles for each gene from parents. In context of genetic testing, zygosity refers to identification of a variant in one or both alleles.

Homozygosity - Both alleles of a gene contain the same variant (eg: c.2376G>C).

Heterozygosity - When one allele contains a variant while the other allele contains the reference sequence (wild type) i.e has one normal and one abnormal copy

Compound heterozygosity - two alleles (chromosomes) of a gene, each contain a different change in different regions or exons of the same gene (eg: c.**2376**G>C and c.**3103**del)

In autosomal recessive disease, the variants should be either homozygous or compound heterozygous (found in trans i.e each of the variant from one parent).

Penetrance: It is a binary function, with a trait or disease either manifesting or not (penetrant or non-penetrant, respectively).

Expressivity: Refers to the range of phenotypes that may manifest in the context of a given disorder, associated with a given pathogenic variant (eg: as NF-B disorders associated with various congenital malformations of kidney such as cystic kidney, echogenic kidneys, VUR, with hyperuricemia, diabetes. All the features may not be present in all the patients with deleterious variant in the gene).

Carrier: Those with a single variant in a recessive disorder

Phenocopy: A phenotypic trait or disease that resembles the trait expressed by a particular genotype, but in an individual who is not a carrier of that genotype.

Genome: The sum total of the genetic material of a cell or an organism

Exome: The entire protein-coding sequences portion of the genome (excludes introns or noncoding DNA between exons/genes).

Coverage: The number of times a portion of the genome is sequenced in a sequencing reaction. Often expressed as "depth of coverage" and numerically as 1X, 2X, 3X. A minimum of 30X required for clinical reporting.

Genetic heterogeneity: A common phenotype caused by more than 1 gene.

Genetic testing methods

Sanger sequencing: A method of DNA sequencing based on the selective incorporation of chain-terminating dideoxynucleotides by DNA polymerase to determine the sequence of nucleotide bases in a piece of DNA.

Massively parallel sequencing (Next generation/high-throughput sequencing): DNA sequencing technology that permits rapid sequencing of large portions of the genome; so called because it vastly increases the throughput over classic Sanger sequencing

a) Targeted gene panel - Only coding portions of a specific set of genes are sequenced.

b) Clinical exome – Sequencing of coding portions of genes that are known to be disease associated and curated from databases such as OMIM, HGMD and ClinVar (4000-6000 genes).

a) Whole exome - Captures nearly all the coding sequences (exons) in an individual's genome (21,000 protein coding genes comprising ~196,000 coding exons). Although the exons of genes constitute only ~1% of the human genome, the rational for exome sequencing is based on the knowledge that the exome harbors up to ~85% of biologically relevant and pathogenic genetic variation, with large phenotypic effects in man

a) Whole genome - covers nearly all regions of the genome (coding and noncoding regions).Not used in clinical setting

Comparative genomic hybridization (CGH)also **array CGH:** Analysis of the entire genome for deletions and duplications, as well as copy neutral changes that may be clinically significant. DNA of test sample is competitively hybridized with a reference sample of DNA of known sequence to a DNA microarray, used to detect copy number changes in the test sample.

MLPA (Multiplex ligation-dependent probe amplification): Laboratory method commonly used for the detection of copy number changes (insertions or deletions) of genomic sequences in a gene or few genes.

Karyotyping: It is a process of preparing, arranging, categorizing chromosomes to know the number of chromosomes as well as structural features of each chromosome.

Fluorescence in situ hybridization (FISH): It is a cytogenetic technique that uses fluorescent probes that bind to only those parts of a nucleic acid sequence with a high degree of sequence complementarity thereby identifying the presence or absence of specific DNA sequences (specific genes or regions) on chromosomes.

Table 1 compares the sanger sequencing with massively parallel sequencing methods

Choosing a genetic testing method: The choice of genetic testing method is based on clinical context, number of potential genes associated with the phenotype and the the type of variant expected.

Sanger sequencing - Single or few gene disorders (eg: cystinosis); confirm a variant identified in MPS; segregation analysis by screening parents and family members; familial disease with a known variant; diagnostic use in prenatal setting; sequence regions that not covered by MPS technique.

Targeted panel - These are phenotype -driven panels chosen when multiple monogenic causes with a syndrome/specific phenotype is present (eg:Bartter's syndrome). Features 10's to 100's genes.

Clinical exome - Most common of the MPS method ordered for genetic testing. Preferred when clinical and pathological phenotypes overlap; no clear clinical diagnosis and a genetic cause is suspected; when copy number variation (CNV) are suspected.

Many MPS- based targeted gene sets are built on clinical exome backbone as a single process for library preparation and sequencing helps in saving cost. In an event the targeted panel returns no pathogenic or likely pathogenic variants, additional relevant gene sets can be "unmasked" and analyzed.

Whole exome - To discover newer genes and for CNVs.

MLPA - When predominant variant associated with a phenotype are large deletions or insertions in a gene (eg: CFHR variants in HUS).

array CGH - Phenotypes associated with copy number variants (eg: syndromes with kidney diseases, CAKUT); to confirm CNV detected on exome sequencing; when a genetic cause is strongly suspected and no variants are identified using MPS method (eg: Alports' syndrome, X linked hypophosphatemic rickets).

Genetic testing process

It is important that a systematic process is followed while ordering a genetic test to ensure that genetic testing will be useful for the patient and their family. It includes identifying patients who are likely to have a genetic cause and benefit form genetic testing, choosing the appropriate test, counselling and conveying the results followed by plan of management based on results. Counselling the family is an important part of the process and includes explaining the reason for genetic testing, setting realistic expectations of utility, informing about technical details of the test including limitations, possibility of uninformative results, need for family screening and management plan based on the results as well as cost. The chances of incidental or secondary findings especially with use of clinical exome or whole exome must also be informed.

Fig 2 provides the key components of the genetic testing process.

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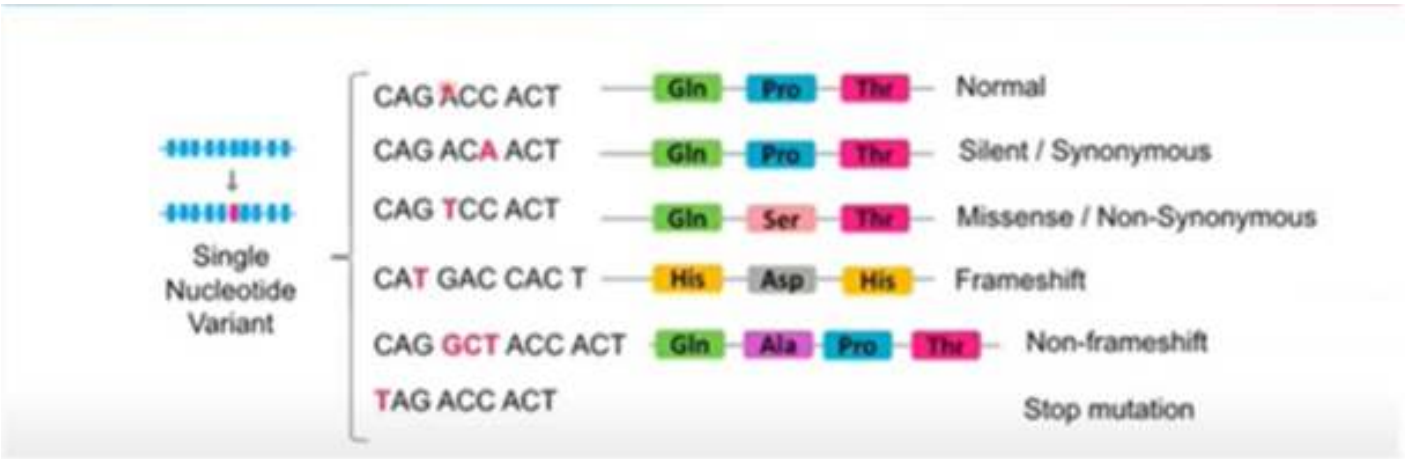

Figure 1: Effect of variant on protein

Fig: 2. Genetic testing process

Table 1. Sanger sequencing and massively parallel sequencing

Features	Sanger sequencing	Massively parallel sequencing (MPS)		
Target	Gene by Gene	Targeted sequencing of Panel of genes	Clinical exome (4000 genes)/ Whole-exome sequencing	Whole genome sequencing
Indications	Single or few gene disorder, confirmation of NGS variant	Multiple monogenic causes with a syndrome/specific phenotype	Atypical phenotype, complex phenotype Negative results on targeted screening	Discovery of mutations including non-coding, untranslated regions
Throughput	Low throughput	High throughput	High throughput	High throughput
Mutations detected	All type except CNV, large deletions	All type except large deletions, repeat regions	All including CNV large deletions missed	All including intronic variants
Analytical Sensitivity/Specificity	High/High	Average/Low	Average/Low	Low/Low
Coverage (Mbp)	NA	~0.5	~0.5	~3200
Average Read Depth	NA	500-100x	100-150x	~30-60x
Incidental findings	NA	Low	Moderate	High
Time and cost	Few days to week Time consuming and expensive for >5 genes	Fast and cost effective	Fast, expensive	Fast, expensive
Pros	High analytical accuracy; Easier & faster sequence interpretation; No risk of secondary/incidental findings	Can be optimized to ensure sufficient coverage; Interrogation of genes associated with clinical indication facilitates interpretation and lowers risks of secondary findings	Ubbiased approach increases diagnostic sensitivity; cost-effective approach: Interrogation of coding regions enriched for known disease causing mutation; Sequence re-analysis and discovery of novel genes	Superior diagnostic and analytical Sensitivity to WES owing to its ability to assess SNVs, indels, CNVs in coding/non-coding regions

Children at Play

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As pediatricians, there is no understating the importance of playing in childhood. Play is an integral part of the development process. I do hope the images of few children at play, taken across various locations across India, do bring you a moment of joy.

As pediatricians, there is no understating the importance of playing in childhood. Play is an integral part of the development process. I do hope the images of few children at play, taken across various locations across India, do bring you a moment of joy.

"In the eyes of a child, there is joy, there is laughter. There is hope, there is trust, a chance to shape the future" – Graham Russell

There are no seven wonders in the Seven Wonders of the World in the eyes of a child. There are seven million." – Walt Streightiff

"In every real man a child is hidden that wants to play." – Friedrich Nietzsche

Image locations:
Vellore, Tamilnadu ; Amritsar, Punjab, Qutub Minar, New Delhi and Chowpatty beach, Mumbai

Guideline Review

In this section we bring for you summary of important guidelines published along with a review. For this issue ISPD guidelines for peritoneal dialysis in acute kidney injury are summarized.

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Summary of ISPD Guidelines for Peritoneal Dialysis in Acute Kidney Injury: 2020 Update (Pediatrics)

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Acute kidney injury (AKI) develops in 5-25% cases in hospitalized children within a week of admission [1] Advanced stage in AKI increases morbidity and mortality. It is associated with longer hospital stay, need for ventilator support, and kidney replacement therapy (KRT) [1] Among KRT modalities, peritoneal dialysis (PD) is most commonly used, especially in low and lower middle-income countries due to paucity of trained personnel, and financial or logistic constraints [2]

The first pediatric guidelines for peritoneal dialysis were published by International Society of Peritoneal Dialysis (ISPD) in 2012, and chiefly focused on catheter-related infections and peritonitis in children [3] Recently, ISPD published a dedicated pediatric guideline- an update on peritoneal dialysis in AKI [4] The strength of each recommendation is graded as level 1 (strong recommendation), level 2 (weak recommendation) and further classified in A to D depending on the level of evidence.

A number of recommendations (12 out of 22) are also categorized as **"Practice point"** where though there was lack of evidence, sufficient clinical experience existed to guide the practice. The recommendations should be followed to achieve optimal standard, and in resource poor settings, minimum standard may be acceptable.

Here we present the summary and highlights of key recommendations. Table 1 shows the comparison with previous ISPD guideline in 2012 [3]

Recommendation:

1.1 Peritoneal dialysis is a suitable renal replacement therapy modality for treatment of acute kidney injury in children (1C).

There is no consensus on superiority of one KRT modality over the others in children with severe AKI. PD is preferred in resource poor settings, where technical and economic support is not adequate. Safety profile of peritoneal dialysis is good in babies of different age groups despite hemodynamic instability or with multi-organ failure [5, 6] PD can be easily implemented as a bed side procedure in a stable child. In fluid restricted state, dextrose content of the PD fluid helps to prevent hypoglycemia [7, 8] Survival rates are high among the children who underwent PD than other modalities of KRT [9, 10] If all modalities are available with equal technical supports, PD is preferred over the other KRT techniques in very low birth weight babies with hemodynamic instability, where blood volume is too small to run extracorporeal measure [11-13] post cardiac surgery cases, deranged coagulation profile where intervention through large vessels can be catastrophic [14,15]

Contraindications of PD

Absolute contraindications to PD are rare as intact peritoneal cavity almost always enables administration of PD. Absolute contraindications include post laparotomy state, abdominal compartment syndrome, and fungal peritonitis. The chief relative contraindications include:

- Recent abdominal surgery
- Paralytic ileus
- Open chest e.g., post cardiac surgery
- Difficult ventilation
- Clinical situations where precise removal of large volumes of fluid are required
- Pleuroperitoneal connection allowing dialysate leak into the chest
- Hypercatabolic renal failure where clearance of small solutes may be insufficient
- Abdominal wall cellulitis or abdominal wall burn.

Recommendation: 2: Access and fluid delivery for acute PD in children

Optimal	Minimum standard
We recommend a tenckhoff catheter inserted by a surgeon in the operating theatre as the optimal choice for PD access. (1B)	Rigid catheters placed using a stylet should only be used when soft Seldinger catheters are not available, with the duration of use limited to <3 days to minimize the risk of complications. (1C)
Insertion of a PD catheter with an insertion kit and using Seldinger technique is an acceptable alternative. (1C)	
Interventional radiological placement of PD catheters combining ultrasound and fluoroscopy is an acceptable alternative. (1D)	
We recommend the use of prophylactic antibiotics prior to PD catheter insertion (1B)	Improvised PD catheters should only be used when no standard PD access is available. ***(Practice point)***
A closed delivery system with a Y connection should be used. (1A) A system utilizing buretrols to measure fill and drainage volumes should be used when performing manual PD in small children. (***Practice point***)	In resource limited settings, an open system with spiking of bags may be used; however, this should be designed to limit the number of potential sites for contamination and ensure precise measurement of fill and drainage volumes. ***(Practice point)***
Automated peritoneal dialysis (APD) is suitable for the management of pediatric AKI, except in neonates for whom fill volumes are too small for currently available machines. (1D)	

Ideally soft tenckhoff catheter insertion should be done in operation theatre by a surgeon [16, 17] Laparoscopic and open surgical approaches have similar safety and complication profile; fluid leakage is avoided with laparoscopic technique [18, 19] Migrated and blocked catheter issues can be sorted out during laparoscopy. In hemodynamically unstable child, bedside PD catheter can be inserted by pediatrician or pediatric nephrologists, using temporary Cook PD catheter, or tenckhoff catheter. The insertion of tenckhoff with seldinger technique and peel-away method, by tunneled or non-tunneled approach are cost effective and safe[18-24]

When soft catheter is not readily available, rigid catheter can be inserted with stylet. This approach is associated with high risk of leakage, peritonitis, dislodgment, visceral injury, and duration should be limited to 2-3days [25, 26] For prolonged need for KRT, a soft catheter should be inserted later on, alternatively HD can be initiated. If no PD catheter is available, central venous or dialysis lines (adult or pediatric), intercostal chest drains, nasogastric tubes (with extra side holes cut) or Foley's urethral catheters can be used for PD as life-saving procedure. Like chronic PD, double cuffed tenckhoff catheter with downward or subcutaneous tunnel configuration is preferred.

Manual PD delivery system are generally used in infants, while automated PD machines are useful when fill volume is ≥100 ml. The components of PD systems and APD options have also been detailed in the guidelines [4]

Sterile technique should be observed during PD insertion including the use of sterile mask, cap, gloves, gown, and sterile drapes. Sterile tray to keep all equipment's (saline bag, connections), povidone iodine for dressing of connections, closed sterile system of tubing, PD fluid, PD catheter, and adequate stuff training must be ensured [4] Guidelines recommend the use of prophylactic antibiotic 60 minutes prior to procedure. Antibiotics should be selected depending on local sensitivity pattern. It should cover gram positive organisms; gram negative organisms should be here bowel perforation suspected.

Recommendation 3: Peritoneal dialysis solutions for acute PD in children

Optimal	Minimum standard
The composition of the acute peritoneal dialysis solution should include dextrose in a concentration designed to achieve the target ultrafiltration (Practice point)	If no facilities exist to measure the serum potassium, consideration should be given for the empiric addition of potassium to the dialysis solution after 12 hr of continuous PD to achieve a dialysate concentration of 3–4 mmol/L. ***(Practice point)***
Once potassium levels in the serum fall to <4 mmol/L, potassium should be added to dialysate using sterile technique. ***(Practice point)***	
Serum concentrations of electrolytes should be measured 12 hourly for the first 24 h and daily once stable. ***(Practice point)***	In resource poor settings, sodium and potassium should be measured daily, if practical. ***(Practice point)***
In the setting of hepatic dysfunction, hemodynamic instability, and persistent/worsening metabolic acidosis, it is preferable to use bicarbonate containing solutions. (1D)	Where these solutions are not available, the use of lactate containing solutions is an alternative. (2D)
Commercially prepared dialysis solutions should be used. (1C)	However, where resources do not permit commercial dialysis solutions, locally prepared fluids may be used with careful observation of sterile preparation procedures and patient outcomes (e.g., rate of peritonitis). (1C)

Commercially available PD fluids contain 1.5% (osmolality 346 mosm/L), 2.5% (396 mosm/L), 4.25% (485 mosm/L) dextrose. We also have commercially available 1.7% (354 mosm/L) PD fluid as 1-2 L bottle. Osmotic gradient between PD fluid and plasma generates ultrafiltration. In minimal or mild fluid overload, 1.5% fluid can be used while in moderate to severe fluid overloaded state, 2.5% fluid is preferred for adequate fluid removal.

Dextrose concentration can be altered by aseptic addition of required amount of 50% dextrose solution to the commercial fluid. Higher dextrose concentration leads to hyperglycemia; therefore, insulin therapy or dextrose concentration titration may be required. As an initial guide, 4-5, 5-7, 7-10U/L insulin may be added to 1.5%, 2.5% and 4.25% PD fluid. A regular insulin infusion may allow tighter regulation. Close blood sugar monitoring is required to prevent hypoglycemia. Heparin should be added (500IU/L) to prevent fibrin clot formation. After initiation of PD, hyperkalemia usually settles in 6-12 hours, and potassium (4 mmol/L) should be added in PD fluid when serum potassium is less than 4 mmol/L. Sterility should be strictly maintained during mixing. If regular serum electrolyte measurement is not feasible, potassium should be added empirically after 12 hours of continuous PD to achieve dialysate concentration 3-4 mmol/L. In bicarbonate based PD, there is risk of developing hypocalcemia. Intravenous (IV) calcium infusion should be considered; adding calcium to PD solution is avoided due to the risk of precipitation. Acute hypertonic PD with rapid cycles promotes free water removal, resulting in hypernatremia [27]. In such cases, dwell time should be increased and dextrose concentration should be titrated depending on volume status. Sometimes IV hypotonic fluid (0.45% saline) can be used to compensate extra fluid loss. In case of hypernatremia, hypertonic saline should be added in PD fluid to maintain sodium concentration of PD fluid within 15 mmol/L of patient's sodium, to prevent abrupt fall in patient's sodium level.

Recommendations: 4: Prescription of acute PD in pediatric patients

- The initial fill volume should be limited to 10–20 ml/kg to minimize the risk of dialysate leakage; a gradual increase in the volume to approximately 30–40 ml/kg (800–1100 ml/m2) may occur as tolerated by the patient. (Practice point)
- The initial exchange duration, including inflow, dwell and drain times, should generally be every 60–90 min; gradual prolongation of the dwell time can occur as fluid and solute removal targets are achieved. In neonates and small infants, the cycle duration may need to be reduced to achieve adequate ultrafiltration. (Practice point)
- Close monitoring of total fluid intake and output is mandatory with a goal to achieve and maintain normotension and euvolemia. (1B)
- Acute PD should be continuous throughout the full 24-h period for the initial 1–3 days of therapy. (1C)
- Close monitoring of drug dosages and levels, where available, should be conducted when providing acute PD. (Practice point)

At initiation of PD, small fill volume is recommended to prevent rise in intra-peritoneal pressure (IPP) and dialysate leakage[28] The guidelines suggest modification of prescriptions depending upon the patient's clinical status, requirement of fluid and solute removal. If patient tolerates well and there is no leakage, gradual increase in fill volume should be tried to increase solute and fluid removal. In <2years of age, maximum fill volume should be 800 ml/m2 to prevent acute rise in IPP and ultrafiltrate (UF) reabsorption through lymphatics, cardiac and respiratory embarrassment [29] Intra-abdominal pressure can be measured through bladder transducer or directly from peritoneal cavity. Raised IPP increases mortality in critically ill children [30]

For adequate fluid and solute removal, initially short duration cycles are preferred. In-flow time and drain time depend on volume of the fluid to be in and out, height difference between the PD and drain bag to the patient, and resistance through the circuits. Generally, in time is 5-10 min and out-time is 10-20 min. Small solute equilibration is rapid in children and dwell time 30-60 min usually suffices [31] The fill volume and dwell time should be optimized depending on the patient's tolerability, fluid balance and requirement solute removal. Fluid balance should be monitored closely in first few hours and as required. If patient's condition permits, weight should be monitored every 12-24 hour.

Recommendation: 5: Continuous flow peritoneal dialysis (CFPD) (Practice point)

- Continuous flow peritoneal dialysis can be considered as a PD treatment option when an increase in solute clearance and UF is desired but cannot be achieved with standard acute PD. Therapy with this technique should be considered experimental since experience with the therapy is limited. (Practice point)
- Continuous flow peritoneal dialysis can be considered for dialysis therapy in children with AKI when the use of only very small fill volumes is preferred (e.g. children with high ventilator pressures). (Practice point)

A second catheter should be placed to run CFPD. Catheter can be placed below umbilicus or either side of umbilicus midway between umbilicus and anterior superior iliac spine. In adult patients, CFPD increases fluid removal and solute removal by three to eight times than conventional PD [32] Pediatric literatures showed fluid and solute removal increases by fourfold in CFPD than conventional PD [33] In some studies, this clearance is comparable to extracorporeal therapy [34]

Prescription of CFPD

- Fill volume: 10-20 ml/kg (can be adjusted according to intra-abdominal pressure)
- Flow rate: 50 -100 ml/1.73m2/min,
- UF flow: start at the rate of 2.5ml/1.73m2/min, then adjust according to UF,
- Dialysate: 1.5% dextrose containing PD fluid. Dextrose concentration can be adjusted according to fluid and solute removal requirement.
- Ultrafiltration: After initial 2 hours of CFPD, UF should be measured. Subsequently assessment at 4-hr intervals may be sufficient.
- Potassium should be added in PD fluid (4 mmol/L) when serum potassium decreases <4 mmol/L.
- Close monitoring is required regarding solute removal and fluid balance, circuit blockage, intra-abdominal pressure, respiratory compromise and need for escalation of ventilation support.

Apart from the guidelines and practice points discussed above, commonly encountered complications and management have also been summarized at the last part of the guidelines. The chief highlights include:

Peritonitis:

In acutely sick child, signs and symptoms of peritonitis may be masked. For early detection of onset of peritonitis, ultrafiltrate leukocyte count should be done on daily basis. Alternatively, ultrafiltrate should be checked for leukocyte esterase using urine dipstick. If it is >2+, treatment should be started while awaiting culture reports. Subsequently antibiotic should be changed according to sensitivity report[35]

Mechanical complications

Obstruction: The following aspects should be initially looked for-

- Bladder should be emptied
- Constipation should be addressed.
- Catheter can be flushed with heparinized saline

- If fibrin clot/visible tissue are seen: fibrinogen inhibitor can be instilled into catheter (2.5 mg in 10 ml normal saline), then heparin should be added (500 IU/L PD fluid).
- Catheter replacement over a guide-wire in same position or replace with a new PD catheter at a different location.

Peri-catheter leak

- Reduction of fill volume
- Consider off dialysis period for some time.
- Consider purse string sutures. Alternatively, fibrin glue can be used between catheter and tunnel wall.
- Multipurpose large gauge cook catheter can be placed at same site over guide-wire
- New catheter can be inserted at a separate location.

Visceral injury: Surgical intervention is needed on urgent basis.

- Bladder injury can be identified by sudden increase in urethral output in filling phase.
- Bowel injury can be identified by sudden onset of watery diarrhea or features of peritonitis.
- In suspected visceral injury, close monitoring is required to look for peritonitis and to prevent sepsis, antibiotic should be added empirically for 72 hours.
- The choice of antibiotic will depend on local bacterial susceptibilities and availability. One can consider amoxicillin-clavulanate (first line), piperacillin tazobactam and amikacin (second line) or ertapenem (third line).
- If PD is absolutely necessary, a new catheter should be inserted at a different place after surgical clearance.

Mechanical complications in tunneled Tenckhoff catheters e.g., catheter tip migration, obstruction, infection, leakage.

- These complications can be reduced by better surgical approach of catheter insertion, post-surgery catheter care, type of catheter used, exit site care, immediate addressing of exit site and catheter infection.
- Access revision can be required in mechanical dysfunction, obstruction.
- Two staged catheter removal and insertion is recommended in fungal, refractory exit site & tunnel infection, surgical peritonitis, refractory peritonitis.

Pleural effusion

- Newly developed or worsening of pleural effusion after initiation of PD is a relative contraindication of continuing PD.
- Pleural fluid sugar should be checked to confirm its origin from the PD fluid.
- Intercostal drain should be inserted and output should be added with UF.
- Consider extracorporeal dialysis modality, if available
- Position patient in semi fowlers position (30o head up)

Metabolic complications

Lactic acidosis and hepatic dysfunction or shock and/or not responding to lactate-based fluids: Use bicarbonate-based PD fluids.

Protein loss: Adequate nutrition and extra protein supplementation should be ensured. As protein loss may compromise nutrition, patients on PD should take protein according to daily dietary reference, in addition to that quantity lost (0.15-0.3 g/kg/day) in dialysis.

Hyperglycemia*:** It leads to loss of osmotic gradient between PD fluid and serum. ***Hyperglycemia is itself a risk factor to increased mortality in critically ill patients[36]

- Dextrose concentration of PD fluid should be titrated
- Insulin infusion is sometimes required to control hyperglycemia: initiate at 0.05 IU/kg/h followed by titration as per blood glucose levels
- Increase exchange duration
- Add insulin to PD bags (discussed above)

Ventilation issues and rise in intra-abdominal pressure

- Respiratory compromise can be identified by sudden fall in tidal volume (in pressure control mode) or rise in peak inspiratory pressure (volume control mode). Respiratory compromise or difficult ventilation may be a relative contraindication of continuing PD (see above).
- If PD is necessary, fill volume should be reduced by 5ml/kg and titrated subsequently.
- Position patient in semi fowlers position (30o head up)
- Intra-abdominal pressure monitoring is required simultaneously.
- Consider CFPD with very low fill volume

In contrast to the guidelines in adult [37], published at the similar time, pediatric guidelines are silent on dialysis efficacy [4] While the prescription and delivery systems have been detailed, the objective parameters e.g. kt/V are not discussed. The guidance on when to consider discontinuation is limited. The clearance studies and cytokine removal aspects in PD need to be examined in future studies. Thus, these pediatric-specific recommendations strengthen our confidence in an (almost) always feasible dialysis modality, with practical guidance on prescription, dialysis delivery, and drug modification. The troubleshooting of commonly encountered complications is expected to enable effective dialysis delivery to sick children with AKI.

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Table 1. Comparison of ISPD 2020 guidelines for peritoneal dialysis in acute kidney injury (Pediatrics) [4] and ISPD guidelines (2012) for prevention and treatment of catheter related infections and peritonitis (Pediatrics) [3]

Feature	ISPD 2020	ISPD 2012
Objective	Guidelines for PD in AKI emphasizing on peritoneal access, dialysis solutions and prescription of dialysis.	Guidelines for prevention and treatment of catheter related infections and peritonitis
Standardization of recommendations	Minimal standard, optimal standard, Practice point	No such standardization.
Training on PD	Recommended but not elaborated	Peritoneal dialysis training and related programs have been emphasized upon.
Special notes on	PD catheter types, insertion techniques, PD prescriptions and modifications, commercially available PD fluid constituents, local preparation of PD fluid	PD catheter entry-exit site care, connection care, intra-peritoneal fluid sample collection, culture technique
Treatment of peritonitis	Recommended as per 2012 ISPD guideline	Discussed in details. Antibiotics and antifungal prophylactic and treatment dosage, administration technique specified
Management for patients with stoma	Not specified	Separately mentioned
PD delivery system	Discussed in details	Not discussed
Complications and management	Complications like poor ultrafiltrate, dyselectrolytemia, difficulty in ventilation or increased intrabdominal pressure, hyperglycemia, mechanical complications (obstruction, leakage), visceral injury, pleural effusion, protein loss have been addressed	Peritonitis related complications addressed

Clinical Quiz

In this section we describe interesting cases with some important teaching points.

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QUIZ 1
AKI in a Neonate… Leaving the Stones Unturned

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Case Report

A month-old female neonate, born of a non-consanguineous marriage, was referred to our hospital with complaints of vomiting and anuria since 2 days. She was born at 30 weeks' gestation, weighed 1.4 kg, and was managed for prematurity in a neonatal intensive care unit. During this period she developed septicaemia for which she received intravenous antibiotics and other supportive treatment. She remained well for 4 days but was re-admitted with complaints of lethargy and poor feeding and was treated with injection piperacillin-tazobactam and amikacin for a week. Two days following discharge from hospital, she was referred to our centre with the above-mentioned complaints. Her family history was unremarkable for any kidney disease. The antenatal ultrasound was reported to be normal.

On admission, she was alert, euthermic, mildly oedematous. No urine drained from the bladder on catheterisation. Laboratory investigations revealed the following: haemoglobin 11.2 gm%, total WBC count 27,140/cu.mm, platelet count 5.2 lacs/mm3, blood gas analysis pH 7.34, PCO2 34, serum bicarbonate of 18 mEq/L, serum potassium of 7.4 mEq/L, blood urea of 38 mg/dl, serum creatinine 2.94 mg/dL. Ultrasonography of kidneys, ureters bladder showed left moderate hydronephrosis, a 16 mm echogenic shadow causing pelvi-ureteric junction obstruction and 2 echogenic shadows measuring 8 mm and 3 mm in the right upper ureter causing right moderate hydroureteronephrosis (Figure 1). The paediatric surgeon planned cystoscopy and placement of stents in both ureters once the neonate's biochemical parameters had improved.

We initiated peritoneal dialysis and after 48 hours, she underwent right pyeloplasty; a DJ stent was left in situ. Pus was sent for urinalysis and culture. Postoperatively she was passing urine at 2 ml/ kg per hour.

Questions

1. What is the likely diagnosis based on the images?
2. How would you manage the condition?

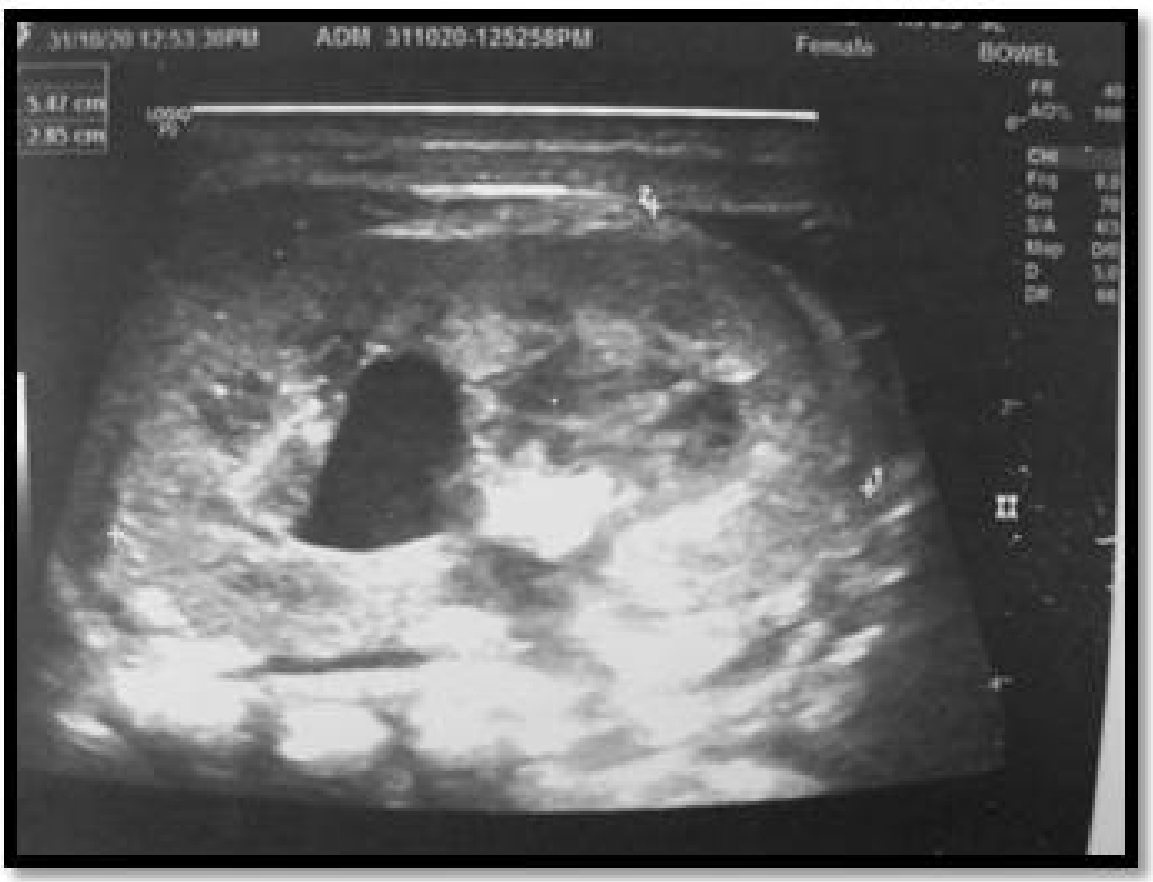

Figure 1. Ultrasonogram of the neonate

QUIZ 2
A Febrile Child with Lower Abdominal Pain and Dysuria


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Case Sinppet

A 7-year-old male child presented with complaints of intermittent high-grade fever for one and a half months, associated with chills and rigor, left sided lumbar and back pain for one month and intermittent dysuria for 15 days duration. On examination, the child appeared sick but hemodynamically stable. Abdominal examination revealed left sided renal angle tenderness with no palpable abdominal mass. An ultrasonography kidney ureter bladder (KUB) showed left sided hydronephrosis with antero-posterior diameter (APD) of 2.3 cm, mild loss of cortico-medullary differentiation, with heterogenous echogenicity. There were features suggestive of evolving renal abscess on left side. Urinalysis showed a pH of 6.5 and 75 leukocytes per high power field along with numerous motile bacteria. Urine dipstick showed leukocyte esterase 3+. Blood investigation revealed total leukocyte count of 23.9 x 103/mm3 (59% neutrophils), and an elevated CRP of 167.9mg/L. Blood urea and creatinine levels were within normal limit. A contrast enhanced tomography (CECT) of the abdomen was done, as shown in Fig. 1 and Fig. 2

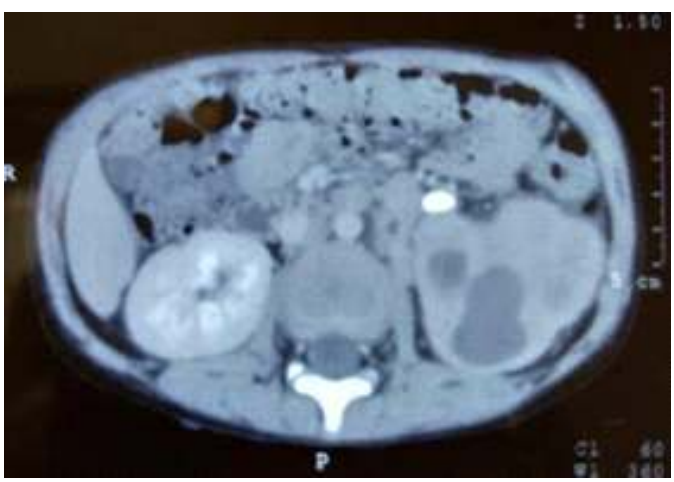

Fig. 1

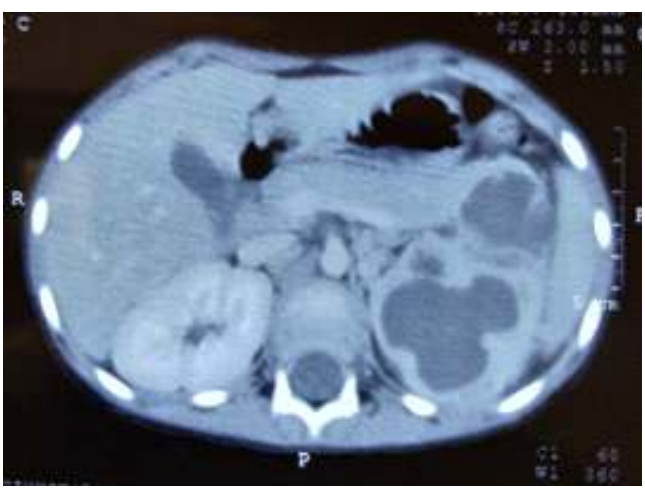

Fig. 2

Questions:

1. What are the chief findings on the CECT?
2. How do you evaluate the child further and decide on subsequent management?

Student Corner

In this section we bring for you a discussion on a topic by paediatric nephrology residents. In this issue Dr Soumya and Dr Mahesh debate on their choice of intravenous fluid in critically

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To Balance OR Not to Balance!

The case of using unbalanced solution

SOUMYA REDDY

Fluid therapy is one of the main interventions provided for critically ill children and adults. More than 40% of hospitalized patients are given intravenous fluid therapy. It is estimated that over 200 million liters of intravenous fluids are used in USA and UK [1,2]

Intravenous fluids differ in their physiochemical properties. The ideal intravenous solution should keep electrolytes and pH at physiological levels and should have the ability to expand intravascular volume. Fluid therapy solutions are classified as colloid or crystalloid solutions. Colloids are solutions composed of large molecules dispersed throughout fluid. Crystalloids are aqueous solutions of ions that show different properties according to their ion concentration. Unbalanced solutions are crystalloids containing sodium chloride that do not match the concentration of ions in plasma and these are not buffered. Balanced solutions, on the other hand, are crystalloid isotonic solutions containing multiple electrolytes. These solutions are isotonic and can help restore electrolyte balance and normalize pH. There is no consensus as to which intravenous fluid therapy must be adopted.

Intravenous fluids were invented in England, early in the 19th century, to treat cholera. Latta, a Scottish doctor, developed a primitive salt water solution to replace through the veins what had been lost through the bowels. The origin of normal saline has been traced to Hamburger's study in 1883. His work suggested, mistakenly, that the concentration of salts in human blood was 0.9%. He argued that a solution of equal concentration would be a "normal" composition for intravenous fluids, hence the name. The ease, convenience and low cost of mixing common salt with water explain the ascendance of normal saline as the default intravenous fluid. The World Health Organization (WHO) and the American Academy of Paediatrics (AAP) recommend the use of normal saline (NS) and ringer lactate (RL) as the first choice for resuscitation fluids[3,4]

There are several other clinical scenarios where chloride rich crystalloid solutions are favourable. In children with hypochloremic metabolic alkalosis and intravascular volume depletion, NS aids in restoration of physiological electrolyte and acid base balance. In salt losing tubulopathies like Bartter syndrome, there is a high chloride requirement making normal saline the preferred intravenous fluid therapy. Normal saline is an appropriate choice of fluid in other clinical conditions predisposing to hypochloremic metabolic alkalosis like cystic fibrosis or pyloric stenosis. It also helps mitigate the risk of cerebral oedema in traumatic brain injury, more effectively than balanced solutions [5]

Use of balanced solutions like RL is associated with increased risk of lactic acidosis and hyperkalaemia. It has been known to contribute to a higher risk of cerebral oedema in diabetic ketoacidosis and traumatic brain injury patients. However these reported disadvantages of acidosis, inflammation and acute kidney injury have not been well established in children.

Balanced solutions offer some theoretical advantages of less metabolic acidosis, less electrolyte disturbances, but the clinical relevance of these remains unknown. A systematic review was done to study the difference in outcomes between buffered solutions versus 0.9% saline for resuscitation in critically ill adults and children. This review included 21 randomized controlled trials (including 20,213 participants) concluded that buffered solutions made little or no difference to overall mortality or worsening renal function [6] The use of balanced solutions in comparison to unbalanced solutions does not seem to impact clinical outcomes and has no added benefits [7,8]

Despite all the technological advances, this is still a lingering debate. A large ongoing meta-analysis is investigating the impact of balanced versus unbalanced fluid resuscitation on clinical outcomes in critically ill children. The conclusion of this review will hopefully help solve this conundrum.

Till the argument is settled, fluid prescriptions must be tailored to each individual child's needs taking into consideration their underlying medical condition, electrolyte and fluid status.

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The case of using balanced solution

MAHESH V

Intravenous fluid therapy is the most common intervention received by acutely ill patients. Historically saline (0.9% sodium chloride) has been most frequently administered intravenous fluids world over. Balanced salt solutions or crystalloid solutions (e.g. Lactated ringer, Plasma Lyte) are increasingly used currently. Balanced crystalloids have sodium, potassium and chloride content closer to that of extracellular fluid and when given intravenously, have fewer side effects on acid base balance. Also known as buffered crystalloids in which chloride ions are replaced with bicarbonate or buffers to reduce the perturbations in acid-base balance. Preclinical research has demonstrated that saline may cause hyperchloremic metabolic acidosis, inflammation and acute kidney injury[1]

In 1998, Kellum and colleagues first quantified the effect of saline on acid base balance with metabolic acidosis and hyperchloremia. There are many trials comparing balanced crystalloids versus unbalanced solutions in acute care with primary end points being acute kidney injury and all-cause mortality[2]

The SPLIT trial compared normal saline and plasma-lyte in 2278 patients admitted in 4 ICUs in New Zealand. The relative risk of in-hospital mortality is 0.87% (95% CI, 0.64-1.18) without much statistical difference[3] The SALT trial comparing ringer lactate and normal saline in 974 adults in a single centre ICU, has reported lower incidence of AKI and all-cause mortality in the balanced solution group [4] The SMART trial compared ringer lactate and normal saline in 15802 patients admitted to ICU, and showed that adverse kidney outcomes at 30 days was 15.4% in the normal saline group as compared to 14.3% in the ringer lactate group [5] In a similar way, SALTED trial compared ringer lactate or plasma lyte and normal saline in 13,347 patients, the major adverse kidney events at 30 days was 4.7% in the balanced solutions group as compared to 5.7% in normal saline group (p=0.01) [6]. A Cochrane systematic review comparing normal saline and balanced solutions concluded that overall there is no much difference in all-cause mortality and acute kidney injury [7]

Data in Children

A multicentric trial from India comparing balanced salt solutions with normal saline for the initial resuscitation of children with shock (N= 708) showed that the risk of acute kidney injury was 20% in balanced solution group as compared to 33% in normal saline group (RR:0.62, 95% CI 0.48-0.80, p=0.0001) and the requirement of any form of renal replacement therapy was 10% in balanced salt solution group as compared to 20% in normal saline group (RR: 0.5, 95% CI 0.34-0.73, p=0.0002)[8] A number of other smaller RCTs have shown the beneficial effects of balanced salt solutions in children with shock.

Areas of Uncertainty

Most trials comparing balanced solutions with saline have occurred in a limited number of centres and generalizing the results may not be feasible. Although balanced crystalloids and saline are similar in availability and cost in many resource intensive settings, the clinical effects and cost effectiveness of these two fluids in low and middle income countries may require additional considerations.

Conclusions

Intravenous fluid therapy is like any other medicine and needs to be used judiciously. For now, the most feasible approach regarding the selection of fluids should be tailored on a case to case basis. Balanced solutions although more expensive should be preferred for volume resuscitation, maintenance fluids and peri operatively. Normal saline to be given in those at risk of raised intracranial pressure and in overt or latent chloride deficiency states. Finally for children there is a need for new fluids to be developed on the basis of better understanding of the physiology in well-designed trials.

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Journal Scan

In this section we bring for you summary of some of the recently published interesting articles.

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Acute pediatric kidney replacement therapies in Europe: Demographic results from the EurAKId Registry.

Nephrol Dial Transplant. 2021 Sep 29:gfab280. doi: 10.1093/ndt/gfab280

Acute kidney injury (AKI) is an independent predictor of mortality and morbidity in hospitalised children. The incidence of mortality, need for longer mechanical ventilation and longer hospital length of stay is even more in the proportion of AKI cases who undergo dialysis. However, there are limited prospective studies describing the epidemiology and long-term outcomes of pediatric patients requiring acute dialysis. The objective of the study was to create a prospective European AKI registry (EurAKId registry, NCT02960867) describing the demographics, clinical characteristics and outcomes in pediatric patients requiring acute dialysis.

The authors conducted a multicentre prospective observational study which enrolled pediatric patients aged 0-18 years requiring acute kidney replacement therapy (KRT) from 14 institutions of the ESCAPE study group. All patients treated inside and outside Pediatric intensive care unit (PICU) with acute dialysis with all three modalities were included.12 categories of primary diseases and five strata of age groups were defined.

Out of the 340 enrolled patients, 86% underwent KRT due to AKI, majority (72%) of which were in AKI stage 3 and 8% had more than 1 episode of AKI needing KRT. 14 % of patients underwent dialysis for non-AKI indications like sepsis, fluid overload, metabolic disorders and drug toxicity. The most representative age groups were infants (32%) and young children (24%), with a male predominance across all age groups. The gender difference was statistically more significant in neonates. Three underlying primary disease noted were renal, cardiac and haematological. A high proportion (72%) of children had one or more than one co-morbidity (need for mechanical ventilation, vasopressors and Multiorgan dysfunction syndrome (MODS).

Acute kidney injury in children with chronic kidney disease is associated with faster decline in kidney function.

Pediatr Nephrol. 2021;36(5):1279-1288. doi: 10.1007/s00467-020-04777-z.

Modifiable risk factors for the progression of chronic kidney disease (CKD) like proteinuria and hypertension are well studied in children. Though acute kidney injury (AKI) has a possible role in accelerating progression, there is a paucity of data on the impact of AKI on the progression of CKD in children. The objective of the study was to evaluate the impact of AKI on disease progression in children with non-dialysis stages 3-5 of CKD.

A single centre retrospective longitudinal observational study including children aged 1-18 years over a 3 year follow up was done. Patients with a baseline eGFR <60 ml/min/1.73m2 at baseline with a minimum follow up period of 1 year and minimum of 3 creatinine measurements per year were included. The estimated glomerular filtration rate (eGFR) was calculated using he modified Schwartz formula and CKD staging was done. AKI was defined as per the KDIGO guidelines. To differentiate AKI from rapid progression, a reversal of creatinine to within 10% of previous creatinine measurement was required. The annualised change in eGFR was calculated and the composite endpoint of 25% reduction in eGFR from baseline or need for renal replacement therapy were considered outcomes.

One hundred and sixteen patients fulfilling inclusion criteria were recruited. Mean GFR at baseline was 29.8 +11.9 ml/min/1.73m2. Fifty six episodes were identified among 39 patients, with urinary tract infections, dehydration, elective surgeries, obstruction to the urinary tract, nephrotoxic medication use. Mean annualised GFR change was -1.08+5.6 ml/min/1.73m2 per year. On multiple regression, age and AKI were independent predictors for accelerated kidney progression.

The study concluded that AKI in established CKD is an independent predictor of progression and should be considered a modifiable risk factor.

Mycophenolic acid area under concentration-time curve is associated with therapeutic response in childhood onset lupus nephritis.

Pediatr Nephrol. 2021;36(2):341-347. doi: 10.1007/s00467-020-04733-x.

Mycophenolic acid (MPA) is used as both induction therapy and maintenance therapy in adults and children with lupus nephritis. In adults with lupus nephritis, therapeutic drug monitoring suggests that area under the curve of MPA of 30-45 mg h/L may be associated with better outcomes. However, there is little data on therapeutic drug monitoring in children with SLE.

This retrospective multicentre study in children <18 years of age with biopsy proven lupus nephritis treated with MPA with at least one pharmacokinetic profile of MPA were included. The association between MPA AUC threshold value and clinical response after 6 months was studied.

A total of 62 AUC values of MPA were analysed in 27 patients. The median value was 44 mg h/L . Tin 32 instances (52%), dose adjustment was required to achieve target AUC levels. At 6 months, 56% were responders and 44% were non-responders. Children with MPA AUC levels of >45, 30-45 and <30 had response rates of 89%, 60% and 0% respectively.

A logistic regression analysis adjusting for age, sex, severity of lupus nephritis and time since initiation showed that an AUC > 45 mg h/L was significantly associated with response to therapy.

MPA AUC has been widely explored in renal transplantation but not in other renal diseases. MPA AUC may be a useful tool to guide dosing of the drug especially in children who are non-responsive to therapy.

Safety and efficacy of sucroferric oxyhydroxide in pediatric patients with chronic kidney disease.

Pediatr Nephrol. 2021;36(5):1233-1244. doi: 10.1007/s00467-020-04805-y.

Hyperphosphatemia, a common complication in CKD contributes to secondary hyperparathyroidism, mineral bone disorder and cardiovascular disease. Along with phosphate restriction, phosphate binders are also used in the management of hyperphosphatemia. Most often in children, calcium based phosphate binders are used. Sucroferric oxyhydroxide is an iron based phosphate binder which has shown a reduced pill burden in adult patients on hemodialysis. The objective of this study was to assess the safety and efficacy of sucroferric oxyhydroxide in children with CKD.

A phase 3, multicentre, randomised, prospective, open label active controlled trial was conducted in 41 centres across 7 countries. Following a screening period of 4 weeks and a washout period of upto 3 weeks for children previously on phosphate binders, the children were randomised stratified by age to sucroferric oxyhydroxide or calcium acetate arms. Children >1 year of age with CKD stages 4, 5 or 5D (on hemodialysis or peritoneal dialysis for at least 2 months) and serum phosphate level greater than the upper limit of normal were included. All randomised subjects were followed up for 2 weeks after stopping the phosphate binder. Sucroferric oxyhydroxide and calcium acetate was initiated on an age dependent dosing regime and increased to achieve serum phosphate within age appropriate levels in the respective randomised groups for < 10 weeks (phase 1 or titration phase). Thereafter, the same dose was continued for 24 weeks (phase 2, safety extension phase).The primary endpoint was change in serum phosphorous from baseline to end of stage 1 in study group. Secondary end points were change in serum phosphorous in calcium acetate groups.

Eight five subjects were randomised to receive sucroferric oxyhydroxide (n=66) or calcium acetate (n=19). Serum phosphate reduction in phase 1 was significant in the study group (-0.488+0.186 mg/dl, p=0.011). Serum phosphate reduction was significant in children 12-18 years of age and in those with higher baseline serum phosphate. Compliance with therapy in the study group varied from 73-93%. Similar proportion of adverse events were reported in both the groups. Withdrawal from the study due to adverse events was more common in the calcium acetate group.

The study concluded that sucroferric oxyhydroxide was safe and effective in reducing serum phosphate levels in children.

Results of the PROPINE randomized controlled study suggest tapering of prednisone treatment for relapses of steroid sensitive nephrotic syndrome is not necessary in children.

Kidney Int. 2021;99(2):475-483. doi: 10.1016/j.kint.2020.09.024.

The dose and duration of steroid therapy for relapses in nephrotic syndrome varies widely between centres. Due to the development of steroid induced side effects, it is important to establish the optimal therapeutic regimen for treatment of relapses. The PROPINE (Prospective Randomized study to Optimize Prednisone therapy for relapses of Idiopathic NEphrotic syndrome in children) study is a multicentric, open-label, randomized superiority trial to optimize the treatment of relapses in children who have not received steroid sparing medications.

The study enrolled children aged 3-17 years with a relapse of steroid-sensitive nephrotic syndrome, comparing two schedules of treatment with oral prednisone with different duration ("short arm" vs "long arm") but the same cumulative dose. Overall, 121 patients were eligible and 78 patients had relapse during the observation period. All relapsed patients received full dose steroids which was continued for 5 more days after remission. After this, 38 were randomized to the short arm and 40 to the long arm. Patients in the short arm received 18 doses of prednisone at 40 mg/m2 on alternate days and in the long arm, the same cumulative amount of PDN divided in 36 doses tapered by steps of six was given. Of the 78 patients included in the first phase of the study, 40 patients were enrolled in a secondary study and were crossed over to the other arm for the subsequent relapse.

The primary outcome in both primary and secondary study was the rate of relapse at 6 months. Secondary outcomes detailed in the current report include differences in blood pressure, weight, and adverse events. In the primary study, at 6 months, 23 patients (58%) had relapsed in the long and 16 patients (42%) had relapsed in the short arm. In the secondary study. At 6 months, 32 patients (80%) and 28 patients (70%) had relapsed in the long and short arm, respectively. For both the primary and secondary study the difference in occurrence of relapse was not statistically different. Survival analysis did not show significant difference in relapse-free survival between the two arms. The time to relapse did not differ for patients with the two different regimens among patients who developed relapse in both the primary and secondary study. No significant changes in blood pressure or weight were observed during the course of the study and between the two treatment arms.

The authors conclude that both the steroid regimens for relapses are comparable in preventing relapses and have similar adverse effects. Hence they do not support the prescription of prolonged tapering schedules for relapses of steroid-sensitive nephrotic syndrome in children.

ISPN Desk

In this section we provide you important academic and administrative information from ISPN secretariate. In this issue we have compiled the activities conducted on World Kidney Day around India and important announcements.

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World Kidney Day Activities

This year world kidney day was celebrated on 11th March 2021 with the theme 'Living well with kidney disease'. It was celebrated across the centres in India keeping in mind the ongoing pandemic. We project here the contributions from our ISPN members and would like to applaud everyone involved in the conduct of these activities.

1. **North Bengal Medical College Department of Pediatrics, Darjeeling**

   The Pediatric Nephrology wing had organised a drawing competition for the children admitted in pediatric ward with various nephrology ailments and prizes/small toys for all participants. The Head of the Department delivered a short speech addressing the patients, their parents and also the nursing staffs and other residents to utilise the platform to create some awareness regarding pediatric renal disease and how to maintain a good kidney health. The chronically ill children were momentarily happy though keeping in mind of current pandemic situation.

With HOD, Pediatrics, NBMC

With parents and nursing staff

Submitted by
Dr Sumantra Raut

2. Sir H N Reliance Foundation Hospital, Mumbai

A webinar was organised to discuss common glomerular diseases in children which was attended by more than 70 paediatricians and paediatric nephrologists

Sir H. N. Reliance Foundation Hospital and Research Centre

RESPECT FOR LIFE

Pediatric Nephrology Clinic, Department of Pediatrics

Webinar on
"Glomerular Diseases in Children
- Strike when the core is HOT"

Thursday, 11th March 2021 | 2:00 pm to 4:45 pm

Organising Secretary: Dr Kiran Sathe
Organising Chairperson: Dr Pankaj Parekh
Patrons: Dr Rumud Mehta, Dr Uma Ali
Compere: Dr Nivedita Pande

TIME	SESSION	SPEAKER
2:00 pm - 2:10 pm	Introduction of the Theme & Welcome	Dr Kiran Sathe
2:10 pm - 2:35 pm	1+, 2+, 3+, 4+: The numbers matter Managing difficult nephrotic syndrome in children	Dr Sudha Dhanbanam (Chennai)
2:35 pm - 3:00 pm	When normal IF is a problem: Emergent approach to a Rapidly progressive glomerulonephritis and ANCA vasculitis	Dr V V R Satyaprasad (Hyderabad)
3:00 pm - 3:25 pm	The 3G team with kidneys: C3 glomerulopathy in children	Dr Kiran Sathe (Mumbai)
3:25 pm - 3:50 pm	When you are over empowered: The approach to atypical Haemolytic Uremic syndrome in children	Dr Aditi Sinha (New Delhi)
3:50 pm - 4:15 pm	When Starry sky doesn't bode well: Lupus Nephritis in Children	Dr Pagan Shah (Surat)
4:15 pm - 4:35 pm	Striking the right balance: Prescribing immunosuppressive medications in children with kidney disease	Dr Kinnari Vala (Ahmedabad)
4:35 pm - 4:45 pm	Q & A session Valediction	Dr Nivedita Pande (Mumbai)

Submitted by:
Dr Kiran Sathe

3. Army Hospital R&R, New Delhi

a. Patient information videos and booklets on Chronic Kidney Disease in children and Nephrotic Syndrome were made by the Pediatric Nephrology team and shared with the patients (links shared below)

Video: https: //drive.google.com/file/d/19j89e89d82dlxSWVL-P4896Bk2bzMBBb/view?usp=sharing

Booklet:https://drive.google.com/file/d/164vvlmU9iyMLIKRuDBYIEOTIrFfXvKN8/view?usp=sharing

b. To encourage and create awareness among the post graduate students, an online Pediatric Nephrology quiz was conducted for the post graduate residents of the Armed Forces Hospital on the e- learning portal of Armed Forces Medical College, Pune. 20 residents from teaching hospitals in Delhi, Pune and Bangalore participated in the same

c. The team at Army Hospital R&R, New Delhi along with Dr Sidharth at Medanta, The Medicity Gurgaon, have been awarded the IPNA WKD Award for their project proposal on Quality of Life Assessment in children with CKD IV-V and post-transplant which will be the first such multicentric study from the SAARC countries.

WORLD KIDNEY DAY 2021

Living well with kidney disease is more than a theme for World Kidney Day; is the goal that everyone who cares for little kidneys everywhere must pursue.

The IPNA Council is pleased to announce the winners of the 2021 World Kidney Day campaign.

After evaluating the 11 projects presented, the jury selected the following winners who will receive the financial grant for the development of their projects:

2. A multicentric prospective assessment of Quality of life in adolescents with CKD by Suprita Kalra from New Delhi, India.

Florencio McCarthy

IPNA World Kidney Day Committee Chair

Submitted by :
Lt Col (Dr) Suprita Kalra

4. TNMC & BYL Nair Hospital, Mumbai

a. Health Awareness Talk

The parents were counselled about adopting a healthy lifestyle that can help to manage the slow progression of CKD and its complications by Dr. Poonam Wade and Dr. Poorvi Agrawal.

b. Poster painting by patients in Pediatric Nephrology OPD

Submitted by :
Dr Nivedita Pande

5. St. John's Medical College Hospital, Bangalore

The Department of Pediatric Nephrology, St. John's Medical College and Hospital, Bengaluru, Karnataka Celebrated "World Kidney Day" 2021 with the global theme of "Living Well with Kidney Disease" on March 11th, 2021. More than 20 families of children with kidney diseases participated. The significance of world kidney day, the theme of world kidney day, and the 8 golden rules for kidney health were highlighted as a part of the event, an art activity based on the theme was organized for children with kidney diseases.

Submitted by :
Dr Nivedita Kamath

6. Lady Hardinge Medical College & associated Kalawati Saran Children Hospital, New Delhi.

The Division of Pediatric Nephrology celebrated "World Kidney Day" on March 11, 2021

The theme of "Living Well with Kidney Disease" and significance of world kidney day were discussed in the patient and parent education activity. The care of children with kidney disease, home monitoring in children with nephrotic syndrome, importance of adherence to therapy and follow up were emphasized. The children participated in the art and drawing activities during the event.

Submitted by :
Dr Abhijeet Saha

7. Mehta Multispeciality hospitals India Pvt Ltd, Chennai

a. Awareness Talk for public: 8th March

As a part of WKD celebration, we have collaborated with ICWA NGO. Dr Sudha E gave an awareness talk to TP Chatharam community people regarding renal problems faced by children. It was an interactive session with community.100 Plus Women, men and children attended the talk.

WKD 2021 Awareness Talk - TP Chatharam,

b. Drawing Competition for children: 9th March

To create awareness on World Kidney Day, Social worker and team conducted a drawing competition on theme “Healthy Kidney and Healthy Living” and an awareness talk on healthy kidney care for orphan and single parent children. The kids enjoyed and participated very enthusiastically. Winners were encouraged with Medal. We have presented a carrom board as an overall prize for the children.

c. Kolam Competition: 10th March

Kolam competition was conducted for Mehta hospital staff on theme of "Empowering kidney patients & care giver". All the staff actively participated in activity. Competition was conducted for one hour and nine teams participated. The winner were awarded with cash prize. 1st prize Rs1500, 2nd prize Rs 1000, 3rd prize Rs 500 and two consolation prize Rs 200 each.

WKD Kolam Competition Winner

d. Hand campaign for patients: 10th - 20th March

We conducted a hand campaign program for patients and their parents to create awareness to public on renal health. The campaign was theme "Living well with Kidney disease". Hand impression with three colour theme Red denotes blood, Blue denotes water, and Yellow denotes urine and also initiated a photo booth session for the patient.

e. Street play: 5th - 21st March

We organised virtual street play competition in view of pandemic with the theme is "living well with kidney disease". It is a great effort of 5 teams who participated from five different colleges. Judge for street play was Dr T Umapathy Assistant professor of D.G Vaishnav College. Winner was awarded with cash prize Rs 7500.

f. Awareness talk and walkathon: 14th March

Awareness talks at various schools were conducted educating the importance of preventive measures on kidney disease progression, followed by an awareness Walkathon covering few kms. The participants in the walkathon were given T-shirts embedded with WKD logo, which took place on Sunday, 14th March 2021 - at Elliot Beach that was flagged off by celebrities Mrs.Namitha (Actress) and Mr.Ramesh Khanna (Director& Actor). We had excellent media coverage. The crowd included around 350 students with their parents holding placards/ banners and raising slogans on kidney disease, which made it a big success!

g. Other activities: 11th March 2021

1. Dietitian talk and question and answer session for patients with nephrotic syndrome and CKD
2. Skit about lifestyle changes and importance of medication compliance by dialysis technicians
3. Distribution of diet recipe pamphlets on eating healthy with kidney disease to patients and family

Submitted by :
Dr Sukanya Govindan

A Proud moment for the ISPN community

On behalf of the entire ISPN community, we would like to express our heartiest congratulations to Lt Gen Madhuri Kanitkar AVSM, VSM for her appointment as Vice Chancellor of Maharashtra University of Health Sciences, Nashik (MUHS). She will be taking charge of this post from 1st November 2021.

Lt General Kanitkar , AVSM, VSM during her recent visit to MUHS, Nashik

33rd Annual Conference of the Indian Society of Paediatric Nephrology
ISPNCON 2021
Translating Evidence into Practice

The 33rd annual conference of the Indian Society of Paediatric Nephrology 2021 is being hosted by AIIMS, Bhopal from 10th to 12th December 2021 on a virtual platform.

Pre-conference workshop -10th December

Paediatric hypertension and ambulatory blood pressure

The abstract submission portal is active and can be submitted online via http://www.ispncon2021.com

Categories for abstracts:

Award papers, free papers and e-posters, Last date of submission- 25th October 2021

Webinar links

a. Pediatric Nephrology -ICH Kolkata

1. **Topic: Tubulopathy meets Sherlock Homes fingerprinting the salt waster**

   Speaker: Detlef Bockhaeuner

   Link: https://youtu.be/z1DpaG_dQA4

2. **Topic: Mycophenolate Mofetil Pharmacology and Therapeutic drug monitoring (TDM)**

   Speaker: Dr Ratna Prabha

   Link: https://youtu.be/d90YSPfayzA

3. **Topic : Framing a good research question**

   Speaker: Dr. Abhijeet Saha

   Link: https://youtu.be/zLKAK1bnRiY

4. **Research Methodology – Data and its interpretation**

   Speaker: Dr Shantanu

   Link: https://youtu.be/zLKAK1bnRiY

5. **Extracorporeal Blood purification in pediatric intensive care unit**

   Speaker: Gabriella Bottari

   Link: https://youtu.be/ftmfmPVB8dc

6. **What is Cytosorb?**

   Speaker: Dr Volker Humbert

   Link: https://youtu.be/ftmfmPVB8dc

7. **Role of Extracorporeal therapies (cytosorbs) in children with multiorgan dysfunction syndrome**

   Speaker: Dr. V.V.R Satya Prasad

   Link: https://youtu.be/ftmfmPVB8dc

8. **Use of PPIs in Pediatric practice**

   Speaker: Dr Gautam Ray

   Link : https://youtu.be/p2WoP3Q6DDg

9. **PPI and kidney: Where do we stand**

   Speaker: Dr Arpita Ray Chaudhury

   Link: https://youtu.be/p2WoP3Q6DDg

IPNA
International Pediatric Nephrology Association
GREAT CARE FOR LITTLE KIDNEYS, EVERYWHERE

ISPN

Dr.Mehta's Hospitals

IPNA Endorsed WEB MASTER SERIES 2021

JOIN US VIRTUALLY FOR
THE ACADEMIC FEAST

"A PEDIATRIC GLOMERULAR DISEASE SYMPOSIUM"

WEBINAR 4

2nd JUNE 2021	TOPICS	SPEAKER
	Approach to a child with proteinuria - How do I go about?	Dr Pankaj Bhansali
	Microscopic hematuria - How do we Approach?	Dr Kalaivani Ganesan
WEBINAR LINK	https://tatatele.webcasts.com/starthere.jsp?ei=1467725&tp_key=5b7a6c8bda	
DOWNLOAD LINK	https://youtu.be/oPQMkkydlyw	POLLING SESSION

WEBINAR 5

5th JUNE 2021	TOPICS	SPEAKER
	Congential Nephrotic Syndrome - Evaluation & Managemnet	Dr. Rajiv Sinha
	Our understanding on Idiopathic Nephrotic Syndrome	Dr. Tej K. Mattoo
WEBINAR LINK	https://tatatele.webcasts.com/starthere.jsp?ei=1467759&tp_key=a353039ec9	
DOWNLOAD LINK	https://youtu.be/7BZeGoTlHoY	POLLING SESSION

WEBINAR 6

9th JUNE 2021	TOPICS	SPEAKER
	Steroid sensitive and Steroid resistant Nephrotic Syndrome - Recent updates	Dr. Susan Uthup
	Role of genetic testing in management of Children with Glomerular disease	Dr. Anil Vasudevan
WEBINAR LINK	https://tatatele.webcasts.com/starthere.jsp?ei=1467760&tp_key=4b9387d7c2	
DOWNLOAD LINK	https://youtu.be/ULWzeOFOV_Q	POLLING SESSION

WEBINAR 7

12th JUNE 2021	TOPICS	SPEAKER
	Clinical Decision making in IgA Nephropathy	Dr. Susmita Banerjee
	Guidelines & treatment of ANCA Associated Vasculities	Dr. Uma Ali
WEBINAR LINK	https://tatatele.webcasts.com/starthere.jsp?ei=1467761&tp_key=ada3c67ffc	
DOWNLOAD LINK	https://youtu.be/E0h8KrbAfs8	

WEBINAR 8

16th JUNE 2021	TOPICS	SPEAKER
	Immune mediated glomerular injury in children	Dr. Menka Yadav
	Infectious & non-infectious complications of Immunosuppressants in Nephrology	Dr. Sukanya Govindan
	Pathophysiology on complement system & it's impact on glomerular injury	Dr. Abhijeet Saha
WEBINAR LINK	https://tatatele.webcasts.com/starthere.jsp?ei=1467762&tp_key=b1527a6b9b	
DOWNLOAD LINK	https://youtu.be/gVxNYiDDiB8	

WEBINAR 9

19th JUNE 2021	TOPICS	SPEAKER
	Glomerular disease in COVID - 19 Pandemic	Dr. Manisha Sahay
	All about Alports Syndrome in Children	Dr. Aditi Sinha
WEBINAR LINK	https://tatatele.webcasts.com/starthere.jsp?ei=1467764&tp_key=f17de21170	
DOWNLOAD LINK	https://youtu.be/DaxCtrpXFhQ	POLLING SESSION

WEBINAR 10

23rd JUNE 2021	TOPICS	SPEAKER
	Infection related glomerular Nephritis in children	Dr. Mehul shah
	Outpatient Evaluation of childhood hypertension	Dr. Joseph T Flynn
WEBINAR LINK	https://tatatele.webcasts.com/starthere.jsp?ei=1467766&tp_key=b3cce9618c	
DOWNLOAD LINK	https://youtu.be/L_cmMa7dI9s	POLLING SESSION

WEBINAR 11

26th JUNE 2021	TOPICS	SPEAKER
	Pediatric membranous Nephropathy in modern era	Dr. Soundararajan P
	Renal Histopathology pertinent to Glomerular Disease	Dr. Anila Abraham Kurien
WEBINAR LINK	https://tatatele.webcasts.com/starthere.jsp?ei=1467767&tp_key=cf41944c05	
DOWNLOAD LINK	https://youtu.be/kpwILy3oVbM	POLLING SESSION

WEBINAR 12

	TOPICS	SPEAKER
30th JUNE 2021	Lupus Nephritis in Children	Dr. Sriram Krishnamurthy
	Bio marker of glomerular injury & it's clinical Signifance	Dr. Nilam Thaker
	Role of plasma exchange and immunoadsorption in Glomerular disease	Dr. Iftikhar Ijaz
WEBINAR LINK	https://tatatele.webcasts.com/starthere.jsp?ei=1467770&tp_key=97a9600dc5	
DOWNLOAD LINK	https://youtu.be/kJd_1NjN2ec	

WEBINAR 13

	TOPICS	SPEAKER
3rd JULY 2021	Hereditary metabolic disease with secondary glomerular involvement	Dr. Jubida Rumana
	Membranoproliferative & C3 mediated GN in Children	Dr. Om Prakash Mishra
	Diet & Nutrition in glomerular disease	Dr. Nivedita Kamath
WEBINAR LINK	https://tatatele.webcasts.com/starthere.jsp?ei=1467771&tp_key=40248b0e06	
DOWNLOAD LINK	https://youtu.be/S5BCAZqOCdQ	

WEBINAR 14

	TOPICS	SPEAKER
7th JULY 2021	Advance in Pediatric AKI	Dr Sidharth Kumar Sethi
	Adsorption in pediatric FSGS - Post Transplant	Dr Rupesh Raina
WEBINAR LINK	https://tatatele.webcasts.com/starthere.jsp?ei=1467772&tp_key=b995538b46	
DOWNLOAD LINK	https://youtu.be/ZDs6KxN_CxI	POLLING SESSION

WEBINAR 15

	TOPICS	SPEAKER
10th JULY 2021	All about Atypical HUS	Dr. Arvind Bagga
	Immunosuppression option for Pediatric Kidney Transplant Recepient	Dr. Minnie M. Sarwal
WEBINAR LINK	https://tatatele.webcasts.com/starthere.jsp?ei=1467773&tp_key=c70ff0448e	
DOWNLOAD LINK	https://youtu.be/lKAdIQNEWM0	

WEBINAR 15-A

	TOPICS	SPEAKER
12th JULY 2021	Clinical Vignettes - Glomerular Disease in Children	Dr. Sadaf Asim
WEBINAR LINK	https://tatatele.webcasts.com/starthere.jsp?ei=1475943&tp_key=8f256d67e5	
DOWNLOAD LINK	https://youtu.be/FqakIrO1Ymg	

WEBINAR 15-B

	TOPICS	SPEAKER
13th JULY 2021	Immunological aspects of Renal Transplantation	Dr Anil Tarigopula
WEBINAR LINK	https://tatatele.webcasts.com/starthere.jsp?ei=1481319&tp_key=6a8db9d092	
DOWNLOAD LINK	https://youtu.be/egf0euNdNaY	

WEBINAR 16

	TOPICS	SPEAKER
14th JULY 2021	Ambulatory Blood Pressure Monitoring (ABPM)	Dr Joseph T Flynn
	Renal Transplant in India - Past, Present and Future	Dr. Georgi Abraham
	Preemptive Pediatric kidney transplantation	Dr. Kumud Mehta
WEBINAR LINK	https://tatatele.webcasts.com/starthere.jsp?ei=1467774&tp_key=90d81c55c7	
DOWNLOAD LINK	https://youtu.be/6J4ahoow36g	

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Course Director
Dr Kalaivani Ganesan
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Answer to Clinical Quiz

Quiz 1

AKI in a Neonate… Leaving the Stones Unturned

JYOTI SINGHAL, JYOTI SHARMA

Paediatric Nephrology Service, Renal Unit, KEM Hospital, Pune

1. The ultrasonography was suggestive of bilateral obstructive calculi. Urolithiasis without nephrocalcinosis in this age is very rare. It can occur secondary to maternal conditions like hyperparathyroidism, Vitamin D intoxication and diuretic therapy, or due to neonatal diseases like hyperparathyroidism, hypothyroidism, idiopathic hypercalciuria, renal tubular acidosis, inborn errors of metabolism, oxalosis and steroids or diuretic therapy.
2. Management: Based on the suspicion of bilateral obstructing renal calculi, the paediatric surgeon planned cystoscopy and stenting of both ureters. However, during the procedure, the guidewire could not be advanced through the right ureter, and the renal tissue was necrotic hence pyeloplasty with double J stenting was performed on the right side. Impacted pus evacuated from the renal pelvis and ureter showed septate fungal hyphae on Gram stain and Candida albicans on culture. Therapy was initiated with neonate injectable amphotericin B and fluconazole. Cerebrospinal fluid (CSF) analysis revealed fungal meningitis due to the same organism so flucytosine was added. A repeat CSF analysis performed 10 days later was free of the fungus and ultrasonography showed that the mass on the left side had resolved. The neonate was transferred back to the primary care physician for completion of 6 weeks of antifungal therapy.

Discussion

Infection of the kidneys and urinary tract by Candida species can lead to acute pyelonephritis, micro-abscesses in the kidneys, papillary necrosis and obstructive lesions. The spread could be hematogenous or as a result of ascending infections from the lower urinary tract. Infiltration of the renal parenchyma, aided by urea metabolism by Candida species, causes inflammation and necrosis of the tips of the renal papillae. Formation of fungal balls, is a rare manifestation but can have serious effects as illustrated by this case. Acute kidney injury due to bilateral ureteral/ pelvi-ureteral junction fungal balls, mimicking calculi on ultrasonography, can be the initial manifestation.

The treatment of fungal urinary tract infection is by a combination of amphotericin B and fluconazole or flucytosine. Surgical intervention is indicated for obstruction due to fungal balls in cases that do not respond to systemic antifungal therapy. Other interventions which have been documented to be effective are local irrigation of the renal pelvis with amphotericin along with streptokinase instillation, in cases where systemic antifungal therapy fails to resolve the infection. Predisposing factors for fungal infection include prematurity, central venous or urinary bladder catheterization, prolonged use of broad-spectrum antibiotics, prolonged duration of endotracheal intubation, persistent neutropenia, immunosuppressive therapy and total parenteral nutrition.

This preterm with poor innate and adaptive immunity was hospitalised for over a month in an intensive care unit and received intravenous antibiotic therapy, thereby predisposing her to fungal meningitis, urinary tract obstruction and acute kidney injury. Relief of urinary obstruction served as treatment for the AKI and provided us with the diagnosis for further medical management.

REFERENCES

1. Kauffman CA. Diagnosis and management of fungal urinary tract infection. Infect Dis Clin North Am. 2014; 28:61-74.
2. Rao S, Ali U. Systemic fungal infections in neonates. J Postgrad Med. 2005;5:27.
3. Knapp K, Flynn P. Candidiasis. In: Kaplan SL, Feigin RD, Demmler-Harrison GJ, Steinbach WJ, Cherry JD, editors. Feigin and Cherry's Textbook of Pediatric Infectious Diseases. 6th edition. Philadelphia, PA: Saunders; 2009.

Quiz 2

A Febrile Child with Lower Abdominal Pain and Dysuria

SUCHISMITA SAHA, ANWESHA ROY, MENKA YADAV

Division of Pediatric Nephrology, LHMC & KSCH, New Delhi, India.

1. Finding in CECT abdomen:

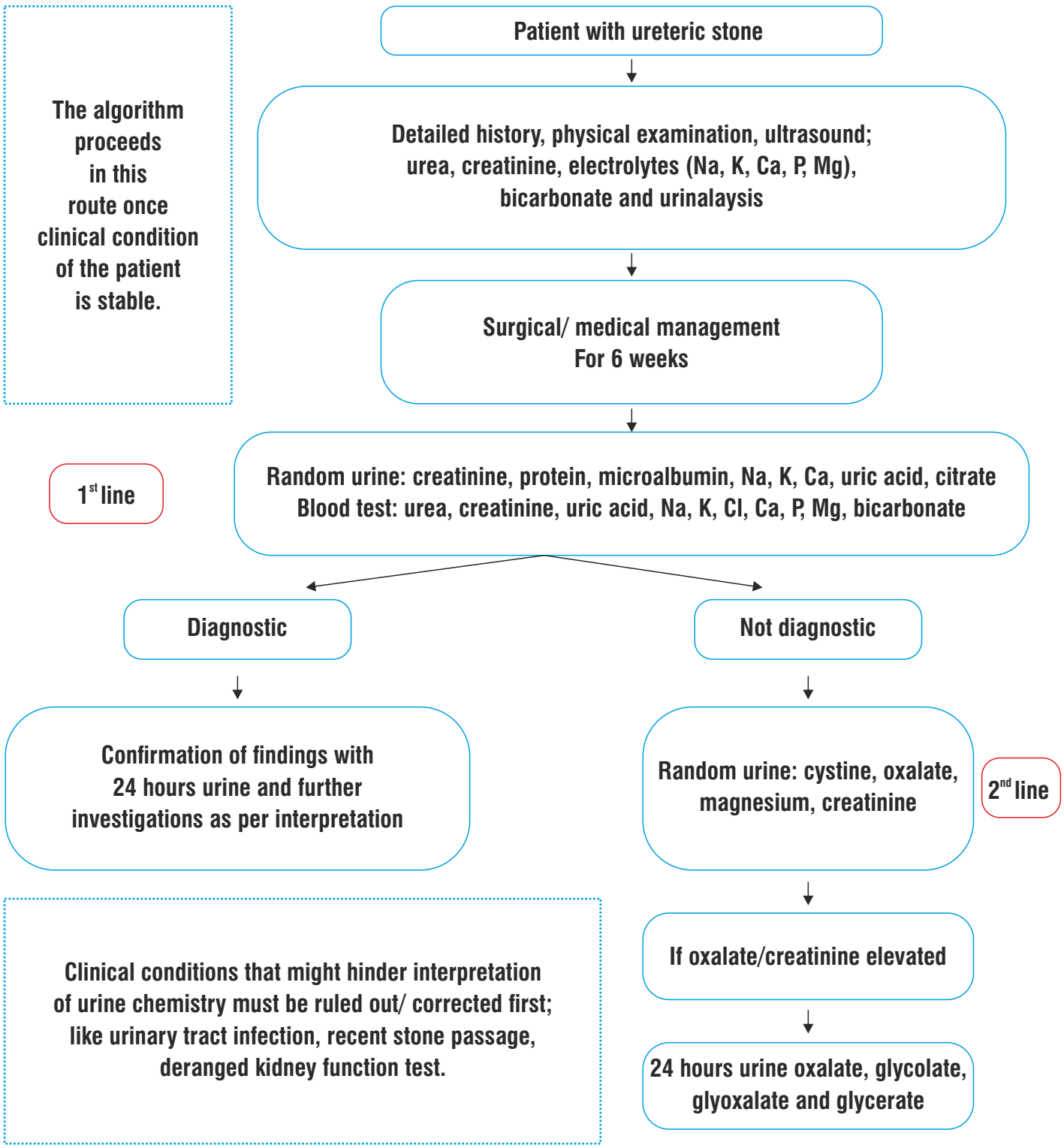
Fig. 1: An obstructive calculus in left ureter causing hydroureteronephrosis.

Fig. 2: A hypodense collection arising from upper pole of left kidney, abutting the tail of pancreas, suggestive of left renal abscess.

2. Management:

With the given amalgamation of symptoms, signs, and radiological findings the child should be treated for a complicated urinary tract infection with immediate institution of parenteral antibiotics. Urinary decompression and drainage may be ensured with stenting to lower the intrarenal pelvic pressure due to stone induced obstruction. Adequate hydration needs to be ensured; the abscess might require surgical drainage if not responding to antibiotics.

Flow chart 1. Workup for evaluation of the ureteric calculi



Instruction to Authors

Educational Reviews:

Articles with broader scope than traditional reviews. Approximately 5000 words and should include figures, tables and references. Subheadings in the text are encouraged. References would not normally exceed 20. They may also contain 5 multiple choice questions with answers.

Clinical Quiz:

We accept this in two forms. First as question/ answer format, which will provide the quiz and the answer separately (1500 words). Second, as a case snippet with approximately one paragraph of answer (200 words).

Text Formatting

Manuscripts should be submitted in Word.

- Use a normal, plain Times New Roman for text, 12 fonts with double spacing, justified alignment.
- Use italics for emphasis.
- Use the automatic page numbering function to number the pages.
- Do not use field functions.
- Use tab stops or other commands for indents, not the space bar.
- Use the table function, not spreadsheets, to make tables.
- Save your file in docx format (Word 2007 or higher) or doc format (older Word versions).

Citation

Reference citations in the text should be identified by numbers in square brackets.

Example:

1. Renal malformations are the most common causes of CKD in India [3]

Reference list

The list of references should only include works that are cited in the text and that have been published or accepted for publication. The entries in the list should be numbered consecutively.

- **Journal article: Use et al after six authors.**

  Goyal KK, Saha A, Sahi PK, Kaur M, Dubey NK, Goyal P, et al. Hepcidin and proinflammatory markers in children with chronic kidney disease: A case-control study. Clin Nephrol. 2018; 89:363-70.

- **Article by DOI**

  Peritoneal dialysis in critically ill children in resource-limited setting: A prospective cohort study. Choudhary P, Kumar V, Saha A, Thakur A. Perit Dial Int. 2020 Dec 4: doi: 10.1177/0896860820975897

- **Book**

  Rees L, Bockenhauer D, NJA Webb, Purano MG (2019) Pediatric Nephrology. Oxford, New York.

- **Book chapter**

  Saha A (2018) Refractory Rickets. In: Gupta P, Memon PSN, Ramji S, Lodha R (ed) PG Textbook of Pediatrics, 2rd edn, Jaypee, New Delhi, pp 2366-2368.

Tables

- All tables are to be numbered using Arabic numerals.
- Tables should always be cited in text in consecutive numerical order.
- For each table, please supply a table caption (title) explaining the components of the table.
- Identify any previously published material by giving the original source in the form of a reference at the end of the table caption.
- Footnotes to tables should be indicated by superscript lower-case letters and included beneath the table body.