# 79266_Auto_EditedC.docx

**Name of Journal:** *World Journal of Nephrology*

**Manuscript NO:** 79266

**Manuscript Type:** MINIREVIEWS

**'Children Kidney Care Centers': Rationale, requirements and recommendations for best facilities and better future**

Jain S. Children Kidney Care Centers

Sunil Jain

**Abstract**

Specialized centers are needed for nephrology and urology care of children. The justifications are the specialized nature of care needed and the growing incidence and prevalence. Chronic kidney disease (CKD) children are at risk of morbidity, mortality, and decreased quality of life. Current pediatric practice structures apparently are poorly suited for the increasing demands of chronic disease in children. Kidney diseases account for around 8%-10% of total outpatients and 12% of admissions to pediatric ward in hospitals. The major causes of pediatric CKD in registries are congenital anomalies of the kidney and urinary tract (around 50%), followed by inherited nephropathies and glomerulonephritis. Nephrologist's role is important for specialized investigations and treatment. Urologist's services are essential for the wide variety of conditions from birth to early adult age for complete cure and complementing medical management. Children have a right to treatments and to resources that are as sophisticated and advanced as those available to adults. Simple and sophisticated care for all children with ailments of the kidneys and related structures is important for ensuring 'health for all'. Availability of 'Child Kidney Care Centers' will go a long way in improving the lives of the affected children.

**Key Words:** Chronic kidney disease; Congenital anomaly; Hereditary nephropathy; Glomerulonephritis; Nephrology; Urology

Jain S. 'Children Kidney Care Centers': Rationale, requirements and recommendations for best facilities and better future. *World J Nephrol* 2022; In press

**Core Tip:** Current pediatric practice structures are apparently poorly suited to meet the growing demands of chronic disease. Serious childhood morbidity and mortality is resulting from chronic disorders. Specialized centers provide opportunity for systematic and focused delivery of high-quality clinical care in a sophisticated manner. An understanding of the etiology of chronic renal failure amongst children guides efforts and excellence goals. Availability of specialized investigations in a center is required, and ensures prompt care, avoiding unnecessary referrals, which delays things. 'Children Kidney Care Centers' will ensure right treatments, both nephrology and urology, with sophistication for success.

## INTRODUCTION

Kidneys are the most important for maintaining the milieu interior and hence in children for ensuring growth, for preventing morbidity, and for obviating mortality all affections of the kidneys need focused attention. The urinary system disorders and diseases spectrum is diverse & distinct, incidence a cause of concern, investigations specialized, and treatment specific and timely. Hence the need for centers for nephrology and urology care for children and the necessity for review and recommendations. Also, it has been commented that current pediatric practice structures are not suitable in meeting the growing demands of chronic disease in children. All this points to the need of major reform in organization, financing, and training[1]. Specialized centers provide opportunity for systematic and sophisticated focused delivery of high-quality clinical care[2]. Specialized care is often challenging but universal access to treatment services is possible with commitment[3]. 'Children Kidney Care Centers' will be an important step in the right direction.

The International Pediatric Nephrology Association (www.ipnaonline.org) role in enhancing knowledge and communication among pediatric nephrologists, aligned practitioners, and other health professionals has been critical for progress and praiseworthy[4]. Establishment of 'Children Kidney Care Centers' will go a long way in specialized practices with sophisticated protocols. All the latest research developments need to be put in proper perspective for practice and future developments.

The leading causes of global U5MR are preterm birth complications (15.9%) and pneumonia (15.5%). The third largest is other causes (13.5%)[5,6]. It is high time that we focus on these other causes also. The evolving trend, as suggested by the past several decades' analysis is that chronic disease prevalence has risen, and serious acute illness incidence in children has fallen. This has resulted in an increasing concentration of serious childhood morbidity and mortality due to chronic disorders[1]. Chronic kidney disease (CKD) children are at risk of increased lifelong morbidity, mortality, and decreased quality of life[7].

The CKD problem magnitude varies in different geographical areas. This is due to genetic and environmental factors. The major causes of pediatric CKD in registries are congenital anomalies of the kidney and urinary tract (UT) (approximately 50%), followed by the inherited nephropathies and glomerulonephritis[8]. In India, the true incidence and burden of CKD in children is not known, for want of national registry. In one of Command Hospitals in India the work load of kidney disease in children has been approximately 8%-10% of total outpatient attendance. These have accounted for 12% of admissions to the pediatric ward[9]. Alarmingly, it has been reported that 58% of children with renal failure presented at end stage renal disease (ESRD)[10]. Thus, prompt diagnosis and proper management is essential. Evidence points that children fare better than adults if they receive kidney replacement therapy including dialysis and transplantation. Access to care disparities exist. All this justifies effective efforts for children with kidney disease. These should be for all regions and including all economic strata[11]. These distinctive features justify dedicated facilities.

Similarly, the statistics of newborn period reveal 0.8% have abdominal masses, and renal origin masses account for the majority of these. The common etiologies are: (1) polycystic kidneys; (2) multicystic dysplastic kidney; (3) hydronephrosis; and (4) renal vein thrombosis. There is a need of specific and specialized management[12]. Thus, the need for focused committed comprehensive centers.

High quality systems of healthcare delivery require health leaders and managers with adaptable and relevant capabilities. This has been thought of as critical[13]. Our justifications given above based on epidemiological evidence and the importance of timely intervention point to need for adaptation to establishment of 'Children Kidney Care Centers'. Further, relevant capabilities' building requires understanding of the spectrum of illness, the specialized investigations, the specific treatments. These are elaborated for sophisticated establishment and scientific execution.

## THE SPECTRUM

In a study of the etiology of Paediatric chronic renal failure (ages 0-18 years) the common causes reported are obstructive nephropathy (31.8%), chronic glomerulonephritis (27.5%), and reflux nephropathy (16.7%). The less common causes are hereditary nephropathy (7.5%), renal dysplasia (4.9%), neurogenic bladder (4.5%), and hemolytic uremic syndrome (1.6%)[14]. All this guides efforts and excellence goals at 'Children Kidney Care Centers'.

***Obstructive uropathy***

Most childhood obstructive lesions are congenital. In a study of the etiology and burden of comorbidities across stages of CKD in children it was concluded that kidney and UT congenital anomalies were the commonest cause of CKD[15]. Common causes are posterior urethral valve, pelviureteric junction obstruction or hydronephrosis, and nephrolithiasis.

***Glomerulonephritis***

The common renal disorder and a leading cause of ESRD is glomerulonephritis[16,17]. It's presentations are protean. The general features include proteinuria, hematuria, renal failure, and hypertension. Therapeutic intervention early is warranted and leads to renal function improvements and long-term preservation of renal function. All this is required for prevention of the progression to end-stage renal failure. Hence it is important to evaluate early in proper centers.

Glomerulonephritis types presenting with recurrent haematuria are immunoglobulin A nephropathy (Berger nephropathy) and Alport syndrome. Membranoproliferative glomerulonephritis (also termed as mesangiocapillary glomerulonephritis) most commonly occurs in children or young adults. The presentation is varied and equally as: (1) nephrotic syndrome; (2) acute nephritic syndrome (hematuria, hypertension, and some level of renal insufficiency); and (3) persistent asymptomatic microscopic hematuria and proteinuria. The rapidly progressive glomerulonephritis and crescentic glomerulonephritis presentation in most children is with acute nephritis (hematuria, some degree of renal insufficiency, and hypertension). These children usually have concomitant proteinuria, often with nephrotic syndrome. Other important ones are systemic lupus erythematosus (SLE) associated glomerulonephritis, Henoch-Schonlein purpura nephritis, and Goodpasture disease. A common cause of community acquired acute kidney injury in young children is Hemolytic-uremic syndrome (HUS). It's characteristic triad is: (1) microangiopathic hemolytic anemia; (2) thrombocytopenia; and (3) renal insufficiency. Expert diagnosis and early treatment is especially suited in specialized centers.

***Reflux nephropathy***

Vesicoureteral reflux (VUR), the reverse flow of urine from the bladder to the ureter and kidney, is a risk for kidney infection (pyelonephritis). The reaction due to inflammation caused by pyelonephritis results in renal injury or scarring. Renal function is impaired with extensive renal scarring. This also leads to hypertension (renin-mediated), renal insufficiency/ESRD, and somatic growth impairment.

## THE SPECIALIZED INVESTIGATIONS

The kidney injury occurs from a variety of different mechanisms. The investigations for the type of injury and the degree of injury and its progression assessment involves laboratory tests, diagnostic imaging, and also tissue sample studies often. All investigations available in a specialized center is required. 'Children Kidney Care Centers' can ensure this. This will ensure prompt care and avoid unnecessary referrals, which delays things. The best evidence based practices are as follows.

***Glomerular filtration rate***

Glomerular filtration rate (GFR) best measures the kidney function. The GFR can be measured optimally by the clearance of inulin. However, in clinical practice it is cumbersome. Hence the GFR estimation is commonly done by the endogenous creatinine clearance test. The Schwartz formula is the most widely used bedside pediatric formula[18,19].

More recently estimation of GFR is done with cystatin C, an endogenous marker of renal function. This non-glycosylated protein is produced in all cells in relative constancy. The advantage being cystatin C not influenced by age, gender, body habitus or composition[20].

***Protein measurement***

Proteinuria assessment for diagnosis, prognosis, and monitoring therapy response is done routinely. Proteinuria on urinalysis is often the first clue to renal injury. Subtle and early glomerular injury is picked up using microalbuminuria measurements. The 24 h urinary protein was the gold standard for defining proteinuria. It has been largely replaced by the spot protein/creatinine ratio measurement in a random urine sample. This correlates to 24 h urine protein reasonably well[21].

***Hematuria***

Hematuria is a nonspecific finding. It indicates some injury, and does not provide more information. However, dysmorphic red blood cells (RBCs) study with phase contrast microscopy is useful for pointing the injury site along the UT. If 75% or more of the RBCs seen are dysmorphic, the site of injury is the kidney, and most likely the glomerulus. If less than 25% of the seen RBCs are dysmorphic, the injury site is the UT from renal pelvis downwards[22].

***Tubular function***

The commonly used dynamic tests of tubular function are fractional calcium, phosphate or sodium excretion calculations. The general formula for calculations is: (urine concentration of analyte × serum creatinine)/(serum concentration of analyte × urinary creatinine). A very low fractional excretion of calcium indicates Familial benign hypercalcaemia. Increased fractional excretion of phosphate indicates hypophosphataemic rickets. Fractional excretion of sodium (FENa) calculation is useful to differentiate volume depletion from acute tubular necrosis. In volume depletion the tubules avidly conserve sodium and FENa is typically less than 1.0. In acute tubular necrosis the tubules are damaged and are less able to conserve sodium, and FENa is typically more than 1.0.

Facilities for measurement of 24 h excretion of solutes (calcium, phosphate, oxalate, uric acid, and dibasic amino acids) are useful in diagnosis of renal stone disease. The 24 h collection is best, but random measurement of urine calcium (mg/dL): Urine creatinine (mg/dL) ratio can be used for diagnosis of hypercalciuria[23].

### *Immunology*

The diagnosis of renal disease secondary to SLE is done with anti-nuclear antibodies tests. These include antibodies to extractable nuclear antigens and the anti-double-stranded DNA antibodies. In glomerulonephritis secondary to systemic vasculitis, antineutrophil cytoplasmic antibodies detection aids diagnosis. In Goodpasture's syndrome antibodies to glomerular basement membrane are seen. Low levels of complement is seen in SLE, systemic vasculitis and Hemolytic-uremic syndrome .

Complement levels measurements are required for fixed proteinuria and glomerular haematuria initial evaluation.

## DIAGNOSTIC IMAGING

### *Ultrasound*

Ultrasound (US) for visualization of the UT is the principal imaging modality. For children US is advantageous. The availability of transducers with high-frequency (7-11 MHz) and lower-frequency (3.5-5 MHz) is recommended. High frequency sound waves have less penetration, but provide greater resolution. Ideally one must use the maximum frequency that penetrates to the depth where study is required. As compared to large or obese individuals, high frequency US can be readily used in infants and small children producing excellent resolution.

Doppler US should be available for blood flow evaluation. It is useful in study of: (1) renal artery disease; (2) renal vein thrombosis; (3) tumor thrombosis in the renal vein, inferior vena cava; and (4) arteriovenous fistulas thrombosis. Power Doppler mode allows blood flow detection with increased sensitivity. It is better than color Doppler US. Power Doppler is useful in detecting intrarenal blood flow, and in identifying areas of decreased perfusion within the kidney. It should be utilized for detecting acute pyelonephritis[24].

US contrast imaging many potential applications. These include: (1) characterization of complex renal cysts; (2) assessment of renal vascular disorders, infection, and transplant kidneys; and (3) differentiation of complex renal cysts and solid lesions, and between renal pseudomasses and tumours[25].

### *Voiding cystourethrography*

Voiding cystourethrography (VCUG) is the gold standard for the diagnosis of VUR. It is the only modality that detects VUR and gives detailed information about the bladder and urethra[26]. Availability of pulsed fluoroscopy importantly reduces VCUG-radiation exposure side effect[27].

### *Intravenous pyelography*

US and magnetic resonance urography availability has dramatically decreased the need for and use of intravenous pyelography (IVP)[28]. As such bowel gas and immaturity of renal function in children often results in suboptimal IVP images. Also, IVP has risks of radiation and contrast exposure.

### *Antegrade pyelography*

This is done with percutaneous nephrostomy tube insertion and contrast agent injection. The indications are nephrostomy tube placement to drain an obstructed infected kidney or to provide percutaneous nephrolithotomy access. In cases in which retrograde studies are prevented by obstruction at the extreme lower end of the ureter, antegrade pyelography is useful.

***Computed tomography***

Excellent anatomic resolution of the UT is provided. Thin-section helical imaging [the spiral computed tomography (CT) scan] gives multiplanar reformatted images quickly. The uses are: (1) initial evaluation of possible symptomatic nephrolithiasis, as a preferred modality; and (2) diagnosis of suspected trauma of the UT, as the optimal modality. It is useful for renal tumor staging. Assessment of renal artery stenosis is with CT angiography.

***Magnetic resonance imaging***

The advantages of magnetic resonance imaging (MRI) are: (1) multiple planes images; (2) resolution excellent; and (3) good distinction between different tissue types. All this is without radiation exposure. As compared to iodinated contrast studies, the Gadolinium-based contrast studies at standard doses are significantly less nephrotoxic. However, when gadolinium-based contrast is used at radiographic doses for angiographic procedures it is nephrotoxic[29,30]. MRI is valuable in evaluating congenital abnormalities.

***Nuclear medicine***

Nuclear medicine imaging provides accurate evaluation of renal function and useful renal imaging in many clinical situations. The requirements are radiotracers (radio-pharmaceuticals) and scintillation detector/gamma camera. Exposure to radiation is there, but it is less as compared to other modalities such as VCUG, IVP, or CT.

Dynamic renal scintigraphy is performed for functional information. This is done using mercaptoacetyltriglycine labelled with technetium ($^{99m}$Tc-MAG$_3$). For most indications, $^{99m}$Tc-MAG$_3$ is better than $^{99m}$Tc-DTPA. This is due to rapid excretion of $^{99m}$Tc-MAG$_3$ and hence providing a superior renal/background ratio. $^{99m}$Tc-MAG$_3$ scan provides information about the perfusion of each kidney, valuable in various clinical settings. It is useful in diagnosis that the collecting system dilatation is caused by obstruction. In cases with obstruction of the outflow tract that is significant, $^{99m}$Tc-MAG3 persists in the renal pelvis and a loop diuretic fails to accelerate its descent (diuresis scintigraphy). The functional significance of a 'baggy' or equivocally obstructed collecting system is distinguished, without undertaking pyelography.

Static renal scintigraphy is used for structural information. This uses dimercaptosuccinic acid labelled with technetium ($^{99m}$Tc-DMSA). It has the property of being taken up by proximal tubular cells. Its intravenous injection is followed by the renal cortex images capturing. These show the show the shape, size and relative function of each kidney. The method is sensitive in demonstrating cortical scarring in reflux nephropathy and thus a way of assessing the function of each kidney individually. It usefully quantifies the amount of renal cortex in patients with renal dysplasia and hypoplasia.

***Endoscopy***

Small calibre flexible fibrescopic cystoscopes are useful in diagnostic cystourethroscopy, and retrograde ureterography. Posterior urethral valves are definitively diagnosed using this.

***Urodynamic studies***

The indications are urinary incontinence or other urinary symptoms investigations for making a definitive, objective diagnosis. A Cochrane review had concluded that "While urodynamic tests have been found to change clinical decision making, there is also some evidence that this does not result in better outcomes, as urinary incontinence rates difference after treatment"[31]. For further research for better outcomes, special facilities can play an important role.

Urodynamic studies evaluate parameters of filling and emptying of the lower urinary tract. The bladder is filled with either water, or carbon dioxide while monitoring the pressure in the bladder (*via* bladder catheter) and in the abdomen (*via* rectal balloon). Simultaneously the the pelvic floor EMG activity is measured by needle or surface electrodes placed in the perineum. The study is often done with fluoroscopy–"the video urodynamics". This is done for obtaining information about the appearance of the bladder wall, presence/absence of vesico-ureteral reflux, emptying efficiency, and most importantly, the bladder neck and urethra appearance, along with their respective pressures recording for evaluation. The anatomy and physiology of the lower urinary tract study requires careful performance of the study with proper patient cooperation. The later, being the real limiting factor for its use in evaluation of children.

Noninvasive urodynamics study involves: (1) voided volume measurement; and (2) flow pattern assessment with a flowmeter. Essential information gathered is displayed graphically, and includes: (1) the measured urine flow rate; (2) urine volume voided along the shape of the voiding curve; and (3) the maximum flow rate. US is used for determination of post void residual urine volume.

***Kidney biopsy***

The facilities for kidney biopsy are desirable. The most common method in vogue is percutaneous renal biopsy. Automatic spring-loaded biopsy systems are now-a-days used, as the technique is simple and easy to use[32,33]. Biopsies examination requires special light microscopy, immunofluorescence techniques, and electron microscopy providing the most accurate diagnosis.

In the transplant setting fine-needle aspiration biopsy technique is most often used for immunologically activated cells analysis. As this is less invasive, it is useful for makes possible serial monitoring of interstitial cellular infiltrates in transplanted kidneys[34].

**THE SPECIFIC TREATMENTS**

Children have a right to treatments and to resources that are as sophisticated and advanced as those available to adults. Pediatricians, pediatric nephrologists, pediatric urologists are integral of ‘Children Kidney Care Centers’. The multi-disciplinary teams required for comprehensive care provisioning for children with kidney disease & their families requires: geneticists, genetic counselors, nurse specialists, dialysis personnel, nutritionists, social workers, and mental health professionals. All this under one roof distinctively is desirable. Regular supply of all consumables need to be ensured. All medicines including immunomodulatory drugs should be readily available. Relevant clinical practice guidelines are an important component of specialized centers. The facilities, features, and functioning in ‘Child Kidney Care Centers’ is discussed below.

***Dialysis***

The choice of dialysis modality to be utilized in managing a specific patient is influenced by several factors. These are: (1) the goals of dialysis; (2) the unique advantages and disadvantages of each modality; and (3) institutional resources[35]. The last should not limit the management of these important conditions.

In the United States, peritoneal dialysis (PD) continues to be the most utilized dialysis modality (~55%) as compared with hemodialysis (~44%). However, hemodialysis (HD) as the initial maintenance dialysis therapy is being increasingly utilized. In dialysis modality selection age is a defining factor. In the age group from birth to 5 yr of age maintenance dialysis treatment using PD is preferred (85%). In children ≥ 13 yr of age initiation of maintenance dialysis treatment is commonly with hemodialysis (50%)[36].

There are some universal rules for the choice of dialysis modality: (1) hemodialysis avoidance in the infant due to difficulties with vascular access; and (2) hemodialysis use when PD cannot be used due to technique failure, intra-abdominal pathology, or social difficulties.

***PD***

PD is preferred and a convenient modality of treatment for acute kidney injury (AKI) and patients with hemodynamically unstability[37]. Recent trend is towards Continuous renal replacement therapy (CRRT) increased utilization vis-à-vis peritoneal dialysis for treating pediatric AKI. PD is still the most common modality used in children younger than 6 years of age[38].

The cornerstone of successful PD is a reliable peritoneal catheter. The PD catheters made of soft material (silicon rubber or polyurethrane) are suitable for long term. Development of a number of dialysate transfer sets and associated devices has been done for reducing the risk of bacterial contamination during either the catheter-to-transfer set or the transfer set-to-dialysate bag connections. All this has contributed to simplify PD connecting maneuvers[39].

Second generation PD solutions are more biocompatible. For the standard nighttime automated PD the solution is neutral pH bicarbonate/lactate-buffered. For a long daytime dwell the solution is icodextrin. For malnourished patients the solution is amino acid based. These provide safety and effectiveness[40].

For ESRD PD can be provided as (i) continuous ambulatory peritoneal dialysis (ii) automated therapy using a cycler (continuous cyclic peritoneal dialysis/intermittent peritoneal dialysis/nocturnal intermittent peritoneal dialysis).

***HD***

Intermittent HD is useful in children with relatively stable hemodynamic status. Pediatric hemodialysis machines with specific features for children need to be provisioned. These are useful with low blood flow speeds capability and can function with lines of varying blood volumes. With capability to measure and remove very small amounts of fluid these are suitable even for infants. The volumetric fluid removal system allows fluid removal accurately. New machines have advanced systems for continuous online monitoring and automatically adjust parameters using a biofeedback system.

The online hemodiafiltration (OL-HDF) module incorporation into the dialysis proportioning machine hardware makes the handling procedure simple. It secures the process by keeping the safety regulation of the monitor. This has the advantage of virtually unlimited amounts of sterile and nonpyrogenic substitutive solution[41].

Incorporating OL-HDF in the RRT of children is beneficial, and improves most of the clinical and laboratory parameters measured[42].

The crucial factor for success of dialysis is a good vascular access. The best form of access is an arterio-venous fistula. Otherwise a line that is tunnelled sub-cutaneously is used, or shunts/grafts may be required rarely[43]. Tunnelled sub-cutaneous lines are used in: (1) children too young for an a-v fistula; and (2) children not expected to be on dialysis long *e.g*. children awaiting a living related transplant.

CRRT is advantageous in patients with: (1) unstable hemodynamic status; (2) concomitant sepsis; and (3) multiorgan failure in the intensive care setting. CRRT can be performed as: (1) continuous venovenous hemofiltration; (2) continuous venovenous hemofiltration dialysis; and (3) continuous hemodiafiltration. Modern CRRT machines are very user-friendly, and with computer modules from which physicians choose the CRRT modality[44].

Wearable and implantable artificial kidneys are the future of hemodialysis, and should be designed for specifically for children also.

***Interventional nephrology***

The interventions assuming importance and impacting advantageously are insertion of tunnelled haemodialysis and peritoneal dialysis catheters, endovascular procedures, percutaneous nephrostomy, ureteral stent placement, *etc*.

## UROLOGY

Urologist's services are essential for a wide variety of conditions from birth to early adult age for complete cure and complementing medical management. The specialized management that should be available in the 'Child Kidney Care Centers' is discussed below.

***Obstructions of the urinary tract***

**Ureteropelvic junction obstruction:** This anomaly correction requires pyeloplasty. Success rate range is 91%-98%. Pyeloplasty can be done using laparoscopic techniques, and is often robotic-assisted using the da Vinci robot. Surgery conducted by surgical robots provide the advantage of: (1) small incision; (2) very minimal blood loss; (3) quick recovery; (4) shorter hospital stays; and (5) faster return to normal life. The advantages provisioned for the surgeon are: (1) a magnified, high-definition, three-dimensional view; and (2) tiny surgical instruments for manipulation, that enjoy flexibility better than that of human hands.

**Posterior urethral valves:** Definitive treatment is done by destruction of the valves endoscopically. The continuing supportive treatment is required for: (1) dilated urinary tract; (2) recurrent urinary infections; and (3) uraemia.

Other conditions for which surgery may be required are ectopic ureter, ureterocele, megaureter, *etc.*

***Urolithiasis***

Calculus removal is necessary if: (1) the calculus does not pass; (2) seems unlikely to pass; and (3) if there is associated urinary tract infection. Lithotripsy of bladder, ureteral, and small renal pelvic calculi can be done using the holmium laser through a flexible or rigid ureteroscope. This is quite effective. Extracorporeal shock wave lithotripsy is the other option, can be used in children with renal and ureteral stones. This has a success rate of more than 75%. Percutaneous nephrostolithotomy is another alternative. In this the renal collecting system is accessed percutaneously, and breaking of the calculi is done using ultrasonic lithotripsy. If these modalities are unsuccessful, laparoscopic removal is an alternative. The da Vinci robot can be utilized for this procedure.

***Vesico-ureteric reflux***

Surgery is needed to minimize the risks of ongoing VUR. Nonsurgical therapy is required for infection prophylaxis and follow-up testing. VUR correction options include: (1) lower abdominal or inguinal incision (open); (2) laparoscopically (with or without robotic assistance); and (3) endoscopically with sub-ureteral injection.

***Neuropathic bladder***

Reconstructive urinary tract surgery is needed in cases of incontinence persisting despite medical therapy. This can provide complete or satisfactory continence, almost always.

The two categories and comprehensive tact are as follows.

Low urethral resistance: bladder neck reconstructive procedures (such as a periurethral sling) often are successful. Alternatively, an artificial sphincter implantation usually is successful. The components of this are: (1) an inflatable cuff placed around the bladder neck; (2) a pressure-regulating balloon implanted in the extraperitoneal space; and (3) pumping mechanism implanted in the scrotum of boys and in the labia majora of girls.

Low bladder capacity or compliance, or persistent uninhibited contractions despite anticholinergic therapy: enlargement of the bladder with a patch of small or large intestine, termed augmentation cystoplasty or enterocystoplasty, is effective. Following this there is still need to perform clean intermittent catheterization. If there is difficulty in urethral catheterization, a continent urinary stoma may be incorporated into the urinary tract reconstruction. Mitrofanoff procedure is a useful and is commonly performed. In this the appendix is isolated from the cecum on its vascular pedicle and is interposed between the bladder and abdominal wall. This is done to allow intermittent catheterization through a dry stoma.

***Hypospadias***

The indications for surgery are: (1) to improve sexual function; (2) to correct problems with the urinary stream; and (3) for cosmetic reasons. The plastic surgical procedures used correct the chordee and re-site the urethral opening. The available procedures are: (1) meatal advancement and glanuloplasty repair; (2) transverse island flap repair; and (3) island tube repair.

Except for the proximal hypospadias, all cases are repaired in a single operation on an ambulatory basis. The proximal hypospadias may require a 2-stage repair.

***Renal transplant***

This is the optimal therapy for children with ESRD. Survival rates with kidney transplantation are better than hemodialysis or peritoneal dialysis. Children and adolescents with ESRD need renal transplant more than adults. This is justified so as to achieve normal growth and cognitive development. Successful transplantation advantageously leads to: (1) linear growth improvement; (2) school attending possible; and (3) dietary restrictions freedom.

***Future directions***

Pediatric Centers of Excellence in Nephrology are need of the hour and the National Institutes of Health is promoting these. Grants are provided for accelerating basic, translational and clinical research in pediatric kidney disease. Important research being funded for paediatric patients include: (1) CKD in Children study; (2) Nephrotic Syndrome Study Network; (3) Cure Glomerulonephropathy; and (4) Polycystic Kidney Disease Research Resource Consortium.

Basic sciences research projects include: (1) The (Re) Building a Kidney Consortium; (2) the GenitoUrinary Development Molecular Anatomy Project; and (3) the Kidney Precision Medicine Project. All this is inspiring the pediatric nephrology research community. Progress has been made in molecular and genetic analyses. Specific gene products have been linked to normal and abnormal kidney growth and development causation in a few human pediatric kidney diseases. It has been commented that much remains to be explored. Future is exciting.

## CONCLUSION

Health for all should include all children with ailments of the kidneys and related structures. Availability of 'Child Kidney Care Centers' will go a long way in improving the lives of the affected children. Pertinent and professional care, both simple & sophisticated is likely to reap rewards. Strategies suggested for focused attention and favorable actions can lead to success with smiles for happiness and health.

# 79266_Auto_EditedC.docx

ORIGINALITY REPORT

25%
SIMILARITY INDEX

PRIMARY SOURCES

| | | |
|---|---|---|
| 1 | Pediatric Nephrology, 2009. Crossref | 243 words — 5% |
| 2 | archive.org Internet | 230 words — 5% |
| 3 | basicmedicalkey.com Internet | 111 words — 2% |
| 4 | link.springer.com Internet | 72 words — 1% |
| 5 | Elder, Jack S.. "Neuropathic Bladder", Nelson Textbook of Pediatrics, 2011. Crossref | 57 words — 1% |
| 6 | Michael E. Mitchell. "Bladder Dysfunction in Children", Pediatric Nephrology, 2009 Crossref | 41 words — 1% |
| 7 | www.alliedacademies.org Internet | 39 words — 1% |
| 8 | Pediatric Nephrology, 2016. Crossref | 38 words — 1% |
| 9 | "Diagnostic Imaging of the Child with Suspected Renal Disease", Pediatric Nephrology, 2014. Crossref | 34 words — 1% |

| | | |
|---|---|---|
| 10 | Van Why, Scott K., and Ellis D. Avner. "Membranoproliferative Glomerulonephritis", Nelson Textbook of Pediatrics, 2011.<br>Crossref | 33 words — 1% |
| 11 | Ashima Gulati, Arvind Bagga. "Management of Acute Renal Failure in the Pediatric Intensive Care Unit", The Indian Journal of Pediatrics, 2010<br>Crossref | 32 words — 1% |
| 12 | "Urethra and penis", Bailey & Love s Short Practice of Surgery 25th Edition, 2008.<br>Crossref | 28 words — 1% |
| 13 | Paul H. Wise. "The Future Pediatrician: The Challenge of Chronic Illness", The Journal of Pediatrics, 2007<br>Crossref | 28 words — 1% |
| 14 | "Urinary symptoms and investigations", Bailey & Love s Short Practice of Surgery 25th Edition, 2008.<br>Crossref | 26 words — 1% |
| 15 | www.science.gov<br>Internet | 26 words — 1% |
| 16 | B. Canaud. "Online Hemodiafiltration", S. Karger AG, 2007<br>Crossref | 25 words — 1% |
| 17 | dokumen.pub<br>Internet | 23 words — < 1% |
| 18 | Aaron Friedman. "Laboratory Assessment and Investigation of Renal Function", Pediatric Nephrology, 2009<br>Crossref | 21 words — < 1% |
| 19 | "Hemodialysis in Children", Pediatric Nephrology, 2015. | |

Crossref

17 words — < 1%

---

20 spheres.dost.gov.ph
Internet

17 words — < 1%

---

21 "GEORGE M. O'BRIEN KIDNEY RESEARCH CORE CENTERS (P30): RFA-DK-11-008", Journal of Investigative Medicine, 2015
Crossref

16 words — < 1%

---

22 www.nationalchildrensresearchcentre.ie
Internet

16 words — < 1%

---

23 Elder, Jack S.. "Anomalies of the Penis and Urethra", Nelson Textbook of Pediatrics, 2011.
Crossref

15 words — < 1%

---

24 es.scribd.com
Internet

15 words — < 1%

---

25 quizlet.com
Internet

12 words — < 1%

---

26 onlinelibrary.wiley.com
Internet

10 words — < 1%

---

| | | | |
|---|---|---|---|
| EXCLUDE QUOTES | OFF | EXCLUDE SOURCES | OFF |
| EXCLUDE BIBLIOGRAPHY | OFF | EXCLUDE MATCHES | < 10 WORDS |