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MINIREVIEWS

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Editorial Board Member of *World Journal of Nephrology*, Jia-Fu Feng, MD, Professor, Reader, Departmant of Clinical Laboratory, Mianyang Central Hospital, School of Medicine, University of Electronic Science and Technology of China, Mianyang 621000, Sichuan Province, China. jiafufeng@foxmail.com

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MINIREVIEWS

Obstructive uropathy – acute and chronic medical management

Julian Yaxley, William Yaxley

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Julian Yaxley, Division of Medicine, Queensland Health, Brisbane 4001, QLD, Australia

Julian Yaxley, School of Medicine and Dentistry, Griffith University, Southport 4215, Australia

William Yaxley, Department of Urology, Queen Elizabeth II Jubilee Hospital, Coopers Plains, 4108, Australia

Corresponding author: Julian Yaxley, MBBS, FRACP, Doctor, Division of Medicine, Queensland Health, 33 Charlotte Street, Brisbane 4001, QLD, Australia.
julianyaxley@yahoo.com.au

Abstract

Obstructive uropathy is an important cause of acute and chronic kidney disease. Decompression of the urinary tract is an essential aspect of treatment. The cause and aetiology of obstruction typically determine the surgical approach. Acute relief of obstruction is frequently complicated by fluid and electrolyte imbalance. Standard therapeutic interventions for acute or chronic renal failure also apply for cases of obstructive uropathy. This narrative review summarises the early and long-term medical management of obstructive uropathy.

Key Words: Obstructive uropathy; Nephrology; Urology; Post-obstructive; Diuresis

Core Tip: Obstructive uropathy is a prevalent cause of acute and chronic kidney disease. Urinary tract decompression is the single most beneficial aspect of management; renal impairment is frequently reversible and the long-term renal prognosis is generally excellent. Subsequent medical care is an important but underappreciated supplement to surgical treatment. Acute relief of obstruction is often complicated by disorders of sodium and potassium balance and post-obstructive diuresis. Longer-term management principles are similar to those for other forms of chronic kidney disease.

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INTRODUCTION

Obstructive uropathy is an important and potentially reversible cause of acute and chronic kidney disease. It may be broadly defined as a functional or structural impediment to urinary flow with resulting renal injury. Some sources label obstructive 'uropathy' as the condition causing a blockage to the flow of urine and obstructive 'nephropathy' as the ensuing renal parenchymal disease. With an incidence of 1.7 per 1000 people[1], obstructive uropathy accounts for approximately 10% of all cases of both acute and chronic kidney disease[2,3], including 5% of the chronic dialysis population[4]. Post-renal causes of kidney disease are particularly common in paediatric and geriatric groups.

Obstructive uropathy can be classified as acute or chronic, unilateral or bilateral, partial or complete, and intrinsic or extrinsic. There is an array of causes (Table 1) affecting both the upper and lower urinary tract; obstruction may occur anywhere from the renal calyces to the urethral meatus. The single most common cause of obstructive uropathy is benign prostatic hyperplasia, probably followed by neurogenic bladder[2]. In women the most frequent aetiology is a pelvic mass, while ureteric calculi are the major contributor in middle-aged adults and patients with a solitary kidney[2,5].

Prompt urinary system decompression is vital, which may be achieved through a variety of methods depending on the cause and site of blockage. Urologists are primarily responsible for relieving obstruction and for treatment of the underlying lesion. However, collaboration with nephrologists may be requested because sudden decompression is frequently complicated by abnormal fluid and electrolyte balance and long-term renal insufficiency. Although longstanding experience and high-quality data support a spectrum of urologic interventions, limited published evidence exists to guide the medical management of obstructive kidney diseases in the acute and chronic context. Obstructive uropathy is less represented in the literature than other causes of medical kidney disease. This evidence-based narrative review outlines the acute and post-decompression medical management of obstructive uropathy.

SEARCH METHODS

A structured search of the PubMed database was undertaken from inception to September 2022, using a range of applicable search terms in various combinations, such as "obstructive uropathy", "post-obstructive diuresis", and "bladder decompression". Results were screened for relevance. A broad selection of articles were obtained, including clinical trials, commentaries, and case series. Additional papers were retrieved by manually searching guidelines or article reference lists. Articles were limited to the English language. Results of this literature search were synthesised to generate this narrative review.

PATHOPHYSIOLOGY OF URINARY TRACT OBSTRUCTION AND DECOMPRESSION

Obstructive uropathy pathogenesis begins with a post-renal obstructing lesion that impedes urinary flow. A sequence of physiologic and pathophysiologic events develop thereafter, the severity of which is related to the degree of obstruction. Continuous urine production is initially maintained through normal glomerular filtration and urinary tract peristalsis, resulting in increased pressure proximal to the blockage. The high-pressure system is perpetuated by compensatory smooth muscle stretching and hypertrophy (shown macroscopically by hydroureteronephrosis). Raised upper tract pressure reduces net hydraulic pressure thereby lowering the glomerular filtration rate (GFR), and reduces renal perfusion which subsequently causes ischaemic injury. These processes beget inflammation, tubular atrophy, and interstitial fibrosis within 2 h of total obstruction[3,4]. Urinary acidification and concentration mechanisms become impaired ('hyposthenuria'), manifesting as blood electrolyte derangements and polyuria, which are relatively unpredictable and determined by affected sections of renal cortex and medulla[6].

Unremitting obstruction will eventually lead to scarring and atony and culminate in end-stage renal failure (ESRF), over days to months. In experimental models, some renal function persists for at least 2 wk after ureteric ligation but not longer than approximately 4 wk[7,8]. The onset of complete obstruction does not induce an abrupt cessation of kidney function because once a pressure threshold is met, backward urine leakage into the interstitium occurs ('pyelointerstitial backflow') with subsequent lymphatic drainage[9]. This safety mechanism also explains why spontaneous rupture of the obstructed collecting system is very rare.

Relief of urinary tract obstruction results in reversal of the processes above. Convalescence may be brisk owing to functional hypertrophy of unaffected nephrons, but incomplete renal recovery is common.

Table 1 Causes of urinary tract obstruction by anatomical level

Level of urinary tract obstruction	Causes
Upper tract (kidney, ureter)	Calculi
	Tumour
	Upper tract bleeding (*e.g.*, bleeding renal cancers, traumatic)
	Anatomic abnormality (*e.g.*, pelvi-ureteric junction obstruction)
	Papillae sloughing (*e.g.*, pyelonephritis, tuberculosis)
	Ureteric stricture
	Ureterocoele
Lower tract (bladder, prostate, urethra)	Calculi
	Tumour
	Neurogenic bladder
	Benign prostatic hyperplasia
	Prostatitis
	Cystocoele
	Bleeding (*i.e.*, clot retention)
	Urethral stricture
	Posterior urethral valves
Extrinsic	Retroperitoneal fibrosis
	Aneurysm
	Pregnancy
	Faecal impaction
	Pelvic organ prolapse
	Phimosis

SURGICAL ISSUES

The site and aetiology of urinary tract obstruction determine the surgical approach. For example, an upper tract process may necessitate ureteric stenting or placement of a nephrostomy tube to achieve adequate decompression of the blocked collecting system, while lower tract pathology (which is typically prostatic in nature for men) may benefit from pharmacotherapy, bladder catheterization, or bladder outlet surgery depending on the acuity and degree of obstruction. There is a myriad of surgical options and techniques employed in the management of urinary tract obstruction, for which a full discussion is beyond the scope of this article.

Definitive urologic surgery should be delayed if possible until after the patient is medically stable and urgent decompression has been accomplished. Resuscitation and emergency drainage are particularly important in cases of obstruction-related severe renal failure or in the setting of an 'infected obstructed' kidney. Temporising interventions, such as percutaneous nephrostomy or bladder catheter insertion, almost always precede a secondary corrective procedure performed at a later date. Medical issues requiring optimisation are often encountered at this initial presentation rather than the time of elective surgery.

Rapid bladder drainage may result in decompression haematuria, or haematuria *ex vacuo*. Relief of a chronically distended bladder, which is associated with a friable bladder wall and capillary damage, leads to macroscopic bleeding in approximately 10% of cases[10]. Decompression haematuria is almost always transient and of little clinical importance. Irrigation is sometimes required. A small randomised control trial demonstrated no benefit in gradual bladder drainage compared to rapid drainage with respect to the risk of macrohaematuria[11].

It should be recognised that urgent decompression is not indicated for all patients with urinary tract obstruction. Those with chronic symptoms, for example men seen in the outpatient setting with lower urinary tract symptoms and bladder outflow obstruction, in the absence of complications are generally suitable for a trial of medical therapy which can be complemented by elective surgery where needed. Complications that should trigger immediate bladder catheterisation include hydronephrosis, chronic urinary retention (usually defined as post-void residual bladder volumes of greater than around 300

mL), and renal impairment (obstructive uropathy).

FLUID MANAGEMENT

Clinical background and genesis

Sudden reversal of obstruction is followed by a polyuric phase in approximately two-thirds of patients with obstructive uropathy[12]. Polyuria is typically a physiologic response in which the kidney aims to restore euvolaemia and normal plasma concentrations, conceptually similar to the polyuric phase of recovering acute tubular necrosis. This osmotic diuresis of retained fluid, urea, and other nitrogenous solutes usually resolves within 24 h.

Prolonged or marked polyuria may be pathologic and extend beyond the reestablishment of homeostasis. The working term for this clinical situation is post-obstructive diuresis (POD). POD is defined as urine output greater than 200 mL/h for at least 2 consecutive hours or a urine output exceeding 3 L in 24 h[12,13]. POD seldom lasts longer than 48 h. Mechanisms of POD include impaired urinary concentrating ability due to aquaporin downregulation and loss of medullary tonicity, and dysfunction of tubular transporters because of cell apoptosis. POD affects approximately 2% of patients with complete unilateral obstruction and up to 50% of patients with bilateral obstruction[14,15]. Risk factors include complete or chronic obstruction. Risk is also proportionate to the creatinine elevation and residual bladder volume at the time of presentation; a bladder volume greater than 1500 mL prior to decompression is often associated with POD[13,16].

Treatment

Mild polyuria typically resolves without any intervention within a few hours or days and oral hydration as an outpatient therapy is generally sufficient. Patients are generally asymptomatic apart from occasional postural hypotension. Patients should be instructed to drink to thirst and avoid dehydration with a minimal daily fluid intake of approximately 2 L or 25 mL/kg. Self-monitoring of urine colour can be a simple guide allowing patients to assess their hydration status.

POD, a significant diuresis beyond 2 d, or any episodes of hypotension warrant hospitalisation for observation and fluid replacement because of the risk of electrolyte abnormalities or hypovolaemia, which may precipitate cardiovascular collapse. Regular monitoring of vital signs, an accurate fluid balance chart, and daily weighs are essential. Postural blood pressure checks are also useful. Hourly urine output measurement is indicated until patient condition settles. The urine drainage catheter should be allowed to drain freely without intermittent clamping as this allows accurate assessment of urine output; historical concerns surrounding rapid decompression are unfounded, as free drainage has not been reliably shown to be associated with more complications than gradual decompression[17,18].

There is no consensus on the best fluid replacement strategy in POD and treatment must be individualised. Controlled trials to inform practice are absent. Fluid prescribing can be complex in post-obstruction patients with ongoing losses, haemodynamic instability, and electrolyte abnormalities. POD is a unique scenario where replacement fluid is administered to patients who are volume-overloaded, in anticipation of steady ongoing losses. A useful strategy is to mentally separate the patient with POD into a volume-overloaded phase and a volume-depleted phase. In the initial volume-overload phase, a preferred method is to administer intravenous fluids at 50% the rate of the preceding hour's urine output. This allows for controlled weight loss and downward titration of intravenous fluid replacement without driving endless diuresis. Crystalloid solutions are recommended rather than colloid; the type of crystalloid depends on the subject's biochemical parameters. Enteral solutions may be appropriate in reliable patients who can manage comfortably. Should an ensuing hypovolaemic phase occur, standard resuscitation principles apply; therapy should account for deficits, maintenance requirements, and ongoing losses. Most patients do not reach a hypovolaemic phase as they successfully achieve homeostasis and diuresis abates with decremented fluid replacement.

ELECTROLYTE DERANAGEMENTS

Clinical background and genesis

Obstructive uropathy may be complicated by a number of electrolyte abnormalities, both before and after acute relief of obstruction, particularly in the context of high-grade chronic obstruction[19]. Laboratory findings vary depending on the degree of corticomedullary damage, GFR, and volume status. Early post-renal obstruction generally produces a state of tubular solute wasting, notably of sodium, potassium, bicarbonate, magnesium, calcium, and phosphate. As renal function declines, these abnormalities may be accompanied by gradual retention of potassium, hydrogen, chloride, and ammonium. Obstructive uropathy is a relatively common cause of proximal and distal renal tubular acidosis. Findings may be indistinguishable from other causes of acute or chronic kidney injury.

Sodium and potassium disorders are the most serious and frequent considerations in practice. Although the majority of cases are mild, life-threatening or refractory presentations are sometimes encountered. An overview of the management of sodium and potassium disorders in the setting of urinary tract obstruction is presented below. Other acid-base and electrolyte problems are clinically insignificant without ESRF and will not be discussed in this review.

Hyponatraemia

Hyponatraemia as a consequence of plasma dilution and tubulopathy is a common finding. It often takes several weeks following decompression before plasma sodium concentration returns to a normal range[20]. Mild hyponatraemia between 130-135 mmol/L requires no specific treatment because it should not be associated with symptoms or clinical complications. Liberal fluid intake should be avoided and a normal diet encouraged, effectively being a fluid restriction in the face of post-decompression polyuria. However, for obvious hypervolaemic hyponatraemia, standard fluid restriction is appropriate.

Moderate or severe hyponatraemia requires strict monitoring of fluid balance and plasma sodium. The frequency of blood testing must be decided on a case-by-case basis. Severe hyponatraemia is defined as a plasma sodium level below 120 mmol/L or the presence of hyponatraemia with neurological dysfunction. Like all electrolyte disturbances, the basic treatment strategy for severe hyponatraemia must establish the body's electrolyte deficit, the desired rate of correction, and the ongoing losses. There are many methods to estimate sodium balance and suitable replacement regimens, one of which is shown in Supplementary Table 1. While useful, prediction formulas are relatively inaccurate and should be interpreted within the overall clinical picture. Sodium replenishment should be adjusted according to patient progress and serial blood sampling; gradual correction is preferable. With respect to POD, although precise sodium calculations can be attempted, administration of intravenous 0.9% sodium chloride at half the urine output rate is ultimately sufficient in the majority of cases.

Transurethral resection of the prostate (TURP) is a widespread surgical treatment for patients with obstructive uropathy, and the TURP syndrome therefore warrants special mention. TURP syndrome is characterised by dilutional hyponatraemia developing early post-TURP due to absorption of hypotonic irrigation solution through open prostatic venous sinusoids. Patients can absorb more than 1 L of fluid intraoperatively in this way. This potentially life-threatening syndrome is becoming increasingly rare as recognition and preventative measures improve. Use of bipolar diathermy with isotonic irrigation solution has reduced its incidence. TURP syndrome is usually effectively managed with fluid restriction and diuretics.

Hypernatraemia

Prolonged diuresis of dilute urine may result in a hypernatraemic volume-depleted state. Such patients require net rehydration rather than tapered chasing of the urine output. The incidence of hypernatraemia in obstructive uropathy is unknown but appears relatively small. Onset is typically several days post-decompression. All episodes are serious due to the risk of cerebral oedema; hypernatraemia is probably among the strongest predictors of death in individuals with POD.

Like the management of hyponatraemia, treatment is based on an estimate of water deficit and ongoing losses and is regularly adjusted according to response. Hypotonic crystalloid such as 5% glucose should be used to reach a target plasma sodium at the upper limit of normal at 145 mmol/L (Supplementary Table 2).

Hypokalaemia

Hypokalaemia is the commonest electrolyte abnormality of obstructive uropathy. It is most often encountered immediately after relief of obstruction due to urinary wasting and is self-limiting; approximately 30% of episodes of POD are associated with hypokalaemia[21]. Potassium supplementation can be difficult to predict and usually requires repeated assessment and titration. As a general rule, each 1 mmol/L fall in plasma potassium concentration equates to a body deficiency of around 200 mmol. Oral potassium replacement is generally adequate and is guided by biochemistry results, ensuring a serum level greater than at least 2.5 mmol/L but ideally above 3.5 mmol/L. Insoluble and effervescent potassium tablets each contain approximately 8 mmol and 14 mmol of potassium, respectively. Severe hypokalaemia with plasma potassium below 2.5 mmol/L deserves cardiac monitoring and intravenous replacement. The maximum daily dose by any route must be less than 400 mmoL to avoid malignant arrhythmias. Simultaneous magnesium supplementation is necessary for concurrent hypomagnesaemia.

Hyperkalaemia

Post-renal obstruction complicated by severe renal impairment or focal injury of the distal tubules may give rise to hyperkalaemia. Hyperkalaemia is mostly a sign of established renal failure from a chronic process but can also occasionally evolve after prolonged post-decompression diuresis in subjects with normal kidney function.

Potassium-lowering therapies are not usually necessary since potassium homeostasis rapidly resets following collecting system decompression. Although hyperkalaemia treatment has not been widely studied in the specific context of uropathies, it is a well-known medical emergency and typical pharmacologic regimens apply. Readers should refer to standard reference texts. Retrospective data demonstrates that haemodialysis is utilised in fewer than 15% of acute hospitalisations for obstructive uropathy[22]. Patients requiring dialysis from the time of index presentation almost always imply undetected chronic urinary tract obstruction.

PERIOPERATIVE MEDICATION MANGEMENT

Medication adjustments are frequently necessary following urinary tract decompression. For example, dosing is influenced by kidney function which is frequently poor and fluctuating in this scenario, and nephrotoxins should be withheld. Common considerations are listed in Table 2.

PHARMACOLOGIC THERAPY FOR OBSTRUCTIVE UROPATHY

It is usually appropriate for patients with obstructive uropathy to receive nephrology follow-up. There is no directly proven reno-protective medical therapy for obstructive uropathy beyond standard measures such as cardiovascular risk factor reduction and proteinuria-lowering agents. Statins have improved renal recovery in animal studies but there is no supporting data in humans[23].

Angiotensin-converting enzyme (ACE) inhibitors appear similarly as effective for long-term renal preservation as in other causes of chronic kidney disease (CKD), but may aggravate injury if introduced too early post-obstruction[3,24-26]. Hypertension is prevalent among individuals with obstructive uropathy and, like in all forms of CKD, is associated with worse outcomes. Guideline-directed antihypertensive therapy is recommended[27].

Sodium-glucose transport protein 2 (SGLT2) inhibitors demonstrated an anti-fibrotic effect when introduced in laboratory rats exposed to iatrogenic ureteric obstruction[28]. In the Dapagliflozin in Patients with Chronic Kidney Disease (DAPA-CKD) randomised control trial, the group randomised to SGLT2 inhibitor treatment, including a small number of subjects with obstructive uropathy, experienced significant renal and cardiovascular benefits[29]. SGLT2 inhibitor use in the presence of an indwelling catheter or instrumentation may increase the risk of urological infection.

Given the prevalence of bladder outlet obstruction from prostatic hyperplasia, nephrologists also require some understanding of basic pharmacologic therapies for this problem (Table 2). Other specific causes of uropathy which benefit from adjuvant medical therapy include retroperitoneal fibrosis, with immune-modulators, nephrolithiasis in the form of calcium channel blockers, and cancer through chemotherapy.

PROGNOSIS

The most important predictors of renal recovery are the completeness and duration of obstruction, and the presence or absence of coexisting infection. There is an inverse relationship between chronicity and reversibility; urinary tract obstruction for less than 1 wk is typically associated with complete recovery. The majority of patients experience complete recovery of kidney function with reversal of obstruction. Most improvement occurs in the first fortnight following decompression but ongoing renal recovery may be seen for up to 6 mo. High-grade obstructive uropathy for more than 6-8 wk is said to be irreversible. However, with good preventative care the trajectory of CKD related to obstructive uropathy tends to be benign with only 3% of patients progressing to dialysis at 10 years[22]. A significant minority of patients commenced on dialysis at the time of diagnosis gradually improve and are freed from dialysis after several months[7].

Total destruction of an infected obstructed kidney may occur within a matter of days. Without decompression the infected obstructed kidney is associated with a 40% mortality[30], compared to a mortality rate of less than 5% following successful decompression[31].

Positive prognostic features for renal recovery include POD, younger age, a normal pre-morbid GFR, and lower grades of hydronephrosis as opposed to higher[14,32]. Obstruction severity is more important for renal outcome than aetiology, though bladder outflow obstruction appears to yield a better prognosis than upper tract obstruction because vesical trabeculation and hypertrophy protect the renal parenchyma from a high-pressure system.

Although obstructive uropathy is associated with low short-term mortality, intermediate- and long-term outcomes are poor, particularly for those older than 85 years of age[5]. The median 12-mo survival for patients presenting with malignant and non-malignant obstruction is roughly 40% and 90%, respectively[22].

Table 2 Common perioperative considerations and medical therapies for obstructive uropathy

Medication class	Comments
Perioperative care	
Non-steroidal anti-inflammatory drugs	Should be avoided or used cautiously in any form of acute or chronic kidney disease
	There is ample experimental and clinical evidence suggesting that non-steroidal anti-inflammatory drugs (NSAIDs) may worsen kidney function in patients with renal impairment, especially during a concomitant physiologic insult, and delay renal recovery from acute kidney injury (AKI)[33-36]. NSAIDs interfere with renal auto-regulation and can directly induce *de novo* AKI through several mechanisms.
Antihypertensives	Hypertension is frequently seen in patients with obstructive uropathy, due to volume expansion and upregulation of renin and erythropoietin release because of focal hypoxia[37,38]
	Hypertension may reverse rapidly following acute relief of obstruction and diuresis, so antihypertensive medications should be rationalised accordingly
	Renin-angiotensin system blockade, with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, should be avoided or prescribed carefully due to the well-recognised risks of pre-renal AKI and hyperkalaemia
Antibiotics	Leucocytosis and raised inflammatory markers are commonly seen in acute presentations of urinary tract obstruction as part of the stress response. A low threshold for empiric antimicrobial coverage for urinary infection is prudent
	Renal drug clearance declines roughly in proportion to the drop in GFR. Antibiotic dosing or frequency may need to be reduced, depending on the agent. Antibiotics considered 'nephrotoxic' may need to be withheld, such as vancomycin and gentamicin
	Urosepsis in the context of an obstructed collecting system is tissue-invasive. Therefore, selected antibiotics must be broad-spectrum and penetrant, and reach therapeutic levels quickly. Intravenous ampicillin or ceftriaxone are typical choices, which can be modified based on culture sensitivities
Obstructive uropathy pharmacologic therapies	
Alpha-1 adrenergic receptor antagonists	Common uses: Benign prostatic hyperplasia, urolithiasis (medical expulsive therapy)
	Rationale: Induce smooth muscle relaxation, thereby enlarging ureteral and urethral calibre and improving flow
	Examples: Prazosin (non-selective), tamsulosin (selective), silodosin (selective)
5-alpha reductase inhibitors	Common uses: Benign prostatic hyperplasia
	Rationale: Targeted antiandrogen effect, thereby reducing prostate volume and the static component of bladder outlet obstruction
	Examples: Dutasteride, finasteride
	Combination tablets with alpha-1 adrenergic receptor antagonists are also widely available
Phosphodiesterase-5 inhibitors	Common uses: Benign prostatic hyperplasia, erectile dysfunction
	Rationale: Exact mechanism of action in lower urinary tract symptoms is unclear but may antagonise phosphodiesterase (PDE) receptors on smooth muscle cells, thus inducing urethral relaxation and improved urine flow, or increase bladder and prostate perfusion Examples: Sildenafil, tadalafil, vardenafil
	PDE-5 inhibitors are commonly prescribed for men with erectile dysfunction and coexisting features of prostatism.
	PDE-5 inhibitors may also be used in combination with alpha-1 adrenergic receptor antagonists or 5-alpha reductase inhibitors

TAKEAWAY POINTS

The therapeutic approach to obstructive uropathy is less well understood than in other forms of acute or chronic renal failure. A joint effort between urologists and physicians is necessary. Priorities include catheterisation and surgical correction of the underlying lesion.

An early post-decompression polyuric phase with electrolyte losses is common, requiring judicious monitoring and replacement. Although usually mild, post-obstructive diuresis may be a complex process that quickly transitions from volume overload to dehydration and an attentive fluid management protocol is warranted. Nephrologists should be particularly wary of evolving hypernatraemia, which must be treated urgently.

Many patients develop CKD and should receive long-term nephrology follow-up. Cardiovascular risk factor reduction is pertinent and evidence-based, including blood pressure control and use of ACE inhibitors and SGLT2 inhibitors for reno-protection. The kidney-specific prognosis is generally favourable with few patients proceeding to dialysis.

CONCLUSION

Obstructive uropathy is a potentially reversible condition. Surgical decompression of the urinary system is the key component of care, but many surrounding medical issues must also be considered. Most cases of obstructive uropathy experience complete renal recovery, but a significant minority develop chronic kidney disease or require dialysis. Patients therefore benefit from inter-speciality collaboration between urologists and nephrologists.

FOOTNOTES

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Country/Territory of origin: Australia

ORCID number: Julian Yaxley 0000-0002-0587-276X.

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MINIREVIEWS

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

Sunil Jain

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Sunil Jain, Department of Paediatrics, Military Hospital Secunderabad, Secunderabad 500015, India

Corresponding author: Sunil Jain, MBBS, MD, Professor, Department of Paediatrics, Military Hospital Secunderabad, P.O. Trimulgherry, Secunderabad 500015, India.
sunil_jain700@rediff.com

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. Children with chronic kidney disease (CKD) are at risk of morbidity, mortality, and decreased quality of life. Current pediatric practice structures are apparently 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 the 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. The 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'. The availability of 'Child Kidney Care Centers' will go a long way in improving the lives of affected children.

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

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

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INTRODUCTION

Kidneys are important for maintaining the interior milieu and hence in children for ensuring growth, for preventing morbidity, and for obviating mortality all diseases of the kidneys need focused attention. The urinary system disorders and diseases spectrum is diverse and distinct, incidence is a cause for concern, investigations are 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 for major reform in organization, financing, and training[1]. Specialized centers provide the 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 on 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 into proper perspective for practice and future developments.

The leading causes of global under-five year of age mortality rate 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 also focus on these other causes. The evolving trend, as suggested by analysis in the past several decades, 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]. Children with chronic kidney disease (CKD) are at risk of increased lifelong morbidity, mortality, and decreased quality of life[7].

The magnitude of CKD 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, due to the lack of a national registry. In one of the Command Hospitals in India the work load of kidney disease in children is approximately 8%-10% of total outpatient attendance. This has accounted for 12% of admissions to the pediatric ward[9]. Alarmingly, it has been reported that 58% of children with renal failure presented with end stage renal disease (ESRD)[10]. Thus, prompt diagnosis and proper management is essential. Evidence shows that children fare better than adults if they receive kidney replacement therapy including dialysis and transplantation. Disparities in access to care 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, statistics for the newborn period reveal that 0.8% of cases have abdominal masses, and renal origin masses account for the majority of these. The most common etiologies are: (1) Polycystic kidneys; (2) multicystic dysplastic kidney; (3) hydronephrosis; and (4) renal vein thrombosis. There is a need for specific and specialized management[12]. Thus, there is a 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 the need for adaptation to establish 'Children Kidney Care Centers'. Furthermore, relevant capabilities' building requires understanding of the spectrum of illness, the specialized investigations, and the specific treatments. These are elaborated for sophisticated establishment and scientific execution.

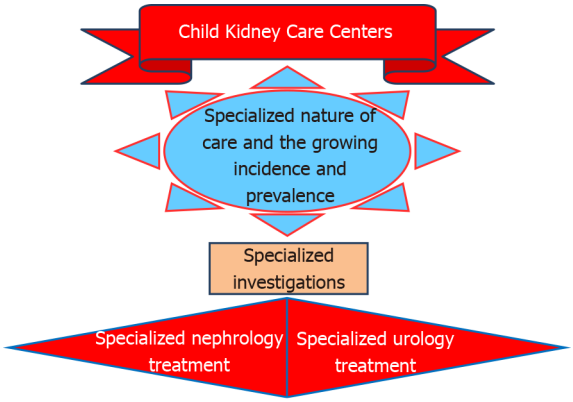

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Figure 1 'Children Kidney Care Centers' need and necessary facilities.

Conceptual frameworks illuminate and magnify illustratively. These simplify ways of representing how complex things work. A conceptual framework pictorial representation for need and necessary facilities of 'Children Kidney Care Centers' is given at Figure 1.

SPECTRUM

In a study of the etiology of pediatric 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]. Pictorial depiction of various etiologies is given at Figure 2. 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

A common renal disorder and a leading cause of ESRD is glomerulonephritis[16,17]. Its presentations are protean. The general features include proteinuria, hematuria, renal failure, and hypertension. Early therapeutic intervention is warranted and leads to renal function improvements and long-term preservation of renal function. All this is required to prevent the progression to end-stage renal failure. Hence, early evaluation is important in appropriate centers.

Glomerulonephritis types presenting with recurrent hematuria are immunoglobulin A nephropathy (Berger nephropathy) and Alport syndrome. Membranoproliferative glomerulonephritis (also termed mesangiocapillary glomerulonephritis) most commonly occurs in children or young adults. The presentation is varied and includes: (1) Nephrotic syndrome; (2) acute nephritic syndrome (hematuria, hypertension, and some level of renal insufficiency); and (3) persistent asymptomatic microscopic hematuria and proteinuria. The presentation of rapidly progressive glomerulonephritis and crescentic glomerulonephritis in most children is acute nephritis (hematuria, some degree of renal insufficiency, and hypertension). These children usually have concomitant proteinuria, often with nephrotic syndrome. Other important presentations 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). The characteristic triad of HUS 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.

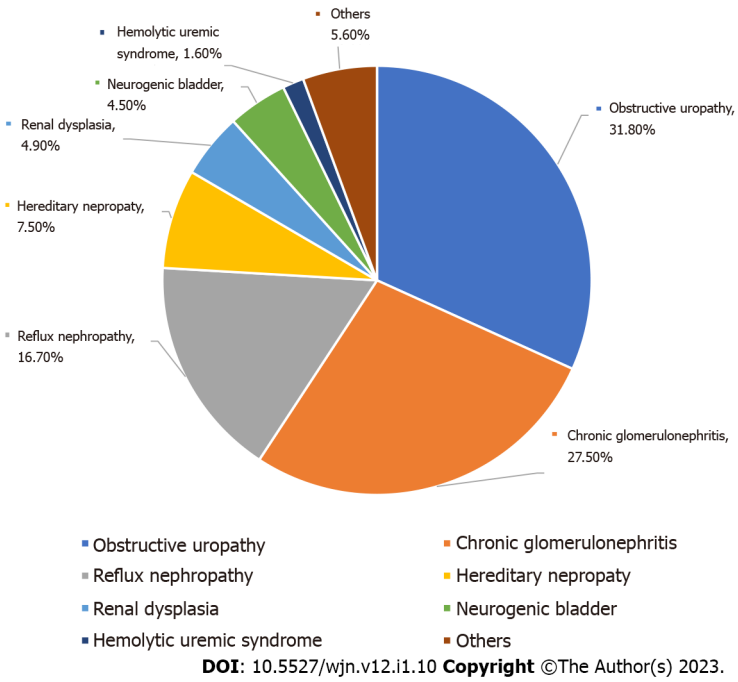

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Figure 2 Chronic renal failure etiological spectrum.

SPECIALIZED INVESTIGATIONS

Kidney injury occurs due to a variety of different mechanisms. Investigations into the type of injury, the degree of injury and assessment of progression involve laboratory tests, diagnostic imaging, and often tissue sample studies. All investigations available in a specialized center are required, and 'Children Kidney Care Centers' can guarantee this. This will ensure prompt care and avoid unnecessary referrals, which causes delays. The best evidence-based practices are as follows.

Glomerular filtration rate

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

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

Protein measurement

Proteinuria assessment for diagnosis, prognosis, and monitoring therapy response is carried out routinely. Proteinuria on urinalysis is often the first clue to renal injury. Subtle and early glomerular injury is identified by microalbuminuria measurements. Twenty-four-hour urinary protein is 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 identifying the injury site in the UT. If 75% or more of the observed RBCs are dysmorphic, the site of injury is the kidney, and most likely the glomerulus. If less than 25% of the observed RBCs are dysmorphic, the injury site is the UT from the 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 hypercalcemia. Increased fractional excretion of phosphate indicates hypophosphatemic rickets. Calculation of fractional excretion of sodium (FENa) is useful for differentiating 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 the diagnosis of renal stone disease. Twenty-four-hour collection is best, but random measurement of the urine calcium (mg/dL): Urine creatinine (mg/dL) ratio can be used in the diagnosis of hypercalciuria[23].

Immunology

The diagnosis of renal disease secondary to SLE is performed by 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 syndrome, antibodies to glomerular basement membrane are seen. Low levels of complement are seen in SLE, systemic vasculitis and HUS.

Complement level measurements are required for fixed proteinuria and glomerular hematuria initial evaluation.

DIAGNOSTIC IMAGING

Ultrasound

Ultrasound (US) for visualization of the UT is the principal imaging modality. For children US is advantageous. The use 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 used 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 and inferior vena cava; and (4) arteriovenous fistula 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 has 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 tumors[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 on the bladder and urethra[26]. The use of pulsed fluoroscopy importantly reduces VCUG-radiation exposure side effects[27].

Intravenous pyelography

The availability of US and magnetic resonance urography has dramatically decreased the need for and use of intravenous pyelography (IVP)[28]. 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 carried out 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 by computed tomography (CT). Thin-section helical imaging (spiral CT scan) gives multiplanar reformatted images quickly. Its uses include: (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 carried using CT angiography.

Magnetic resonance imaging

The advantages of magnetic resonance imaging (MRI) are: (1) Multiple plane images; (2) excellent resolution; and (3) good distinction between different tissue types. All this is without radiation exposure. As compared to iodinated contrast studies, 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 assessing 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 a scintillation detector/gamma camera. Exposure to radiation occurs, but is less compared to other modalities such as VCUG, IVP, or CT.

Dynamic renal scintigraphy is performed for functional information. This is carried out 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$_3$ hence providing a superior renal/background ratio. A ^{99m}Tc-MAG$_3$ scan provides information on the perfusion of each kidney, which is valuable in various clinical settings. It is useful in diagnosis when collecting system dilatation is caused by obstruction. In cases with significant obstruction of the outflow tract, ^{99m}Tc-MAG$_3$ 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. The intravenous injection is followed by the renal cortex images captured. These show the shape, size and relative function of each kidney. The method is sensitive in demonstrating cortical scarring in reflux nephropathy and is 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 caliber flexible fiberscopic cystoscopes are useful in diagnostic cystourethroscopy, and retrograde ureterography. Posterior urethral valves are definitively diagnosed using endoscopy.

Urodynamic studies

Investigations for urinary incontinence or other urinary symptoms are required to make 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 to achieve 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 pelvic floor electromyography activity is measured by needle or surface electrodes placed in the perineum. The study is often carried out with fluoroscopy-"the video urodynamics". This is done to obtain information on the appearance of the bladder wall, presence/absence of VUR, emptying efficiency, and most importantly, the bladder neck and urethra appearance, along with their respective pressure recording for evaluation. The anatomy and physiology of the lower urinary tract requires careful performance with proper patient cooperation. The latter, being the limiting factor in its use in the evaluation of children.

A 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 commonly used method is percutaneous renal biopsy. Automatic spring-loaded biopsy systems are now used, as the technique is simple and easy to use[32,33]. Biopsy examination requires special light microscopy, immunofluorescence techniques, and electron microscopy providing the most accurate diagnosis.

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

SPECIFIC TREATMENTS

Children should have access to treatments and resources that are as sophisticated and advanced as those available to adults. Pediatricians, pediatric nephrologists, and pediatric urologists are integral in 'Children Kidney Care Centers'. The multi-disciplinary teams required for comprehensive care provision in children with kidney disease and their families are: geneticists, genetic counselors, nurse

specialists, dialysis personnel, nutritionists, social workers, and mental health professionals. All these professionals under one roof is desirable. A regular supply of all consumables needed should 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' are discussed below.

Dialysis

The choice of dialysis modality to manage 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 factor 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 the selection of dialysis modality age is a defining factor. In the age group from birth to 5 years of age maintenance dialysis treatment using PD is preferred (85%). In children ≥ 13 years of age initiation of maintenance dialysis treatment with HD is common (50%)[36].

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

PD

PD is preferred and is a convenient treatment modality for acute kidney injury (AKI) and patients with hemodynamically instability[37]. There is a recent trend towards increased continuous renal replacement therapy (CRRT) 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 placement. A number of dialysate transfer sets and associated devices have been developed to reduce the risk of bacterial contamination during either the catheter-to-transfer set or the transfer set-to-dialysate bag connections. This has contributed to simplifying PD connecting maneuvers[39].

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

For patients with ESRD, PD can provide continuous ambulatory peritoneal dialysis and automated therapy using a cycler (continuous cyclic peritoneal dialysis/intermittent peritoneal dialysis/nocturnal intermittent peritoneal dialysis).

HD

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

Incorporation of the online hemodiafiltration (OL-HDF) module into the dialysis proportioning machine hardware makes the handling procedure simple. It secures the process by maintaining 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 good vascular access. The best form of access is an arteriovenous (a-v) fistula. Otherwise a line that is tunneled subcutaneously is used, or shunts/grafts may rarely be required[43]. Tunneled subcutaneous lines are used in: (1) Children too young for an a-v fistula; and (2) children not expected to be on dialysis long-term *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 can choose the CRRT modality[44].

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

Interventional nephrology

The interventions assuming importance and impacting advantageously are insertion of tunneled

hemodialysis 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: Correction of this anomaly requires pyeloplasty. The success rate ranges from 91% to 98%. Pyeloplasty can be carried out using laparoscopic techniques, and is often robot-assisted using the da Vinci robot. Surgery conducted by surgical robots has the advantages of: (1) Small incision; (2) very minimal blood loss; (3) quick recovery; (4) shorter hospital stay; and (5) faster return to normal life. The advantages for the surgeon are: (1) A magnified, high-definition, three-dimensional view; and (2) tiny surgical instruments for manipulation, that have better flexibility than human hands.

Posterior urethral valves: Definitive treatment is performed by destruction of the valves endoscopically. Continuing supportive treatment is required for: (1) Dilated urinary tract; (2) recurrent urinary infections; and (3) uremia.

Other conditions for which surgery may be required are an 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, and 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 where the renal collecting system is accessed percutaneously, and breaking of the calculi is carried out 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 almost always provide complete or satisfactory continence.

The two indications and comprehensive treatments are as follows.

Low urethral resistance: bladder neck reconstructive procedures (such as a periurethral sling) are often successful. Alternatively, an artificial sphincter implantation is usually successful. The components used in this technique 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 a 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. The Mitrofanoff procedure is a useful and commonly performed technique. During this procedure, 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 proximal hypospadias, all cases are repaired in a single operation on an ambulatory basis. 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 require a renal transplant more than adults. This is justified in order to achieve normal growth and cognitive development. Successful transplantation leads to: (1) Improvement in linear growth; (2) possible school attendance; and (3) freedom from dietary restrictions.

Future directions

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

Basic science 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. The future is exciting.

CONCLUSION

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

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ORCID number: Sunil Jain 0000-0002-3935-9243.

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