Original Article

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Retrospective Audit of a Pediatric Nephrology Clinic at a Tertiary Care Teaching Hospital

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Abstract

Background and Aim: To provide basic renal data in the pediatric age group in a poorly resourced hilly state of India, which might be used by researchers and health planners.

Methods: The case records of children presenting to pediatric nephrology clinic from April 2016 to March 2017 were analyzed retrospectively. Registered cases were broadly categorized into various groups and subgroups based upon clinical presentation and investigation findings.

Results: Two hundred and five children presented to the pediatric nephrology clinic with renal diseases over a period of one year. Registered children presenting to pediatric nephrology clinic were broadly categorized into 10 groups. Nephrotic syndrome (NS) was the most common renal disease accounting for 45.6% of registered cases followed by congenital anomalies of the kidney and urinary tract (CAKUT) comprising 26.8% of the cases. Edema was the most common presenting symptom and proteinuria was the most common urinary finding. Focal segmental glomerulosclerosis was the most common histopathological finding reported on renal histopathology and peritoneal dialysis was found to be the most frequently used modality for renal replacement therapy.

Conclusion: Our data reflects geographical variations of the patterns of renal diseases in a resource poor hilly state of northern India. Improvement in pediatric renal services and targeted training of healthcare workers would help in early diagnosis and treatment of children with renal diseases resulting in reduction in their morbidity and mortality.

Keywords: Pediatrics; Nephrology; Nephrotic Syndrome; Glomerulonephritis; Biopsy.

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Introduction

The pattern of childhood renal disease varies from one geographic region to another, even within the same country. This variation is influenced by factors such as genetic predisposition, environmental background, and, to a large extent, the level of awareness. The spectrum of renal diseases is different in developing countries as compared to developed ones. In general, pediatric renal disease accounts for about 4.5–8.7% of total pediatric admissions (1). In developed countries, proper documentation and established renal registries often provide data to guide stakeholders in resource allocation (2,3). This is in contrast to developing countries like ours, where low priority is accorded, partly due to the focus on communicable diseases as well as a lack of data on pediatric kidney diseases, resulting in an overall poor outcome in this group of patients (4). The prevalence of renal disease in a developing country like ours is very difficult to estimate as available reports are very scarce and are mostly hospital based (5). Uttarakhand, a hilly state

of India, has many challenges in developing an acceptable health infrastructure that is readily accessible to its population. There is absolutely no data regarding the spectrum of renal diseases in this resource poor and environmentally challenged state. Improved diagnostic facilities and initiation of pediatric nephrology fellowship programs in recent years has led to much better care and reporting of renal diseases in children. This retrospective study was conducted to find out the pattern and spectrum of pediatric renal diseases at a tertiary care teaching hospital in the state of Uttarakhand, India.

Methods

This study was conducted at the Pediatric Nephrology Clinic of the Department of Pediatrics, SGRR Institute of Medical and Health Sciences, Dehradun, Uttarakhand, India. This retrospective study was conducted over a period of 1 year from April 2016 to March 2017. The retrospective data of all the children aged 0-18 years presenting to the Pediatric Nephrology Clinic during the study period was recorded in a predesigned checklist. Data from children admitted with renal diseases or their complications in the pediatric ward or pediatric intensive care (PICU) were not included in the study. The children presenting with non-renal conditions and those presenting with renal conditions but reporting 2nd time or further were also excluded from the study. Data included demographic details, clinical history, investigations, diagnosis, and details of procedures such as renal biopsy and renal replacement therapy (RRT). Case records were analyzed and broadly categorized into various groups based on their clinical presentations and investigation findings.

These groups were further divided into subgroups to provide more insight about the pattern of these diseases. Disease outcomes could not be ascertained, as it required long-term follow up of the children presenting with variable renal conditions. The hematological and biochemical investigations included complete blood count (CBC), urinalysis and culture, kidney function test (KFT), liver function test (LFT), serum albumin, serum cholesterol, serum anti-streptolysin O (ASO) titer, serum C3, serum C4, anti-nuclear antibody (ANA) profile, anti- neutrophil cytoplasmic antibody (ANCA) profile, anti-double stranded DNA (anti dsDNA), and viral markers (HBsAg, HCV, HIV). Radiological evaluations included ultrasonography (USG) of the kidney and urinary bladder (KUB), micturating cystourethrogram (MCU), DTPA (diethylenetriaminepentaacetic acid) scan and DMSA (dimercaptosuccinic acid) scan. Percutaneous real time ultrasound guided renal biopsy was performed in children where it was needed for the diagnosis as per the standard guidelines (6,7). Renal replacement therapy included both peritoneal dialysis and hemodialysis depending upon the clinical indication. Continuous renal replacement therapy (CRRT) was not utilized as a RRT modality because of unavailability at our center. Plasma exchanges were performed in few children if indicated. Data recorded in predesigned checklists were entered into an Excel sheet and later analyzed using Statistical Package for Social Science (SPSS) software version 18.0. Independent t-test was used for continuous variables and chi-square test was used for categorical variables.

Results

A total of 205 children presented to the pediatric nephrology clinic with renal diseases during the aforementioned study period. An obvious male predominance was noted, as 139 (67.8%) cases were males as compared to 66 (32.19%) females with a male/female ratio of 2.1:1.0. The maximum number of cases belonged to the age groups 1-5 years (31.2%) and 5-10 years (30.7%). Forty-eight (23.4%) cases were in the age group 10-15 years and 24 (11.7%) were <1 year.

The maximum male representation was found in the 5-10 years age group (35.2%) while the maximum female representation was seen in the 1-5 years age group (34.8%). Overall, the mean age at presentation was 6.45 years ±4.708 (Table 1). The mean age was 6.32 years ± 4.51 for males and 6.71 years ± 5.12 for females. Edema was the most common presenting symptom in 85 (41.5%) cases followed by pallor (22.4%), hypertension (10.7%), hematuria (7.8%), rashes (4.9%) and joint pain (3.9%). Registered children presenting to pediatric nephrology clinic were broadly categorized into 10 groups (Table 2) based on their diagnosis.

Nephrotic syndrome (NS) was the most common diagnosis in our study (n=94, 45.6%) followed by congenital anomalies of kidney and urinary tract (CAKUT) (n=55, 26.8%). Twenty-two (10.7%) children were diagnosed with acute glomerulonephritis (AGN) and 10 (4.9%) of them

presented with renal calculi. Chronic kidney disease (CKD) was found in 8 (3.9%) cases while 7 (3.4%) patients presented with enuresis. Out of all the patients presenting with NS, 86 (91.4%) had steroid

Table 1: Age and gender distribution of cases (N=205)

Age (Years)	Male, N (%)	Female, N (%)	Total, N (%)
<1	16 (11.5)	8 (12.1)	24 (11.7)
1-5	41 (29.5)	23 (34.8)	64 (31.2)
5-10	49 (35.2)	14 (21.2)	63 (30.7)
11-15	30 (21.5)	18 (27.2)	48 (23.4)
>15	3 (2.15)	3 (4.5)	6 (2.92)
Total	**139 9 (67.8)**	**66 (32.2)**	**205 (100)**
Mean Age= 6.45 years ± 4.708 Mean (Females) = 6.71 years ± 5.12, Mean (males)= 6.32 years ±4.5			

Table 2: Spectrum of pediatric kidney diseases (N=205)

Diagnosis	N (%)
Acute glomerulonephritis	22 (10.7)
Acute kidney injury	4 (2.0)
CAKUT*	55 (26.8)
Chronic kidney disease	8 (3.9)
Enuresis	7 (3.4)
Nephrotic syndrome	94 (45.8)
Renal calculi	10 (4.9)
Renal tubular acidosis	2 (1.0)
Hemolytic uremic syndrome	2 (1.0)
Post malarial TMA**	1 (0.5)
***Congenital anomaly of kidney and urinary tract, **Thrombotic microangiopathy**	

sensitive nephrotic syndrome (SSNS) and 8 (8.5%) had steroid resistant nephrotic syndrome (SRNS). Eighteen (11.7%) patients with SSNS had steroid dependent nephrotic syndrome (SDNS). Twenty-three (24.4%) were diagnosed with frequently relapsing nephrotic syndrome (FRNS) as compared to 33 (35.1%) with infrequently relapsing nephrotic syndrome (IFRNS).

Of all the steroid resistant cases, 3 (3.2%) had initial resistance (SRNS-IR) and 5 (5.3%) had late resistance (SRNS-LR). Sixty-five (69.1%) children with NS were treated with steroids alone while 29 (30.8%) required alternate steroid sparing drugs. Only 38 children (40.4%) received steroid treatment as per the standard protocols (6,7) during their 1st episode as compared to 56 patients (59.6%) in whom treatment was erratic.

In the CAKUT group, 16 (29%) had pelvi-ureteric junction obstruction (PUJO) and 13 (23.6%) had posterior urethral valve (PUV). Six patients (10.9%) had vesico-ureteric reflux (VUR), 6 (10.9%) had neurogenic bladder, and 4 (4.2%) were diagnosed with multicystic dysplastic kidneys (MCDK). Two children (2.1%) had autosomal dominant polycystic kidney disease (ADPKD), 2 (2.1%) had a duplex system and transient hydronephrosis. One child (1%) had megaureter, 1 (1%) had bladder outlet obstruction, 1 (1%) had autosomal recessive polycystic kidney disease, and 1 (1%) had vesico-ureteric junction obstruction (VUJO). In the AGN group, post infectious glomerulonephritis (PIGN) was the most common diagnosis in 7 (31.8%) out of 22 children. Four children (18.1%) had lupus nephritis and 4 (18.1%) and Henoch Schönlein purpura (HSP) nephritis. One child (4.5%) presented with C3 glomerulonephritis (C3GN), 1 (4.5%) with dense deposit disease (DDD), 1 (4.5%) with Wegener's granulomatosis (WG), 1 (4.5%) with Alport syndrome and 1 (4.5%) with anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis.

A comparative analysis of children presenting with nephrotic syndrome and AGN was performed for different variables (Table 3). The mean age at presentation was 6.11 ± 3.63 years for NS as compared to 12.95±3.24 years for AGN (p=0.001). A significant male predisposition was observed in the nephrotic syndrome group as compared to the AGN group where females were more affected (p<0.001).

Edema and proteinuria were significantly more common in the nephrotic syndrome group (p<0.001). Hematuria, pallor, hypertension, rashes, joint pain, and uremia were significantly more prevalent in AGN group (p<0.001).

Table 3: Comparative analysis of nephrotic syndrome and acute glomerulonephritis

Parameters	Nephrotic Syndrome (N=94)	Acute glomerulonephritis (N=22)	P value
Age (Years)	Mean: 6.11 years ± 3.63	Mean: 12.95 years ± 3.24	0.001*
Gender **Male** **Female**	 68 (Mean age: 6.22 years ± 3.42) 26 (Mean age: 5.84 Years ± 4.20)	 9 (Mean Age: 13.44 years ± 3.04) 13 (Mean age: 12.61 years ± 3.04)	 <0.001** <0.001**
Edema	69 (73.4%)	10 (45.4 %)	0.006**
Pallor	16 (17 %)	13 (59 %)	<0.001**
Hematuria	3 (3.1%)	13 (59 %)	<0.001**
Proteinuria (>2+)	89 (94.7 %)	22 (100 %)	<0.001**
Rash	0	10 (45.4%)	<0.001**
Joint Pain	0	8 (36.4 %)	<0.001**
Hypertension	3 (3.1 %)	9 (40.9 %)	<0.001**
High Urea **(Ref >40 mg/dl)**	48 (51 %) Mean: 37.7±27.4	22 (100 %) Mean: 60.23±48.1	<001** 2.48*
High Creatinine **(Ref >0.8 mg/dl)**	48 (51 %) Mean: 0.86 ±2.24	22 (100 %) Mean: 1.37± 1.26	0.528** 0.992*
***Student's t-test **Chi-square test**			

Creatinine was high in all AGN cases although the difference was not significant. Proteinuria was the most common manifestation and was present in 121 (59%) patients of whom 91 (44.4%) had nephrotic range proteinuria (urine protein ≥3+/4+). Hematuria detected in 52 (25.4%) children was the 2nd most common urinary symptom. Amongst patients with hematuria, 23 (44.2%) had AGN, 22 (42.3%) had CAKUT (VUR, PUV and neurogenic bladder), 4 (7.7%) had renal calculi, and 3 (5.7%) had NS. Hypertension was present in 32 (15.6%) children while 10 (4.8%) presented with rashes and 8 (3.9%) had joint pain. Ninety-seven (47.3%) children had hypoalbuminemia (serum albumin <3.5 g/dl) and 82 (40%) had hypercholesterolemia (serum cholesterol >200 mg/dl). Urine culture was performed in 46 (22.4%) patients and 20 (43.5%) showed growth of Escherichia coli. USG KUB was performed in 84 (40.9%) patients of whom 45 (53.5%) had hydronephrosis (HDN). Twenty-one (46.6%) children had unilateral HDN and 24 (53.4%) had bilateral HDN. Twelve children (14.3%) were diagnosed with echogenic kidneys and 9 (10.7%) had shrunken kidneys. Renal calculi were detected on USG in 10 (11.9%) patients while 5 (5.95%) were diagnosed with dysplastic kidneys. MCU was performed in 44 (21.4%) children of whom 20 (45.5%) had VUR and 9 (20.5%) had posterior urethral valve (PUV). Nuclear scans were performed in 29 (14.1%) patients, including 19 (65.5%) DTPA scans and 10 (34.5%) DMSA scans. Kidney biopsy was done in 11.2% of the children and all the biopsies were percutaneous real time USG guided biopsies. The most common histopathological diagnosis was focal segmental glomerulosclerosis followed by diffuse proliferative glomerulonephritis (Figure 1).

Renal replacement therapy was required in 22 (10.7%) patients. Peritoneal dialysis (PD) was performed in 9 (40.9%) and hemodialysis (HD) was required in 13 (59.1%) children. Plasma exchange was performed in 5 (2.4%) children of whom 2 (40%) were diagnosed with hemolytic uremic syndrome, 1 (20%) had lupus nephritis, 1 (20%) had dense deposit disease, and 1 (20%) had p-ANCA associated vasculitis.

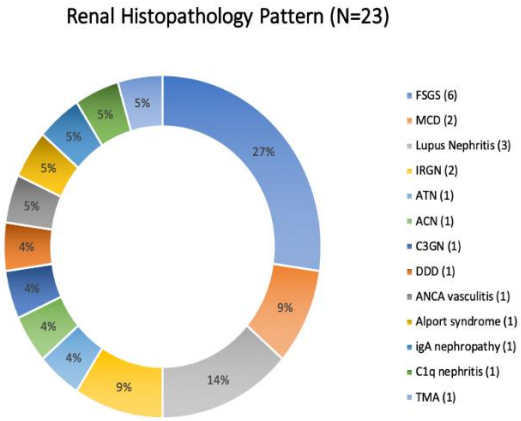

Figure 1: Pattern of renal histopathology findings
FSGS: Focal segmental glomerulosclerosis, IRGN: Infection related glomerulonephritis, ATN: acute tubular necrosis, ACN: Acute cortical necrosis, C3GN: C3 glomerulonephritis, DDD: Dense deposit disease, ANCA: Ani neutrophilic cytoplasmic antibody, TMA: Thrombotic microangiopathy

Discussion

The pattern of childhood renal disease varies from one geographic region to another, even within the same country. Factors responsible for such variations included genetic predisposition, environmental factors and level of awareness in the general population (8). Early detection of renal diseases in children leads to better management and reduced the morbidity and mortality. Data describing the spectrum of renal diseases in children is scanty because of the lack of a pediatric renal disease registry. The pattern of pediatric renal disease is different in developing and developed countries accounting for 4.5-8.7% of total pediatric admissions (9,10). In the present study, pediatric renal disease accounted for 1.1 % of the total outpatient registry over the study period, which was comparable to a few studies (9) but lower than most of the previous studies (1,4,11,12). Standard criteria and guidelines were utilized for the diagnosis of children presenting with features of kidney diseases (13,14,15). Although most of the previous studies included admitted patients, our study was different as it was based on the records of outpatient registry. Another reason for the lower than expected prevalence could be non-registry of not very serious renal conditions like urinary tract infections (UTIs), which were managed in general pediatric OPD and were not referred to the pediatric nephrology clinic. Poor disease characterization and under development of a pediatric sub-specialty clinic in the hilly state of Uttarakhand also contributed to the low prevalence. In our study, a male predominance was observed, which was consistent with many previous studies (1,4,11). Nephrotic syndrome was the most common diagnosis in our study accounting for 45.6% of all registered cases. Similar observations were noted by Bhatt et al and others where it was the most common renal disease responsible for 34.1% patients and other similar studies (9,16,17). However, a study from Kashmir found that acute kidney injury (AKI) and urinary tract infection (UTI) were the leading diagnoses (10). This suggests wide variations in referral practices to the pediatric sub-specialty clinics amongst pediatricians from different states of this country. In the present study, not a single case of uncomplicated UTI was registered and those who had UTI had some form of CAKUT and were grouped accordingly. Similarly, no AKI cases were observed in the outpatient registry as most of these cases were probably managed in PICU and pediatric wards and were caused by reversible etiologies. These patients were evaluated and managed in the PICU and were not included in this study. The children whose AKI was found to be a complication of other renal conditions like AGN, nephrotic syndrome, vasculitis, or CAKUT needed follow-up and were referred to the pediatric nephrology clinic and further grouped under the primary renal disease conditions. CAKUT was the 2nd most common renal disease condition diagnosed in our study, which was different from most of the previous studies in which AGN was the leading or the 2nd leading diagnosis (1,9,11,12). Hydronephrosis was a presentation in almost all of the CAKUT cases diagnosed on ultrasonography either incidentally or during work-up for other etiological conditions. In a study from Iran, CAKUT and CKD accounted for 46% of all cases and the majority of them had VUR with or without neurogenic bladder (11). Such a high proportion of CAKUT diseases suggests advances in the antenatal care and postnatal follow-up of affected babies through improved pediatric nephrology services. This also reflects geographical and epidemiological variations in the spectrum of renal diseases in the pediatric age groups in different countries or states within the same country. AGN was the 3rd most common renal disease found in our study accounting for 10.7% of the cases. Post

infectious glomerulonephritis (PIGN) was responsible for 31.8 % of all AGN cases followed by lupus nephritis and Henoch Schönlein purpura (HSP). Almost similar observations were noted in a study from Nepal where AGN was responsible for 37.1% of renal diseases and amongst all AGN, PIGN accounted for 33% of the cases followed by lupus nephritis and Henoch Schönlein purpura (HSP) nephritis (1). The prevalence of AGN in our study was much lower compared to reports from other countries such as China (30%), Nigeria (37.7%) and South Africa (45%) (18,19,20). In our study, only 8 children (3.9%) were diagnosed with CKD, which was comparable to a report from Nepal (4.2%) and a very recent study from Sudan (4%) (21,22). However, a much higher prevalence has been reported from other developing countries such as Nigeria (20.3%) and Iran (14.9%). A significant 10 (4.9%) children were found to have nephrolithiasis, which was much higher than previous reports (1,8). Such a high prevalence of renal and ureteric stones in the hilly state of Uttarakhand may be related to genetic predisposition, environment factors and food preferences of the population. However, in a study from Sudan, 15.5 % of the children had nephrolithiasis, which was much higher than our study (22). Further studies are required to evaluate the possible etiologies and the wide variation in the prevalence of nephrolithiasis in different parts of the world. Percutaneous real-time USG guided renal biopsy was conducted in 23 (11.2%) children and focal segmental glomerulosclerosis (FSGS) was the most common histopathological finding seen in 26% of the all biopsies. Our findings were very similar to the results of a prospective study conducted by Sinha et al (23) that found FSGS accounting for 25% of histopathological diagnosis amongst all renal biopsies. However, in another study from India, mesangioproliferative glomerulonephritis (MesPGN) was the most common histopathological finding seen in 38% of all biopsies (24). Four children developed perinephric hematoma and two developed transient hematuria following biopsy. No major complications were observed in the children who underwent biopsy in our study. PD was the most common dialysis modality followed by HD in children who required RRT. Continuous renal replacement therapy (CRRT) was not available at our center and hence could not be carried out for children requiring RRT. PD with stiff catheter was found to be the most commonly employed modality for RRT in acute kidney injury in a cross-sectional survey from India (25). Vasudevan et al. reported that in India, despite the availability of PD, hemodialysis, CRRT, and SLED in 23 of 26 centers surveyed, acute intermittent PD with rigid catheter was the most commonly used modality due to its low cost and simplicity (26). A limitation of this study was its retrospective nature due to which the accuracy of data collection could be doubted and some children might have been inadvertently excluded from the registry. Common renal conditions like uncomplicated UTI and AKI were not referred from general pediatric OPDs and hence the true incidences of such diseases might be underestimated. Many rare renal diseases such as hereditary nephropathies and renal malignancies might have been missed because of lack of diagnostic facilities and referral to other higher centers.

Conclusion

This study was conducted to provide a basic data regarding the burden of renal diseases, their relative frequency, clinical profile, diagnosis and management. There is a need for routine screening of renal diseases in children, so that children with evidences of kidney diseases can be identified early and treated appropriately. This can be achieved by improving pediatric health services and strengthening training programs of health workers in resource constrained settings like ours. It can be further strengthened by wider availability of pediatric nephrology teaching and training programs to improve the expertise and skills required for diagnosing and managing such children.

Conflict of Interest

The author declares no conflicts of interest.

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