Clinico-epidemiological Profile of Children with Chronic Kidney Disease in Tertiary Care Referral Center in Nepal: Prospective observational study

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ABSTRACT

Background

Chronic kidney disease in children has been increasing over the years and is associated with high degree of morbidity and mortality. The cost of treating children with chronic kidney disease is also substantial. Prevention of this disease is the only long term solution in our context. Till date, there is limited data on chronic kidney disease in Nepalese children.

Objective

To study the epidemiological, clinical and etiological profile of children with Chronic Kidney Disease from 2 to 16 years of age presenting for the first time in tertiary care hospital.

Method

This is the prospective observational study carried out at the tertiary care hospital over a period of 3 years. Children between 2-16 years who were first time diagnosed of chronic kidney disease and had estimated glomerular filtration rate < 60 ml/min/1.73 m^2 for last 3 months were enrolled.

Result

There were total of 124 patients, of whom 78 were male with male to female ratio of 5:3 with mean age of 11.8±2.2 years. Chronic glomerulonephritis (23%), reflux nephropathy (23%) and nephrolithiasis (16%) were the commonest etiological diagnosis. Rapidly progressive glomerulonephritis and systemic lupus erythematous accounted for 85% cases of chronic glomerulonephritis. Vesicoureteric reflux and posterior urethral valve accounted for 85% cases of reflux nephropathy. In 32%, the cause could not be determined. Swelling (45%) and dyspnea (20%) were the chief presenting complaints. Pallor were seen in all cases (100%) followed by hypertension in 68% and short stature in 64%. Majority (60%) of the patients with chronic kidney disease presented in the stage V.

Conclusion

Chronic glomerulonephritis and reflux nephropathy were the commonest etiologies of chronic kidney disease, majority of them following rapidly progressive glomerulonephritis, systemic lupus erythematosis, vesicoureteric reflux and posterior urethral valve. The commonest clinical features were swelling, dyspnea, pallor and hypertension.

KEY WORDS

Chronic kidney disease, Clinical profile, Epidemiological profile, ESRD, Etiology of CKD, Nepalese children

INTRODUCTION

Chronic kidney disease (CKD) encompasses a spectrum of clinical and laboratory derangements manifesting with chronic and progressive decline of renal functions. While CKD affects 500 per million populations per year of adults, pediatric age group accounts for only 1-4%.[1-3] However, CKD is associated with high degree of morbidity and mortality in children, compared to adults. When a child with CKD reaches to the terminal stage, commonly referred to as end stage renal disease (ESRD), the survival is only possible with renal replacement therapy (RRT) either dialysis or renal transplantation. But RRT services in resource limited settings are usually available for only small number of patients with ESRD. Data from India in adult population had also shown that only 3 to 5% of ESRD get some form of RRT.[4] Even for those, who had initiated RRT, there has also been significant drop rate of dialysis seen in our population due to poor socioeconomic background and is another major cause of death while awaiting renal transplantation. Irrespective of lower incidence of CKD in children, compared with adults, the cost of treating ESRD is also still significant.[5] Studies have shown that mortality rate for children with ESRD receiving dialysis therapy is between 30 and 150 times that of the general pediatric population and the expected remaining lifetime for a child 0–14 years of age and on dialysis is only 20 years.[6,7] Therefore screening and identifying at the risk population is the only practical solution to minimize the burden of CKD.

Most epidemiological information on CKD originates from data available on ESRD. Little information is available on the prevalence of earlier stages of CKD, as patients are often asymptomatic. Warady BA and Chadha V also recommended that more epidemiological studies on pediatric CKD would be needed because of geographic, environmental, racial, genetic, and cultural differences if a better understanding of the full extent of the problem, areas for study, and the potential impact of intervention is desired.[8]

Because of lack of pediatric CKD registry, data in the epidemiological, etiological and clinical profile of pediatric CKD in Nepal is scanty. Hence, this study was conducted with the aim to study the clinico-epidemiological profile of patients presenting for the first time with chronic kidney disease.

This study is expected to add further information on current data and guide health planners to formulate strategies for the prevention of CKD in days to come.

METHODS

This was the prospective observational study carried out in the Department of Pediatrics of Tribhuvan University Teaching hospital (TUTH) in Kathmandu, Nepal for the period of 3 years (April 2017 to March 2020). TUTH serves as one of the main referral tertiary hospitals for pediatric patients with kidney disease across the country. The study was approved by Institutional Ethics Committee.

All patients from 2 to 16 years whose estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73 m^2 for last 3 months or patients when visited first time to pediatric emergency and OPD diagnosed to have CKD on the basis of serum creatinine and ultrasound features of contracted kidney were included for the study. Chronic kidney disease stage I, II, acute on chronic kidney disease on evaluation and readmitted patient were excluded. Staging of CKD was done based on eGFR estimated from modified Schwartz formula {0.413* (height in cm/serum creatinine in mg/dl)}.[9] CKD staging is categorized into I, II, III, IV and V if eGFR is ≥ 90-120, 60-89, 30-59, 15-29 and ≤ 15 ml/min/1.73 m^2 respectively.[10]

All the data regarding the age, gender, geography, ethnicity, socioeconomic status, etiology, clinical feature, lab investigation, need of dialysis, mode of dialysis and outcome was documented in case proforma of the patient after getting informed consent.

The collected data were entered in MS Excel and converted into Statistical Package for Social Sciences version 20 (IBM Corp. Armonk, NY, USA) for statistical analysis. The descriptive data was expressed in frequency, percentage, mean, standard deviation, median, etc. along with graphical and tabular presentation. Continuous variables were expressed as mean ± standard deviation or median {interquartile range (IQR)}, depending upon the normality of distribution. Categorical variables were expressed as number of observations (proportion).

RESULTS

Out of the 1458 children with renal diseases seen in last 3 years, 124 patients were diagnosed to have CKD which accounts for 8.5%. Out of 124 children with CKD, 78 were male with male to female ratio of 5:3 with age ranging from 2 to 16 years (mean age of 11.8±2.2) (fig. 1).

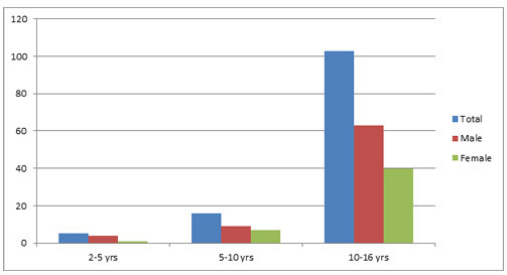

Figure 1. Age and sex wise distribution of studied population

Brahmin/Chhetri (32%) and Hill Janjati (28%) were the ethnic group commonly affected (table 1). Eighty seven percentage of children with CKD belong to lower middle class and 13% from upper lower class as derived from Kuppuswami scale.

Table 1. Ethnical Distribution of CKD children

Ethnicity/Age	2-5years (n=5)	5-10 years (n=16)	10-16 years (n=103)
Brahmin/Chhetri	2	5	33
Terai/Madheshi	1	3	7
Hill Dalit	0	2	5
Hill Janjati	1	3	31
Madhesi/Muslim	0	1	16
Newar	0	1	5
Terai Janjati	1	1	6

The commonest etiological diagnosis identified were chronic glomerulonephritis (23%), reflux nephropathy (23%) and nephrolithiasis (16%). There were 3 cases of chronic tubulointerstitial disease (2.5%), 3 cases of HIV associated nephropathy (2.5%) and 1 case of CKD caused by chronic use of nonsteroid antiinflammatory drug (naproxen) prescribed for juvenile idiopathic arthritis (1%). In 32% of the patients (n=40), cause could not be determined. Rapidly progressive glomerulonephritis (RPGN) and systemic lupus erythematosis (SLE) accounted for 85% cases of chronic glomerulonephritis and vesicoureteric reflux (VUR) and posterior urethral valve (PUV) for 85% cases of reflux nephropathy (table 2).

Table 2. Etiological diagnosis of pediatric kidney diseases

Pathology	Etiology	Number (%)
Chronic glomerulonephritis (n=28)	RPGN (MPGN, SLE, IgA nephropathy, unknown)	13 (46)
	SLE	9 (32)
	IgA nephropathy	5 (18)
	Alport syndrome	1 (4)
Reflux nephropathy (n=28)	VUR	13 (46)
	PUV	10 (36)
	Neurogenic bladder	3 (11)
	Bilateral PUJO	2 (7)
Nephrolithiasis (n=20)	Hypercalciuria	8 (40)
	Hypocitraturia/hypo-kaliuria	7 (35)
	Hyperoxaluria	3 (15)
	Renal tubular acidosis	2 (10)

Majority (60%) of the patients presented in the stage V (fig. 2). Swelling (45%), dyspnea (20%) and vomiting (19%) were the commonest presenting features and pallor (100%), hypertension (68%) and short stature (64%) were the commonest finding in our population (table 3). Proteinuria {non nephrotic (79%), nephrotic (21%)} and low serum albumin (< 3.5 gm/dl) were seen in all cases. Metabolic acidosis (84%) and Vitamin D deficiency (81%) were other commonest laboratory findings detected in our patients (table 4).

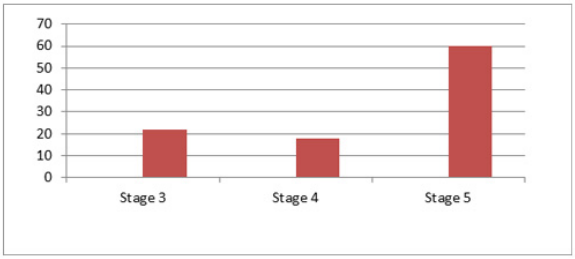

Figure 2. Stages of CKD at the time of presentation

Table 3. Clinical profile of children with CKD

Clinical features	N (%)
Swelling	56 (45)
Dyspnea	25 (20)
vomiting	23 (19)
weakness	11 (9)
Red urine	11 (9)
Decreased urine output	10 (8)
Pallor	124 (100)
Hypertension	84 (68)
Short stature	79 (65)
Underweight	68 (55)
Respiratory distress	40 (32)
Rickets	8 (6.5)

Table 4. Laboratory findings in pediatric CKD patients

Laboratory parameters	N (%)
Proteinuria	124 (100)
Low albumin	124 (100)
Vitamin D Deficiency	104 (84)
Metabolic acidosis	100 (81)
Anemia	96 (78)
Hypocalcemia	94 (76)
Hyperphosphatemia	59 (48)
Hyponatremia	22 (18)
Hyperkalemia	11 (14)

DISCUSSION

The current study provides the information of clinico-epidemiological profile of pediatric CKD patients admitted in our hospital. Chronic kidney disease was found more frequently among adolescent male from the low socioeconomic status. Brahmin, Chhetri and Hill Janjati were most commonly affected ethnic groups, however, Newar and Hill Dalit ethnic groups were least affected. Chronic glomerulonephritis, reflux nephropathy and nephrolithiasis were the leading cause of CKD. Most of the patients presented were in the stage V. Swelling, dyspnea, vomiting, pallor, hypertension, short stature, proteinuria and hypoalbuminemia were seen in majority of our patients.

A total of 1458 children with renal disorders were identified during the study period, of whom CKD was diagnosed in 124 (8.5%). However, in the study conducted in 206 cases of pediatric renal disorders by Yadav et al. in BP Koirala Institute of Health Sciences, CKD accounts for only 1.2%.[1] Bhatta et al. and Malla et al. in their study on pediatric renal disorders in different center of Nepal found chronic renal failure in 4.2% and 2.5% respectively.[2,3] This difference could be due to the varying incidence of pediatric renal disorders in different regions of the Nepal. Also, our study being done at tertiary care hospital where the patients are usually referred for RRT, this prevalence might not reflect the true prevalence of CKD existing in our community.

In the current study, most of the patients with CKD (83%) belong to adolescent age group which was in consistent with many reports from developing countries.[8] Mangia CMF and Andrade MC in their study also found out that the highest proportion attributed to kidney failure hospitalization occurred among children between 10 to 19 years (57.5%).[11] There could be various reasons why adolescent age group was found to have more incidence of CKD. In the present study, all the CKD cases below 2 years of age were excluded there by excluding congenital kidney diseases which is the most common cause of CKD at younger age. Chronic glomerulonephritis, being the most common acquired cause of CKD, is common in adolescent age group, predominantly in children between 10-19 years old. Other reason could be the delayed fall in GFR below 60 ml/min/1.73 m^2 in children with congenital anomalies of kidney and urinary tract (CAKUT), which may not have been detected in early age. Many studies in the past had also shown that cases with CKD following glomerulonephritis were common in adolescent period.[12]

In the present study, of the 124 children with CKD, 69% were males. In the study by Sathyan et al. in adult population, of the 333 patients with CKD, 65.17% were males.[13] Gheissari et al. reported that out of 268 CKD pediatric patients, 144 were male (54%).[14] This shows that male gender is an important factor in the development of CKD and probably hormonal influence is responsible for faster decline in GFR in males as compared to females. However, parents' early health seeking behavior for the male child in our society might be the reason for this difference, and should be interpreted precisely.

Chronic kidney disease was more predominant in Brahmin, Chhetri and Hill Janjati people in the current study. However, higher prevalence of CKD among these ethnic groups needs to be confirmed by larger studies. We also observed that children with CKD belong to family with poor socioeconomic status. However, we cannot establish the relationship between socioeconomic status and CKD from this study as our hospital mostly caters children from poor socioeconomic background.

In the presently studied population, chronic glomerulonephritis (23%), reflux nephropathy (23%) and nephrolithiasis (16%), were found to be the commonest cause of CKD in children and in 32% cases, the cause could not be ascertained. This finding is consistent with the study by Ghessari et al. in 268 CKD children in which the most frequent etiology of CKD was also glomerular diseases and reflux nephropathy seen in 34% and 16.7% respectively. In 21.7% of pediatric CKD patients, the etiology was unknown.[14] Similar findings also observed in study by Peco-Antic et al.[15] Even in the study by Khakurel et al. in adult ESRD, unidentified cause accounted for 18%.[16] The significant proportion of unknown etiology could be because of late presentation to the tertiary center of developing countries in which case establishing the cause is extremely difficult. As chronic glomerulonephritis and reflux nephropathy being the commonest pathology identified in several studies, early diagnosis and prompt treatment of the cause such as vesicoureteric reflux, posterior urethral valve and rapidly progressive glomerulonephritis could decrease the burden of CKD to greater extent.

Current study had identified that 60% of CKD children were presented in the stage V at the time of first arrival to hospital. Almost the similar result was found in one of the studies in the past in which case 74.8% had GFR less than 15 ml/min/m^2 i.e. stage V when diagnosed.[17] In the context of Nepal, expertise in the field of pediatric nephrology and the pediatric dialysis facilities are not available in peripheral center. Therefore almost all children with advanced stages of CKD need to be referred to tertiary pediatric facility. This also reflects the lack of awareness about CKD among the public and the failure of medical practitioners to screen the at risk population and to diagnose CKD at an early stage, which would enable appropriate treatment to be instituted so as to prevent or reduce the rate of progression of CKD.

Swelling was the most common symptom (45%) followed by dyspnea in 20% and vomiting in 19%. The most common findings at the time of presentation were pallor (100%), hypertension (68%) and short stature (64%). Similar clinical findings have been reported by Ghessari et al. where hypertension (HTN) was the most prevalent sign (more than 50% of patients) followed by anemia.[14] In another cohort study on 366 children, HTN was observed in more than 70% of patients, while anemia and growth retardation were reported in 37% and 12% respectively.[18] Thus emphasizing the need for a high index of suspicion even in patients presenting with symptoms and signs related to other systems.

Presence of proteinuria and hypoalbuminemia were seen in all CKD cases in present study followed by metabolic acidosis in 84%, Vitamin D deficiency in 81%, anemia in 78%, hypocalcemia in 76% and hyperphosphatemia in 48%. However, study by Wong et al. found anemia in 36.6%, proteinuria in 11.5%, and metabolic bone disease in 16.9%.[18] This difference could be due to the inclusion of all stages of CKD by Wong et al. but in the present study patients with only moderate and advanced CKD (stage 3

and beyond) have been included. According to Wong et al. study, the prevalence of all complications increased with worsening stage of kidney disease (all P-values significant). However in this study the complications in different stages of CKD have not been compared.

Hyponatremia has been observed in 14% of CKD cases and hyperkalemia in 11% especially in ESRD patients in the current study. Furth et al. reported that while comparing the individuals with a GFR ≥ 50 ml/min per 1.73 m^2 with GFR < 30 ml/min per 1.73 m^2, there was a three-fold higher risk of acidosis and growth failure and a four to five fold higher risk of anemia and elevated potassium and phosphate. Similar results were obtained in the other studies also.[19-21]

The main limitations of this study are the exclusion of children below 2 years of age and children with earlier CKD stages. The reason behind not including patients less than 2 years is that there has not been any consensus on definition of CKD and normal GFR value in this age. Especially in early stages of CKD, the patient donot have any clinical symptoms so parents usually donot take their children for routine check up for CKD detection during asymptomatic stage. This makes the epidemiology of CKD very difficult to study and therefore may underestimate real incidence and prevalence of CKD stages I and II. For all these reasons, in the majority of studies, estimates of CKD take into account patients with moderate to severe CKD or end-stage renal disease (ESRD) so larger population based study is needed to find the exact prevalence of CKD including stage I and II in our part of the world. Also being a single center study, the prevalence of moderate and advanced Pediatric CKD identified from this study might not be true representative of the whole community.

CONCLUSION

Of all the CKD cases, glomerular disease and reflux nephropathy were the leading and majority was following RPGN, SLE, VUR and PUV. In one third of pediatric CKD cases, the etiology is unknown.

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REFERENCES

1. Yadav SP, Shah GS, Mishra OP, Baral N. Pattern of renal diseases in children: A developing country experience. *Saudi J Kidney Dis Transpl.* 2016 Mar;27(2):371-6.
2. Bhatta NK, Shrestha P, Budhathoki S, Kalakheti BK, Poudel P, Sinha A, et al .Burden of kidney disease in children: Nepalese perspective. *Kathmandu Univ Med J (KUMJ)*. 2008 Apr-Jun;6(2):191-4.
3. Malla T, Malla K, Thapalial A, Sharma MS. An overview of renal diseases in children. *J Nepal Paediatr Soc*. 2007 Jul-Dec;27(2):75-8.
4. Mani MK. Prevention of chronic renal failure at the community level. *Kidney Int Suppl.* 2003 Feb;63:86.
5. Lysaght MJ. Maintenance dialysis population dynamics: current trends and long-term implications. *J Am Soc Nephrol.* 2002 Jan;13:37-40.
6. United States Renal Data System. 2020 USRDS Annual Data Report: Epidemiology of kidney disease in the United States. National Institutes of Health. Bethesda, MD: National Institute of Diabetes and Digestive and Kidney Diseases, 2020.
7. McDonald SP, Craig JC. Long-term survival of children with end-stage renal disease. *N Eng J Med.* 2004 Jun;350:2654–62.
8. Warady BA, Chadha V. Chronic kidney disease in children: the global perspective. Pediatr Nephrol. 2012 Dec;22(12):1999-2009.
9. Schwartz GJ, Munoz A, Schneider MF, Mak RH, Kaskel F, Warady BA, et al. New equations to estimate GFR in children with CKD. *Journal of the American Society of Nephrology*. 2009 Mar 1;20(3):629-37.
10. National kidney foundation. KDOQI clinical practice guidelines for chronic kidney disease: Evaluation, Classification, and Stratification. *Am J Kidney Dis*. 2002 Feb;39(2 Suppl 1):S1-S266.
11. Mangia CMF, Andrade MC. Epidemiological aspects of kidney failure in hospitalized children in Brazil. *J Nephrol Ther.* 2016; 6: 245.
12. Ferris ME, Miles JA, Seamon ML. Trends in treatment and outcomes of survival of adolescents initiaing end-stage renal disease care in USA. *Pediatr Nephrol*. 2006 Mar;21(7):1020-26.
13. Sathyan S, George S, Vijayan P, Jayakumar M. Clinical and epidemiological profile of chronic kidney disease patients in a tertiary care referral centre in South India. *Int J Community Med Public Health*. 2016 Dec;3(12):3487-92.
14. Gheissari A, Hemmatzadeh S, Merrikhi A, Fadaei Tehrani S, Madihi Y. Chronic kidney disease in children, A report from a tertiary care center over 11 years. *J Nephropathology*. 2012 Oct;1(3):177-82.
15. Peco-Antić A, Bogdanović R, Paripović D, Paripović A, Kocev N, Golubović E, et al. Epidemiology of chronic kidney disease in children in Serbia. *Nephrology Dialysis Transplantation*. 2012 May 1;27(5):1978-84.
16. Khakurel S, Agrawal RK, Hada R. Pattern of end stage renal disease in a tertiary care center. *J Nepal Med Assoc.* 2009 Apr-Jun;48(174):126-30.
17. Chan JC, Williams DM, Roth KS. Kidney failure in infants and children. *Pediatrics in Review.* 2002 Feb;23(2):47-60.
18. Wong H, Mylrea K, Feber J, Drukker A, Filler G. Prevalence of complications in children with chronic kidney disease according to KDOQI. *Kidney Int*. 2006 Aug;70(3):585-90.
19. Furth SL, Abraham AG, Jerry-Fluker J, Schwartz GJ, Benfield M, Kaskel F, et al. Metabolic abnormalities, cardiovascular disease risk factors, and GFR decline in children with chronic kidney disease. *Clinical Journal of the American Society of Nephrology*. 2011 Sep 1;6(9):2132-40.
20. Harambat J, Van Stralen KJ, Kim JJ, Tizard EJ. Epidemiology of chronic kidney disease in children. *Pediatr Nephrol*. 2012 Mar;27(3):263-73.
21. Mong Hiep TT, Janssen F, Ismaili K, Khai Minh D, VuongKiet D, Robert A. Etiology and outcome of chronic renal failure in hospitalized children in Ho Chi Minh City, Vietnam. *Pediatr Nephrol*. 2008 Jun;23(6):965-70.