Journal of Muhammad Medical College
Website: jmmc.mmc.edu.pk

Original Article

Etiological factors and clinical presentation of chronic kidney disease among pediatric patients in Hyderabad, Sindh.

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Abstract:

Introduction: Chronic kidney disease (CKD), though a relatively uncommon in children yet a devastating disease with serious conditions that may leads to several complications like end-stage renal disease (ESRD) and even premature mortality.

Objective: To evaluate the etiological factors linked with chronic kidney disease among pediatric patients in Isra University hospital, Hyderabad, Sindh.

Methodology: Cross-sectional study was conducted at Isra University Hospital, Hyderabad from July 2019 to August 2020. Pediatric patients between the ages 6 months and 14 years, belongs to either gender, admitted during the study duration and diagnosed as having chronic kidney disease were included. Patient's information related to etiological factors of disease and its symptoms was collected using written questionnaire. Collected data was analyzed using SPSS ver. 23.

Results: Out of total 62 pediatric patients, majority 53.2% were males and 46.7% were females. Mean age was 8.68±4.2 years (range from 6 months to 14 years). Majority, 29.0% patients were suffering from CKD stage III while 22.6% patients were suffering from stage II and IV. Renal hypoplasia or dysplasia (congenital small sized kidneys) was the most common (22.6%) underlying etiological factor followed by neurogenic bladder (19.3%) and unknown etiology (17.7%). Polyuria and bed-wetting were more prominent complaint among males compared with female patients. Whereas, stunted growth was more prominent among female patients. There was a statistically significant ($p<0.05$) difference between polyuria, stunted growth, bed wetting among male and female patients.

Conclusion: Renal hypoplasia (congenital small sized kidneys) and neurogenic bladder are the major etiological factors of CKD among pediatric patients. While amongst the presenting complaints polyuria, nocturnal enuresis and stunted growth along with pallor are the chief presenting complaints.

Key words: Chronic kidney disease, neurogenic bladder, nocturnal enuresis .

Introduction:

Chronic kidney disease (CKD), though a relatively uncommon in children yet a devastating disease with serious conditions that may leads to several complications like end-stage renal disease (ESRD) and even premature mortality.[1] In children, there are five stages of CKD that is; first stage when there is a damage to kidney with normal or increased glomerular filtration rate (GFR) that is ≥90 mL/min while in second stage there is kidney damage with mild GFR decreased (60-89 mL/min). In third stage there is a moderately decline in GFR (30-59 mL/min) with damage to the kidney, in fourth stage there is a severely declined in kidney functions (GFR 15-29 mL/min) while fifth stage or end stage renal disease (ESRD) is linked with extremely decline in the kidney function with

GFR <15 mL/min that requires dialysis.[2, 3] According to the estimations, the prevalence of stage 2 or lower of CKD has been reported in approximately 18.5-58.3 per million children worldwide.[4] In United States of America (USA) alone, the prevalence CKD has been increased nearly 90% with increase in mortality and morbidity during the last three decades.[4, 5] In children, CKD if progresses may lead to extremely declined renal functions or ESRD that is associated with high mortality and morbidity in this age group.[6, 7] The etiological factors responsible for CKD among children vary from those in adults; these includes congenital anomalies of kidney and urinary tract, urinary tract calculi, infections, glomerular diseases, obstructive uropathies {posterior urethral valves (PUV) in male}, vesicoureteral reflux (VUR) and dysplasia of renal tissues.[3, 8, 9] Pediatric nephrology is a newfangled sub-specialty in Pakistan and only few medical centers providing services related to the disease with inadequate facilities for the renal replacement therapy.[9, 10] Moreover, at country level, appropriate data regarding renal diseases including CKD among children is lacking. This scarce data related to epidemiology of early stages of CKD among children leads to delay in diagnosis and management of CKD.[11] Furthermore, deprived primary health care system of the province with limited diagnostic facilities and skills, dearth of proper health education services, absence of centrally managed record keeping at the national as well as provincial levels and limited resources of tertiary care hospitals are responsible factors for increasing burden of this disease among children.[9, 11] Keeping in view, the current study was designed with an objective to demonstrate the clinical spectrum and etiological factors associated to CKD among children in Hyderabad, Sindh.

Objective:

To provide a snapshot of the condition of CKD and its associated factors among children in Sindh province; with a hope that the resultant data might help the healthcare providers and managers to prevent and manage the progression of CKD to ESRD.

Methodology:

This cross-sectional study was conducted at the Pediatric unit of Isra University Hospital, Hyderabad from July 2019 to August 2020 after getting approval from institutional review board of Isra University, Hyderabad. All pediatric patients belongs to age between the ages 6 months and 15 years, of either sex, admitted during the study duration and diagnosed as the case of CKD, with elevated level of creatinine and estimated GFR < 90 ml/min for over a duration of three months were included in the study. Moreover, patients with acute kidney injury (AKD), history of any organ, bone marrow or stem cell transplantation, those had a dialysis in last 3 months duration before enrollment in the study and defrayal of raised serum creatinine were excluded. A formal informed consent was taken from the guardians/parents of patients after explaining the purpose of the study. A pre-designed and tested written proforma was used for collecting the patient's information. All the information including socio-demographic information, age, sex, presenting complaints, symptoms of disease, history of polyuria and bedwetting along with family history were collected from the parents/guardian. Weight, height, BMI and blood pressure were also measured and documented. While general examination findings including; pallor, stunted growth, blood pressure and weight were also documented in the proforma.

Random urine sample of each patient was collected for urinary screening for protein using Urinary dipstick. Proteinuria on dipstick with specific gravity of ≤1.015 was labelled as +1, while +2 proteinuria was labelled when urine spe-cific gravity was >1.015.[12] Blood samples of all patients for serum urea and creatinine was collected. Schwartz formula for glomerular filtration rate 30 to 90 mL/min per 1.73 m^2 was used for estimating the GFR of participants.[13] Blood pressure was measured using aneroid sphygmomanometer while weight was measure with standard weighing machine.

The collected data was entered and analyzed by using SPSS ver.23. The data was presented as frequencies and percentages as well as mean and standard deviation. Chi square test was applied for comparison of nominal data with p value < 0.05 taken as significant.

Results:

Total 297 patients admitted in pediatric ward during the study duration of which 62(20.8%) patients were diagnosed as having chronic renal disease. Majority, 33 (53.2%) were males and 29 (46.8%) were females. Age of participants ranged from 6 months to 14 years. Majority, 49 (79.0%) of patients were over 5 years of age while 8 (13.0%) patients between 2 to 5 years of age and 5 (8.0%) patients were less than 2 years. (Tab

Table-1: Characteristics and examination findings of study participants (n=62)

Variables	Min	Max	Mean ±SD
Age (years)	0.6	14.0	8.68±4.2
Weight (Kg)	3.78	38.60	19.20±8.8
BP Systolic (mm Hg)	69.8	200	109±28.7
BP Diastolic (mm Hg)	51	140	73±20.8
Serum Urea (mg/dl)	41	598	197.8±146.3
Creatinine (mg/dl)	1.50	19.58	5.43±5.5

Table II shows the difference of male and female patients in different stages of CKD. Majority, 29.0% patients were suffering from CKD stage III while 22.6% patients were suffering from stage II and IV. None of the patient reported in stage V. (Table II).

Table II: Gender wise distribution of different stages of CKD (n=62)

Stage	Gender		Total
	Male	Female	
I	05	11	16 (25.8)
II	08	06	14 (22.6)
III	11	07	18 (29.0)
IV	09	05	14 (22.6)

Out of total, proteinuria was positive in 05 (8.0%) of the pediatric patients. Patients were presented with different complaints. Total 33 (53.3%) patients were present with complaint of polyuria while 18 (29.0%) and 23(37.1%) patients were presented with complaints of nocturnal enuresis and stunted growth respectively. Pallor was observed in 36 (58.0%) while 5 (11.6%) patients reported to have a family history of CKD.

Table III below is demonstrating the common underlying pathologies of CKD patients in the study. Based on the findings, the presence of renal hypoplasia or dysplasia (congenital small sized kidneys) was the most common underlying pathology among participant followed by Neurogenic bladder and unknown etiology. (Table III). Patients presented with different complaints; 33 (53.3%) patients presented with complaint of polyuria while 18 (29.0%) and 23(37.1%) patients were presented with complaints of nocturnal enuresis and stunted growth respectively. Pallor was observed in 36 (58.0%) while 5 (11.6%) patients reported to have a family history of CKD. Polyuria and bedwetting were more prominent complaints among males compared with female patients. Whereas, stunted growth was more commonly found among female patients. There was a statistically significant ($p<0.05$) relation between polyuria, stunted growth, nocturnal enuresis (bedwetting) and gender as shown in table IV.

Table III: Frequency and underlying diagnosis of participants (n=62)

Diagnosis	Frequency	Percent
Unknown etiology	11	17.7
Vesico-ureteral reflux nephropathy	07	11.4
Neurogenic Bladder	12	19.3
Obstructive Uropathy	09	14.5
Renal hypoplasia (Congenital Small sized kidneys)	14	22.6
Renal tubular acidosis	05	8.1
Focal Segmental Glomerulosclerosis	04	6.4

Table IV: Cross table gender with stunted growth, polyuria and nocturnal enuresis (n=62)

	Male	**Female**	**p-value**
Polyuria Yes No	 23 10	 13 16	 *0.04**
Stunted growth Yes No	08 25	15 14	 *0.02**
Nocturnal Enuresis Yes No	17 16	05 24	 *0.004**

Discussion:

Number of serious consequences of CKD have been demonstrated among pediatric patients including anemia, growth impairment, developmental problems, poor quality of life and even premature deaths.[7] Early diagnosis and timely treatment of CKD not only halt the progression of disease but also help in reducing the health care burden resulting from consequences the disease. Whereas, inappropriate or

delayed diagnosis and management of CKD leading to ESRD, ultimately necessitates hemo or peritoneal dialysis and even renal transplantation.[9]

The increasing prevalence of CKD in developing countries have been reported by different studies.[14] Data related to the prevalence of CKD among children in Pakistan is scarce and limited studies have been conducted to highlight this issue in Pakistan.[9, 15] The prevalence of CKD in this present study was 20.8% which is bit lower than that reported in another Pakistani study (29.0%) carried out at Pediatric Nephrology center in Karachi among children by Moorani et al.[16] Furthermore, a recent study by Shah SH. et al. in their study reported prevalence of 29% of CKD among hospitalized patients.[11] Moreover, a study by Goel M. et al reported the prevalence of 27.6% which is bit higher than the present study.[17]

Patients in this study presented at different stages of CKD as majority, 29.0% patients were suffering from CKD stage III while 22.6% patients were suffering from stage II and IV. None of the patient reported in stage V. There was no statistically significant difference between gender and different stages of CKD; as majority of the patients were recently diagnosed in stage III and IV of CKD. These findings are consistent with those reported by Kamath N. et al.[18] from India. This higher proportion of diagnosis of late-stage disease may be due to the delayed or improperly diagnosis of CKD.

In currennt study, renal hypoplasia or dysplasia (congenital small sized kidneys) was found to be the main etiology as 22.6% of patients were suffering from it followed by neurogenic bladder (19.3%), unknown etiology (17.7%), obstructive uropathy (14.5%), vesico-ureteral reflux nephropathy was identified in 11.4%; renal tubular acidosis and focal segmental glomerulosclerosis (FSGS) were 8.1% and 6.4% respectively. Findings of the present study are consistent with Shah SH et al and Kamath N. et al that also reported higher prevalence of renal hypoplasia or dysplasia (congenital small sized kidneys) in their study.[11, 18] Moreover, Kamath N. et al. reported that out of the all etiological factors, majority in their study cohort were non-glomerular diseases including renal hypoplasia/dysplasia (small kidneys), obstructive uropathy, neurogenic bladder and reflux nephropathy.[18] These findings are partially consistent with the present study. Sharifian M. et al from Iran also reported different etiological factors of CKD among pediatric patients; however neurogenic bladder was the most frequent (27.8%) etiological factors among study participants.[14] Becherucci F et al, in their review discussed the etiological factors of CKD in pediatric patients. The foremost etiologies reported were inherited anomalies of kidneys and urinary tract followed by glomerulonephritis, nephrolithiasis, renal infections, renal hypoplasia and the obstruction of bladder outlet.[19] Out of total patients in the present study, 8.0% were having problem of the significant clinical proteinuria and 9.7% of our study patients were obese. Ezeonwu BU et al conducted study on children for evaluating the risk factors for CKD concluded that proteinuria is one of the significant risk factor for developing CKD as 3% of their participant were having problem of clinical proteinuria and 10.1% of their participants were obese.[20]

Patients in our study presented with different complaints. Total 37.1% patients had stunted growth while pallor was observed in 58.0% of patients. Number of studies have reported the effect of CKD on nutritional factors as well as growth and stature of patients. Moreover, several features are there that challenges significantly to the upkeep an adequate nutrition and linear growth among patients with CKD.[21] Silverstein DM. et al. in his systematic review on growth and nutritional related issues among patients with CKD highlighted that velocity of growth and development declines with the progression of CKD while the impairment of the growth is observed at all stages of CKD. Furthermore, malnutrition and developmental problems along with the anemic state was reported in his systematic review.[22] Ahn SY et al al emphasized upon early diagnosis and prompt management of CKD among children as the disease poses impact on neurological, cognitive and developmental functions of children.[23] It is very vital to observe the etiological factors of CKD among children to initiate management at earliest stages.

In CKD, there is a decrease in renal functions due to which there is a decline in concentrating ability and increase in urinary volume resulting in the new onset

urinary incontinence in patients of CKD.[9] Because of this decline in functions and increased urine volume, children suffering from CKD are also at risk of diurnal or nocturnal enuresis and polyuria.[18] The present study also demonstrated that children suffering from CKD have complaints of persistent urinary incontinence and polyuria. Over 53.3% of our patients had complaints of polyuria while 29.0% were reported to have problem of nocturnal enuresis. With strengths, there were some limitations in the present study. Firstly, this study was conducted in single tertiary care hospital in the private sector; the finding of the current study may not be generalized. Second, due to limited resources and time constraints the inclusion of pediatric patients in the present was based on the elevated levels of estimated GFR and serum creatinine levels only. Lastly, due to the design and set objectives of the study, follow up of patients was not done to assess the progression of disease in study participants.

Conclusion:

The present study concludes that renal hypoplasia (congenital small sized kidneys) and neurogenic bladder are the major etiological factors of CKD among pediatric patients. While amongst the presenting complaints polyuria, nocturnal enuresis and stunted growth along with pallor are the chief presenting complaints.

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