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A Study of Clinical Characteristics and Complications in Children with Chronic Kidney Disease

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Abstract **Original Research Article**

Chronic kidney disease is characterized by permanent decline of renal function that steadily proceeds to End Stage Renal Disease (ESRD). CKD is a major public health problem worldwide. Incidence rate reported is 12.0 pmarp (per million of the age related population) in children 1-18 years' age group. Causes of CKD differ in children from that reported in adult patients. Children are particularly vulnerable to the complications of CKD. Main objective of present study was to determine the clinical characteristics, etiology and complications in children age 1-18 years with chronic kidney disease (CKD) in pre-dialytic stage. It was an observational study of 100 children who presented to us with CKD in Pediatric nephrology division of SMS Medical college Jaipur. Schwartz formula was applied to calculate the Glomerular Filtration Rate (GFR). M:F ratio was 1.7:1. Mean age of presentation was 4.36 yrs. The stage 5 was the most common presentation. Hypoplastic kidney/Dysplastic kidney was the most common cause of CKD. Anemia was the most common complication followed by hypertension and failure to thrive. The presence of CKD complications generally increased with the worsening stage of CKD. The study reveals the characteristics, etiologies and complications of chronic kidney disease to help in early detection, and create awareness about complications.

Keywords: Chronic Kidney Disease (CKD), Glomerular Filtration Rate (GFR), End Stage Renal Disease (ESRD), Hypoplastic kidney, Dysplastic kidney, Anaemia.

INTRODUCTION

Chronic Kidney disease (CKD) is defined as abnormality of kidney structure or function, with GFR <60 ml/min/1.73 m^2, presenting with implications for health [1].

CKD is a major public health problem worldwide and economic burden as well. In contrast to the extensive epidemiological research done on adult population, little is known about the epidemiology of CKD in the paediatric population [2]. Incidence rates reported is 12.0 pmarp (per million of the age-related population) in children 1-18 years age group [3, 4].

Children are particularly vulnerable to the complications of CKD. Growth failure and neurocognitive dysfunction are common and often irreversible having profound impact on both physical and psychological wellbeing of children with CKD [1].

Little information is available regarding the clinical characteristics and prevalence of complications in children with CKD most specifically in early or pre-dialytic stages [2]. Most complications observed in CKD patients are uncontrolled blood pressure, anaemia, hyperlipidaemia, short stature, proteinuria and failure to thrive. Prevalence of these complications increase with worsening stages of CKD [1].

CKD is a major public health problem and worsening with time, but its prevalence in paediatric population is unknown; necessitating the need for an epidemiological study to acquire knowledge for early detection and appropriate intervention in children which can prevent or slow down the progression of CKD.

SUBJECTS AND METHODS

It was an observational study, which included 100 children (1 year to 18 years of age) diagnosed with CKD, presented over a period of one year (2017-2018)

in the paediatric nephrology division of SMS Medical College Jaipur, a tertiary care centre.

Their GFR was calculated by Schwartz formula. Children with GFR ≤60 ml/min/1.73m^2 were included. Staging of chronic kidney disease was done on basis of the Kidney Disease Improving Global Outcome (KDIGO) working group of the National Kidney Foundation[2]. For each case we recorded demographic data (gender, date of birth, age at diagnosis of CKD), age at which the patient reached ESRD (if applicable) associated malformations, comorbidities like premature birth, low birth weight, recurrent urinary tract infections (UTI), hypertension, pallor. After a thorough clinical assessment, they underwent blood investigations, urinalysis, and imaging to determine probable aetiology and later, a renal histology was performed wherever required. These data were constantly updated during the entire study period. Linear data were represented as percentage and mean ±Standard Deviation (SD).

Children <1 yr and >18 yrs, renal transplant recipient and patients who received chronic dialysis in last 3 months were excluded from our study.

RESULTS

A total of 100 children with CKD were included, out of which 64 were males and 36 were females. They were divided into Glomerular CKD which was present in 15 children and Non-Glomerular CKD in 85 children. Mean age of presentation was 4.361±3.773 years. Most of the cases were in stage 5 (65%) followed by stage 4 (29%) and stage 3 (6%) (Table-2). Most common cause of CKD in children in our study was hypo-dysplasia (61%) followed by chronic glomerulonephritis (15%) and reflux nephropathy (8%). Other causes were Neurogenic bladder 7%, obstructive nephropathy 6% and cystic kidney disease (Table-3).

Mean weight was 18.385±8.611 kg and mean height was 110.47±23.769 cms. Mean BMI (kg/m^2) was 14.285±2.003. Mean GFR was 14.027±8.784 ml/min/1.73m^2 (Table-5). The most common clinical presentation was pallor in 93% followed by short stature (74%), growth failure (54%), hypertension (50%), failure to thrive (20%), mineral bone disease (20%), seizure (15%), encephalopathy (9%) and polyuria (1%) (Table-4). Among laboratory parameters haemoglobin, calcium, phosphorus, PTH and Serum bicarbonate were also measured. The laboratory parameters defined in study were Anaemia as defined by KDIGO clinical practice guidelines using NHANES-III reference data to cite normative values among children [5]. Other parameters were hypocalcaemia (<8.5 mg/dl), hyperphosphatemia (>4.5 mg/dl), hyperparathyroidism (PTH) (>150 pg/ml) and acidosis (serum bicarbonate <22meq/l). 22 % of cases were proteinuric; serum alkaline phosphatase was high in 47.45% patients and 20% patients showed radiological features of renal osteodystrophy.

Out of 100 patients 50 had blood pressure in normal range, 5% had blood pressure in 90th-95th centile, 9% in stage 1 hypertension, 36% in stage 2 hypertension and 5% patients presented with Hypertensive encephalopathy (Table-6). The most common complication in CKD patients was Anaemia 93 (93%) followed by Short stature in 74 (74%), Hypertension in 50 (50%), Hyperlipidaemia in 23 (23%), Failure to thrive and Renal osteodystrophy in 20 (20%) each and Proteinuria in 14(14%) patients of CKD (Table-7). Majority of patients were on conservative therapy.

Table-1: Age and Sex distribution of patients

Age in years	Sex				Total	
	Male	%	Female	%	No.	%
<3	25	25	12	12	37	37
3-5	17	17	9	9	26	26
5-7	8	8	3	3	11	11
7-9	2	2	9	9	11	11
9-11	2	2	2	2	4	4
11-13	6	6	1	1	7	7
13-15	4	4	0	0	4	4
15-17	0	0	0	0	0	0
Total	64	64	36	36	100	100

Table-2: Stages of Chronic Kidney Disease

Stages			Sex	
	Male	%	Female	%
Stage G3	3	3	3	3
Stage G4	20	20	8	8
Stage G5	41	41	25	25

Table-3: Causes of Chronic Kidney Disease

Etiology in CKD	No. (n=100)	%
Hypodysplasia	61	61
Chronic glomerulonephritis	15	15
Reflux nephropathy	8	8
Neurogenic bladder	7	7
Obstructive uropathy	6	6
Cystic kidney disease	3	3

Table-4: Clinical Presentation of Chronic Kidney Disease

CLINICAL PRESENTATION OF CKD		
	No.	%
Pallor	93	93
Short Stature	74	74
Growth failure	54	54
Hypertension	50	50
Failure To Thrive	20	20
Mineral Bone Disease	20	20
Seizure	15	15
Encephalopathy	9	9
Polyuria	1	1

Table-5: Clinical presentation and laboratory parameters

Mean age of presentation (SD)	4.361±3.773
Mean weight (SD)	18.385±8.611
Mean height (SD)	110.47±23.769
Mean GFR(SD)	14.027±8.784
Mean Haemoglobin (SD)	7.342±2.380
Mean body surface area (SD)	0.7247±0.2590
Hyperphosphatemia	59%
Hypocalcaemia	60%
Raised serum alkaline phosphatase	57%
Hyperparathyroidism	65%
Acidosis	80%

Table-6: Blood Pressure in CKD

Stages of Hypertension		
	No.	%
Normal blood pressure	50	50.0
Elevated (>90th to<95th centile) blood pressure	5	5.0
Stage 1 (>95th centile to <95th centile+12 mmHg) Hypertension	9	9.0
Stage 2 (>95th centile+12 mmHg) Hypertension	36	36.0
Hypertensive Encephalopathy	5	5.0

Table-7: Complications in CKD Patients

Complications	No.	%
Anaemia	93	93
Short stature	74	74
Hypertension	50	50
Hyperlipidaemia	23	23
Failure to thrive	20	20
Mineral bone disease	20	20
Proteinuria	14	14

***Above figures are overlapping.**

DISCUSSION

Chronic kidney disease (CKD) in children is a progressive and intractable disease, with devastating effects on the patient's growth, development and quality of life. If left untreated, paediatric CKD eventually progresses to end-stage renal disease (ESRD), which requires long-term dialysis or repeated renal transplantation. The mortality rate for children with ESRD on dialysis is estimated to be 30–150 times that of the general paediatric population [5]. Therefore, it is particularly important to detect CKD as early as possible, possibly by applying simple but accurate screening of at-risk children to detect and eventually

prevent the progression of this disease. The present study was conducted to find out the prevalence of CKD, its clinical characteristics and complications in children.

The present study was an observational study, where mean age of presentation of CKD was 4.361±3.772 yrs. which was comparable to study by Gianluigi *et al*., [4] from the Italkid project on CKD (6.9 ± 5.4 yrs.). The age at presentation of CKD was lower compared to other studies [1, 6, 7] which suggests improved referral and early detection of these patients.

Among the Glomerular group, majority of patients (40%) presented in age group 5-7 yrs. while in Non-Glomerular group, maximum patients presented at <3 yrs. of age group.

The CKD was more common among boys. Male:female ratio was 1.77:1. The results of the present study were in concordance with other studies [6, 8, 9]. A male preponderance could be due to higher incidence of Congenital Anomalies of Kidney and Urinary Tract (CAKUT) including renal hypo dysplasia as well as obstructive uropathy including posterior urethral valves among males. Also, it may be due to male dominated society where more male children are presented to OPD than females.

In the present study, the most common cause of CKD was hypo-dysplasia (61%), followed by Chronic Glomerulonephritis (15%), Reflux Nephropathy (8%), Neurogenic Bladder (7%), Obstructive Uropathy (6%) and Cystic kidney disease (3%). In a study by Miller *et al*., [6] the commonest cause of CKD was PUV (24%), Renal dysplasia (24%), Glomerulonephritis (25%). Chiou *et al.*, [7] reported that 52.1% had CKD due to a structural abnormality or genetic disease, and 47.9% due to nephritis or hemodynamic changes. The most common diseases in the structural abnormalities or genetic diseases group were reflux nephropathy (23.1%), renal dysplasia (19.6%), and renal agenesis (15.6%). The most common diseases or disorders in the nephritis or hemodynamic change group were lupus nephritis (37.2%) and IgA nephritis (17.5%). The study by Saland *et al.*, [10] stated the causes for CKD, 67% were due to genitourinary/cystic/hereditary diseases, 22% were due to glomerular disease, and 11% had other or unknown causes.

Data from the ItalKid project [4] have revealed similar results that Hypo-dysplasia, with or without urologic malformations, accounts for as many as 57.6% of all cases, whereas glomerular diseases account for as few as 6.8% of CKD in children. In patients that had reached ESRD, the relative percentage of glomerular diseases increased from 6.8% to 15.2% whereas that of hypo dysplasia decreased from 57.6% to 39.5%. EDTA Registry [11] reported that in the CKD cases hypoplasia/dysplasia and hereditary diseases were the commonest causes for ESRD in the 0-4 yrs. age group, whereas glomerulonephritis and pyelonephritis became progressively more common with increasing age.

The mean GFR (ml/min/1.73m^2) of CKD patients under study was 14.027± 8.784; 10.599±7.131 in the Glomerular group while 14.632±8.944 in the Non-Glomerular CKD. Mean eGFR (mL/min per 1.73 m^2) was 83.6 ml/min/1.73 m2; 80.8 ml/min/1.73m^2 among non-Glomerular CKD patients while 87.7 ml/min/1.73 m2 among Glomerular CKD patients in a study conducted by Chiou *et al.*, [7]. In another study by Rodig *et al.*, [8] the median baseline GFR was 49.9 mL/min/1.73 m^2. The mean estimated GFR was 58±18 ml/min per 1.73 m2 in study by Saland *et al.*, [10]. The variation in GFR could be because of variation in number of patients taken in different stages of CKD in different studies.

The mean height and weight SD scores are – 3 and –3 respectively. In comparison to their fit, population-based peers, children and adolescents in the Chronic Kidney Disease cohort demonstrate height deficits across the complete range of GFR that develop into more prominent with declining GFR levels. Children with Chronic Kidney Disease are well thought-out at high danger for protein-energy malnutrition. In the Indian circumstances, where malnutrition is extensively prevailing in the general population, the crisis becomes even more severe. The dominance of growth failure augmented with each declining category of GFR, signifying that declining GFR influences caloric intake or metabolism.

A large number of our patients (93%) were anaemic; the mean (SD) haemoglobin at presentation was 7.342±2.380 gm/dl. Anaemia is the main complication and is caused by reduced erythropoietin which is mainly produced in the kidneys; concomitant iron deficiency, folate deficiency and B12 deficiency were other causes. In Glomerular group mean Hb was 5.973±1.553 gm/dl while in the Non-Glomerular group it was 7.584±2.425 gm/dl which was statistically significant. Gheissari *et al.*, [12] reported that Anaemia was present in 85% of patients of CKD. Similar findings were also reported by Saland *et al*., [10] in a cross-sectional analysis of 340 children enrolled in CKiD where the mean haemoglobin was 12.5±1.5 g/dl, and 45% children were classified as anaemic. As shown in our study and different studies around the world anaemia contributes to a large proportion of morbidity and mortality in CKD patients, worsening as the disease progresses As anaemia is a treatable cause, regular evaluation and early use of iron and erythropoietin could diminish the associated cardiovascular problems and the quality of life of these children becomes better.

In our study CKD children had biochemical irregularities proposing development of Mineral bone

disease. These are hyperphosphatemia (70%), hypocalcaemia (54%), and hyperparathyroidism (85%). Radiological features indicative of renal osteodystrophy were noticed in 20% of Chronic Kidney Disease children. The bone disease of Chronic Kidney Disease is known as CKD-Bone Mineral Disorder (CKD-MBD). In our study, patients with Renal MBD and rickets were as high as 20%. In a similar study by Wong *et al.*, [13] stated that one-sixth (16.9%) of patients had metabolic bone disease also, Bhargava *et al.*, [14] found 16.95% patients with metabolic bone disease. Findings of our study were very close to findings of above mentioned studies. This can be explained by the fact that low calcium, release of PTH and decreased dietary intake of phosphorus stimulate the kidney to convert 25-dihydroxyvitamin D into calcitriol. This in turn promote intestinal calcium absorption, phosphorus reabsorption and Bone mineralisation. This leads to bone modelling and remodelling and growth impairment.

In our study hypertension (50%) and proteinuria (14 %) was significant clinical finding among CKD patients. Of these 10% had Elevated blood pressure, 18% had stage 1 Hypertension and 72% had stage 2 Hypertension. Chou *et al.*, [1] in their study reported that the overall prevalence of Hypertension was 44.1%. Similarly, in study by Gheissari *et al*., [12] 55% of patients had either systolic and/or diastolic hypertension. Our findings were very similar to findings of these studies. Authors concluded that hypertension is extremely important and independent predictor for development of CKD in children. As hypertension is a treatable state, early involvement may avoid or holdup CKD development.

80 % children were acidotic on presentation. Acidosis arises early in children with Chronic Kidney Disease because of disruptive or tubulointerstitial renal disease which arises due to less functioning of nephrons to maintain ammonia excretion essential for acid base balance. The outcome is retention of hydrogen ions leading to metabolic acidosis. The (NKF, KDOQI) guidelines proposed that chronic metabolic acidosis is the chief reason for growth failure. Serum bicarbonate must be measured three to six times monthly in early CKD and monthly once the disease progresses.

As kidney failure develops, signs and indications of Uremic encephalopathy originate. In our study, 24% of CKD patients showed uremic encephalopathy.

Short stature was defined as height below 3rd centile or more than 2 standard deviations below the median height. In present study 74% cases were having Short Stature. However, in study by Chou *et al*., [1] with 757 children with CKD reported overall prevalence of short stature was 10.3%. Study by NAPRTCS [16] registry data revealed that about 33% of paediatric patients have short stature. The study also reports that even after initiation of CKD therapy 30-60% patients have Short Stature. Similarly, in study by Rodig *et al*., [8] stated that 12% of the CKD patients exhibited severe short stature for age. Difference in findings of present study and the above-mentioned study could be due to differences in sample size and different stages of CKD patients taken for study. As in most studies stage G1 and G2 patients are in majority while in the present study no patients of G1 and G2 were found.

CONCLUSION

Chronic Kidney Disease is generally silent till the disease reaches very advance stage. Most common presentation were Anaemia, Hypertension, Short stature, failure to thrive and management are necessary to prevent progression. Regular follow-up with proper intervention may prevent the occurrence of complications and delay the progression of renal function impairment. Children with CKD and their families must be educated regarding the progression of disease and future likely transplantation.

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