Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2016; 4(5B):1530-1535 **ISSN 2347-954X (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com DOI: 10.36347/sjams.2016.v04i05.017

Original Research Article

Profile of Chronic Kidney Disease in Children

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Abstract: Chronic kidney disease is characterized by permanent decline of kidney function that steadily proceeds to End-Stage Renal Disease (ESRD) which is evolving as a serious public health problem. Causes of CKD differ in children from that reported in adult patients. Main objective of present study was to determine the causes, clinical presentation and biochemical disturbances in children with chronic kidney disease (CKD). This was an observational study of 59 children who presented to us with CKD in Pediatric nephrology division of a tertiary care center in India. In this study, CKD was common among males. Schwartz formula was applied to calculate the Glomerular Filtration Rate (GFR). The stage 5 was the most common presentation among both males and females. Hypoplastic kidney/Dysplastic kidney was the most common cause of CKD. Anemia was the most common presentation. Most of the children were on conservative management.
Keywords: Chronic Kidney Disease (CKD), Glomerular Filtration Rate (GFR)

INTRODUCTION

CKD is a common public health problem globally. A better understanding of CKD in children is important to make accurate and untimely diagnosis, discover preventable or reversible causes of progression, and predict prognosis and counseling of children & parents. The definition and classification of chronic renal disease may help to identify affected individuals, probably resulting in the early institution of effective therapy. The Kidney Disease Outcomes Quality Initiative (KDOQI) which is the working group of the National Kidney Foundation (NKF) defined CKD as an "evidence of structural or functional kidney abnormalities (histology, abnormal urinalysis, or imaging studies) that persist for at least 3 months, with or without a decreased GFR, as defined by a GFR of less than 60 mL/min per 1.73 m^2" but it is not valid for children younger than 2 years, because they generally have a low Glomerular filtration rate [1-3]. In these patients, to detect renal impairment, calculated GFR based on serum creatinine can be compared with normative age-appropriate values. The increasing number of younger children being treated now as the relative distribution of primary renal diseases has changed over time. Also, the prognosis for children with CKD has changed immensely over the past 25 years, from almost certain fatality to now, a good prospect of long-term survival and rehabilitation. Technological advances have made it possible to offer dialysis and transplantation to almost all children with ESRD including the very young. We conducted a prospective study to determine the major causes, clinical expression and biochemical changes in CKD children.

SUBJECTS AND METHODS

It was an observational study, which included 59 children (up to 16 yrs of age) with the diagnosis of Chronic kidney disease (CKD), presented over a period of one year (2013-1014) in the pediatric nephrology division of SMS Medical College Jaipur , a tertiary care center catering to the needs of patients from all over state. Their GFR was calculated by Schwartz formula[4]. Children with GFR less than 60 ml/min/1.73m^2 were included. Staging of chronic kidney disease was done on basis of the Kidney Disease Outcomes Quality Initiative (KDOQI) working group of the National Kidney Foundation. 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, co-morbidities like premature birth, low birth weight ,recurrent urinary tract infections (UTI), hypertension and treatment (transplanted, hemodialysis (HD) or continuous ambulatory peritoneal dialysis (CAPD). After a thorough clinical assessment they underwent

blood investigations, urinalysis, and imaging to determine probable etiology, Scintigraphy, urodynamic study and renal histology were performed wherever required. These data were constantly updated during the entire study period. Linear data were represented as percentage and mean ±SD.

RESULTS

A total of 59 children with CKD were included, wherein 47 were males and 12 were females. Four groups were chosen as per the age, less than 4 years, 4-8 years, 8-12 years and 12-16 years, with 12, 18, 10, and 19 children respectively (Table 1). Most of the cases were in stage 5 (66%) followed by stage 4 (25%) (Table 2) Most of the children had hypodysplasia(47.3%) followed by chronic glomerulonephritis (16.8%) and reflux nephropathy (13.8%). Other causes were obstructive nephropathy 11.8%, cystic kidney disease, neurogenic bladder and chronic pyelonephritis(Table 3). Mean age of presentation was 7.16±3.87 yrs. Mean weight was 15.33±6.33 kg and mean height was 106.47±23.69cm. Mean GFR was13.80±9.32 ml/min/1.73m^2(Table 5). The most common presentation was anaemia in 71.19%, failure to thrive (66.10%), hypertension (27.12%), encephalopathy (22.03%), bony deformities (16.95%), and cardiac failure (5.08%). 1.69% children had antenatally detected anomalies whereas in 6.78 %, CKD was incidentally detected (Table 4). Among laboratory parameters hemoglobin, calcium, phosphate, PTH and Serum bicarbonate were also measured. The laboratory parameters defined in study were Anaemia as defined by NKF-KDOQI 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). 23 % of cases were proteinuric; serum alkaline phosphatase was high in 47.45% patients and 16.9% patients showed radiological features of renal osteodystrophy. Most of the patients were on conservative therapy.

Table 1: Age and Sex Distribution of Subjects

Age in Years	Sex				Total	
	Male	%	Female	%	No.	%
<4 yrs	9	15.2	3	5.08	12	20.33
4-8	13	22.03	5	8.47	18	30.5
8-12	10	16.9	Nil	Nil	10	16.9
12-16	15	25.4	4	6.77	19	32.2
Total	47	79.6	12	20.33	59	100

Table 2: Stages of Chronic Kidney Diseases

Stages	Sex			
	Male	%	Female	%
Stage-III	4	6.77	1	1.69
Stage-IV	13	22.03	2	3.38
Stage-V	30	50.84	9	15.2

Table 3: Causes of Chronic Kidney Diseases (CKD)

	Male		Female	
Hypoplasia & Dysplasia	20	33.8	8	13.5
Reflux Nephropathy	8	13.5	-	
Chronic Glomerulonephritis	8	13.5	2	3.38
Obstructive Nephropathy	7	11.8	-	
Cystic Kidney Disease	1	1.69	-	
Medullary Nephrocalcinosis	1	1.69	-	
Neurogenic Bladder	1	1.69	2	3.38
Chronic pyelonephritis	1	1.69	-	-

Table 4: Clinical Presentations

	Percentage of patients
Anaemia	71.19
Hypertension	68.8
Failure to Thrive	66.10
Acidosis	44.07
Proteinuria	23
Encephalopathy	22.03
Bony Deformity	16.95
Incidental detection	6.78
Left Ventricular Failure	5.08
Antenatal Anomalies	1.69

Table 5: Clinical presentation and laboratory parameters

Mean age of presentation (SD)	7.16±3.87
Mean weight(SD)	15.339±6.33
Mean height(SD)	106.47±23.69
Mean GFR(SD)	13.80±9.32
Mean Hemoglobin	7.085±2.03
Hyperphosphatemia	69%
Hyperparathyroidism	68%
Hypocalcemia	50.8%
Serum alkaline phosphatase	47.45% have high levels

DISCUSSION

The incidence of CKD differs in different parts of the world. In most developed countries, it varies from 4-10 per million-children below the age of 18 years[6,7]. In contrast, from Asia, where 57% of the world's population resides, a geographic region characterized by a very high proportion of children, epidemiological information is very scanty and is primarily based on patients referred to tertiary medical centers[8,9]. There has been a rise in CKD patients being registered in India.

The present study was prospective observational study,where mean age of presentation of CKD was 7.1±6.87 years. The age at presentation was comparable to that of North American Pediatric Transplant Cooperative Studies (NAPRTCS), which inferred that 36% of children registered as chronic renal insufficiency were below 5 years of age [10] .The age at presentation of CKD in this study was higher as compared to reports from developed countries suggesting delayed detection and referral of these patients.

The CKD was more common among boys. Male female ratio was 4:1.This was is in accordance with the other studies[8-11]. A male preponderance could be due to higher incidence of Congenital Anomalies of Kidney and Urinary Tract (CAKUT) including renal hypodysplasia as well as obstructive uropathy including posterior urethral valves among males.

Most of the children had hypo dysplastic kidneys (47.45%) as the primary cause of Chronic Kidney Disease in the study. In the ItalKid project the principal causes of Chronic Kidney Disease were hypodysplasia associated with urinary tract malformations (43.6%), while 13.9% had isolated hypodysplasia[12]. However other studies depicted a lower incidence of 12% and 24% [13,14]. Our values were higher owing to exact measurements of kidney size and more precise ultasonography. The data of NAPRTCS Registry from over 7,000 children who were less than 21 years old gives much information on the etiology of Chronic Kidney Disease in childhood[15]. In this report CAKUT (48%) and hereditary nephropathies (10%), were the main causes.

Chronic glomerulonephritis (CGN) accounted for 16.94% patients. CGN was detected by presence of nephrotic range of proteinuria with gradual deterioration of renal function with or without RBC cast and or hypertension, some established with renal biopsy. Principal cause of chronic glomerulonephritis was steroid resistant nephrotic syndrome. In several studies from Latin America, India, Caribbean area, Southeast Asia and sub-Saharan Africa, incidence of CGN ranged from 30 to approximately 60% [8,9,16–22]. In India second annual report by CKD registry of India (CKDRI) recommended chronic glomerulonephritis to be the most common cause of CKD (28.2%) [23]. Reflux nephropathy was diagnosed on account of presence of scarred kidney(irregular renal

outline) confirmed by ultrasonography, radio nuclide imaging and presence of either primary VesicoUretral Reflux (VUR) showed on micturatingcystourethrography or laboratory evidence of past urinary tract infection. Obstructive uropathy was diagnosed if urinary tract dilatation was diagnosed by radiography or scinitigraphy, in the absence of VUR and bladder dysfunction.

The avoidable causes of Chronic Kidney Disease include obstructive uropathy and reflux nephropathy that together accounted for 25.39% of cases in our study, like the reports from other parts of the world[8, 24]. Reflux nephropathy owing to primary VUR was viewed in 13.8% as against 16.7% in other study. [9] However, the amount of cases of Chronic Kidney Disease as a result of reflux nephropathy were very less in North American children, whereas not a single case had been reported in Swedish children from 1986-1994 [6,7]. It is projected that a decline in the amount of patients with reflux nephropathy is primarily because of quick detection and management of urinary tract infections, subsequently cautious screening for underlying anomalies. Screening for urinary tract anomalies by antenatal ultasonography is likely to identify major structural disorders that can be treated postnatally.There is a study which points out decline in the amount of ESRD caused by reflux nephropathy, whereas incidence of obstructive uropathy and hypodysplasia augmented[25]. This fashion may be discovered by an adjustment in reporting the primary diagnosis, in view of the fact that the combined proportion of hypodysplasia and reflux nephropathy has stayed stable over the past 30 years.

Neurogenic bladder was viewed in 1.69% patients, which is lesser than the NAPRTCS data [10] and study by Sirin*et al* [26] who reported that amount of patient owing to neural tube defect and secondary VUR was 15.4% in Turkish children.

The mean GFR at presentation was 13.80±9.32 ml/min/1.73m^2 whereas in another study it was 18.5[9]. 66% cases were by now in end stage renal failure. Patients presenting with ESRD in our study was very high as compared to NAPRTCS report however lesser than that reported by a study from India [8]. Late detection and transfer of patients to tertiary care centers are diverse factors responsible in our region. Early-stage Chronic Kidney Disease is often asymptomatic or with non-specific symptoms and ESRD is a late clause that is excessively late for referral in view of the fact that Renal replacement therapy (RRT) is not available in majority of the centers in developing countries.

The mean height and weight SD scores are –2.1 and –2.0 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 amount of our patients (71.19%) were anemic; the mean (SD) hemoglobin at presentation was 7.08±2.03 g/dL. Anaemia is the main complication and is caused by reduced erythropoietin which is mainly produced in the kidneys; concomitant iron deficiency, folate deficiency, B12 deficiency and aluminum excess. It generally arises when GFR falls to 60 ml/min/1.73m^2. In a study of Chronic Kidney Disease children the mean hemoglobin at presentation was 7.2 ±2.6g/dL[27]. As anaemia is a treatable clause, 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 (69%), hypocalcaemia (50.8%), and hyperparathyroidism (68%). Radiological features indicative of renal osteodystrophy were noticed in 16.9 % of Chronic Kidney Disease children. The bone disease of Chronic Kidney Disease is known as CKD-Mineral Bone Disorder (CKD-MBD). Altered calcium phosphorus and vitamin D metabolism takes place early in Chronic Kidney Disease and each patient with GFR of less than 60 ml/min/1.72m^2 needs to be supervised. The pathogenesis of CKD-MB is on account of decreased clearance of phosphorous with consequential increase of serum PTH. There is decrease in production of calcitriol also. Supervision of blood levels of PTH, calcium, alkaline phosphatase and phosphate is crucial. Various factors like anaemia, hypocalcaemia, hypoalbuminemia and hyperphosphatemia are related with the rate of Chronic Kidney Disease progression, entailing probable measures to preserve renal function[28, 29].

44.07 % 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.

In our study hypertension (68.8%) and proteinuria (23 %) was significant clinical finding among CKD patients. Hypertension is there in about 50% of children with CKD and masked hypertension i.e., normal casual but elevated ambulatory blood pressure is often present [30, 31]. 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.

When the kidney failure develops, signs and indications of Uremic encephalopathy originate. In our study, 22% of CKD patients showed uremic encephalopathy. It arises in patients with chronic renal breakdown, generally when the estimated glomerular filtration (eGFR) level goes down and stays below 15 mL/min. Manifestations differ from gentle symptoms such as lassitude and fatigue to severe symptoms such as seizures and coma. Quick recognition of uremia as the source of encephalopathy is vital for the reason that symptoms are readily reversible pursuing initiation of dialysis. [32-34].

Left ventricular hypertrophy too was a significant finding which can be secondarily to hypertension, volume overload and anaemia. More violent control of hyperparathyroidism, anaemia and BP may be essential in avoiding the progress of LVH in these patients.

Owing to shortage of state funded renal replacement program, a large amount of patients cannot afford renal transplantation. The incidence of renal transplantation in children from other centers in India as well as in some other underdeveloped countries is also less on account of similar reason[8, 24]. The parents usually go for conservative management and hardly ever for long-term dialysis because of financial limitations. An active cadaver organ donation program is still in its emerging phase.

CONCLUSION

Chronic Kidney Disease is generally silent till the disease has reached to a very advance stage. The occurrence and frequency rates are normally greater for boys. Most common presentation is hypertension, anaemia and failure to thrive. Early diagnosis and involvement is vital to hold up the advancement of the disease and to curtail related morbidity and mortality. Children with CKD and their families must be given education regarding the significance of fulfillment of secondary preventive actions, natural disease development, prescribed medications along with their possible benefits and unpleasant outcomes, diet and kinds of long-term renal replacement modalities.

When estimated GFR goes down to less than 30 mL/min / 1.73 m^2 and the child has stage IV CKD, necessary information associated with hemodialysis, preemptive kidney transplantation and peritoneal dialysis must be provided to the family as soon as possible.

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