ORIGINAL ARTICLE

CLINICAL SPECTRUM AND AETIOLOGY OF CHRONIC KIDNEY DISEASE IN CHILDREN —AN EXPERIENCE AT AYUB TEACHING HOSPITAL, ABBOTTABAD

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Background: Chronic kidney disease (CKD) is devastating and major health issue with long term consequences. This study was done to enlighten the clinical spectrum and aetiology of CKD in children attending Ayub Teaching Hospital, Abbottabad. **Methods:** This descriptive study was carried out at Ayub Teaching Hospital, Abbottabad form April 2019 to September 2020. Children of either sex, 6 months to 15 years old, diagnosed as CKD were included. Children with syndromic features, or acute kidney injury were excluded. A specifically designed questionnaire/proforma was used to record information like socio-demographic details, medical history including polyuria, polydipsia, pallor, stunted growth, bedwetting and family history of participants. Blood pressure and weight of all participants was also recorded. Data was analysed using SPSS-20. **Results:** Out of 43 patients, 23 (53.5%) were males and 20 (46.5%) were females. Mean age was 8.71±3.96 years. Mean creatinine was 6.06±4.59 mg/dl. Small size kidneys were in 46.5% patients and reflux nephropathy in 14% patients. Polyuria was present in 23 (53.5%) patients. There was significant relationship between polyuria and polydipsia (p<0.001). Pallor was in 58.1% and stunted growth in 53.5% patients. Bed wetting was present in 30.2% patients and there was significant relationship between bed wetting and gender (p=0.007). Bed wetting also had significant relationship with polyuria and stunted growth (p<0.001 and 0.043 respectively). **Conclusion:** Small size kidneys and reflux nephropathy are major aetiology, while polyuria, progressive pallor and stunted growth are the major clinical presentation of CKD in children.

Keywords: Children, chronic kidney disease, clinical spectrum

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INTRODUCTION

Chronic kidney disease (CKD) is devastating disease with long term consequences. Though relatively uncommon in children yet a major health issue.[1] Kidney Disease: Improving Global Outcomes (KDIGO) defines CKD as 'abnormalities of kidney structure or function, present for more than 3 months, with implications to health'.[2]

Chronic kidney disease is a serious condition leading to multiple complications including premature mortality and end-stage renal disease (ESRD).[3] According to literature it is estimated that 1 in 7 to 10 adults have CKD worldwide and approximately 10% survive and progress to ESKD. Due to cost issue, half of these survivors receive dialysis or kidney transplant.[4] In USA during last three decades, CKD prevalence has increased almost by 90% and there has been increase in mortality and morbidity.[5] In children CKD progression can lead to ESRD, which is related with high mortality and morbidity.[6] The aetiology of CKD is different from as that of adults.[7] As major causes of CKD are congenital anomalies of the kidneys and urinary tract including obstructive uropathy, e.g., posterior urethral valves (PUV) in male, vesicoureteral reflux (VUR), kidney dysplasia, glomerular diseases, urinary tract calculi and infections.[8]

Paediatric nephrology is new subspecialty in Pakistan and only few centres are there with limited facilities of renal replacement therapy. At national level, there is no registry and proper data regarding childhood kidney diseases is lacking. Due to limited information regarding epidemiology of CKD stages, children with early CKD are not being diagnosed and properly managed which can prevent advancement of CKD to ESRD. This study will help in targeting the children with specific aetiology and clinical features, so they can be managed in proper way to prevent progression of CKD to ESRD, which requires costly renal replacement therapy and renal transplant. The objective of this study was to enlighten the clinical spectrum and aetiology of childhood CKD.

METHODOLOGY

This descriptive study was carried out at Paediatrics B Unit of Ayub Teaching Hospital, Abbottabad over a period of one and half year form April 2019 to September 2020, after getting approval from Institutional Review Board. Children diagnosed as case with CKD were included in this study, who were having

increase in serum creatinine for age and estimated glomerular filtration rate (GFR) <90 ml/min/ 1.73 m^2 for more than 3 months. Children of either sex from 6 months to 15 years of age were included. Patients were included after taking proper consent. Children with syndromic features, acute kidney injury responded to treatment or settlement of raised serum creatinine were excluded. Sample size was calculated by open epi sample size calculator with taking prevalence of CKD in children as 2%.[9] Calculated sample size was 37 patients with 97% confidence interval. We included 43 patients in our study. Patients presenting symptoms including history of polyuria, polydipsia, pallor, stunted growth, blood pressure (systolic and diastolic), bedwetting at night, family history of CKD, age, sex, weight and diagnosis were documented on specific proforma. Data was analysed using SPSS-20. Chi-square test was applied for comparison of nominal data with $p<0.05$ taken as significant.

RESULTS

There were total of 43 patients, 23 (53.5%) males and 20 (46.5%) females. Age ranged from 6 months to 15 years with mean age 8.71±3.96 years. Majority, (35, 81.4%) of patients were above 5 years of age while 5 (11.6%) patients were 2–5 years of age and only 3 (7%) patients were less than 2 years old. Weight of patients ranged from 3.6 to 39 Kg with mean weight 19.20±8.83 Kg. Serum creatinine ranged from 1.3 to 20.6 mg/dl with mean creatinine of 6.06±4.59 mg/dl (Table-1).

The most common underlying pathology was congenital small size kidneys and it accounted for 20 (46.5%) patients followed by reflux nephropathy in 6 (14%) patients (2 patients with PUV, 2 patients with primary VUR, 2 patients with neurogenic bladder) (Table-2).

Patients' presenting features were documented subjectively. Polyuria as presenting complains was present in 23 (53.5%) patients. Polydipsia was there in 14 (32.6%) patients. There was significant relationship between polyuria and polydipsia ($p<0.001$). The chief complain of progressive pallor was present in 25 (58.1%) patients, while 23 (53.5%) presented with history of stunted growth and parents were worried about short height or less weight. Bed wetting was present in 13 (30.2%) patients. There was significant relationship between bed wetting and gender ($p=0.007$), as males had more issue of bed wetting. Bed wetting had significant relationship with polyuria ($p<0.001$). Bed wetting was also related with stunted growth ($p=0.043$). Family history of CKD was present in 5 (11.6%) patients. There was significant relationship between polyuria and pallor as patients who were having polyuria were also having significant pallor ($p=0.025$) (Table-3).

There was significant relationship of gender with stunted growth and polyuria ($p=0.023$) respectively (Table-4 and 5). Stunted growth and polyuria was more in males as compare to females. There was also significant relationship between polyuria and stunted growth ($p=0.023$).

Table-1: Age, weight, BP, urea, creatinine in patients

Variables	Minimum	Maximum	Mean±SD
Age (years)	0.50	15.00	8.71±3.96
Weight (Kg)	3.60	39.00	19.26±8.83
Systolic BP (mm Hg)	70	200	123.86±29.03
Diastolic BP (mm Hg)	50	140	80.79±21.43
Urea (mg/dl)	39	608	206.95±147.07
Creatinine (mg/dl)	1.30	20.60	6.06±4.59

Table-2: Underlying diagnosis in patients

Diagnosis	Frequency	Percent
Small size kidneys	20	46.5
Reflux nephropathy	6	14
Polycystic kidneys	2	4.7
Renal calculi	3	7
SLE nephritis	1	2.3
Bartter syndrome	2	4.7
Unknown aetiology	7	16.3
Renal tubular acidosis	1	2.3
Focal Segmental Glomerulosclerosis	1	2.3
Total	43	100

Table-3: Cross table between polyuria and pallor

	Pallor			
Polyuria	Yes	No	Total	*p*
Yes	17 (39.3%)	6 (13.95%)	23 (53.49%)	0.025
No	8 (18.60%)	12 (27.91%)	20 (46.51%)	
Total	25 (58.14%)	18 (41.86%)	43 (100%)	

Table-4: Cross table gender with stunted growth

	Stunted growth			
Gender	Yes	No	Total	*P*
Male	16 (37.21%)	7 (16.28%)	23 (53.49%)	0.023
Female	7 (16.28%)	13 (30.23%)	20 (46.51%)	
Total	23 (53.49%)	20 (46.51%)	43 (100%)	

Table-5: Cross table gender with polyuria

	Polyuria			
Gender	Yes	No	Total	*P*
Male	16 (37.21%)	7 (16.28%)	23 (53.49%)	0.023
Female	7 (16.28%)	13 (30.23%)	20 (46.51%)	
Total	23 (53.49%)	20 (46.51%)	43 (100%)	

DISCUSSION

There are serious consequences of CKD in children including growth failure, developmental delay, and increase risk of cardiovascular diseases, poor quality of life and early death. Recognition of CKD in early stage and tools to predict progression and outcome of CKD are important not only for risk stratification but also help in identification of potential therapeutic targets to halt progression of CKD and reducing the burden of health loss associated with this disease.[10] Studies have shown that CKD incidence in increasing more in developing countries.[11] Missing the diagnosis or not properly treating the patient with CKD leads to progression of disease to ESRD necessitating either haemodialysis or

peritoneal dialysis and renal transplant.[12] The CKD has rising trend in Pakistan due to multiple factors including poor primary health care system and facilities, lack of proper health education, absence of central data registry at national level and under funding of tertiary care hospitals.[13]

Though exact prevalence of CKD in children in not known in Pakistan, yet one study by Jessani *et al*[14] reported prevalence of CKD as 12.5% in adults population of Karachi. Moorani KN *et al*[15] did one study in one of Paediatric Nephrology centre in Karachi about pattern of renal diseases in children. Out of total of their patients with kidney issues, 29% patients were having CKD. The patients with CKD were having different aetiology including urinary stone renal 25.6%, hypoplasia-dysplasia 39.3%, PUV19%, juvenile nephronophthiasis 10.4%, neurogenic bladder 7.5%, VUR 8.6%, and cystic renal disease 5.2%. The Moorani study[15] was done is one of dedicated paediatric nephrology centre, while our centre is dealing with general paediatric diseases including paediatric nephrology patients. This may be the reason for the aetiology differences between the two studies. Bek K *et al*[16] studied CKD patterns in children. Their male to female ratio was 1.29:1 and mean age was 8.05±5.25 years, about 71% patients were more than 5 years of age, and the main underlying diseases were VUR 18.5%, neurogenic bladder 15.1% and obstructive uropathy 10.7%. In our study male to female ratio was 1.15:1, which is almost similar. Mean age of patients in our study was 8.71±3.96 years. In our study 81.4% patients were above 5 years. The most common underlying pathology in our patients was small size kidneys in 46.5% patients and reflux nephropathy in 14% patients.

Harambat J *et al*[17] described that in developed countries congenital anomalies affecting kidneys and urinary tract along with nephropathies are major causative factor of CKD. In developing countries acquired causes are main reason for CKD in children. Gheissari A *et al*[9] did one retrospective study in Iran and included records of patients over ten years. In their study 54% were male and 46% were female. Mean age was 11.01±0.39 years. The most aetiology was glomerulopathies and reflux nephropathy but still in 21.7% the aetiology was unknown. Small size kidneys were seen in 65.8% patients. Anaemia was present in 85% of patients. In our study males were 53.5% and 58.1% patients were having history of progressive pallor. An only patient with FSGS was having CKD. Ezeonwu BU *et al*[18] did one cross-sectional study and screened children for risk factors for CKD including hypertension, proteinuria and obesity. The study results showed asymptomatic hypertension in 3.7%, proteinuria in 3% and obesity in 10.1% children as risk factor for developing CKD.

In one of review by Becherucci F *et al*[1], discussed the aetiologies of CKD in children. The main aetiologies are congenital anomalies of urinary tract and kidneys, glomerulonephritis, tubulopathies, nephrolithiasis, infections involving kidney, structural anomalies including renal hypoplasia and bladder outlet obstruction. Ahn SY *et al*[19] in their editorial emphasized on the studies regarding the CKD. Though prevalence of CKD is low in children yet timely diagnosis and management is important due to long term impact on health including growth failure, neurocognitive and development delay and cardiovascular involvement. Also there is 30 times more mortality in children with CKD as compare to normal population of children. Therefore it is important to find out the aetiology in order to properly manage the CKD patient.

Regarding limitations of our study, we only included children with CKD on basis of raised creatinine and estimated GFR, due to non-availability of plasma markers including TNFR-1, TNFR-2 and KIM-1 in children. We did not classify the CKD. Follow up should have been done of patients with CKD to check for progression of the disease.

CONCLUSION

Congenital small size kidneys and reflux nephropathy are the leading cause of CKD. The main presenting clinical features are polyuria, progressive pallor and stunted growth. Multi-centre studies are required to augment the data and findings.

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