Manjuri Sharma, Gayatri Pegu, Anup Kumar Barman, Satyakam Kakaty, Pranab Jyoti Mahanta, Pallavi Bordoloi Clinical profile of chronic kidney disease in children

ORIGINAL PAPER

Clinical Profile of Chronic Kidney Disease in Children

Sharma Manjuri¹, Pegu Gayatri², Barman Anup Kumar³, Kakaty Satyakam⁴, Mahanta Pranab Jyoti⁵, Bordoloi Pallavi⁶

Received on March 20, 2017; editorial approval on June 20, 2017

ABSTRACT

Background: CKD is an important cause of mortality, morbidity and impaired quality of life in children. Data in paediatric population is sparse from this part of the country. A better understanding about the epidemiology and preventable factors can help in better management of these children. Aims: To study the etiology and clinical profile of the children with chronic kidney disease who attended Gauhati Medical College and Hospital, Assam. Materials and methods: The demographic, clinical profile and biochemical data of the children diagnosed with CKD, admitted in our Institute from August 2013-July 2016 were analysed retrospectively. CKD was defined according to NKF-K/DOQI 2002 clinical practice guideline with GFR below 60ml/min/1.73m² estimated by modified Schwartz formula. Records were reviewed to search for their etiology and clinical profile like height, weight, BMI, presence of anaemia or hypertension. Also outcome where available were recorded. Results: Among 101 children diagnosed as CKD, 65 (64.35%) were boys. The mean age of presentation was 14.87 years of age (range 3 yrs to 18 yrs). Only 4 children were less than 5 years of age. The mean GFR at presentation was 14.67ml/min/1.73m².61% of the children were already in CKD stage 5. The causes of CKD included glomerular diseases (35.6 %,), interstitial and obstructive causes (38.61%), miscellaneous (6.9%) and undetermined (18.81%). Among glomerular causes chronic GN (15.84%) was most common, followed by FSGS (8.91%) and IgA nephropathy (4.95%). Reflux nephropathy was seen in 10.89% and obstruction in 9.9%. Most patients were anaemic with mean haemoglobin at time of admission of 6.4gm/dl. By the end of the study period 8 children had undergone transplantation, 22 children were undergoing conservative therapy, and 42 children were lost to follow up. **Conclusions:** Obstructive and interstitial nephritis comprises a large subgroup of CKD in children from this region. Most of the children carry poor prognosis in view of their late presentation. Majority of the children were unable to undergo any effective

therapy and were lost to follow up in view of limited availability and high cost of therapy.

Keywords: Glomerular diseases, chronic interstitial nephritis

INTRODUCTION

Rubella or German measles is a exanthematous fever characterized by transient macular rash and lymphadenopathy. In itself, the disease is trivial but rubella in the pregnant woman may lead to congenital malformation in the baby.¹ But in the world, half a million pregnant women die each year, many from such infection. Rubella virus infection acquires a special significance in pregnant women as the virus may enter the fetal circulation through the placenta.² Unfavourable outcome to pregnancy has become a serious problem in the society. Rubella virus infection during pregnancy can be a serious threat to the fetus with possible loss of pregnancy and dieases of newborn of which, encephalitis,

INTRODUCTION

Chronic Kidney disease is increasingly recognised as a major public health problem.^{1, 2} As Chronic kidney disease is an irreversible condition that eventually progresses to End stage renal failure, it becomes an important cause of morbidity, mortality and impaired quality of life in children.³⁻⁵ The magnitude of CKD varies from one geographical region to another depending on the genetic factors, environmental factors and local practice.

Unlike in adult population, where extensive epidemiological research is available, data in paediatric population is sparse.⁶⁻⁹

Address for Correspondence:

¹Associate professor and Head of Nephrology

(Corresponding Author)

Email: manjurisharma@yahoo.com

Mobile: +919435553482

^{2,6}Registrar, ³Professor, ⁴Associate Professor, ⁵Assistant Professor of dept of Nephrology, Gauhati Medical College & Hospital (GMCH), Guwahati -32, Assam, India CKD in early stages is mostly asymptomatic and hence remains undetected or under-diagnosed. In developing country like ours where optimal health care is still out of the reach to many people, early detection of CKD is rare and patients mainly present late with all the complications. Knowledge about the magnitude, etiology, risk factors and outcome of CKD will help in proper allocation of limited resources in a developing country.

The aim of the present study was to examine retrospectively the clinical profile of CKD in paediatric patient who attended our centre.

METHODSAND MATERIALS

We reviewed the medical records of all paediatric CKD patients between 2-18 years of age, who were admitted at Nephrology department of Gauhati Medical College & hospital, Guwahati between the periods of August 2013- July 2016. Clinical features like pallor, edema, oligoanuria, hematuria or any other urinary or voiding dysfunction were recorded. Examination findings included weight, height, BMI, blood pressure. Hypertension was defined as BP e"95th percentile or as self-reported hypertension plus current treatment with antihypertensive medications. Laboratory data included blood biochemistry, urinary findings & radiological studies. Renal histopathology, where available were included. CKD was defined according to 2002 NKF-K/DOQI criteria for classification of CKD, as presence of markers of kidney damage for > 3month with evidence of structural/functional abnormalities of the kidney with or without decreased GFR that is manifested by either pathological abnormalities or other markers of kidney damage in the blood, urine or imaging tests or eGFR <60ml/min/1.73 m² for >3month as estimated by modified Schwartz formula with or without kidney damage. 10-12 Children less than 2 years of age were excluded, as NKF-K/DOQI classification criteria apply to children above 2 years.

The patients of CKD were classified in four broad categories based on etiology.

- a) Glomerular causes; chronic glomerulonephritis either biopsy proven or when biopsy was not done, a probable diagnoses of chronic GN was made based on history of prolonged duration of oedema and proteinuria.
- b) Interstitial or Obstructive causes; when there was obvious finding of reflux, hydronephrosis, neurogenic bladder, dysplastic kidney or obstruction in radiological studies. A subgroup of unknown aetiology of chronic interstitial nephritis was made if therewere any features suggestive of recurrent urinary tract infection, indigenous medicine intake, scarred kidney or proteinuria <1000mg/m²/day.</p>
- c) Miscellaneous causes; included cystic kidney diseases, as evidenced by radiological study. Alport disease was diagnosed based on presence on presence of sensorineural deafness, lenticonus and family history of Nephritis.
- d) Chronic Kidney Disease of Unknown etiology; included patients where clear-cut diagnoses regarding the aetiology could not be made.

Manjuri Sharma, Gayatri Pegu, Anup Kumar Barman, Satyakam Kakaty, Pranab Jyoti Mahanta, Pallavi Bordoloi

RESULTS

After reviewing the records, we found 101children with CKD, where data was adequate for evaluation. The median age of the children was 13years (range 3-18 years). Mean age (SD) at presentation was 14.87years \pm 3.65. The youngest child was 3 years of age and there were only 4 children below the age of 5years (figure 1). There were 65 male children with a sex ratio of 1.8: 1(figure 2). At presentation, majority of our patients were in CKD stage 4 and 5 with a mean eGFR of 14.64 /min/1.73m² (**Table 1**). 27 (26.73%) children had an eGFR <10 ml/min/1.73m².

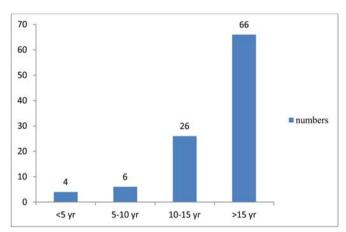


Figure 1 Age distribution of children with CKD

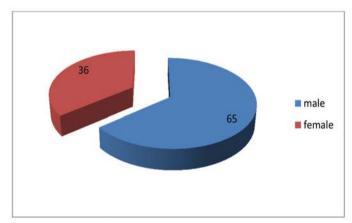


Figure 2 Sex distributions of children with CKD

35 children had presented with facial or pedal edema, while 49 patients presented with history of oligoanuria. Voiding dysfunction was present in 25 children. Anaemia was very common, seen in 74 children, with a mean haemoglobin level of $6.1 \text{gm/dl} (\pm 2.1)$. Hypertension was found in 58(57.42%) children. Etiology of CKD is shown in **Table 2**.

Table 1 Stages of CKD at presentation

Stage of CKD at presentation	Frequency	Percentage
Stage 3(30-59ml/min/1.73m ²)	4	3.96
Stage 4 (15-29 ml/min/1.73m ²)	36	35.64
Stage 5 (<15 ml/min/1.73m ²)	61	60.39

Table 2 Etiology of CKD

Etiology	Frequency	Percentage
Glomerulonephritis	36	35.64%
Chronic Glomerulonephritis (Unknown)	16	15.84%
FSGS	9	8.91%
IgA nephropathy	5	4.95%
SLE	6	5.94%
Obstruction & Interstitial causes	39	38.61%
Primary reflux	11	10.89%
CAKUT-PU	5	4.95%
CAKUT- Hypo plastic -Dysplastic Kidney	2	1.98%
Neurogenic Bladder	2	1.98%
Obstruction	10	9.90%
CIN (unknown)	9	8.91%
Miscellaneous	7	6.93%
Cystic kidney disease	4	3.96%
Alport syndrome	2	1.98%
Ischemic Nephropathy	1	0.99%
CKD (Unknown)	19	18.81%

Out of 101 patients, till last follow up, 22 patients were undergoing conservative management, 18 patients expired, 12 patients were undergoing maintenance haemodialysis. 8 patients underwent live related renal transplantation, of which 6 patients are doing well with a functioning allograft, while 2 expired following sepsis. A majority of the patient, 42 (41.58%) were lost to follow up.

DISCUSSION

Globally, the numbers of CKD patients are increasing markedly to the extent that it has become a major public health concern. The incidence and aetiology of CKD varies in different parts of the world. The paediatric incidence of CKD in Europe is reported to be around 11–12 per million of age-related population (pmarp) for stages 3–5, while the prevalence is <"55–60 pmarp. 13-15 The median incidence of renal replacement therapy (RRT) in children < 20 years worldwide range from 4-18 per million age related population. ¹⁶There is limited information about the epidemiology of CKD in paediatric population around the world, especially from developing or low income countries. Precise incidence of CKD in children is lacking from our country. In a study from SGPGIMER, Lucknow showed that children constitute 5.3% of total cases of CRF cases referred. Our study being retrospective in nature was unable to comment of the exact incidence and prevalence of the same.

The median age of our patient was 13 years, and only 4 patients were under the age of 5 years. This was in contrast to an earlier report from AIIMS, New Delhi, where the median age of the patient was 8 years and 96 children below 5 years of age. In the study from Lucknow, the median age was 13 years. In our study, 66 (65.35%) children were above 15 years. The delayed presentation may be due to delayed diagnoses and referral. The incidence and prevalence of CKD is greater in males than females because of the higher frequency of congenital abnormalities of the kidney and urinary tract (CAKUT) in males. In our study 65.35% of the patients was male.

In our study, 60% of the children were in ckd stage 5. The mean eGFR at presentation was 14.67ml/min/1.73m², which indicates

delayed presentation at an advanced stage. The delayed presentation in our study population may be because of poor public health awareness, delayed detection and poor access of patients from rural and remote areas with patients presenting for the first time only when there is rapid deteoriation of kidney functions with onset of puberty.

In our study, glomerulonephritis (35.64%) was the commonest cause of CKD in children. Obstructive & Interstitial causes together comprised of 38.61% cases. Correctable causes of CKD like obstructive uropathy, reflux nephropathy together accounted for a majority of these cases in our study. Unlike in developed countries, where early antenatal detection of congenital anomalies and prompt surgical correction is done, diagnoses and hence intervention were late in our setup. Earlier detection and treatment would have prevented their progression to chronic renal failure. In a recent NAPRTCS report(2014) congenital causes, including congenital anomalies of the kidney and urinary tract (CAKUT) (15.8%), obstructive uropathy (15.3%), FSGS (11.7%), Reflux nephropathy (5.1%) and chronic Glomerulonephritis (3.1%) were the five most common causes. ¹⁷In 18.8% of the patients, the etiology couldn't be identified from clinical history and investigation as they presented late.

All patient had identifiable clinical features with common presentation being oligoanuria, edema and voiding dysfunction. Anaemia was very common, seen in 74 children with a mean Hb of 6.4gm/dl (±2.1). 45% of children with CKD were found to be anaemic in the CKiD cohort, with a more rapid decline as GFR fell below 43ml/min/1.73m² at a rate of -0.3g/dl per 5ml/min/ 1.73m². ^{16,18}In our study, hypertension was found in 58 children. The North American Pediatric Renal Trials and Collaborative Studies' chronic renal insufficiency database had hypertension in 48% of the enrolled children and also demonstrated that it plays a role in progression of CKD in children. 19 Various studies have found prevalence of hypertension in children with chronic kidney disease (CKD) to be more than 50%. 20,21 The risk of hypertension is more closely associated with the type of underlying disease than with the degree of renal insufficiency; children with acquired glomerulopathies or polycystic kidney disease tend to have higher blood pressure than patients with renal hypoplasia and/or uropathies. The results of ESCAPE trial shows that intensified blood-pressure control delays the progression of renal disease in children with chronic kidney disease who receive a fixed high dose of an ACE inhibitor.²²

In our study a majority of the patients (41.6%) were lost to follow up, which may be due to financial constraints, as patient attendant themselves had to bear the expenses in absence of any state funding. 22 children were undergoing conservative therapy, 12 patient were getting maintenance haemodialysis and 8 had undergone live-related renal transplantation, till last record 6 of the post-transplant patients were doing well with a functioning allograft. 2 patient expired due to infection with functioning allograft.

We conclude from our study that, Glomerulonephritis is still the most common cause of CKD in our children. At the same time obstructive and interstial nephritis comprises a big subgroup, which can be easily prevented by detection and aggressive intervention at an early stage. Most of the children carry poor prognosis in view of their late presentation. Also majority of the children were unable to undergo any effective therapy and were lost to follow up in view of limited availability and high cost of therapy. Further studies to understand the epidemiology, causes and progression of ckd in children can help in delaying the onset of ESRD and hence the need for renal replacement therapy. This will also help in formulating health policy and allocation of limited resources.

Acknowledgments: Residents, Staff of Nephrology department, GMCH.

Conflict of interest: No conflict of interest associated with this work.

Contribution of authors: I (We) declare that this work was done by the author(s) named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

Ethical clearance: Taken Source of Funding: Nil

REFERENCE

- Levey AS, Atkins R, Coresh J, Cohen EP, Collins AJ, Eckardt KU et al. Chronic kidney disease as a global public health problem: Approaches and initiatives - A position statement from Kidney Disease Improving Global Outcomes. Kidney International 2007 Aug;72(3):247-259.
- Greenbaum LA, Warady BA, Furth SL. Current advances in chronic kidney disease in children: growth, cardiovascular, and neurocognitive risk factors. Semin Nephrol 2009;29:425–434.
- 3. Wong CJ, Marva MM, Judith JF, Bradley AW, Susan LF. CKiD (CKD in children) prospective cohort study: a review of current findings. Am J Kidney Dis 2012; 60: 1002–1011.
- 4. Shroff R, Ledermann S. Long-term outcome of chronic dialysis in children. Pediatr Nephrol 2009;24:463-474.
- Kaspar CDW, Bholah R, Bunchman TE. A Review of Pediatric Chronic Kidney Disease. Blood Purif 2016;41:211-217.
- Col M Kanitkar. Chronic Kidney Disease in Children: An Indian Perspective. Medical Journal Armed Forces India 2009:65:45-49.
- Gulati S, Mittal S, Sharma RK, Gupta A. Etiology and outcome of chronic renal failure in Indian children. Pediatr Nephrol 1999;13:594-596.
- 8. Hari P, Singla IK, Mantan M, Kanitkar M, Batra B, Bagga A. Chronic renal failure in children . Indian Pediatr 2003;40:1035-42.
- CKD registry of India: Indian Society of Nephrology. [online] [cited 2017 June 12]; Available from: URL: http://www.ckdri.org

- National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis 2002;39:S1.
- 11. Hogg RJ, Furth S, Lemley KV, Portman R, Schwartz GJ, Coresh J et al. National Kidney Foundation's Kidney Disease Outcomes Quality Initiative clinical practice guidelines for chronic kidney disease in children and adolescents: evaluation, classification, and stratification. Pediatrics 2003; 111:1416-1421
- Schwartz GJ, Muñoz A, Schneider MFM, Mak RH, Kaskel F, Warddy BA et al. New equations to estimate GFR in children with CKD. J Am Soc Nephrol 2009; 20:629.
- 13. Ardissino G, Daccoʻ V, Testa S, Bonaudo R, Claris-Appiani A, Taioli E et al. Epidemiology of chronic renal failure in children: data from the ItalKid project. Pediatrics 2003 April e382-387
- 14. Harambat J, van Stralen KJ, Kim JJ, Jane Tizard E. Epidemiology of chronic kidney disease in children. Paediatric Nephrology 2012; 27: 363-373
- 15. ESPN/ERA-EDTA Registry. European registry for children on renal replacement therapy. 2016. [cited 20117 June 12]; Available from: URL:http://www.espn-reg.org
- Copelovitch L, Warady BA, Furth SL. Insights from the chronic kidney disease in children (CKiD) study. CJASN 2011;6:2047–2053.
- 17. North American Pediatric Renal Transplant Cooperative Study (NAPRTCS) 2014 Annual report. [cited 20117 June 12]; Available from: URL:https://web.emmes.com/ped/annlrept
- Fadrowski JJ, Christofer BP, Stephen RW, Marva MM, Bradley AW, Furth SL. Hemoglobin decline in children with chronic kidney disease: baseline results from the chronic kidney disease in children prospective cohort study. CJASN 2008: 3: 457–462
- 19. Mitsnefes M, Ho P-L, McEnery PT. Hypertension and progression of chronic renal insufficiency in children: a report of the North American Pediatric Renal Transplant Cooperative Study (NAPRTICS). J Am Soc Nephrol 2003;14:2618–2622.
- Wong H, Mylera K, Feber J, Drukker A, Filler G. Prevalence of complications in children with chronic kidney disease according to KDOQI. Kidney Int 2006;70:585–590.
- 21. Flynn JT, Mitsnefes M, Pierce C, Cole SR, Parekh RS, Furth SL, et al. Blood pressure in children with chronic kidney disease: a report from the chronic kidney disease in children study. Hypertension 2008;52:631–637.
- The ESCAPE Trial Group. Strict blood-pressure control and progression of renal failure in children. NEJM 2009;361:1639–1650.