RESEARCH PAPER

Clinical Profile and Outcome of Emergencies in Pediatric Chronic Kidney Disease

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Objective: To describe the clinical profile and outcome of emergencies in children with chronic kidney disease (CKD). **Methods**: This retrospective analysis studied children with CKD presenting with acute emergencies. The clinical profile, renal and patient outcomes were compared between incidentally diagnosed - iCKD, previously diagnosed not on dialysis - pCKD and those on maintenance dialysis - dCKD groups. **Results**: 82 children (67 boys, median age – 8 years) with 99 visits were included. Uremic encephalopathy was the most common emergency in iCKD (64.7%) and pCKD (38.4 %), and access-related infections (32.1%) in dCKD group. Children with iCKD had higher Pediatric Risk of Mortality score (P<0.001), emergent initiation of dialysis (P=0.03) and discontinuation of treatment (P<0.001) when compared to the pCKD group. **Conclusion**: Uremic encephalopathy and access-related infections were the most common emergencies in children with CKD. Incidentally diagnosed CKD had a worse clinical profile and outcome.

Keywords: *Dialysis, Emergency department, Uremic encephalopathy*.

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Chronic kidney disease (CKD) related life-threatening emergencies like hyperkalemia, severe hypertension, heart failure, have been shown to be preventable by timely care and regular follow up [1]. Unfortunately, for many patients with CKD in developing counties, the first contact with the nephrologist is in the emergency department (ED) when they present with life-threatening complications [2]. These late presentations often require intensive care, and urgent, unplanned initiation of dialysis, leading to poor outcomes with high risk of treatment failure and mortality [2]. In children, delayed diagnosis is not uncommon, especially in resource-poor settings [3]. In children on dialysis, poor compliance to therapy, inadequate therapy, and socio-economic factors may result in unplanned visits to ED and life-threatening complications.

There is limited exploration of ED visits in pediatric CKD from developing countries in literature. This study was conducted to know the clinical profile and outcomes of acute emergencies in children with CKD.

METHODS

The study is an analysis of hospital records of children with CKD presenting with acute emergencies to the ED of a tertiary care hospital between January, 2016 and December, 2018. Clearance of the protocol with waiver of informed consent was obtained from institutional ethics committee. We extracted and included data of children (1 month to 18 years) with CKD stages III-V/VD, presenting with CKD-related emergencies. Emergencies unrelated to CKD and emergencies in children with renal transplan-tation were excluded. Repeated ED visits requiring hospitalization in the same child were considered as separate events. Based on the severity of illness, patients were admitted in pediatric intensive care unit (PICU) or in High-dependency unit (HDU).

Children diagnosed as CKD for the first time during the ED visit, and children with known diagnosis of CKD stage III-V but not on dialysis were categorized as incident-CKD (iCKD) and prevalent-CKD (pCKD), respectively. Those on maintenance continuous ambulatory peritoneal dia-lysis (CAPD) or hemodialysis (HD) were categorized as dialysis-CKD (dCKD).

Estimated glomerular filtration rate (eGFR) was calculated using modified Schwartz formula [4]. Staging of CKD was based on the highest eGFR documented in the preceding three months for pCKD, according to KDIGO guidelines [5]. Definitions of acute CKD-related emergencies were as per standard guidelines [6]. All emergencies were managed according to standard protocols. Pediatric risk of mortality score (PRISM IV) was calculated

at the time of admission to PICU [7]. PRISM IV score <10 and >10 were categorized as mild risk and moderate-to-high risk for mortality, respectively [8]. Renal outcome was defined as dialysis-dependency at discharge among those not on dialysis, while mortality and duration of hospital stay were considered as patient outcomes.

Statistical analysis: All analyses were performed using R statistical software version 3.6.1. Continuous variables were compared using Mann-Whitney *U* test and Kruskal-Wallis test and categorical variables using chi-square test. Odds ratio (95%CI) for outcome measures was calculated using logistic regression.

RESULTS

There were 118 visits to the ED, of which 19 in children with renal transplantation were excluded. Eighty-two children (67% boys) with 99 visits were included. Among these, 17 (20.7%), 26 (31.7%) and 39 (47.5%) children belonged to iCKD, pCKD and dCKD groups, respectively. Fourteen children in dCKD group required more than one hospital admission. Demographic profile of the cohort is described in **Table I**. In dCKD group, 36 (92.3%) were on CAPD and 3 (7.6%) on maintenance-HD through arteriovenous fistula. The median (IQR) eGFR in iCKD and pCKD groups was 11mL/min/1.73m^2 (10,12.1) and 23 mL/min/1.73m^2 (19,35) (P<0.001). About one-third of children (35.3%) required admission to PICU, with a higher proportion in iCKD group (P=0.07).

Children with iCKD had higher number of complications compared to pCKD and dCKD groups (P<0.001) (**Table II**). The most common emergency was uremic encephalopathy in iCKD (64.7%) and pCKD (42.3%), and infections (32.1%) in dCKD group, with peritonitis being the most common infection (25%). Among the 14 children in dCKD group having more than one admission, preventable causes (hypertensive emergencies, hyperkalemia, cardiac failure) accounted for 54.5% admissions. Patients in iCKD group had a higher median PRISM IV scores (P<0.001) and a higher proportion of children with PRISM score >10 (P=0.001) compared to other groups. Serum calcium, bicarbonate and hemoglobin concentrations were significantly lower in the iCKD group compared to other groups.

Hyperkalemia (median potassium 6.4 (6.3, 6.8) meq/L) was seen in 8 children. Six of these had ECG changes of hyperkalemia, none had ventricular tachycardia and five required dialysis. Children with hypertensive encephalopathy (n=19) were managed with sodium nitroprusside (n=9) and intravenous labetalol (n=10). The need for emergent initiation of dialysis was significantly higher in the iCKD (76.47%) compared to pCKD (42.3%) group (P=0.03). Hemodialysis was the most common modality for emergency dialysis (83.3%).

Table I Profile of Children With Chronic Kidney Diseases Presenting With Acute Emergencies

Characteristics	*iCKD (n= 17)*	*pCKD (n= 26)*	*dCKD (n=39)*
Age (y)[a]	5.0 (0.9, 9.0)	9.0 (6.0, 13.8)	9.0 (5.0, 15.0)
Weight (*z*-score)[b]	-2.4 (-3.6, -1.7)	-3.2 (-4.2, -2.6)	-3.5 (-4.5, -2.4)
Height/length (*z*-score)	-3.5 (-4.7, -3.3)	-3.6 (-3.9, -3.3)	-3.6 (-4.3, -3.1)
CKD stage[a]			
III- IV[c]	3 (17.6)	21 (80.7)	-
V[c]	14 (82.3)	5 (19.23)	-
Vd	-	-	39 (100)
eGFR (mL/min/1.73m^2)[c]	11 (10,12.1)	23 (19,35)	-
Etiology of CKD[a]			
Non-glomerular	12 (70.5)	20 (76.9)	32 (82.0)
Glomerular	5 (29.4)	6 (23.0)	7 (17.9)

Values in median (*IQR*) or [a]no. (%). *CKD-chronic kidney disease; iCKD-incident CKD; pCKD-prevalent CKD; dCKD-dialysis CKD; eGFR-estimated glomerular filtration rate.* [b]*P=0.05,* [c]*P<0.001. – indicates not applicable.*

In pCKD group, on comparing the children requiring maintenance dialysis with those continued on conservative management at time of discharge, median (IQR) eGFR prior to admission was comparable (23 (19, 37) vs 22 (19, 31) mL/1.73m^2/min; P=0.815), but lower hemoglobin (7.4 (6.7,8.3) vs (8.8 (8.3, 10.3); P=0.04) and higher number of complications (2 (2,4) vs 1 (1,2); P=0.003) during admission were noted.

Treatment discontinuation was significantly higher in iCKD group (P<0.001) and more prevalent among patients of lower socioeconomic status (11.6%, P=0.25). After adjusting for severity of illness at admission, children in iCKD group were significantly more likely to have emergent initiation of dialysis (OR (95%CI) 4.43 (1.13-17.34); P=0.03) and treatment discontinuation (OR (95%CI) 21.81 (3.90-121.84); P <0.001) compared to pCKD group.

DISCUSSION

This retrospective analysis of emergencies in children with CKD found that about 21% of the cohort was newly diagnosed with CKD while presenting with an acute life-threatening emergency. Uremic encephalopathy was the most common etiology in iCKD and pCKD group. Repeat hospitalizations were more common in dCKD group.

Prevalence of newly diagnosed CKD (21%) in our study is comparable to previous data from India (25%) [3,9]. We

Table II Clinical Profile and Outcome of Children With Chronic Kidney Diseases Presenting to the Emergency Department

Characteristics	*iCKD(n=17 visits)*	*pCKD(n=26 visits)*	*dCKD(n=56 visits)*
Emergencies per admission[a,b]	2 (2,4)	2 (1,3)	1 (1,2)
Biochemical profile[a]			
Hemoglobin (g/dL)[c]	6.1 (5.4, 6.5)	8.4 (7.3, 9.1)	7.6 (6.8, 9.6)
Plasma bicarbonate (mEq/L)[b]	11.3 (8.1,15.3)	14.7 (13,21.4)	20.5 (17.1,21.6)
Serum potassium (mEq/L)	5.4 (4.4, 6.3)	4.7 (3.9,5.7)	4.7 (4.1,5.4)
Serum calcium (mg/dL)[b]	7.8 (7.1, 8.1)	8.8 (7.4, 9.2)	9.2 (8.4, 9.6)
Etiological profile			
Hypertensive emergencies	6 (35.3)	4 (15.4)	15 (26.8)
Severe hyperkalemia[d]	2 (11.8)	2 (7.7)	2 (3.5)
Symptomatic hypocalcemia	4 (23.6)	4 (15.4)	4 (7.1)
Severe anemia	4 (23.6)	6 (23.1)	11(19.6)
Acute cardiac dysfunction	6 (35.3)	2 (7.7)	9 (16.1)
Uremic encephalopathy[c]	11(64.7)	11(42.3)	5 (8.9)
Severity of illness			
Admission to PICU	10 (58.8)	9 (34.6)	16 (28.5)
PRISM IV score [a,b]	11.5 (10.2,13.7)	8 (7.0,9.0)	10.5 (9.2,12.5)
Mechanical ventilation	3 (30)	3 (33.3)	10 (62.5)5 (31.2)
Inotropes	5 (50)	3 (33.3)	
Emergent initiation of RRT[c]	13 (76.4)	11 (42.3)	-
Indications for RRT[e]			-
Uremia	8 (61.5)	5 (50)	
Volume overload	6 (46.1)	6 (60)	
Hyperkalemia[d]	2 (15.4)	1 (10)	
Hemodialysis	11 (84.6)	9 (81.8)	
Acute peritoneal dialysis	2 (15.4)	2 (18.2)	-
Time interval for initiation of dialysis (d)[a]	1 (1,1)	1 (1,1.5)	-
Outcome			
Discharged[b]	11 (64.7)	24 (92.3)	55 (98.2)
Dialysis dependency at discharge	12 (70.7)	11 (42.3)	-
Duration of hospital stay (d)[a]	13.0 (9.0, 23.0)	5.0 (4.0, 10.2)	8.5 (5.0, 16.0)
Discontinuation of treatment[b]	6 (35.3)	2 (7.6)	0 (1 died)

Data presented as no. (%) or [a]median (IQR). - indicated not applicable. CKD-chronic kidney disease; iCKD-incident CKD; pCKD-prevalent CKD; dCKD-dialysis CKD; PICU-pediatric intensive care unit; PRISM IV-pediatric Risk of Mortality IV; RRT-renal replacement therapy; HD-hemodialysis; PD-peritoneal dialysis. [c]P<0.05. [^]Compared only between two groups; [d]With ECG changes; [e]RRT in one child of iCKD group for refractory acidosis.

found that iCKD presented with more severe illness and need for emergent dialysis. Studies in adults have shown that late referral is associated with more severe complications at time of presentation [10-12]. A similar study in adults from Africa found that uremia and sepsis accounted for about 80% admissions [11]. In contrast, a study from the developed world showed that cardiopulmonary complications were the most common emer-gencies in adults with advanced CKD [13]. These differences probably reflect delayed diagnosis and inadequate dialysis in resource-poor settings.

Emergent initiation of dialysis and its indications were similar to the reported proportion seen in adults [11]. In our study, majority of children were initiated on RRT early in contrast to delay in initiation of dialysis noted in other studies [11]. Majority of our CKD patients (42.3%) remained dialysis-dependent at discharge and required unplanned initiation of maintenance dialysis, comparable with previous studies in adults reporting 30% [14]. Cardiovascular disease, low hemoglobin levels and low serum albumin were associated with sudden unexpected fall in eGFR and precipitous initiation of dialysis [14]. Among those who discontinued treatment, all patients were dialysis-dependent and a majority belonged to low socioeconomic status and iCKD group. Low socio-economic status and lack of insurance support were identified as important risk factors for discontinuation of treatment in resource-poor settings [10,11]. A systematic review showed that disease awareness, access to healthcare, and geographical remoteness were important reasons for delayed diagnosis [15].

WHAT THIS STUDY ADDS?

- Children incidentally diagnosed to have chronic kidney disease in the emergency department had more severe complications and were at high risk for emergent initiation of dialysis.

Though our study has the inherent limitations of a retrospective study, it highlights the prevalence of preventable emergencies, and need for multiple admissions in children with CKD, which could potentially be avoided by better ambulatory care. A significant proportion of children in late stages of CKD required unplanned initiation of maintenance dialysis which can be prevented by increased clinical scrutiny and informed decision making for early planned initiation of dialysis in this high-risk group.

Ethics clearance: Institutional Ethics Committee, St John's Medical College, Bengaluru; No. 350/2018, dated Nov. 29, 2018.
Contributions: MA: data collection, analysis of the data and writing of the manuscript; NK: study design, supervision of data collection and analysis and writing of the manuscript; LAV: study design, analysis of data and writing of the manuscript; AV: writing of the manuscript and critical review of the manuscript. All authors approved the final draft of the manuscript.
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