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Clinical Profile and Outcome of Acute Kidney Injury in Children Less than 5 Years: A Two-Year Retrospective Study in a Resource Limited Setting

Denis Georges Teuwafeu[1], Yolande Djike Puepi[1], Ange Erica Maguipa Tsasse[1], Mbua Ronald Gobina[1], Leslie Tasha Mbapah[2], Marie-Patrice Halle[3]

[1]University of Buea, Buea, Cameroon
[2]Triad Research Foundation l, Buea, Cameroon
[3]University of Douala, Douala, Cameroon
Email: d.teuwafeu@yahoo.com, maguipaange@gmail.com, Yolandep2000@yahoo.fr, ronaldgob@yahoo.com, mbapah@gmail.com, patricehalle@yahoo.fr

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Abstract

Background: Younger children are more vulnerable to acute kidney injury. We aimed to determine the prevalence, aetiological factors, clinical features, and outcome of acute kidney injury (AKI) in children aged 29 days to 5 years. **Method:** We retrospectively reviewed hospital records of children less than 5 years admitted in the paediatrics ward and the Intensive care unit from the 1st of January 2021 to the 1st of March 2023. We defined AKI using the Kidney Disease: Improving Global Outcome (KDIGO) criteria. Our outcomes of interest were the need for dialysis, death, and renal recovery at discharge. Data were analysed using STATA version 17 SE. A p-value of less than 0.05 was considered statistically significant. **Results:** Out of 3393 patients, 54 (1.6%) had AKI either on admission or during the course of treatment. The median age of our participants was 22 months. Sepsis (n = 47; 87%), severe malaria (n = 17; 31.5%), and the use of nephrotoxins (n = 15; 27.8%) were the most common aetiologies of AKI. All but one of our participants was in KDIGO stage 3 AKI. Dialysis was indicated for 75.9% (n = 41) of the patients. But done only in 32% (n = 13). The reasons for no dialysis were inappropriate logistics (n = 16, 57.1%), death before initiation of dialysis (n = 8, 28.6%), and family refusal (n = 4, 14.3%). The mortality rate was 66.7% (n = 36). **Conclusion:** About 15 in a thousand children aged 29 days to 5 years developed AKI during hospital stay. Sepsis, severe malaria, and the use of nephrotoxins were the most common aetiologies of AKI. Dialysis was often needed and not done, and the mortality rate was high.

Keywords

Acute Kidney Injury, Children, Outcome, Resource-Limited

1. Background

Globally Acute Kidney Injury (AKI) affects more than 13 million patients resulting in more than 2 million deaths annually [1] [2]. It Affects about 27% of critically ill children, and its prevalence in non-critically ill children is not negligible [3]-[9].

The Kidney Disease: Improving Global Outcome (KDIGO) definition and staging system is the most recently accepted and preferred definition even in the paediatric literature. According to the KDIGO, AKI is defined as an increase in serum creatinine by 0.3mg/dl or more within 48 hours or an increase in serum creatinine to 1.5 times baseline or more within the last 7 days, or urine output less than 0.5ml/kg/h for 6 hours [10].

According to a prospective study on children and young adults done across Asia, Australia, Europe, and North America, 27% of the participants had AKI while 11.6% had severe AKI. This was associated with a mortality rate of 2.5% and 11% in those with AKI and those with severe AKI respectively [11].

Paediatric nephrology is still evolving in Africa. The absence of a comprehensive paediatric renal registry makes the burden of paediatrics AKI difficult to estimate across the continent [12]-[14]. A recent meta-analysis in sub-Saharan (SSA) on the outcome of AKI reported that 66% of children with AKI present with severe forms requiring dialysis, hence high mortality (34%) in a setting with limited access to dialysis [15]. According to a recent study in a referral hospital in Douala the incidence of AKI in children was 9.6% with 32% in stage 3, while another study in a primary health facility reported an incidence of paediatric AKI of 12.3%, with a recovery rate at the discharge of 71.1% [16] [17].

In contrast to developed countries where AKI occurs in older children with comorbidities, the commonest causes of paediatric AKI in our setting include exposure to nephrotoxins (86.7%), sepsis (51.2%), and severe malaria (40%) [17]. In addition most cases of paediatrics AKI in our settings are community-acquired with late presentation to the hospital [15] [18]. This is coupled with scarce means of paediatric dialysis, which reduces the accessibility to every population with severe forms of AKI, resulting in a high mortality rate [17]. Younger children are known to be more vulnerable and there are limited options for diagnosis and treatment [19] [20]. Treatment options available are often not adapted and sometimes do not exist [14]. This research focussed on describing the burden of AKI in children less than 5 years in a setting where paediatric nephrologists are lacking and the only treatment option for severe acute kidney injury is adult hemodialysis with no provision to adapt it to children.

2. Methods

2.1. Study Design and Settings

This was a hospital-based retrospective cohort study. Data were retrieved from hospital records of all children aged 29 days to 5 years admitted to the paediatric wards and intensive care unit from the 1st of January 2021 to the 1st of March 2023.

We conveniently selected two hospitals providing dialysis services: The Buea Regional Hospital (BRH) and the Douala General Hospital (DGH). The Buea Regional Hospital is at the second referral level, according to the health pyramid. It is the referral centre of nephrology cases in the southwest region. The Douala General Hospital is at the tertiary level of the health pyramid. It serves as the national referral centre for nephrology cases. In both centres, there is no paediatric nephrologist and children with AKI are managed by the nephrologist and the paediatricians. In addition, the only method of dialysis available is haemodialysis (HD). No standardized routine investigations are requested on admission, and investigations requested are based on the physician's probable diagnosis and differentials. Therefore serum creatinine levels were not assessed for all patients admitted during our study period.

2.2. Data Collection

We reviewed 1809 files from the DGH of which 33 had AKI and 1584 from the BRH of which 21 had AKI. This gives a total of 3393 files reviewed of which 54 had a diagnosis of AKI during our study duration. We went through the admission records of the paediatrics units to identify our participants. Then we used information derived from the admission records to find the corresponding files in the archives.

AKI was defined in this study as an absolute increase in the serum creatinine of 0.3 mg/l within 48 hours or observed 1.5-fold increase in creatinine in 7 days and/or urine volume less than 0.5 mL/kg/h for at least 6 hours or an anuria for more than 12 hours. We included files of all children less than 5 years old with at least two serum creatinine or a record of the urine output. Newborns with less than 29 days of life were excluded.

All methods were performed following the relevant guidelines and regulations.

The following data were collected from patients' files; Age, gender, weight, height, clinical presentations, duration of symptoms, comorbidities, aetiologies of AKI, and severity of AKI according to KDIGO criteria. The mechanism of AKI was determined using clinical reasoning (kidney biopsy were not performed) and the outcome studied were the hospital length of stay, kidney recovery (total or partial), need for dialysis and death.

Data were entered into a computer then exported from Excel 2016 and analysed using STATA version 17 SE. continuous variables were express in median (IQR). Chi-square, fisher moods median test were used to compare variables. Regression statistical model was used to test for significance of association between the independent and dependent variables. Values were considered significant at $p < 0.05$.

2.3. Definition of Terms

1) AKI Staging: The KDIGO 2012 classification was used to stage the severity.

2) Sepsis was define using sepsis 3 definitions [21] is life-threatening organ dysfunction due to a deregulated host response to infection and Sepsis clinical criteria: organ dysfunction is defined as an increase of 2 points or more in the Sequential Organ Failure Assessment (SOFA) score.

3) Severe Malaria clinical or laboratory proven malaria stage of the disease is defined by clinical or laboratory evidence of vital organ dysfunction [22].

4) Use of Nephrotoxin was defined as a recorded history of ingestion of known nephrotoxic drug (conventional, or herbal remedies)

5) Kidney Function Recovery [23] was assessed and calculated by the ratio of serum creatinine (sCr) to baseline sCr at the time of renal function assessment, according to the following criteria: (1) Total renal function recovery: when creatinine returns to the sCr baseline value; (2) Partial recovery: when sCr does not return to the baseline value but stays within a margin up to 1.5 times the baseline value; (3) No recovery: sCr stays at a value above 1.5 times in relation to the baseline

6) Length of Stay: was considered from the first day of admission.

7) Need for Dialysis was referred to patients with indications for dialysis.

8) Access to Dialysis to those with indications for dialysis and that were actually.

2.4. Ethical Consideration

Ethical clearance was obtained from the Faculty of Health Sciences, University of Buea (FHS), and its Institutional Review Board (ref. 2022/1313-02/UB/SG/IRB/FHS). The confidentiality of participants was maintained by using codes rather than names on questionnaires. Since we were conducting a retrospective study, the need for study participant consent was waived by the Ethics Unit (Institutional Review Board, Faculty of health science university of Buea).

3. Results

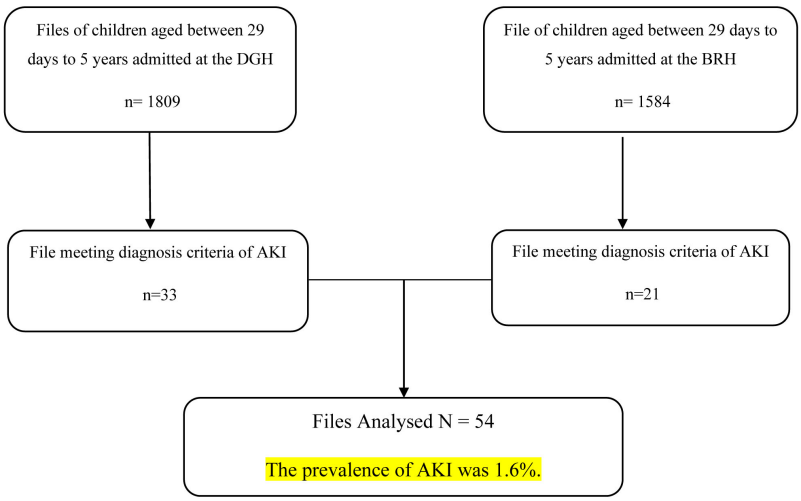

Figure 1. Recruitment flow chart.

A total of 4847 children aged from 29 days to 5 years were admitted during the study period. Thirty per cent of the files were rejected (age not mentioned, no date of admission, file not found). A total of 3393 files were reviewed for AKI (Figure 1).

3.1. Clinical Characteristics of Patients and Aetiological Factors in Children with Acute Kidney Injury

The majority of our population was male (61.11%, n = 33) with a male to female ratio of 1.57:1. The median age was 22 months (IQR, 10 - 35). Most participants presented with fever (n = 48, 88.9%), anuria (51.9%), and anaemia (51.9%). Sepsis was the most common aetiological factor of AKI (n = 47, 87%), followed by severe malaria (31.5%), and use of nephrotoxins (27.8%). Combination of 2 or more aetiological factors were observed (Table 1).

Table 1. Clinical characteristics of patients and Aetiological factors of children with acute kidney injury.

Variable	Categories	Frequency	Percentage
Age	<24 months n (%)	29	53.3
	≥24 months n (%)	25	46.7
Sex	Male	33	61.1
	female	21	38.9
Presenting complaints	Fever	48	88.9
	Anuria	28	51.9
	Anemia	28	51.9
	Vomiting	15	27.8
	Cough	13	24.1
	Oedema	8	14.8
	Convulsion/loss of consciousness	15	27.8
Aetiological factors	Sepsis	47	87
	Malaria	17	31.5
	Use of nephrotoxins	15	27.8
	Dehydration	7	12.9

n: number with characteristics.

3.2. Clinical Characteristics of AKI in the Study Participants

The median duration from the onset of symptoms to consultation was 6.5 days (6.5 - 10). As shown in Table 2, almost all participants were classified according to the KDIGO criteria in stage 3 AKI (98.2%, n = 53). The main complications related to AKI were anuria (n = 43, 79.6%), uraemia (n = 41, 75.9%), and fluid overload (n = 26, 48.2%).

Table 2 highlights that dialysis was needed for 75.9% of the population (n = 41), with 48.8% (n = 20) being less than 24 months. Dialysis was done in only 31.7% (n = 13). The only method of dialysis performed was HD. The most common indications for dialysis were anuria (65.8%, n = 27) and uraemia (58.5%, n =

24), fluid overload (24.39%, n = 10). The most common reason for which dialysis was not done was inappropriate logistics (57.1, n = 16), followed by death before initiation (28.6%, n = 8) (Table 2).

Patients received 1 to 6 dialysis sessions with a median of 2.6 (1 - 4), and dialysis was done about 3.1 days after admission.

Table 2. Clinical characteristics of AKI in the study participants (N = 54).

Variables	Category	Frequency	Percentage
KDIGO staging	Stage 1	0	00
	Stage 2	1	1.9
	Stage 3	53	98
Complications of AKI	Uraemia	41	75.9
	Fluid overload	26	48.2
	Hyperkalaemia	11	20.4
Dialysis	Not needed	13	24.1
	Needed and done	13	24.1
	Needed and not done	28	51.9
Indications for dialysis	Uraemia	24	58.5
	Anuria	27	65.9
	hyperkalaemia	5	12.2
	Fluid overload	10	24.4
Reasons for not doing dialysis	Inappropriate logistic	16	57.1
	Death before initiation	8	28.6
	Family refusal	4	14.3
Median duration of symptoms (IQR)	6.5 days (6.5 - 10)		
Median dialysis frequency (IQR)	1.2 (1-4)		
Median time to start HD after arrival (IQR)	3.1 days (3-6.2)		
Mean creatinine	66 mg/L		

IQR: Inter Quartile Range, AKI: Acute Kidney Injury, KDIGO: Kidney Disease: Improving Global Outcome.

3.3. Outcome of Patients with Acute Kidney Injury

Of those who survived up to discharge, renal recovery was complete for 20% (n = 2), incomplete for 20% (n = 2) and 40% (n = 4) did not recover (Tables 3 - 4). The median length of hospital stay was 2 days (interquartile range 1 to 5).

The mortality rate was 73.5%. Mortality was greater in participants aged less than 24 months as compared to those older (46.9% vs 36.1%), and when dialysis was needed and not done as compared to when it was needed and done (74.1% vs 25.9%) (Table 5).

Table 3. Outcome of AKI in the study participants.

Variables	Category	n	Percentage (%)
Referral	Yes	8	14.8

Continued

	<24 months	5	62.5
	≥24 months	3	37.5
Reason for referral	PD	7	88.9
	Urologic consultation	1	11.1
Renal recovery at discharge	Complete	2	20.0
	Partial	2	20.0
	No recovery	4	40.0
	Unknown	2	20.0
Death	yes	36	66.7
Median length of hospital stay (IQR) (day)	2 (1 - 5)		
Median creatinine at discharge (IQR) in mg/L	17 (10 - 39)		

IQR: *Interquartile Range*; *SD*: *standard Deviation*; *PD*: *Peritoneal Dialysis.*

Table 4. Factors associated with mortality (univariate analysis).

Variable	Category	n	%	95% CI	p-value
Sex	Female	20	66.7	58.9 - 85.1	0.245
	Male	16	33.2	1	
Age	<24	23	46.9	32.53 - 61.7	**0.011**
	≥24	13	36.1	14.95 - 41.1	
	Dialysis not needed	9	25.0	12.12 - 42.2	**0.007**
	Dialysis needed	27	75.0	57.80 - 87.9	
Dialysis	Dialysis done	7	25.9	11.11 – 46.3	**0.025**
	Dialysis needed and not done	20	74.1	53.72 – 88.9	
	2 or less session of dialysis	5	71.5	66.21 – 81.1	**0.014**
	More than 2 sessions of dialysis	2	28.5	21.72 – 39.9	
Aetiological Factors	Sepsis	47	87.0	62.12 – 92.3	0.354
	Severe malaria	17	31.0	21.23– 42.6	
	Use of nephrotoxin	15	28.0	17.23 –35.8	
	Dehydration	7	13.0	12.02 – 23.5	

CI: *Confidence Interval.*

Table 5. Predictors of mortality in children less than 5 years with AKI (Multivariate analysis).

Variable	n	%	AOR	95% CI	p-value
Age < 24 months	23	46.9	12.56	8.53 - 24.7	**0.011**
Dialysis needed	27	75.0	24.4	17.80 - 30.9	**0.001**
Dialysis needed and not done	20	74.1	9.2	7.72 - 18.9	0.568
2 or less session of dialysis	5	71.5	5.23	3.21 - 12.1	**0.014**

4. Discussion

The goal this study was to describe the burden of AKI in children aged 0 to 5 years in the BRH and DGH from January 2021 to March 2023. We aimed specifically at determining the prevalence of AKI, determining the aetiological factors associated with the development of AKI, the clinical presentation and the outcome of AKI in children aged 29 days to 5 years. We found that 1.6% of children in this age range developed AKI before, or during their hospital stay, with more than half presenting with signs of an established AKI. In contrast to developed countries where most cases of AKI are due to cardiopulmonary bypass, sepsis, heart failure, solid organ and stem cell transplantation, tumour lysis syndrome, and exposure to nephrotoxins, we found that sepsis was the most common, followed by severe malaria, and use of nephrotoxins [24]. Social determinants of health such as poverty, poor hygiene and sanitation may play a role in those aetiologies. Furthermore, malaria is endemic in our country. Also, there is a high number of traditional practitioners and high use of herbal concoction which may be nephrotoxic. Our findings are similar to those reported in Malawi by Evans *et al* in 2017 [25]. However, according to a study done in Nigeria by Esezobor *et al* in 2012, primary kidney diseases were the most common causes of AKI, followed by sepsis and malaria [26]. This may be explained by the fact that they included children of all ages, and primary kidney diseases are less common in children of our age group.

Most of our participants presented with fever (88.9%), anuria (51.9%), and anaemia (51.9%). Fever reflects the most common aetiological factor associated with AKI which was sepsis. Anuria may be explained by renal hypo perfusion which may arise in cases of sepsis and severe malaria. In addition, anuria may arise as a side effect of the medication used to treat the underlying disease. Anuria also is the most striking symptom pointing toward AKI. Hence, children who develop anuria may most likely be investigated for AKI, and referred from primary health care settings. Anaemia on the other hand may be associated with the aetiological factor associated with AKI, which was malaria in 31.48% of the cases. Bai *et al*. reported a similar prevalence of fever (78.5%), anuria/oliguria (53.1%), and anaemia (52.3%) in Pakistani children in 2021 [20].

In line with previous studies conducted in developing countries, most of our population presented with stage 3 AKI according to the KDIGO staging, with either anuria or creatinine greater than three times the baseline value, as per the KDIGO criteria [12] [15] [18] [20]. This may be due to late hospital presentation, late referrals from primary health care providers, late diagnosis as creatinine was not done on everyone and only requested when suspicion (so the milder cases were missed and therefore not included in the cohort), and financial constraints. However, in a prospective cohort, Fouda *et al* reported that 47.4% of children had stage 3 AKI. This was lower than our findings and may be explained by the fact that their study was carried out in a primary healthcare facility where there are less severe cases. Also, the prospective design of the study may have led to early diagnosis of AKI in their cohort [16].

Most of our participants needed dialysis (75.9%), as this reflects the severity of AKI in this population. Dialysis was done in only 31.7% of those who required it. The most common reason for this is inappropriate logistics. Haemodialysis in Cameroon is designed for adults so not adapted to children (no children catheter, no children haemodialyser nor bloodlines). The only dialysis technique developed is haemodialysis. Peritoneal dialysis is still embryonic or not available. Dialysis was also started late, about 3 to four days after admission, reflecting delayed recognition, delayed diagnosis and delayed initiation of dialysis. All these factors associated led to a high mortality rate (66.7%). The majority of the patients received only one session, and probably many of these patients died before the next session. This high mortality rate may also be justified by the young age of our participants, the fact that most of them present with sepsis which may be associated with multiple organ failure, and also the unavailability of a paediatric ICU to handle such cases.

The mortality rate was significantly higher in children aged less than 24 months, and this may be explained by the fact that their low weights and the difficulties in getting vascular access, makes haemodialysis (which was the only dialysis modality offered in our setting) not feasible.

Bai*et al* reported a dialysis need of 61.5% in Pakistan in 2021, which was similar to ours. But, their mortality rate was lower (36.1%), probably due to their use of more advanced logistics such as the possibility of PD [20]. Parikh and Tullu reported a dialysis need of only 1.8% in India in 2014, and a mortality rate of 46.6%. This may be due to the prospective design of their study which led to earlier diagnosis [27]. Ezesobor *et al.* also described a lower mortality rate (28.4%) in a setting similar to ours. This is probably because they included children of all ages in their study, with older children being less likely to die from AKI.

The median length of hospital stay was 2 days. This reflects the fact that most of our participants came for consultation in critical states which led to death within a few days.

Renal outcome at discharge was partial in 20%, incomplete in 20%, and no recovery in 40%. This may be justified by the fact that renal recovery was evaluated in just a few survivors and also by our short period of follow-up. This may not reflect the real picture of renal recovery in a larger population. Contrarily to our findings, Abdelraheem *et al.* in Sudan in 2012, described a renal recovery of 68.9%, probably due to the high number of AKI survivors in whom renal recovery was assessed. Our study describes relevant information on AKI in children aged 29 days to 5 years in the BRH and DGH. However some children with AKI may not have been diagnosed, and therefore were omitted in this study.

5. Study Limitations

As a retrospective study, quality of data was dependent on the accuracy of health provider to keep his archives. Over 30% of files reviewed were rejected because of either missing or incomplete clinical information. The lack of baseline creatinine

when defining AKI has been shown to lead to underestimation of AKI and Higher mortality.

Patients with milder stages of AKI may not have been included due to a lack of routine investigating, leading to and underestimated prevalence.

6. Conclusion

About 15 out of a thousand children aged 29 days to 5 years developed AKI before or during the hospital stay. The most common aetiologies of AKI were sepsis, malaria and the use of nephrotoxins. Most children of this age group present to the hospital with severe forms and require dialysis. However this need is not often met. AKI in this age group carries poor outcomes.

Statements and Declarations

Ethical considerations

Ethical clearance was obtained from the Faculty of Health Sciences, University of Buea (FHS), and its Institutional Review Board (ref. 2021/1313-02/UB/SG/IRB/FHS). Administrative clearance was obtained from the Regional Delegate of Public Health of South west region, from hospital authorities of Douala and Buea. The consent to participate and the informed consent were waived by the ethic committee (Intuitional Review Board, Faculty of Health Sciences, University of Buea). All informations were store in a password protected computer to endure confidentiality.

Availability of Data and Materials

The materials described in the manuscript, including all relevant raw data, will be freely available to any scientist wishing to use them for non-commercial purposes. The data that support the findings of this study are then available from the corresponding author (d.teuwafeu@yahoo.com) upon reasonable request.

Authors' Contributions

TDG, MTAE, HMP drafted and revised the work, MTAE, NPY, TDG drafted the work and collected data, TDG, MTAE, HMP, MLT analysed and interpreted data, HMP, AG revised the work.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Abbreviations

AKI	Acute Kidney Injury
BRH	Buea Regional Hospital
DGH	Douala General Hospital
HD	Haemodialysis
KDIGO	Kidney Disease: Improving Global Outcome
PD	Peritoneal Dialysis