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Risk Factors, Epidemiology and Outcome of Acute Kidney Injury among Pediatric Admissions in a Primary Health Facility in Cameroon

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Abstract

Background and aim: Data on the epidemiology of acute kidney injury (AKI) in Sub-Saharan Africa mainly originates from studies in large tertiary hospitals with nephrology units. Little is known about what happens in primary health structures without nephrology care, especially in the paediatric population. We sought describe the epidemiology of AKI in children at risk in district hospitals in Cameroon.

Methods: We prospectively screened consenting children aged 2-18 years of age in paediatric wards of 3 large urban district hospitals over a period of 4 months. We identified children with AKI risk factors on admission then screened for AKI using the creatinine based modified Kidney Disease Improving Global Outcomes (KDIGO) 2012 criteria. Participants with AKI were then followed up till discharge. Outcomes of interest were need and access to dialysis, and renal recovery on hospital discharge. Written assent was obtained from parents or caregivers.

Results: Among the 211 children admitted during the study period, 82% (n=173) were at risk of AKI, of whom 19 (11%) did not consent. Of the 154 children included 54.5% were males and the median age was 6 years [IQ 3-10]. Sepsis and volume depletion were the most common risk factors of AKI. The incidence of AKI was 12.3% (n=19). AKI was mostly community acquired and 47.4% (n=9) patients were in KDIGO stage 3. Pre-renal AKI and acute tubular necrosis accounted for 63.2% and 36.8% respectively. Gastro-intestinal losses, malaria, bacterial sepsis and nephrotoxins were the common aetiologies of AKI. The lone patient in need of dialysis died without it. On discharge, 71.7% of AKI had complete recovery renal function.

Conclusion: Risk factors of AKI are very common in children on admission in general district hospitals in Cameroon. At least one out of 10 admitted children with AKI risk factors will have AKI. AKI is caused largely by preventable community acquired conditions such as diarrhoeal diseases and malaria. Efforts should be made to raise awareness of primary health caregivers about risk assessment, prevention, early recognition and management of AKI in children.

Keywords: AKI; Primary Healthcare hospital; Epidemiology; Cameroon.

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Introduction

Acute Kidney injury (AKI) is a common condition affecting about 13.3 million of people per year in the world (1). It is associated with prolonged hospital stay, increased healthcare costs and poor patient outcomes such as death, cardiovascular

disease and chronic kidney disease. In high income countries, hospital-acquired AKI is more frequent, affecting elderly patients admitted in intensive care unit and with high comorbidity burden, and results mainly from the diagnostic or therapeutic procedures for the comorbid conditions (1). Furthermore, in those settings, the incidence of AKI in children is reported high (2) and is usually linked to post cardiac surgery, sepsis, multi-organ failure and exposure to nephrotoxic agent (2-3). In low-income countries, there is paucity of data on the epidemiology of AKI although it is thought to be high with an estimated 85% of people with AKI living there (1-2). In Sub-Saharan Africa, AKI is usually community-acquired. Young people are mainly affected and mortality is high due to delays in presentation, diagnosis and care (1, 4-5). Olowu et al. reported an overall mortality of 34% in children and 32% in adults which rose to 73% in children and 86% in adults when dialysis was needed but not received.

AKI is found in multiple settings and is commonly first encountered by non-specialized health care providers both in developed and developing areas. Indeed, most AKI cases are managed by non-nephrologist who may be unfamiliar with risk factors and early manifestations of the disease, contributing to delayed recognition and suboptimal management, especially in children. Bhojani et al. in the United Kingdom revealed that only 26% of paediatric AKI was recognised (6). The picture may be worse in low- and middle-income areas where lack of access to appropriate medical care, lack of dialysis facilities and financial constraints are more common. Moreover, available data on AKI epidemiology in those areas are mostly based on studies in single large tertiary specialist hospitals with nephrology services. Little is known about paediatric AKI in health facilities in primary healthcare settings which usually don't have nephrology services. We sought to describe the epidemiology and outcome of AKI among paediatric admission in district hospital in Cameroon.

Methods

Study setting

Cameroon is a lower middle-income country with around 26 million inhabitants, half of whom live in urban areas. Primary health care is provided in line with the health district framework proposed by the World Health Organization (WHO) Regional Office for Africa. Healthcare structures found in a health district include health centers (usually managed by a nurse) and a district hospital (usually managed by a medical doctor). Douala is the most populated city of the country and had seven health districts with six district hospitals at the time of this study. Most of the medical and paediatric admissions are managed by general practitioners as specialized physicians, including paediatricians are usually not available or insufficient to take care of all the patients. We conducted this observational study descriptive study over a 4 months (February to June 2019) period in the paediatric wards of 3 of the 6 district hospitals chosen randomly.

Patients

We prospectively screened children aged 2-18 years on admission for AKI risk factors using the NICE (National Institute for Health and Care Excellence) [CG169] recommendations (Table 1) (7). Consenting children with parental assent with AKI risk factors were included in the study. We excluded children with known chronic kidney disease.

Procedure

For each participant and upon inclusion we collected relevant socio-demographic and clinical data were after a complete clinical examination. We performed a dipstick urinalysis and monitored urine output. Urine was collected in a container for children who were conscious able to express themselves when to urinate and a peniflow/urinary catheter was used for unconscious patients.

A random venous blood sample was thereafter collected for serum creatinine assay and repeated after 48 hours to diagnose AKI. Serum creatinine assay was done by the enzymatic method by spectrophotometry.

All participants were followed up till death or hospital discharge. In addition, for participants with AKI, the severity, plausible mechanism and aetiology of AKI were identified, and creatinine assay was again done on hospital discharge to evaluate renal recovery. For participants without AKI, screening for AKI was done in case of incident risk factors or decrease in urine output. Laboratory parameters such as haemoglobin level, white blood cell count or malaria test were registered if available.

AKI was defined according to the serum creatinine based modified Kidney Disease Improving Global

Outcomes (KDIGO) 2012 and classified using the KDIGO 2012 severity classification. The following definitions were used:

- AKI was defined according to the following criteria:
  - An increase or a decrease in serum creatinine by≥0.3mg/dL between 48 hours.
  - An increase of at least 50% of the baseline creatinine (creatinine at admission) during the hospitalization.
- Pre-renal AKI was diagnosed based on history, sign of hypovolemia with urine dipstick gravity >1020, urea and creatinine ratio of more than 30 and normalization of renal function with volume expansion.
- Anuria was defined for urine volume <0.3 mL/kg/h.
- Polyuria was considered as urine volume >2.5 mL/kg/h.
- Acute tubular necrosis was diagnosed based on history, presence of risk factors, urinary dipstick gravity<1015 and recovery with a polyuric phase.
- Complete renal recovery was defined as normalization of serum creatinine at discharge,
- Partial recovery was registered as decrease in serum creative by at least 50% but without normalization at discharge.
- Nephrotoxins was defined as exposure to know nephrotoxic drug such as non-steroid anti-inflammatory drug (NSAID), aminoglycoside, iodine contrast or traditional medicines.
- Sepsis was diagnosed based on systemic inflammatory response syndrome associated with evidence or suspected infection.
- Malaria was diagnosed based on fever and a positive thick blood smear or rapid antigenic test for plasmodium falciparum. Severe malaria was defined according to WHO criteria (8)
- Anaemia was defined as haemoglobin level <10g/dl and severe anemia by haemoglobin level<7 g/dL.
- Leukocytosis was defined as white blood cell count>10,000 cell/mm^3.

The study was approved by the Douala University Ethic Committee. Analysis of the data was performed using SPSS (Statistical Package for the Social Sciences) version 22. Continuous data was summarized as mean±standard deviation or median (25^{th}-75^{th} interquartile range IQR) as appropriate, while categorical data was presented as percentages.

Table 1: Assessment of risk of AKI according to NICE recommendation (7)

Risk factor of acute kidney injury in acutely ill patient
Chronic kidney disease
Heart failure
Liver disease
Diabetes mellitus
History of acute kidney injury
Neurological or cognitive impairment or disability, which may mean limited access to
Fluids because of reliance on a carer
Hypovolaemia e.g. diarrhoea
Nephrotoxins e.g. NSAIDs, iodinated contrast, aminoglycoside, acyclovir, vancomycine
Symptoms or history of urological obstruction
Sepsis
Hypertension
Antihypertensive medications in the setting of hypotension
Additional factors for children and young people
Cardiac surgery
Diabetes keto-acidosis
Haematological malignancy
Hypotension
Trauma
Severe diarrhoea
Malignancy including leukemia and non-Hodgkin lymphoma
Haemato-oncologic pathologies

Results

In all, 82% (n= 173) of the 211 patients admitted during the study period were at risk for AKI. However, 19 (11%) of the 173 did not consent to the study. Of the 154 participants enrolled, 54.5% (n=84) were male sand the median age was 6 years [IQR 3-10]. Though comorbid conditions were rare, malnutrition and sickle cell anaemia were the most common. Main risk factors for AKI were sepsis, volume depletion and exposure to nephrotoxins (Table 2). Half of patients (n=80, 52%) had more than 2 risk factors.

Table 2: socio-demographic characteristics, comorbidities and risk factors

Variable	Effective (N=154)	Percentage
Sex		
Male	84	54.5
Female	70	45.5
Age		
2-6 years	92	60
6-12 years	42	27
12-18 years	20	13
Residency		
Urban	151	98
Rural	3	2
Comorbidity		
None	136	88.5
Malnutrition	10	6.5
Sickle cell anaemia	9	6
HIV infection	2	1.3
Down syndrome with cardiac malformation	1	0.65
Risk factor of AKI		
Sepsis	149	96.7
Volume depletion	105	68.2
Nephrotoxins (n=60)		
Aminoglycoside	35	22.8
Traditional medicines	27	17.5
NSAIDS	2	1.3
Anaemia with decompensation	24	15.6
Sickle cell crisis	2	1.3
Decompensated heart failure	1	0.65
Lymphoma	1	0.65

NSAIDS non-steroidal anti-inflammatory drugs

Infections, mainly severe malaria, were the main admission diagnosis (Table 3). Most of the children had hypotension (n=102; 66.3%) with median systolic and diastolic blood pressure of 82 [IQR 78-100] mmHg and 40 [IQI 40-60] mmHg respectively. The median urine output was 0.82 [IQR 0.63-1.03] mL/kg/h. Sixteen patients (10.4%) had abnormalities on urinary dipstick.

Anaemia was common (n=81, 52.6%) and 31ts (20.1%) had severe anaemia. Leucocytosis was found in 28.6% of patients and twenty-eight (18%) patients had platelet counts below 100,000/mm3 (Table 4). In all, 19 of the 154 participants had AKI, thus an incidence of 12.3%. Participants with AKI were significantly older and more likely to have febrile diarrhoea than those without AKI (Table 5). The spectrum of AKI risk factors was similar in both groups, but hypovolemia was more prevalent in patient with AKI (84.2% vs. 66%, p=0.08) without any statistically significant difference. Although statistically non-significant, the length of hospital stay was longer in participants with AKI (AKI=4 [IQR 2-8] days, no AKI = 3 [IQR 2-6]; p=0.06) Figure 1A.AKI was mainly community-acquired

(n=16, 84%), and nine of the 19 cases of AKI were in Stage 3. AKI was pre-renal in 12 of the 19 cases (Table 6). All three cases of hospital acquired AKI were associated with aminoglycoside use.

The one patient who had an indication for dialysis (uremic encephalopathy and anuria>24 hours) died without receiving dialysis due to delays (due to lack of funds) in transfer to a dialysis center. Of the 18 survivors in the AKI group, two with prerenal AKI stage 1 left against medical advice, 71.7% (n=14) had complete recovery of renal function, and 2 had partial recovery on hospital discharge.

The median length of hospital stay was significantly longer in participants with AKI stage 3 (stage 1=2 [1-5] days; stage 2=3 [2-4] days; stage 3=8 [4-12] days; p=0.033- Figure 1B) and in those with hospital-acquired AKI (Community acquired=3 [2-8] days; hospital acquired 10 (5-12)] days; p=0.036- Figure 1C).

Table 3: clinical characteristics of patients

Variable	Effective (N=154)	Percentage
Admission diagnosis		
Infections (n=149)		
Severe malaria*	91	59.1
Community acquired Pneumonia	14	9
Pharyngitis / otitis	12	7.8
Febrile diarrhea	10	6.5
Meningitis	9	5.9
Urinary tract infection	7	4.5
Erysipelas/myositis	4	2.6
Septic arthritis	2	1.3
Tuberculosis	1	0.65
Herpes Zooster	1	0.65
Appendicitis	1	0.65
Indeterminate sepsis	6	3.9
Non-infectious (n=5)		
Sickle cell crisis	2	1.3
Decompensated heart failure	1	0.65
Paracetamol intoxication	1	0.65
Lymphoma	1	0.65
Clinical parameters		
Hypotension	102	66.3
Dehydration	80	52
Oliguria/anuria	14	9
urinary dipstick parameters		
Proteinuria	11	7.1
Haemoglobinuria	12	7.8
Leucocyturia	10	6.5

*Nine patients had severe malaria associated with another infection

Table 4: Full blood count data

Variable	Median	[25TH - 75TH Interquartile range]
Haemoglobin level (g/dL)	9.8	[7.3-11.4]
White blood cell count (cell/mm3)	8000	[5700-12100]
Platelet count (cell/mm3)	157500	[113250-246000]

Table 5: comparison of paediatric admission according to AKI

Variable	Participants with AKI (%) n=19	Participants without AKI (%) n= 135	p-VALUE
Demographic data			
Sex (male)	9 (47.4)	75 (55.5)	0.33
Age in years (median) [25th -75th interquartile range IQR]	8 [5-13]	6 [3-8]	0.054
Diagnosis on admission			
Malaria (n= 91)	9 (47.4)	82 (60.7)	0.19
Pneumonia (n=14)	3 (15.8)	11 (8.2)	0.23
Febrile diarrhea (n=10)	5 (26.3)	5 (3.7)	0.001
Meningitis (n=9)	2 (10.5)	9 (6.7)	0.4
Urinary tract infection (n=7)	1 (5.3)	6 94.5)	0.6
Risk factors			
Hypovolemia (n=105)	16 (84.2)	89 (66)	0.08
Sepsis* (n= 68)	8 (42.1)	60 (44.5)	0.57
Nephrotoxin exposure (n= 60)			
aminoglycosides	6 (31.6)	29 (21.5)	0.45
traditional medicine	4 (21)	23 (17)	0.27
NSAIDS	-	2 (1.5)	-
Decompasentated anemia (n=24)	5 (26.3)	19 (14)	0.2
Sickle cell crisis	-	2 (1.5)	-
Cardiac failure	0	1 (0.75)	-
lymphoma	0	1 (0.75)	-

*Malaria excluded

Table 6: AKI characteristics and outcome

Variable	Frequency (n=19)	Percentage
Type of AKI		
Community-acquired AKI	16	84
Hospital-acquired AKI	3	16
Severity of AKI		
Stage 1	6	31.6
Stage 2	4	21
Stage 3	9	47.4
Mechanism of AKI		
Pre-renal	12	63.2
Acute tubular necrosis	7	36.8
Etiologic factors		
Diarrhoea/ vomiting	8	42.1
Malaria (n=7)		
Black water fever	4	21
Dehydration	3	
Nephrotoxins (n=5)		
Aminoglycosides	3	15.8
Traditional medicines	2	21
Sepsis (n=4)		
Bronchopneumonia	2	10.6
Urinary tract infection	1	5.3
Sepsis of unknown aetiology	1	5.3
Outcome at hospital discharge		
Alive with complete renal recovery	14	73.7
Alive with partial renal recovery	2	10.5
Left against medical advice in AKI stage 1	2	10.5
Death	1	5.3

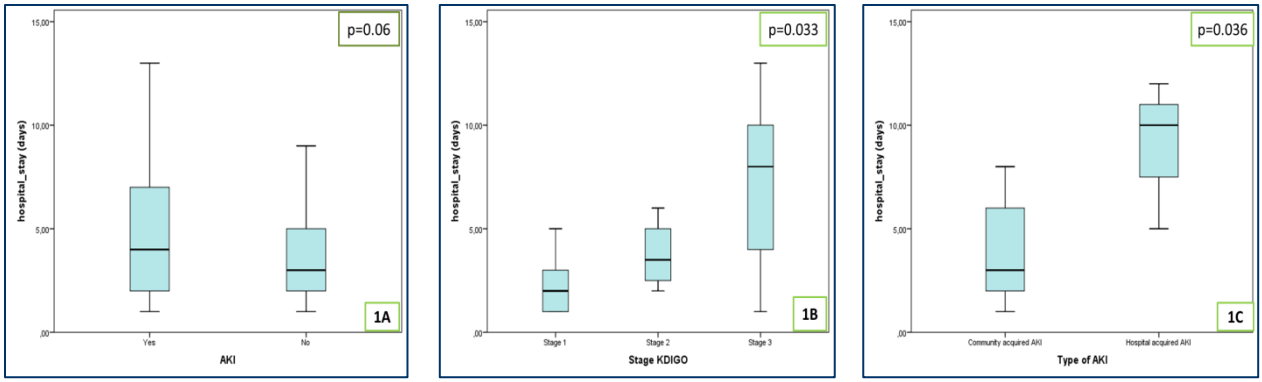

Figure 1: Median length of Hospital stay according to 1A) presence of AKI, 1B) AKI severity, 1C) type of AKI

Discussion

Paediatric admissions in district hospitals in our setting present a high prevalence of risk factor of AKI, with sepsis, hypovolemia and use of nephrotoxin frequent. Among patients at risk, the incidence of AKI was 12.3%. Community-acquired AKI was common (84%, n=16) and nine of the 19 patients with AKI were in stage 3. Pre-renal AKI (63.2%) and acute tubular necrosis (36.8) were the sole mechanisms of AKI seen. Gastrointestinal loss and malaria were the most common aetiologies. Mortality rate was low (5.3%) and 73.7% had complete renal recovery at hospital discharge.

We found that 82% of paediatric admissions were at risk of AKI, suggesting that more than 2/3 of children admitted in district hospital in Cameroon may develop AKI. Sepsis, malaria, hypovolemia were leading risk factor of AKI in our setting as noted by previous reports on paediatric AKI in tertiary hospitals in Cameroon (9-10) and other resource-limited regions (3, 5). Indeed, similar to our observation, infections, malaria and diarrhoeal diseases are the usual pathologies found among paediatric admission in both primary and tertiary health structures in low-income countries (11-12). However, in primary health facilities such as district hospitals, children are usually managed by nurses and general practitioners who may be unfamiliar with risk factors and early manifestations of AKI leading to late recognition.

The incidence of AKI was 12.3% suggesting that one child out of ten admitted in a district hospital may have AKI. This incidence is high compared to previous report in Sub-Saharan Africa. In Nigeria, AKI accounts for 1 to 3% of paediatric hospital admissions (13) while a prevalence of 0.91% is reported in Senegal (13). However, previous publications mostly originated for tertiary hospital with nephrology unit. Moreover, many of them are retrospective, thus they probably revealed only the tip of the iceberg as our result suggested that incidence of AKI among paediatric admission in primary care is high. Active screening of paediatric admission for AKI risk factors and renal function monitoring in those at risk as was done in the present study is more likely to reveal the true picture. Indeed the 5R's strategy proposed by the ISN 0 by 25 initiatives is designed for raising awareness and educating care givers on management of AKI. Its focus on 5 points: Risk assessment by identification of high risk individuals; early Recognition which involved monitoring of risk individual for prompt diagnosis of AKI; adequate Response meaning effective intervention in case of AKI such as hydration, relieve obstruction, remove/avoid nephrotoxin and nephrology referral; Renal support (dialysis) and Rehabilitation which included follow-up, renal recovery and functional assessment. Community acquired AKI was more frequent resulting from community acquired infections as has been previously reported in other low-income settings. All The 3 patients with hospital acquired AKI were associated with aminoglycoside use. Aminoglycoside such as Gentamycin are cost-effective antimicrobial agents very available in sub-Saharan Africa which are commonly used in inpatient care. However, its use is associated with AKI in 20-62% of children (15-16). The high proportion of AKI stage 3 observed in the present study is well known in low income countries and may reflect delays in presentation to hospital (3, 5,

13, 17). Several factors may delay presentation to hospitals for care in low income countries; lack of funds, cultural biases and geographical access to health structures commonly reported (5).

In contrast to the poor short-term outcomes reported in previous studies in low-income settings, we observed a low mortality and good renal recovery in the present study. The systematic screening for patients at risk of AKI, allows for timely correction of risk factors, renal function monitoring and adequate management of those with AKI. The high proportion of pre-renal azotaemia which is amenable to fluid resuscitation may also explain these outcomes. This emphasizes the need for implementation of the 5R's strategy especially in this primary care settings were AKI is dominated by community acquired pre-renal azotaemia from causes which can be corrected when detected early thus preventing AKI (1). Despite major dialysis subsidies by Government in Cameroon, previous studies have shown lack of funds and choice-restriction in children to limit access (17).The sole patient who needed dialysis, died in want of it due to lack of funds. The only public dialysis centre in Douala is situated in a tertiary hospital where a session of dialysis costs about 10USD (150USD in private dialysis centre); however patients have to pay for accessories such as dialysis catheters and laboratory tests. In addition patients must pay the hospital bills out-of-pocket in the primary care setting before being transferred for dialysis in the tertiary hospital where they are equally required to pay a deposit amount as risk in case they are unable to pay for services at the end of care. Moreover, peritoneal dialysis which is thought to be cheaper and more adapted to children is not readily available in the city.

Limitation

This study had some limitations. First, we may have underestimated the true burden of AKI for two reasons: exclusion of neonates and children under 2 years old who have the highest burden of AKI among paediatric populations; and the non-use of the urine output (3, 18, 19). Secondly, we did not assess the response to AKI risk factors and AKI which may have influenced the incidence and outcome of AKI. Thirdly, the presumed mechanism of AKI was not based on robust laboratory parameters. Finally, the small number of AKI events may limit the generalisation of the patient outcomes. Despite these limitations, our study presents several strengths: it is the first study on AKI epidemiology in a primary care setting in Cameroon and one of the few in sub-Saharan Africa. We prospectively identified and followed up participants at risk of AKI using the 5R strategy thus demonstrating its feasibility and utility in a primary care setting of a low income country. We had a very low rate of loss to follow up thus limiting biases in outcomes.

Conclusion

Risk factors of AKI are very common in paediatric admissions in the primary health settings in Cameroon with at least one out of 10 admitted children with risk factors developing AKI. Risk factors are mainly due to preventable and common childhood ailments such as bacterial infections, malaria and diarrhoeal diseases. Routine screening for risk factors, monitoring of renal function in those at risk and appropriate response to risk factors and AKI may limit the incidence and improve outcomes of AKI. Urgent efforts are needed to raise awareness of primary health caregiver on AKI in general and the 5R strategy in particular.

Conflict of Interest

The author declares no conflicts of interest.

Ethics

The study was approved by the Douala University Ethic Committee.

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Authors Contributions

Conceptualization, A.G and F.H; methodology, A.G and K.F; software, MM and N.E; validation, A.G, F.H and H. MP; formal analysis, B.I; investigation, B.I; resources, F.H and B.I; data curation, A.G and K.F; writing original draft preparation, F.H and N.V; writing review and editing, F.H, H. MP and A.G.; visualization, M.M and N.V; supervision, A.G.; project administration, B.I. and N.E.

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