

The Clinical Pattern and Outcomes of Acute Kidney Injury in a Semi-Urban Hospital Setting in Cameroon

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Abstract

Background: Acute kidney injury (AKI) is a common disorder with high morbi-mortality especially in developing countries. In contrast to high income regions, AKI in these areas tend to be more community-acquired and affect young people. As in most Subsahara countries, previous studies on AKI in Cameroon were carried out in urban tertiary hospitals. Data on the clinical pattern and outcomes in semi-urban is lacking and may be quite different of urban setting.

Objective: To describe the clinical pattern and outcomes of AKI in Buea Regional Hospital.

Methods: We conducted an 18 months' hospital-based observational retrospective study in the regional hospital of Buea, a semi-urban second category health facility of the South-West region of Cameroon. We excluded patients with known CKD (Chronic Kidney Disease) and incomplete data. AKI was diagnosed and classified according to the 2012 KDIGO criteria. Renal outcome was evaluated at 1 month.

Results: Of the 196 participants included, 57.7% were males and 10.7% children. The median age was 45 years. HIV infection, hypertension and diabetes were the main comorbidities. AKI was community-acquired in 95% and stage 3 was found in 59%. Sepsis (37.2%), volume depletion (25%) and nephrotoxicity from herbal remedies (15.3%) were the main etiologic factors. Renal AKI was found in 72% of patient and was mostly due to ATN (56.6%). Obstetrical AKI was mainly due to post-abortum sepsis and AKI related malaria were the main etiologies of pediatric AKI. In all, 71 (36%) participants had indications for dialysis but only 52 (73%) accessed it. Lack of appropriate dialysis technique and lack of funds were the main reasons for dialysis non-access. In-hospital mortality was 37.2%. Among survivors, renal recovery was complete in 65%, partial in 21%, and no recovery in 3%. Stage 3 disease was the only predictor of poor renal recovery at one month.

Conclusion: AKI in this semi-urban hospital setting is community acquired and affected young individual with previous comorbidities such as HIV/AIDS, hypertension and diabetes. It is mainly caused by infections, volume depletion and herbal toxins.

Keywords: AKI; ATN; Sepsis; Comorbidity; Volume depletion; Dialysis; Semi-urban setting; Cameroon

Introduction

Acute Kidney Injury (AKI) is an abrupt and sustained decline in kidney function, which can be reversible if detected early enough. Clinically, its manifestation is due to an acute increase in nitrogen waste product measured by blood urea nitrogen and serum creatinine levels—over the course of hours to weeks. AKI is associated with substantial morbidity and mortality worldwide. However epidemiology profile of AKI is quietly different among region. In high income countries, hospital-acquired AKI tend to be more frequent, affect older people generally with several comorbidities [1]. In contrast, in low income region such as Sub-Saharan Africa, AKI tend to be more

community-acquired and affect young otherwise healthy individuals [1]. AKI in these areas is also characterized by poor outcomes. Although recent studies have shown an increased in dialysis access, treatment with dialysis is often unavailable or too costly in developing regions, especially in children [2,3]. Delays in diagnosis and management mainly explain this poor outcome. Increase in dialysis access could be the reflection of programs such as the Saving Young Life (SYL) ISN's program and government effort such as in Cameroon. In this country, hemodialysis services are widely available and hemodialysis is partially funded by the state for both AKI and ESRD (End Stage Renal Disease). However, if recent studies on AKI in sub-Saharan Africa underline the disease burden and its poor outcomes, most of them were conducted in urban tertiary hospital. The picture in rural and semi-urban healthcare setting may be completely different since socio-economic profile of patients, quality of healthcare

personnel and sanitary infrastructure are not the same. The aim of this study was to describe the epidemiology and one month outcome of AKI in a government -funded semi-urban hospital with conventional hemodialysis facilities.

Methodology

The Buea regional hospital is located in the capital of the South-West region and serve as a main reference hospital of this region with an estimated population around 1-5 million. It has 180 beds, a WHO (World Health Organization) certified laboratory, radiology services as well as internal medicine, pediatric, surgery and gynecology-obstetric services with both in and outpatient clinics. It is a teaching hospital of the Faculty of Health Science of Buea. It is also the nephrology and HIV reference center of the region and it host the unique hemodialysis center of the South-West region.

No pediatric nephrologists are available and children with kidney diseases are managed in adult unit, which is held by 2 nephrologists. Bicarbonate dialysate with polysulfone dialyzers are used. Serum creatinine assay are not routine for all patients admitted in the hospital. SYL project with peritoneal dialysis for children is more than 300 km away.

We retrospectively reviewed the medical records of all patients admitted with the diagnostic of AKI from 1st November, 2015 to 28th February, 2017 at the Buea regional hospital. Patients with known CKD and records with insufficient data for the diagnosis of AKI were excluded. We noted relevant clinical data including: etiology, mechanism and type of AKI, access to dialysis, in-hospital mortality and renal recovery at one month of diagnosis.

The diagnostic of AKI was based on the following criteria:

- Increase or decrease in serum creatinine >0.3 mg/dl from baseline within 48 hours
- Increase or decrease in serum creatinine $>50\%$ from baseline within 7 days
- Urine output <0.5 ml/kg/hour over 6 hours
- Baseline creatinine referred to the first creatinine after the admission of the patient.

The KDIGO 2012 classification was used to stage the severity of AKI [4]. Renal outcomes were reported only for survivors at hospital discharge and were evaluate at 1 month. Complete renal recovery was definite as normalization of serum creatinine; partial recovery as persistence of renal failure without need of dialysis in those who were receiving dialysis or decrease of serum creatinine between 1.2-1.5 times baseline and no recovery as decrease of serum creatinine less than 1.2 times baseline or dependency on dialysis.

Diagnosis of etiologies, mechanism and type of AKI were clinical and the following definitions were used:

- Acute tubular necrosis (ATN) was diagnosed based on history, presence of risk factors, urine indices when they were available and recovery with a polyuric phase.
- Pre-renal AKI was diagnosed based on history, presence of risk factor, urea and creatinine ratio of more than 20 and urine indices when they were available.
- Nephrotoxins AKI was diagnosed based on a history of ingestion of know nephrotoxic drug (NSAI: Non-Steroidal Anti-

Inflammatory Drug, ECI: Enzyme Conversion Inhibitor, cisplatin, aminoside, iodine contrast) or herbal remedies.

Need of dialysis referred to patients with indications for dialysis and access to dialysis to those with indications for dialysis and that were actually dialysed.

Analysis of the data was performed using SPSS version 20. Continuous data was summarized as mean or median as appropriate, while categorical data was presented as percentages.

Logistic regression model was used to identify factors associated with poor renal outcome. The level of statistical significance was set at a p-value of <0.05 .

Ethical approval was sought and granted by the Faculty of Health Sciences Institutional Review Board of Buea.

Results

A total of 211 AKI were identified during the study period and 15 were excluded due to incomplete data (n=11) and underlying CKD (n=4).

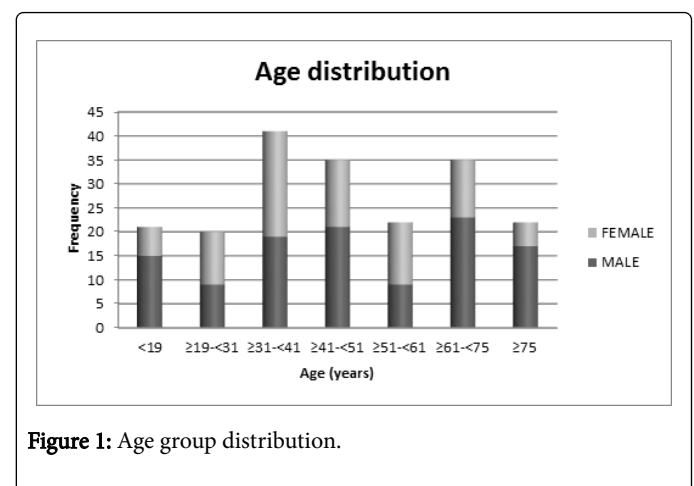


Figure 1: Age group distribution.

Of the 196 patients included, most were male (57.7%) with a median age of 45 years (5.5-86); 21 patients (10.7%) were children (Figure 1).

The main comorbidities (Table 1) were HIV (30.6% n=60), hypertension (28%, n=55) and diabetes (22%, n=43). AKI was community-acquired in 95%, and 59% of cases were in KDIGO stage 3 (Table 2).

Renal AKI was the most frequent type of AKI (72%, n=141) with ATN the main clinical form.

Obstetrical AKI was found in 5 patients (2.5%) and were due to post-abortion sepsis (n=3), post-partum bleeding (n=1) and post caesarian ligation of ureters (n=1).

Pediatric AKI was mainly related to malaria (n=11, 52.4%); other etiologies were diarrhea (n=4), septicemia (n=3), nephrotic syndrome (n=2) and post-infectious acute glomerulonephritis (n=1).

Variables	Frequency (n)	Percentage (%)
Age*		
All patients (n=196)	45 [5.5 - 86] years	-
Adult patient (n=175)	48 [21 - 86] years	-
Pediatric patient (n=21)	11 [5.5 - 14.5] years	-
Sex		
Male	113	57.7
Diagnosis setting		
Buea regional hospital services	121	62
Medicine	84	43
Pediatrics	21	11
Surgery	10	5
Emergency	6	3
Gynecology/obstetric	-	-
Other health facilities	75	38
First category	59	31
Second category	14	7
Co-morbidities		
HIV	60	30.6
Hypertension	55	28.1
Diabetes	43	21.9
Malignancy	27	13.8
Heart Failure	20	10.2
Liver disease	13	6.6
Malnutrition	3	1.5
*median [extremes]		

Table 1: Patients characteristics.

Variables	Frequency	Percentage
Severity of AKI		
Stage 1	52	26.5
Stage 2	28	14.3
Stage 3	116	59.2
Mechanism of injury		
Prerenal	41	21
Intrinsic	141	72

ATN	111	56.6
AIN	16	8.2
Glomerular lesion	7	3.6
Vascular lesion	1	0.5
Unknown	6	3.1
Post-renal	14	7
Etiologic factors¹		
Bacterial infection*	86	-
Volume depletion [#]	50	-
Drug	30	-
Malaria-related	21	-
Heart failure	15	-
Pelvic tumors ^{&}	14	-
Herbal remedies	13	-
Hepato-renal syndrome	5	-
Obstetrical	5	-
Acute glomerulonephritis	4	-
Nephrotic syndrome	3	-
ATN: acute tubular necrosis, AIN: acute interstitial nephritis, 1 most patients had multiple etiologic factors *Bacterial infection included 73 septicemia, 5 pneumonia and 8 pyelonephritis; # Volume depletion included 47 gastro-enteritis and 3 post-operative bleeding; & Pelvic tumors included 8 prostate tumor and 6 cervix cancer.		

Table 2: AKI characteristics.

Dialysis (Table 3) was indicated in 71 patients (36%) but done in only 52 participants (73%). In-hospital mortality was 33% (n= 64). At one month of post hospital discharge, 86(65%) patients had complete

renal recovery and 14 (11%) patients were lost to follow-up (Figure 2). Stage 3 disease (Tables 4 and 5) was the only independent predictor of poor renal recovery at one month (OR 2.8, CI 1.2-6.5, p=0.01).

Variables	Frequency	Percentage
Need of dialysis	71	36
Access to dialysis	52	73
Reasons for no dialysis n= 19		
Lack of appropriate materials	6	30
Financial constraints	13	70
Indication of dialysis included 52 uremia sign, 36 prolong anuria, 10 refractory pulmonary edema and 5 refractory hyperkalemia		

Table 3: Dialysis access.

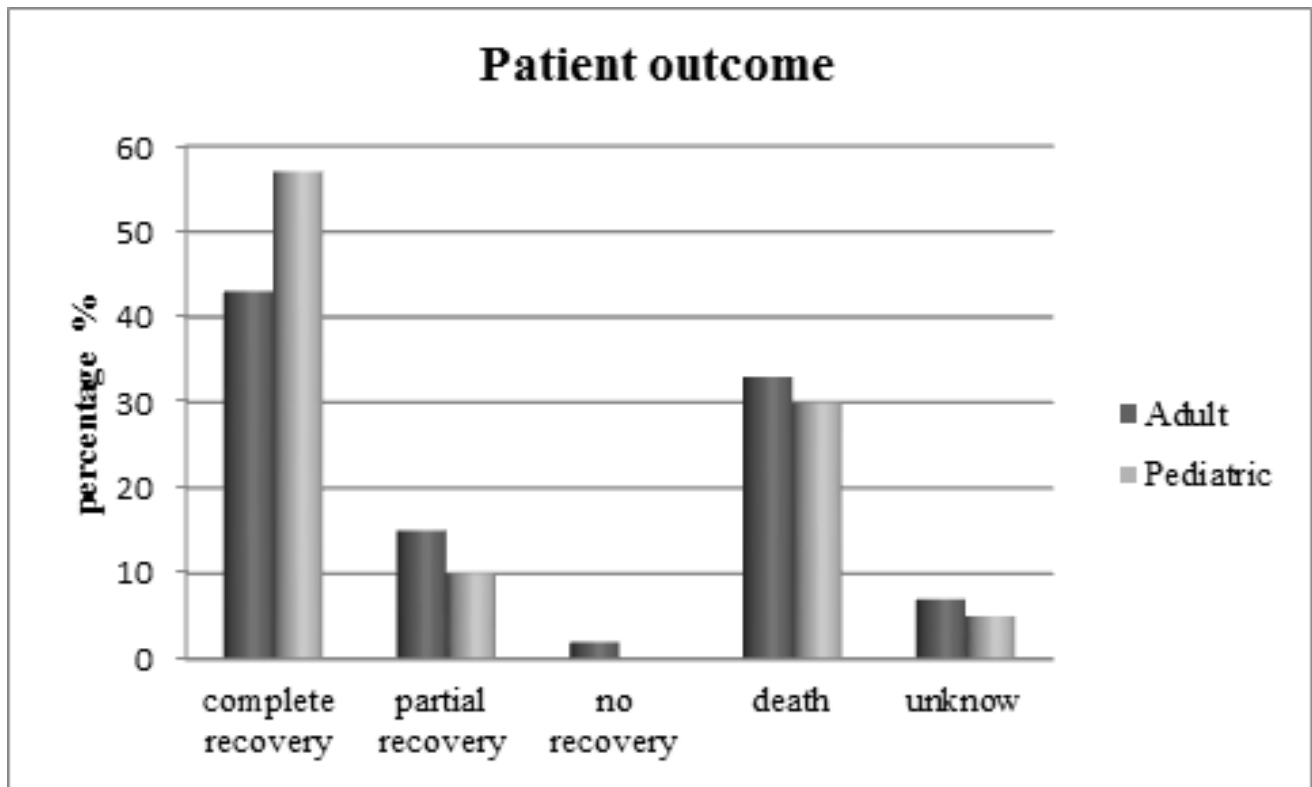


Figure 2: Overall patient outcome.

Variables	Poor recovery n=32	Complete recovery n= 86	OR (95% CI)	p value
Gender				
Female	12 (23.5)	39 (76.5)	0.8 (0.4 - 1.8)	0.7
Male	20 (29.8)	47 (70.2)		
Advanced age				
>60	5 (17.8)	23 (82.2)	1.03 (0.5 - 2.3)	0.9
≤ 60	27(30)	63 (70)		
Stage				
Stage 3	30 (60)	20 (40)	2.4 (1.1 - 5.1)	0.02
Stage 1 and 2	2 (3)	66 (97)		
Mechanism				
Intrinsic	30 (33.7)	59 (66.3)	1.9 (0.8 - 4.4)	0.1
Pre-renal and postrenal	2 (6.9)	27 (93.1)		
Type of AKI				
c-AKI	44 (34.9)	82 (65.1)	1.1 (0.2 - 5.0)	0.9
h-AKI	2 (33.3)	4 (66.7)		

Comorbidity				
≥1	29 (36.3)	51 (63.7)	2.5 (0.9 - 5.0)	0.07
None	3 (7.9)	35 (92.1)		
Hypertension				
Yes	12 (31.6)	26 (68.4)	1.7 (0.8 - 3.3)	0.2
No	20 (25)	60 (75)		
Diabetes				
Yes	3 (12)	22 (88)	0.8 (0.3 - 2.0)	0.6
No	29 (31.2)	64 (68.2)		

Table 4: Factors associated with poor renal recovery in bivariate analysis

Variables	Poor recovery n= 32	Complete recovery n= 86	Adjusted OR (95% CI)	Adjusted p value
Stage 3	30 (60)	20 (40)	2.8 (1.2 - 6.5)	0.01
Intrinsic AKI	30 (33.7)	59 (66.3)	1.6 (0.7 - 3.9)	0.4
At least one comorbidity	29 (36.3)	51 (63.7)	2.0 (0.8 - 5.0)	0.4

Table 5: Factors associated with poor renal recovery multivariate analysis

Discussion

As noted by previous Sub-Saharan studies, AKI in our setting is mainly a community-acquired condition affecting young adults. Infection including malaria, volume depletion and nephrotoxic agents are the main etiologic factors. Many authors have reported that AKI in low income countries typically affects previously healthy individual [5], we found a high burden of comorbidities in our series. More than 40% of our patients already have comorbid condition mostly HIV/AIDS, hypertension and diabetes - before the diagnostic of AKI. This high burden of comorbidities was also noted in a Cameroonian urban tertiary hospital [3] and probably reflects the epidemiological transition from communicable to non-communicable diseases reported in resource-limited settings.

Unlike in developed countries, AKI in developing countries mainly affected young people. More than 75% of our patient was less than 60 years. The disparities in age between low-income and high-income countries may reside in the differences of risk factors of AKI in these populations. While AKI in low income countries is mainly community-acquired resulting from infections and volume depletion; in the high-income countries, AKI is often hospital-acquired due to complications of diagnostic procedures and therapies of multiple cardiovascular disease and malignancies which are more frequent in the elderly.

In high-income countries no gender-bias in the incidence of AKI has been reported. Although higher female frequencies have been reported in some studies in Nigeria with a high proportion of pregnancy-related AKI [6,7], a male predominance is typically found in sub-Saharan Africa [2,5]. Our results and previous urban Cameroonian studies confirm it [3]. This male predominance may reflect the bias in access to healthcare seen in these areas. Males who

are usually the breadwinners access hospitals more frequently and; even in children, males are more considered than girls and therefore are more likely to be taken to hospital [8].

This study shown that AKI is predominantly community-acquired in our setting as noted by others reports in Sub-Saharan Africa. Olowu and al in a systematic review reported the proportion of community-acquired acute kidney injury between 72.8% and 82.9% [2]. Poverty, poor sanitation and ignorance may explain the high prevalence of communicable diseases. As they also facilitate the use of alternate medicines (such as herbal remedies), leading to either nephrotoxicity or delays in presentation to hospitals for the appropriate care [9,10]. Delays in AKI recognition also result from the low awareness of physicians [11]. Over half of our patients were at KDIGO stages 3 on diagnosis and similar results were found in a previous study in an urban area of Cameroon. Contrary to previous studies in Sub-Saharan African [2,9,12], we did not identify pre-renal AKI as a major mechanism of injury. Most of our patients, as in previous report in Cameroon [3] had intrinsic renal disease. Since sepsis and volume depletion were common, it plausible that these patients originally had prerenal disease but present late; underlying again the burden of delay diagnostic and late presentation.

Malaria and herbal remedies remain a major cause of AKI in sub-Saharan Africa. As noted by other [3], malaria was the main etiology factor of AKI among pediatric. High parasitemia, age under 5 years, pregnancy and HIV are known risk factors [13]. Used of herbal remedies was also comparable to that of urban setting [3] and may be related to low socioeconomic status and cultural habits. Surprisingly, we observed a low prevalence of obstetric AKI of 2.6%. Obstetric AKI is usually prevalent in developing countries ranging from 4.8% to 19.8% [12,13]. Our result is also inferior to the 11% observed in a Cameroonian urban study [3]. This lower prevalence could be explain

by under diagnosis due to the non- recognition of AKI risk factors and consequently, a low rate of renal function monitoring in our obstetrics and gynecological wards as it has been reported elsewhere [14]. The patients with obstetric AKI in our study were all referrals from other health facilities.

Globally about 36% of our patients required dialysis with the need being higher in children (67%) than adults (30%). Olowu et al. showed a pooled average need for dialysis of 66% in children and 70% in adults with AKI in sub-Saharan Africa [2]. They also reported an improve of access to dialysis increased from 32% in the period 1990-2009 to 82% in the period 2010-2014 in children and from 17% to 47% in adults during the same time periods [2]. Dialysis access in our setting was also high (100% in children and 66.7% in adult) similar to what we found in urban tertiary hospital. As access to dialysis in most Sub-Saharan countries is dependent on availability and ability to pay, the high dialysis access rate found in Cameroon reflects the subsidized cost of hemodialysis as well as the widely availability of dialysis center in the country. Financial constraint and lack of appropriate material were the main causes of non-dialysis access. This was also noted in a previous urban study but financial constraint was less prevalent in urban setting [3].

AKI mortality mainly depends of comorbidity and access to dialysis. We found an hospital mortality rate of 32.7% consistent with findings from urban Cameroonian setting as well as other low-income countries [2,3,15,16]. We observed that non-access to dialysis was responsible for 22% of deaths. At 1 month, 73% of survivors had achieved complete renal recovery; sharply contrast to the 55%, 3 months complete renal recovery rate recorded in urban tertiary setting [3]. The lower renal recovery rates in this study may be explained by the higher rate of severe AKI. Compared to our semi-urban setting, urban AKI patient was more severe (77.4% in stage 3), had more hospital induced AKI (29.4%) and less ATN (25%).

Limits of the Study

This was a retrospective study which tries to describe to clinical pattern of AKI in a semi-rural setting. Indeed, it has all the limits of retrospective study. Diagnosis and type of AKI was mainly based on clinical judgement and urinary dipsticks findings which may have influenced the frequency of the different mechanisms. No histology was available. We also evaluated renal recovery at one month so long term outcomes such as end-stage kidney disease could not be evaluated.

Conclusion

Similar to previous urban studies, AKI in Cameroon semi-urban milieu is frequent and mainly affected young people with previous

comorbidities such as HIV/AIDS. Infection including malaria, nephrotoxic agents and volume depletion are the main etiologic factors. Mortality rate and access to dialysis are also comparable to urban milieu. However, in contrast with urban setting, AKI in semi-urban hospital seem to be more community acquired, less severe and of better renal prognostic.

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