ORGINAL ARTICLE

Aetiologies and Short-term Outcomes of Acute Kidney Injury in a Tertiary Centre in Southwest Nigeria

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ABSTRACT

BACKGROUND: *Acute kidney injury (AKI) has become a global health problem and is associated with increased morbidity, mortality and overall health expenditure. Information on the epidemiology and outcomes of AKI will help to audit practice and advocate for policies that will reduce this burden. This study determined aetiologies, short term outcomes and their predictors in AKI patients in a tertiary hospital in Southwest Nigeria.*

METHODS: *This was an 18-month retrospective study that involved 91 patients with AKI. The socio-demographic information, aetiology, severity and the treatment given to patients were recorded. Outcomes and their predictors were determined using multivariate analysis. P value < 0.05 was taken as statistically significant.*

RESULTS: *The mean age of the study population was 45.12 ±20.67 years. Common causes of AKI were sepsis in 50(54.9%), hypovolaemia in 23(25.3%), cardiac failure in 7(7.7%) and eclampsia in 6(6.6%). Fifty-seven (62.6%) presented with stage 3. Thirty-one (34.1%) had haemodialysis. Forty-eight (52.7%) had complete renal recovery, 35(38.5%) died and 3(3.3%) left against medical advice while five (5.5%) were referred to other hospitals. Stage 3 AKI (Adjusted odd ratio: 6.79, confidence interval: 1.21:38.04, p = 0.029) and age ≥ 65 years (Adjusted odd ratio: 4.14, confidence interval: 1.32-13.04, p = 0.015) were significant predictors of mortality in AKI patients.*

CONCLUSION: *Sepsis and hypovolaemia were the commonest causes of AKI. The associated mortality is still high and factors associated with mortality were late presentation and older age. Early presentation, treatment and making haemodialysis affordable are key to improving AKI outcomes.*

KEYWORDS: *aetiologies, outcomes, acute kidney injury*

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INTRODUCTION

Acute kidney injury (AKI) has become a global health problem due to its increasing incidence in both developing and developed countries.(1,2). The true incidence of AKI is not known especially in developing countries due to poor data collection, underreporting and non-uniform criteria for diagnosis (3,4). Some cases of AKI also go unrecognized while some patients with AKI do not present in the hospitals (5). The hospital-pooled incidence of AKI in a met-analysis that mainly involved studies from Asia, America and Europe in both adults and children was reported by Susantitaphong et al to be 22% and 14% respectively (2). The incidence of AKI ranges between 20-50% among patients admitted in the intensive care unit (6).

It is well established that the burden of AKI is quite enormous. It is associated with increased morbidity, mortality and overall health expenditure (7-9). Acute kidney injury has been reported to be an important risk factor for chronic kidney disease (CKD), rapid progression to end stage renal disease (ESRD) later in life and longterm non-renal morbidity and mortality (10,11). Therefore, measures aimed at reducing the burden of AKI would also translate into reducing the burden of CKD which is beyond what most developing countries like Nigeria could cope with.

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Collaborative efforts of government, international organizations, health care providers and corporate organizations are key to achieving the initiative of the International Society of Nephrology (ISN) of eliminating AKI by 2025. Data on the epidemiology and outcomes of AKI is required to enlighten the public to advocate for policies from the government and corporate organizations that will help reduce the burden of AKI. Determining the aetiologies and outcomes of AKI will also serve as audit of practice of health care workers with the aim of improving practice and reducing the burden of AKI. This will help in directing preventive strategies towards the common aetiologies of AKI.

The aim of this study was to determine the aetiologies, short term outcomes and their predictors in AKI patients in a tertiary health centre in Southwest Nigeria.

METHODS

This study was a retrospective study carried out in Kidney Care Centre, Ondo, Ondo state, Nigeria, which is a state-government owned tertiary hospital located in Southwest Nigeria and receives referrals from other departments within the hospital complex, other hospitals within and outside Ondo state, Nigeria. This study was a retrospective study that covered a period of 18 months between March 2014 and August 2015. Ethical clearance was obtained from ethical committee on research of the Ondo state hospital management board. Inclusion criteria were patients ≥ 15 years of age presenting with AKI or who developed AKI while in the hospital. Patients with CKD or acute or chronic kidney disease were excluded.

Case notes and dialysis records of all patients who fulfilled the inclusion criteria were retrieved and reviewed. Data obtained from patients' records were age, gender, aetiology and stage of AKI at presentation, investigations done, estimated glomerular filtration rate (GFR) at presentation, treatment given, fluid input and output records, number of haemodialysis sessions for those who had renal replacement therapy (RRT) and outcomes following treatment. The estimated GFR was calculated using Modification of Diet in Renal Disease formula which has been validated in Nigerians (12). The possible outcomes in this study were left against medical advice, referral to another hospital, in-hospital mortality, recovery of renal function or dialysis dependence beyond 12 weeks.

Acute kidney injury was defined and staged using Kidney Disease Improving Global Outcome criteria (KDIGO) (13).Acute kidney injury was defined as increase in serum creatinine by 0.3 mg/dl (26.5micromol/L) within 48 hours, or increase in serum creatinine to 1.5 times baseline, which is known or presumed to have occurred within the previous 7 days, or urine volume 0.5 ml/kg/h for 6 hours.

Stage 1: Serum creatinine rise of ≥26 micromol/L within 48 hours or 50-99% rise from baseline within 7 days or urinary output of <0.5ml/kg per hour for more than 6 hours

Stage 2: 100-199% rise in serum creatinine from baseline within 7 days or urinary output of <0.5mls/kg per hour for more than 12 hours

Stage 3: ≥ 200% rise in serum creatinine from baseline within 7 days or concentration of ≥ 354 micromol/L within 48 hr or ≥ 50% rise from baseline within 7 days or any requirement for RRT or urinary output of < 0.3ml/kg per hour for 24 hours or anuria for 12 hours.

Operational Definitions

Renal recovery after AKI: Dialysis independence at hospital discharge (14)

Sepsis: Presence of a proven or suspected microbial infection in the presence of at least two of the following- temperature > 38^0C or < 36^0C, pulse rate >90/minute, respiratory rate > 24cycles/minute, white cell count of > 12,000cells/mm^3 or < 4000 cells/mm^3 (15)

Hypovolaemia: Significant fluid loss with features of dehydration and changes in the cardiovascular system such as tachycardia and hypotension

Surgical AKI: Acute Kidney Injury caused by surgical problems such as intestinal obstruction, enterocutaneous fistula, bone fractures or following surgical procedures

Obstetric/Gynaecologic: Acute Kidney Injury caused by obstetric or gynaecologic conditions such as eclampsia, abortion, ante-partum or post-partum haemorrhage and ectopic pregnancies

Medical AKI: Acute Kidney Injury caused by medical conditions such as gastroenteritis, heart

failure or following medical treatment such as use of nephrotoxic medications

Data were analyzed using the statistical Package for Social Sciences (SPSS) version 17.0 by Chicago Inc. Results were presented in tabular form. Discrete variables were presented as frequency and percentages. Continuous variables were presented as mean and standard deviation for unskewed data and median, interquartile range for skewed data. Chi-square test was used to determine the significance of the observed differences for categorical variables while chi-square with trend was used where the categorical variable was ordinal. Binary logistic regression was used to determine the significant independent predictors of outcomes of AKI. P values < 0.05 were considered statistically significant.

RESULTS

A total of 91 patients (50 males and 41 females) were involved in the study with a mean age of 45.12 ±20.67 years. Sixty-nine (75.8%) of these patients were less than 65 years. The median value and interquartile range of serum creatinine, urea and estimated GFR of these patients were 584.4(304.0)micromol/L, 19.6(15.0)mmol/L and 12.9(12.6) mls/min/1.72m^2 respectively (Table 1).

The causes of AKI in this study were sepsis 50(54.9%), hypovolaemia 23(25.3%), cardiac failure 7(7.7%) eclampsia 6(6.6%) and others 5(5.5%). Medical causes of AKI accounted for 53(58.2%), surgical causes for 20(22.0%) and obstetric and gynaecologic causes for the remaining 18(19.8%) (Table 1).

Table 1: Characteristics of study population

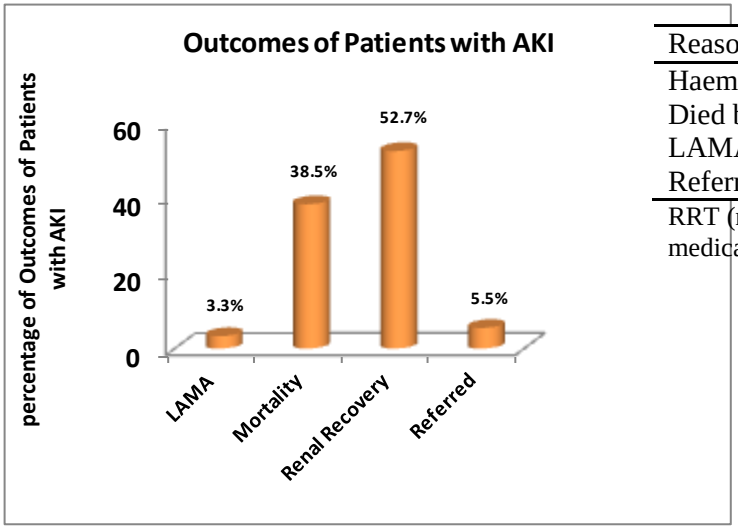
Parameter	Frequency (percentages)/Mean (SD)/Median(IQR) (N=91)
Mean age* (years)	45.12(20.67)
Median serum creatinine†(micromol/L)	584.4(304.0)
Median serum urea† (mmol/L)	19.6(15.0)
Median eGFR† (mls/min/1.72m^2)	12.9(12.6)
Median HD sessions†	3(2)
Age groups	
≤65 years	69 (75.8)
> 65 years	22(24.2)
Gender	
Male	51 (45.1)
Female	40 (54.9)
Aetiology by specialty	
Medical	53(58.2)
Obs&Gyn	18(19.8)
Surgical	20(22.0)
Aetiology	
Cardiac failure	7(7.7)
Eclampsia	6(6.6)
Sepsis	50(54.9)
Hypovolaemia	23(25.3)
Others	5(5.5)
KDIGO Stage of AKI	
1	12(13.2)
2	22(24.2)
3	57(62.6)
Dialysis Required	
Yes	50(54.9)
No	41(47.1)
Dialysed	
Yes	31(34.1)
No	60(65.9)

OBY&GYN (obstetric and gynaecology), LAMA (left against medical advice), eGFR (estimated glomerular filtration rate), IQR (interquartile range), SD (standard deviation),*expressed as Mean (SD), †expressed as Median(IQR)

Fifty-seven (62.6%) of the patients presented with stage 3 AKI, 22(24.2%) with stage 2 AKI and the remaining 12 (13.2%) with stage 1 AKI. Thirty-one (38.5%) of the patients were managed with haemodialysis with a median of 3 dialysis sessions.

The in-patient mortality rate of the patients in this study was 38.5% while 52.7% survived with complete renal recovery. Three patients (3.3%) left against medical advice while five (5.5%) were referred to other hospitals (Figure 1).

Fig 1: Outcomes of Patients with AKI



Ten (52.6%) of the AKI patients who had indication for RRT could not be dialyzed due to haemodynamic instability, 3(15.8%) died before haemodialysis could be administered, 3(15.8%) left against medical advice and the remaining 3(15.8%) were referred to other hospitals (Table 2).

Table 2: Reasons for not receiving RRT despite indication

Reasons for not receiving RRT	n(%)
Haemodynamic Instability	10(52.6)
Died before HD could be administered	3(15.8)
LAMA	3(15.8)
Referred	3(15.8)

RRT (renal replacement therapy), LAMA (left against medical advice)

Table 3: Association between patients' characteristics and outcomes

	Death (n=35) n (%)	Renal recovery(n=48) n (%)	OR	95% CI	P value
Gender					
Male	18(40.0)	27(60.0)	0.82	0.34-1.97	0.416
Female	17(44.7)	21(55.3)			
Age					
<65 years	22(35.5)	40(64.5)	2.96	1.06-8.22	0.034
≥65 years	13(61.9)	8(38.1)			
AKI Staging					
Stage 1	2(16.7)	10(83.3)	1		
Stage 2	7(36.8)	12(63.2)	2.92	0.49-17.32	0.046
Stage 3	26(50.0)	26(50.0)	5.00	0.99-25.08	
Aetiology					
Sepsis	23(50.0)	23(50.0)			
Hypovolaemia	6(30.0)	14(70.0)			
Cardiac Failure	4(57.1)	3(42.9)			0.190
Eclampsia	2(33.3)	4(67.7)			
Others	0(0)	4 (100)			
Specialty					
Medical	21(43.8)	27(56.2)			
OBGY	7(41.2)	10(59.8)			0.935
Surgical	7(38.9)	11(61.1)			

OBY&GYN (obstetric and gynaecology), OR (odd ratio), CI (confidence interval), AKI (acute kidney injury)

The proportion of AKI patients with mortality was higher in those who were 65 years and above (OR: 2.96, 95% CI: 1.06-8.22, p=0.034). There was a significant increase in mortality rate of AKI patients across stages 1 to 3 from 16.7% to 50% (OR: 5.0 95% CI: 0.99-25.08, p=0.046). Mortality was the highest in patients who had AKI from cardiac failure and sepsis compared with other aetiologies, although this was not statistically significant. Mortality rate across the three specialties was not significantly different (Table 3).

Age ≥ 65 years (Adjusted OR: 4.14, CI: 1.32-13.04, p = 0.015) and AKI stage 3 (Adjusted OR: 6.79, CI: 1.21-38.04, p= 0.029) were still independent predictors of mortality in AKI patients on binary logistic regression (Table 4).

Table 4: Binary logistic regression showing independent predictors of mortality in AKI patients.

	P value	AOR	95% Confidence interval
Age 65 years and above	0.029	6.79	1.21-38.04
AKI KDIGO stage 3	0.015	4.14	1.32-13.04

DISCUSSION

Acute kidney injury is a common disorder worldwide that is associated with high morbidity, mortality and cost (1, 2, 7-9). The majority of patients with AKI in this study were young and middle aged which is similar to previous reports from tropics (7, 16-18), unlike in developed countries where the elderly are commonly affected (19, 20). The more affected population in this study are the economically productive age group of the nation. Hence AKI, contributes to socioeconomic loss in developing countries like Nigeria. There were more males with AKI than females in this study which is similar to previous reports (21, 22),although some other authors have reported female predominance in their studies (16, 23). This may be due to the fact that males have better access to health care compared to females in Nigeria as reported by Onah et al (24).

The commonest causes of AKI were sepsis and hypovolaemia. This finding is similar with reports of previous studies (7, 8, 16, 21, 23). Medical causes of AKI were also the most predominant when the aetiology were studied across specialties, therefore patients admitted to medical wards should be monitored regularly in order to prevent or diagnose AKI early. The common causes of AKI identified in this study are largely preventable and treatable by regular health education of the public, early diagnosis and adequate treatment by health care workers. Amongst the causes of AKI, heart failure and sepsis had the highest mortality. This is comparable to earlier report by Soliman (25).

More than half of the patients presented late in stage 3 AKI, according to KDIGO criteria. Other studies in different parts of Nigeria reported similar findings (7, 23).This may be related to poor health care seeking attitude of Nigerians even amongst those who are educated as reported by Chukwuezi et al. (26). Most cases of AKI are treatable and often reversible if managed adequately and promptly (27). Stewart et al reported that only 50% of patients with AKI received good care in the hospital (28).It was also reported that up to 23.5% of over 1500 patients admitted in a hospital in Glasgow with AKI were undiagnosed (29). Thus, primary health care givers also need to be regularly educated on how to recognize AKI early and when it becomes expedient for them to refer patients with AKI to nephrologists. Educational intervention was reported to have improved clinicians' knowledge and awareness of acute kidney injury (AKI), which led to better management and outcome in patients with AKI (30).

About 62% of patients with AKI who needed RRT were dialyzed in this study which is higher compared to 21.4% reported by Effal et al (23). This may be because the cost of dialysis is relatively cheaper in our centre compared to the latter hospital. Also, AKI patients are treated as emergency in our centre, and those who could not readily afford dialysis immediately are given the opportunity to have one or two sessions of

dialysis on deferred payment terms. However, the cost of dialysis is still beyond the reach of most Nigerian patients with AKI and places huge financial burden on these patients and their relatives. The majority of these patients stay longer in the hospital after discharge due to inability to settle their hospital bills. It is therefore highly imperative for the government to subsidize renal care in order to reduce overall mortality of patients with AKI.

Ten of our patients who had indication for RRT could not be dialysed due haemodynamic instability from severe hypotension that was refractory to inotropes and fluids. Continuous Renal Replacement Therapy (CRRT), which is the choice of modality of RRT in such critically ill patients, is not available in our centre and in most tertiary health institutions in Nigeria. This mode of therapy is very expensive, and most patients cannot afford it unless it is well subsidized.

The mortality rate of patients with AKI was 38.5% which is comparable to 39.4% reported by Bamgboye et al (7) but higher than 18% reported by Kaballo et al.(31).The lower prevalence in the latter study may be the result of exclusion of major surgical and intensive care unit patients that were included in the index study. However, mortality rate in our study was lower than 46.8% reported by Emem-Chioma et al. This may be due to the fact that they studied patients with severe AKI who required RRT unlike this study which involved stages 1 to 3 AKI patients (21). The mortality rate is still unacceptably high, and efforts must be intensified in order to achieve ISN vision 0 by 2025.

Significant factors associated with mortality in this study were older age and late presentation. Elderly patients with AKI were four times more likely to die compared to the young and middle aged patients. This associated increase in mortality in the elderly may be related to the presence of other co-morbidities such as hypertension, diabetes mellitus and heart failure which are common in this age group, although these were not accessed in our study. There was significantly increased mortality across AKI stages 1 to 3 with stage 3 patients having about eight times more risk of mortality compared to AKI stage 1. Similar findings were reported in other studies. (7,21-23) Therefore, early presentation with prompt, adequate care and easy access to all forms of RRT will significantly reduce mortality associated with AKI.

The limitation of this study was that we depended on the accuracy of previous documentations in the patients' case notes and dialysis records because it was a retrospective study. Secondly, the study had a relatively smaller sample size compared to some earlier studies. However, this is the first study in Southwest Nigeria that used the new KDIGO staging of AKI. It also determined the independent predictors of outcomes in AKI patients. The findings in this study will be very useful in advocating for health care policies that will reduce the burden of AKI.

Regular education of the public and health care workers should be done in order to encourage early presentation, prompt diagnosis and treatment. Also, the government should implement policies that will make RRT easily accessible and affordable to those who require it.

In conclusion, sepsis and hypovolaemia were the commonest causes of AKI affecting more of the young and middle aged population. Acute kidney injury-related mortality is still unacceptably high and factors associated with mortality were late presentation and older age.

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