



ORIGINAL ARTICLE

Acute kidney injury among adult patients undergoing major surgery in a tertiary hospital in Nigeria

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Abstract

Background. Acute kidney injury (AKI) is an underreported but major cause of morbidity and mortality among patients undergoing major surgical interventions in sub-Saharan Africa (SSA). Whereas AKI is often seen following major cardiac surgery in high-income countries, a similar spectrum of surgical diseases and interventions is not seen in developing countries. The impacts on surgical outcomes have also not been well characterized in SSA. This study aimed at identifying risk factors, incidence and determinants and short-term outcomes of AKI among patients undergoing major surgery.

Methods. This was a cohort study of adult patients undergoing major surgery at the University College Hospital, Ibadan, Nigeria. Data obtained were sociodemographic details, risk factors for AKI, details of surgery, anaesthesia and intra-operative events and short-term outcomes. Blood samples were obtained for pre-operative (pre-op) full blood count, serum electrolytes, blood urea and creatinine (SCr). Post-operatively (Post-op) SCr was determined at 24 h, Day 7 post-op and weekly until each patient was discharged.

Results. A total of 219 subjects who had major surgery (86.3% elective) were enrolled. The median age of the patients was 46 (range 18–73) years and 72.6% were females. The surgeries performed were mostly simple mastectomies (37.4%), exploratory laparotomies (22.8%) and total thyroidectomies (16.4%). The incidences of AKI were 18.7% at 24 h and 17.4% at Day 7 post-op, while cumulative AKI incidence was 22.5% at 1-week post-op. Pre-op elevated SCr [odds ratio (OR) 3.86], sepsis (OR 2.69), anaemia (OR 2.91) and duration of surgery >120 min (OR 1.75) were independently associated with AKI. In-patient mortality was 20.4% in individuals with AKI and 5.3% in those without AKI ($P < 0.01$).

Conclusion. Peri-operative risk factors for AKI are common among patients undergoing major surgery in SSA hospitals. The cumulative incidence of AKI was high and independently associated with pre-op sepsis, anaemia, pre-existing kidney dysfunction and duration of surgery >120 min.

Key words: acute kidney injury (AKI), incidence, risk factors, sub-Saharan Africa, surgery

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Background

Acute kidney injury (AKI) is a major cause of morbidity and mortality among patients undergoing major surgical interventions worldwide and contributes to prolonged hospital stays and increased cost of treatments [1, 2]. The epidemiology of AKI appears different between high-income countries (HICs) and low- and middle-income countries (LMICs) [3, 4]. Whereas it is often seen following major cardiac surgery in the former, this is not the case in LMICs [4–6].

A review by Adu et al. [7] estimated the incidence of AKI among hospitalized patients in the sub-Saharan Africa (SSA) region to be 1.9%. In contrast, a recent study by Evans et al. [8] reported the incidence of AKI among 892 cases of medical admissions in a Malawian hospital to be 17.2%, with an in-hospital mortality rate of 44.4%. The outcome of AKI in the SSA region is poor compared with HICs. Olowu et al. [9] reported that only 64% of 1042 children and 33% of 178 adults with AKI across many studies received dialysis when needed. While the overall mortality was 34% in children and 32% in adults, the mortality rose to 73% in children and 86% in adults when dialysis was needed but not received [9]. Most of the reports from the SSA region are on community-acquired AKI, while reports on the epidemiology of AKI among individuals undergoing surgery are sparse. With the increase in volume of surgical procedures performed in SSA [10], it has been hypothesized that most cases of surgery-related [peri-operative (peri-op)] AKI are underdetected. The impact of delayed or undetected AKI is enormous in patients undergoing surgical interventions and it is associated with increased morbidity and mortality, prolonged hospital stay and higher cost of treatment [11, 12].

Despite peri-op AKI being a preventable disease with enormous benefits of early detection and intervention, which is feasible through identification of risk factors and prompt institution of appropriate treatment during the peri-op period, very limited data are available on the incidence of AKI and its risk factors among patients undergoing surgery in the SSA region. The primary objective of this study was to identify peri-op risk factors and determine the pattern of AKI among patients undergoing major surgery in a leading tertiary hospital in Nigeria and the secondary objective was to determine the short-term outcomes of AKI among the participants.

Materials and methods

Study design and participants

This was a short-term follow-up study of 219 adult patients undergoing major surgical interventions at the University College Hospital, Ibadan, Nigeria. Consecutively presenting patients requiring elective or emergency surgery were enrolled in the study between 1 October 2015 and 31 January 2016. Inclusion criteria were individuals 18–74 years of age while exclusion criteria were individuals with <18 or >74 years of age, primarily obstructive urological disease, end-stage renal disease (ESRD) or on renal replacement therapy (RRT). Standard case report forms were used to collect data from the participants. Data obtained included sociodemographic details, risk factors for AKI [pre-operative (pre-op) sepsis, diabetes mellitus, pre-existing kidney disease, presence of comorbidity, anaemia, emergency surgery, prolonged duration of anaesthesia, prolonged duration of surgery, intra-op blood loss, intra-operative (intra-op) hypotension, intra-op hypertension, post-operative (post-op) sepsis, post-op fluid loss through the surgical drain,

use of multiple antibiotics and analgesics], lifestyle, medical histories, clinical diagnosis, types and duration of surgery, episodes of hypotension and details of anaesthesia. Pre-, intra- and post-op serum electrolytes, urea and creatinine and full blood count were carried out while noting the vital signs, intra-op blood loss, fluid input and output, use of inotropic agents and the need for blood transfusion. Post-op blood samples were also collected for serum creatinine (SCr) within 24 h of surgery, Day 7 post-op and weekly until participants were discharged home.

AKI was defined and graded in accordance with the Kidney Disease: Improving Global Outcomes (KDIGO) 2012 criteria (Table 1), while pre-existing kidney dysfunction, anaemia, sepsis, hypertension, intra-op hypertension and hypotension, diabetes mellitus, prolonged and major surgery and recovery of kidney function are defined as shown in Table 1.

Statistical analysis

Statistical analyses were done using the Statistical Package for Social Sciences (SPSS) version 20 (IBM, Armonk, NY, USA). Continuous variables are expressed as means or medians and categorical variables are expressed as proportions. Paired t-test was used to test for association between continuous variables that were normally distributed and continuous variables that were not normally distributed were compared using the Mann–Whitney U-test. Associations between categorical variables were compared using the chi-square test or Fisher's exact test as appropriate. Linear and multiple logistic regression analyses were conducted to identify factors that were independently associated with the development of AKI. Associations between variables were considered to be significant for P-values <0.05.

Ethical approval

This study adhered to the Declaration of Helsinki and ethical approval was obtained from the Joint University of Ibadan and University College Hospital, Ibadan Institutional Review Board. All participants gave written informed consent.

Results

Clinical characteristics of the participants

A total of 219 participants who had major surgery were recruited into the study; the median age of the patients was 46 (range 18–73) years and 159 (72.6%) were females. The median duration of surgery was 100 (range 30–433) min and the median pre-op systolic blood pressure (SBP) and diastolic blood pressure (DBP) was 120 (range 70–190) mmHg and 80 (range 50–150) mmHg, respectively. A total of 189 (86.3%) participants underwent elective surgery while 30 (13.7%) had emergency surgical interventions. The medians were significantly higher among the participants with AKI compared with those without AKI for the duration of surgery and pre-op, 24-h and 1-week post-op SCr, while the median estimated glomerular filtration rate (eGFR) was significantly lower in the participants with AKI compared with those without AKI (Table 2). In addition, AKI at the end of 1 week was significantly associated with gender. The spectrums of surgical diseases among the participants were predominantly breast carcinoma, simple multinodular goitre, abdominal ventral hernia and acute appendicitis (Table 2). The surgical interventions carried out were mainly simple mastectomies, exploratory laparotomies, total thyroidectomies, appendectomies and wide excision of soft tissue sarcomas and the proportions were similar in participants with and without AKI

Table 1. Definitions of diagnostic criteria

Variable	Definition
AKI	Increase in serum creatinine by ≥ 0.3 mg/dL (≥ 26.5 $\mu\text{mol/L}$) within 48 h OR increase in SCr to >1.5 times baseline that is known or presumed to have occurred within the prior 7 days OR urine volume <0.5 mL/kg/h for 6 h [13]
Pre-existing kidney dysfunction	eGFR <60 mL/min/1.73 m ² [14]
Anaemia	Haemoglobin <11 g/dL [15]
Sepsis	The presence of confirmed (culture) or presumed identifiable microbes with two or more features of SIRS. Features of SIRS include fever (temperature >38 °C) or hypothermia (temperature <36 °C), tachycardia (pulse rate >90 /min), tachypnoea (respiratory rate >20 /min) and leucocytosis (WBC $>11 \times 10^6$ /mm ³) or leucopenia (WBC $<4 \times 10^6$ /mm ³) [16, 17]
Hypertension	SBP ≥ 140 mmHg or diastolic DBP ≥ 90 mmHg, presence of hypertension previously diagnosed by a physician or use of antihypertensive medications to control BP [18]
Diabetes mellitus	Fasting plasma glucose >7 mmol/L, diabetes mellitus diagnosed previously by a physician or use of anti-diabetic medications to control blood sugar [19]
Intra-operative hypotension	Increase in mean arterial BP $>20\%$ from the baseline, lasting 5–10 min. Intra-op hypotension was defined as absolute SBP <80 mmHg or a drop in the baseline SBP of $>20\%$ lasting at least 5–10 min [20, 21]
Major surgery	Any surgical procedure that required at least a regional or general anaesthesia, surgery that lasts >120 min in duration or surgery requiring in-hospital care
Full recovery of kidney function	SCr return to baseline value or below [22]
Partial recovery of kidney function	Change from higher AKI severity stage to a lower one but not below Stage I or a reduction in SCr of $>25\%$ from the highest value attained [22]
Prolonged surgery	Surgical interventions lasting >120 min [23]
KDIGO staging of AKI	
Stage I	Increased SCr 1.5–1.9 times from the baseline OR urine output <0.5 mL/kg/h for 6–12 h
Stage II	Increased SCr 2.0–2.9 times from baseline OR urine output <0.5 mL/kg/h for ≥ 12 h
Stage III	Increased absolute SCr to >4.0 mg/dL (>353.6 mmol/L) OR initiation of RRT OR increased SCr 3.0 times from baseline OR 0.3 mL/kg/h for ≥ 24 h OR anuria for ≥ 12 h [13]

SIRS, systemic inflammatory response syndrome; WBC, white blood cell count.

(Table 2). General anaesthesia was administered to 198 (90.4%) patients while spinal anaesthesia was the choice in the remaining [21 (9.6%)] participants (Table 2).

Peri-op risk factors

Pre-op sepsis, pre-op anaemia, pre-existing kidney dysfunction and emergency cases were observed to be significantly higher among participants with AKI on bivariate analysis, while diabetes mellitus and hypertension were not associated with AKI (Table 3). Pre-op sepsis was significantly higher among participants who had emergency surgery [8 (26.7%)] compared with elective cases [17 (8.9%); $P < 0.01$]. A duration of surgery >120 min, a duration of anaesthesia >120 min and the need for intra-op blood transfusion were the identified intra-op AKI risk factors that were significantly higher among the individuals with AKI (Table 3), while the post-op risk factors for AKI were similar in individuals with AKI and those without AKI (Table 3).

Incidence of AKI

The incidences of AKI were 18.7% ($n = 41$) and 17.4% ($n = 38$) within 24 h and Day 7 post-op, respectively, while the cumulative AKI incidence at 1-week post-op was 22.5% ($n = 49$). The proportion of diagnosed AKI varied with the diagnostic criteria employed; the highest incidence (22.5%) was observed when either SCr or urine output-based criteria was used (Table 4). The severity of AKI using KDIGO grading among participants with AKI showed 32 (65.3%) in Stage I, 11 (22.4%) in Stage II and 8 (16.2%) in Stage III.

Factors associated with AKI

On multivariate analysis, only pre-existing kidney dysfunction, pre-op sepsis, anaemia and duration of surgery >120 min independently predicted AKI at the end of the 1-week post-op period (Table 5).

Outcome data

Of the 219 participants enrolled, 49 (22.5%) had AKI; at the end of 30 day, 33 (67.3%) and 16 (32.7%) of those with AKI had full and partial recovery of their kidney function, respectively. Six participants (12.2%) among those with AKI required and had haemodialysis. The crude mortality rates (30 days post-op) among those with AKI and those without AKI were 10 (20.4%) and 9 (5.3%), respectively ($P < 0.01$).

Discussion

The incidence of AKI (22.5%) in our study was higher than the 1.9% reported among hospitalized adult patients by Adu *et al.* [7]. Our finding was similar to the 17.2% reported by Evans *et al.* [8] and 16.7% by Bagasha *et al.* [24] among adult hospitalized patients in a Ugandan and a Malawian hospital, respectively. Also, the AKI incidence in our study agreed with the 16.3% reported by Skinner *et al.* [25] among South African patients admitted with trauma. Of note is that the case mix of sepsis and trauma differs from ours because of specialty bias. The low incidence of AKI reported by Adu *et al.* [7] in their review is probably due to underestimation of the true incidence of AKI in SSA, as the low incidence might have resulted from the non-uniformity of definition of AKI across the studies included in their review. Supporting this explanation

Table 2. Baseline characteristics of patients who underwent major surgical interventions

Variables	Peri-op AKI (n = 49)	No peri-op AKI (n = 170)	P-value
Gender, n (%)			
Female	29 (59.2)	129 (76.3)	0.02*
Male	20 (40.8)	41 (23.7)	
Age (years), median (range)	49 (19–73)	46 (18–74)	0.23
SBP (mmHg), median (range)	120 (70–180)	120 (80–190)	0.96
DBP (mmHg), median (range)	80 (52–150)	80 (50–115)	0.75
Duration of primary surgical illness (months), median (range)	6 (1–96)	10.5 (1–205)	0.12
Duration of surgery (min), median (range)	105 (45–433)	96 (30–350)	0.03*
Pre-op SCr ($\mu\text{mol/L}$), median (range)	106 (44.5–371.3)	79.6 (61.7–97.2)	0.01*
24-h post-op SCr ($\mu\text{mol/L}$), median (range)	106 (30.4–344.8)	88.4 (23.2–132.5)	0.01*
Day 7 post-op SCr ($\mu\text{mol/L}$), median (range)	105 (32.0–319.5)	92 (34.6–138.3)	0.01*
eGFR (mL/min/1.73 m^2), median (range)	77 (39.7–160.4)	96 (73.4 \pm 153.0)	0.01*
Haemoglobin (g/dL), mean \pm SD	7.4 \pm 1.6	7.2 \pm 1.4	0.86
Types of surgery, n (%)			
Emergency	14 (28.6)	16 (9.4)	0.01*
Elective	35 (71.4)	154 (90.6)	
Presence of at least one comorbidity, n (%)	15 (30.6)	56 (32.9)	0.76
Surgical diagnoses, n (%)			
Breast carcinoma	17 (34.5)	63 (37.1)	0.86
Thyroid tumour	10 (20.4)	26 (15.2)	
Abdominal wall hernia	4 (8.9)	10 (5.8)	
Acute appendicitis	3 (6.1)	11 (64.7)	
Intestinal obstruction	3 (6.1)	7 (4.1)	
Pancreatic carcinoma	2 (4.1)	7 (4.1)	
Soft tissue sarcoma	0 (0)	8 (4.7)	
Colorectal carcinoma	1 (2.0)	5 (2.9)	
Enterocutaneous fistula	1 (2.0)	4 (2.4)	
Others	8 (16.3)	29 (17.1)	
Surgical interventions, n (%)			
Mastectomy	21 (42.9)	59 (34.7)	0.38
Exploratory laparotomy ^a	13 (26.5)	40 (23.5)	
Thyroidectomy	2 (4.1)	34 (20.0)	
Appendectomy	5 (10.2)	6 (3.5)	
Wide excision (sarcoma)	1 (2.0)	10 (5.9)	
Herniorrhaphy	1 (2.0)	9 (5.3)	
Axillary clearance	2 (4.1)	1 (0.6)	
Cholecystectomy	1 (2.0)	2 (1.2)	
Others	3 (6.1)	11 (1.8)	
Types of anaesthesia used, n (%)			
GA with isoflurane plus propofol	36 (73.4)	134 (78.8)	0.43
GA with halothane	7 (14.3)	20 (11.8)	
GA with ketamine	1 (2.0)	3 (1.8)	
Spinal anaesthesia	5 (10.3)	13 (7.6)	

BP, blood pressure; GA, general anaesthesia; SD, standard deviation.

*P-value less than 0.05.

^aExploratory laparotomy in 30 cases (13.7%) were with additional surgical procedures such as bowel resection, appendectomy, splenectomy or adhesiolysis.

further is the similarity of the AKI incidence in our study to those reported by Evans et al. [8] and Skinner et al. [25] among patients who were admitted for medical- and trauma-related AKI, respectively. The general increase in the volume of surgical procedures may have also contributed to the increasing incidence of peri-op AKI in the SSA region, where mostly medical AKI had been previously reported [7, 9, 26].

The incidence of AKI in our study is similar to the pattern observed from the HICs among patients who underwent surgical interventions [27–30]. Although the incidence of AKI in our study is similar to the reports from HICs, the spectrum of surgical procedures performed was different in our cohort. Simple

mastectomies with axillary clearance, exploratory laparotomies and total thyroidectomies were the predominant surgical procedures, unlike in HICs where cardiopulmonary surgery was the leading surgical procedure causing peri-op AKI [29–32].

Most of the identified AKI risk factors were modifiable and therefore preventive strategies for their early identification and prompt treatment should be part of the protocol for managing patients undergoing major surgical interventions to reduce the burden of AKI in this group of patients. Pre-op anaemia was observed to be associated with an increased risk of peri-op AKI by 3-fold. This is in agreement with the observations by Karkouti et al. [33] and De Santo et al. [34], who also reported

Table 3. Peri-op characteristics of participants with AKI and those without AKI

Risk factors	Peri-op AKI (n = 49)	No peri-op AKI (n = 170)	P-value
Pre-op risk factors, n (%)			
Age >60 years	8 (16.3)	20 (11.8)	0.69
Pre-op sepsis	12 (28.6)	12 (7.1)	0.01*
Presence of at least one co-morbidity	16 (32.6)	56 (32.9)	0.76
Elevated pre-op BP	16 (32.5)	62 (36.5)	0.60
Hypertension	9 (18.4)	40 (23.5)	0.48
Diabetes mellitus	4 (8.1)	10 (5.9)	0.56
Proteinuria	11 (22.5)	20 (11.8)	0.06
Pre-op anaemia	22 (44.9)	40 (23.5)	0.01*
Pre-op leucocytosis	7 (14.2)	12 (7.1)	0.09
Pre-existing kidney dysfunction	13 (26.6)	6 (3.5)	0.02*
Intra-op risk factors ±			
Prolonged duration of surgery >120 min	32 (65.3)	29 (17.1)	0.01*
Prolonged duration of anaesthesia >120 min	33 (67.3)	40 (23.5)	0.01*
Intra-op hypotension	4 (4.1)	9 (5.3)	0.23
Intra-op hypertension	2 (2.1)	6 (3.5)	
EBL >500 mL	15 (30.6)	31 (18.2)	0.09
Intra-op blood transfusion	28 (57.1)	34 (20.0)	0.02*
Need for >3 L intra-op	12 (24.5)	23 (13.5)	0.07
Need for inotropic support	1 (2.0)	2 (1.2)	0.65
Post-op risk factors ±			
Drain >500 mL/day	10 (20.4)	28 (16.5)	0.52
Had 2 or more post-op antibiotics	11 (22.5)	46 (27.1)	0.53
Post-op analgesic	47 (95.9)	166 (97.6)	0.67
Post-op sepsis	11 (22.5)	46 (27.1)	0.53
Post-op blood transfusion	47 (95.9)	166 (97.6)	0.67

BP, blood pressure; EBL, estimated blood loss.

*P-value less than 0.05.

Table 4. Incidence of AKI based on different KDIGO diagnostic criteria

KDIGO criteria for AKI diagnosis	n (%) (total; N = 219)
Increased serum creatinine >26.7 µmol/L	28 (12.7)
SCr criteria >1.5-fold from baseline	36 (16.2)
Urine output criteria alone: urine volume <0.5 mL/kg/h for 6 h	11 (5.0)
Combination of both SCr and urine output-based criteria	21 (9.6)
Diagnosis based on either SCr or urine output-based criteria	49 (22.4)

anaemia as a predictor of peri-op AKI among patients who had cardiac surgery and coronary artery bypass graft, respectively. Optimizing the haemoglobin concentration prior to and during surgery has the potential of reducing the incidence of peri-op AKI and this can be achieved through pre-op blood transfusion in emergency settings or during surgery and using erythropoiesis stimulating agents in elective cases. Intra-op blood transfusion is a common occurrence in SSA, particularly in emergency surgical procedures [35–36]; not surprisingly, a quarter of our cohort required intra-op blood transfusions while 12.8% required further post-op blood transfusions.

Another factor that was associated with AKI in our study was sepsis. Sepsis causes AKI through multipronged injury pathways that include ischaemia-reperfusion injury, direct inflammatory injury, coagulation and endothelial cell

dysfunction and apoptosis [37, 38]. Prompt treatment of severe sepsis prior to surgery using the international guideline for management of sepsis (Surviving Sepsis Campaign Guideline) is recommended [39]. This aggressive treatment of sepsis prior to surgical procedures is a cost-effective way of preventing peri-op AKI and its attendant outcomes, most especially in emergency cases, which are at higher risk of developing sepsis.

For surgery lasting >120 min, adequate fluid balance both prior to and during surgery must be ensured, in addition to optimal BP control to prevent episodes of intra-op hypotension and hypertension. These steps will reduce the risk of AKI in patients undergoing major surgery.

Pre-existing kidney dysfunction was identified as a predictor of AKI among our patients, although we couldn't establish whether the pre-existing kidney dysfunction was chronic kidney disease (CKD) or AKI. This is because most of the participants had no baseline urinalysis and SCr records that were at least 3 months prior to admission for the surgical procedures. The existence of pre-existing kidney dysfunction in our study increased the risk of developing peri-op AKI by 4-fold. This finding is in keeping with previous reports that classified CKD as a risk factor for AKI [40]. Although CKD may not be reversible, prompt identification of modifiable peri-op risk factors for AKI and instituting preventive measures may safeguard against development of AKI, which is a known risk factor for CKD progression. Also, early involvement of nephrologists in the optimal care of at-risk patients prior to surgery will go a long way in reducing the burden of AKI among individuals undergoing surgical interventions.

This study is not without limitations, and these include the definition of pre-existing kidney dysfunction as eGFR

Table 5. Logistic regression analysis of factors predicting AKI

Risk factors	Odds ratio	95% CI	P-value
Female gender	0.83	0.3949–1.0574	0.71
Pre-op sepsis	2.67	1.1198–7.3341	0.03*
Pre-existing kidney dysfunction	3.86	1.8075–9.7942	0.01*
Pre-op anaemia	2.91	1.0829–5.2254	0.02*
Duration of anaesthesia >120 min	1.03	0.7324–5.9186	0.12
Duration of surgery >120 min	1.75	1.3912–11.4267	0.04*
Emergency surgery	1.44	0.5269–3.9106	0.48
Need for blood intra-op blood transfusion	0.93	0.8594–4.1937	0.65

*P-value less than 0.05.

<60 mL/min/1.73 m², given that eGFR is not accurate when the kidney function is near normal. Second, due to limited funds, SCr was only measured pre-op, 24 h post-op, 7 days post-op and weekly until patients were discharged and thus some cases of AKI may have been missed. SCr as a marker of AKI has been shown to lag injury to the kidney, but the high cost of using early markers of AKI was prohibitive. Also, diabetes mellitus was based on self-reported history and/or the use of antidiabetic medications, as no plasma glucose was measured.

Conclusion

This study showed a high incidence of peri-op risk factors for AKI among patients undergoing major surgical procedures in a tertiary hospital in SSA. The cumulative incidence of AKI was high and independently associated with pre-op sepsis, anaemia, pre-existing kidney dysfunction and duration of surgery >120 min. The presence of AKI increased the mortality rate among individuals undergoing major surgical interventions. Prompt identification and aggressive treatment of peri-op AKI risk factors offer the potential of reducing the burden of AKI in this group of patients.

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Conflict of interest statement

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