Tropical Journal of Nephrology Vol.18 Nos 1 & 2, June & Dec., 2023 7 - 16

Acute Kidney Injury among Trauma Patients Seen at the National Trauma Center Abuja: Risk Factors and Short-Term Outcomes

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ABSTRACT

Background: Patients who have experienced trauma may develop acute kidney injury (AKI), which is associated with greater morbidity and mortality rates. We aim to identify the incidence, risk factors and short-term outcome of AKI in trauma patients admitted to the National Trauma Centre in National Hospital Abuja.

Methods: This was a cohort study of trauma patients aged 18 years and above. AKI was defined according to the Kidney Disease Improving Global Outcome guidelines. Demographic, physical, and laboratory data were obtained from patient record, semi-structured questionnaires, physical assessments and blood and urine samples. Outcome of AKI, and in-hospital mortalitywithin 30 days of admission were observed. Multiple logistic regression analysis was used to determine risk factors associated with AKI development.

Results: Of the 239 patients analysed, 20.9% developed AKI.The risk factors identified were older age (AOR 1.04, 95% CI 1.00-1.09, P= 0.04), admission to intensive care unit (AOR 4.12, 95% CI 1.1-15.35, P=0.04), abdominal trauma (AOR 22.41, 95% CI 6.66-75.36, P <0.001), multiple injuries (AOR 3.34, 95% CI 1.33-8.4, P= 0.01), and length of hospital stay (AOR 1.04, 95% CI 1.0- 1.08, P= 0.04).Among AKI patients, rapidreversal of AKI occurred in 74%, Acute Kidney Disease in 8% and persistent AKI in 18%. In-hospital mortality was higher in those with AKI vs no AKI (20% versus 0.5%)and mortality was even higher in AKI patients who had RRT vs those managed conservatively. (83.3% vs 11.4%, P=0.001).

Conclusion: Increased vigilance and prevention of AKI is warranted in managing trauma patients, given the increased risk.

Keywords: *Acute kidney injury, trauma patients, KDIGO criteria, risk factors, short-term outcome.*

INTRODUCTION

Acute Kidney Injury (AKI) is a common and serious complication in trauma patients that is associated with increased morbidity and mortality [1]. Major risk factor for AKI in trauma patients include hypoperfusion as a result of hemorrhage, older age, presence of comorbidities, systemic inflammation, hypovolemic shock, rhabdomyolysis and major surgery [1]. Admission into the intensive care unit (ICU), African American race, diabetes mellitus, body mass index? 30 kg/m2, abdominal abbreviated injury scale score? 4 and prolonged hospitalization are also recognised risk factors of AKI post-trauma [2,3].

The outcome of AKI as a result of trauma is not fully established but global studies of survivors of AKI of various etiologies have revealed an increased risk of chronic kidney disease (CKD), cardiovascular

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disease and death [4,5]. Studies done in Nigeria have also demonstrated high mortality rate among AKI patients, and important predictors of death observed were depressed sensorium, ICU admission, and late initiation of dialysis [6,7].

Acute Kidney Injury (AKI) as defined by Kidney Disease Improving Global Outcome (KDIGO) 2012 is an increased creatinine by 0.3mg/dl within 48 hours or 1.5 times baseline within 7 days or low urine output (<0.5mls/kg/hr.) [8]. AKI requiring long-term dialysis or progressing to CKD, leads to a further increase in health care cost as well as adverse effects on overall quality of life [1].

There are limited studies on AKI among trauma patients in Nigeria and also a lack of information on specific risk factors and short-term outcomes in this patient population.

In view of this, the study aims were to determine the incidence, the risk factors associated with AKI developmentand to determine the short-term outcomes of AKI among trauma patients seen at the National Trauma Center (NTC) in Abuja. By this, we hope to enhance the understanding of AKI in trauma patients and its implications for clinical management while also providing valuable insights for developing preventive strategies and improving patient outcomes.

METHODS

This study was conducted at the NTC within the National Hospital Abuja, which serves as a regional traumatology training and referral center located centrally in the Abuja Municipal Area Council, the capital city with a population of 3.3 million inhabitants [9]. The NTC has a specialized team of experts, including trauma surgeons, orthopedic surgeons, neurosurgeons, plastic surgeons, and general surgeons. It houses an 80-bed center with a well-equipped intensive care unit, an operating theater, a laboratory, and a radiology unit. On average, the NTC attends to approximately 10 patients daily in the trauma emergency and resuscitation ward.

The study was a prospective cohort study design, that recruited patients over a six-month period. All adult patients (? 18 years) with a primary trauma diagnosis who consented, were recruited. We excluded the following groups from the study: Patients with pre-existing CKD, those with a history of direct kidney trauma, deceased individuals who passed away within 24 hours of traumatic injury, those admitted to the hospital for less than 24 hours and pregnant patients.

Being an incidence study, we determined the sample size needed to obtain a valid result using Fisher's statistical formula (n = z2pq/d2) [10]. Assuming an estimated prevalence of AKI in trauma patients of 17%, [11] a tolerable margin of error at 5% and an attrition rate of 10%, a sample size of 239 was obtained.

We consecutively recruited patients who met the inclusion criteria until the target sample size was attained. Using a semi-structured questionnaire we obtained information from the participants such as, demographics, clinical history, injury cause and site, treatment received, risk factors for AKI (e.g., hypertension, diabetes, CKD, co-morbidities, and nephrotoxic drug use). Medication and in-hospital care were extracted from the patients'charts. A detailed examination and documentation of the trauma-affected body parts was carried out. The severity of trauma was assessed using the revised trauma score. Vital signs were recorded at presentation and during each review to identify dehydration, hypotension, and other AKI risk factors. Vital signs were temperature, weight, blood pressure, pulse rate, respiratory rate, and Glasgow coma score.

Urine output (UO) was measured 2 hourly for the first 7 days after trauma, then, daily subsequently. The hourly UO (ml/kg/hr) was estimated from the 2-hour urine output.Serum creatinine level was assayed on days 1,2,3,5,7,14,21,28 and at discharge or day 30 if still on admission. Other tests such as urea, sodium, potassium and bicarbonate levels were done on days 1,2,7,14,21,28 and at discharge or day 30. White blood cell count and haemoglobin levels were assayed in all patients at presentation and in patients suspected to have sepsis. AKI was determined by comparing the highest SCr value with the baseline SCr. Patients with AKI were categorized by severity using the KDIGO staging system. Outcomes were observed up till Day 30 after trauma.

Definition of cases, risk factors and outcomes

AKI was defined based on the KDIGO 2012 Criteria [8] as an Increase in SCr by ≥0.3mg/dl(26.5µmol/l) within 48hrs orIncrease in SCr to ≥1.5times baseline, which is known or presumed to have occurred within the prior 7 days or SCr value of >4mg/dl (354µmol/l) in the absence of history or clinical features to suggest background CKD orUO <0.5mls/kg/h for 6 consecutive hours.

Staging of AKI was according to KDIGO staging using both urine output and SCr criteria [8]. The higher stage from either criterion was used. Baseline Creatininewas the lowest SCr level recorded during the period of hospitalization [12]. CKD was defined as either of the following: History of renal impairment for ≥3months, Previous records of elevated urea and creatinine levels with baseline eGFR <60mls/min and markers of kidney damage (proteinuria/albuminuria and sonographic evidence of shrunken kidneys), Patients on renal replacement therapy or Previous renal transplant [13].

Sepsis was defined as proven or suspected microbial infection with the occurrence of one or more of the following components of systemic inflammatory response syndrome (SIRS) - temperature >38°C or <36°C, pulse rate >90 beats per minute, RR >24cycles/minute, white cell count of >12,000cells/mm^3 or <4000 cells/mm^3 [14]. White blood cell count was used as an indirect marker of sepsis in this study. Participants had anaemia if haemoglobin levels were <12.0g/dL in women and <13.0 g/dL in men [15]. HYPOVOLAEMIC SHOCK - Significant fluid loss, dehydration and cardiovascular signs such as tachycardia and hypotension [16].

Hypotension was Mean Arterial Pressure (MAP) <60mmhg, [17] while Hypertensionwas systolic and diastolic BP ≥140mmHg and ≥90mmHg respectively or use of antihypertensive medications [18].

Nephrotoxic therapy was defined as the administration of a known nephrotoxic medication associated with AKI, such as aminoglycosides, amphotericin B, and non-steroidal anti-inflammatory drugs (NSAIDs). Diabetes mellitus was fasting plasma glucose level ≥126mg/dL (7mmol/L) or random plasma glucose level ≥200mg/dL (11.1mmol/L) in a patient with symptoms of hyperglycaemia or a patient on treatment for diabetes mellitus [19].

Oliguria wasUO of <400mls/day despite adequate fluid replacement, [20] while anuria was UO <100mls/day [20].

The Trauma Severity Score in this study was assessed using the revised trauma score (RTS) and was graded into mild (score of 12), moderate (score of 11) and severe (10-3) [21].

Outcomes in Patients with AKI

Outcome were, rapid reversal of AKI defined as Complete reversal of AKI within 48hours of AKI onset, [22] persistent AKI (the continuance of AKI beyond 48h from AKI onset to <7 days, [22]) and acute kidney disease (AKD) defined as any stage of AKI persisting for ≥7 days but < 90 days after exposure to an AKI initiating event [22]. Outcome of AKD include recovery, recurrence of AKI, progression of AKD.

Outcome in All Participants

In-Hospital Mortality was any death occurring within 30 days of hospitalization. Outcomes will be determined up till day 30 of admission or death if these occured earlier.

Recovery from AKD- defined as a reduction in peak AKI stage (based on KDIGO criteria) and can be further refined by a change in SCr, GFR, biomarkers of injury and repair and/or return of renal reserve [22].

Statistical analysis

Statistical analyses were performed in Statistical Package for Social Sciences (SPSS) statistical software version 21.0.Continuous variables are expressed as mean ± 1 standard deviation or as median and interquartile range; categorical variables, as frequency and percent. Participant characteristics were compared using the t-test, or Mann-Whitney-U test, if they were continuous variables or Chi-square χ^2 or Fisher exact tests if they were categorical variables. Incidence of AKI was determined using proportions and person-time incidence rate.

Binary logistic regression was performed to identify the risk factors associated with AKI development. Clinically relevant risk factors with a p<0.05 valuein bivariate analysis were entered into a multivariable models. All tests were 2 sided and p<0.05 was considered significant.

Ethical clearance

Ethical clearance was obtained from the National Hospital research and ethics committee (NHA/EC/048/2018) and ethical guidelines and research protocols were followed including obtaining written informed consent from all patients or their caregivers, maintaining confidentiality, and not denying treatment for non-participation.

RESULTS

During the study period, 260 patients with trauma were seen but 18 patients declined, and 3 patients were excluded from the study (1 patient had direct renal injury while 2 had CKD). Fifty of the 239 patients (20.9%) had AKI and the incidence rate of AKI was 3 cases per 1000 person days. Seventy percent of patients with AKI developed it on day 1 while 94% developed it within the first 7 days of admission. The in-hospital mortality rate in the AKI group was significantly higher than that in the non-AKI group (20%(n=10) vs. 0.5%(n=1) p<0.001). Twelve percent of patients with AKI required intermittent hemodialysis in the course of their management and the mortality rate in the haemodialysis group was significantly higher than that in the group that had conservative care (83.3% vs 11.4% p=0.001).

Table 1: Socio-demographic characteristics of all trauma patients

Variables	Total (n=239)	AKI n (%) n=50	No AKI n (%) (n=189)	P value
Mean age (±SD)		38±10	33±11	0.010*
Age group (years)				
18-45	208(87.0)	40(80.0)	168 (89.0)	0.090
46-65	28(12.0)	10 (20.0)	18 (10.0)	
>65	3(1.0)	0(0)	3 (2.0)	
Gender				
Male	201(84.0)	48 (96.0)	153 (64.0)	0.005*
Female	38(16.0)	2(4.0)	36(36.0)	
Marital Status				
Single	99(41.0)	14 (28.0)	85 (45.0)	0.126
Married	136(57.0)	36 (72.0)	100 (53.0)	
Divorced	2(1.0)	0 (0.0)	2 (1.0)	
Widowed	2(1.0)	0 (0.0)	2 (1.0)	
Educational Status				
No formal education	14 (6.0)	2 (4.0)	12 (6.0)	0.651
Primary	33(14.0)	7 (14.0)	26 (14.0)	
Secondary	114(48.0)	21 (42.0)	93 (49.0)	
Tertiary	78(33.0)	20 (40.0)	58 (31.0)	
Employment Status				
Employed	223(93.0)	46 (92.0)	177 (94.0)	0.750
Unemployed	16(7.0)	4 (8.0)	12(6.0)	

**significant p-value, SD= standard deviation*

Table 2: Univariate comparison of clinical characteristics of all trauma patients seen at NHA

Variables	AKI n (%) n=50	Non-AKI n (%) n=189	p-value
Type of Injury			
Assault	12 (24.0)	43 (23.0)	0.402
Burns	2 (4.0)	14 (7.0)	
Falls	4 (8.0)	7 (4.0)	
RTA	24 (48.0)	107 (57.0)	
Gun shot	5 (10.0)	9 (5.0)	
Others	3 (6.0)	9 (5.0)	
Site of Injury			
Abdomen	6 (12.0)	7 (4.0)	<0.001*
Chest	1 (2.0)	16 (8.0)	0.210+
Multiple injury	20 (40.0)	46 (24.0)	0.023*
Musculoskeletal	11 (22.0)	68 (36.0)	0.062
Brain	12 (24.0)	52 (28.0)	0.618
Method of Presentation			
From accident scene	12 (24.0)	54 (29.0)	0.632
Inter-hospital transfer	32 (64.0)	106 (56.0)	
Others	0 (0.0)	6 (3.0)	
Unknown	6(12.0)	23(12.0)	
Intervention prior to presentation			
Yes	9(18.0)	28(15.0)	0.580
No	41(82.0)	161(85.0)	
Medication used prior to presentation			
NSAID use	0(0.0)	13(7.0)	0.080
Herbal drug use	12(24.0)	30(16.0)	0.179
Comorbidities			
Hypertension	5 (10.0)	6 (3.0)	0.055
Diabetes Mellitus	5 (10.0)	0 (0.0)	<0.001*
Revised trauma score ×	11.2±1.3	11.6±0.8	0.002*
Mild injury	30 (60.0)	145 (77.0)	
Moderate/mild Injury	7 (14.0)	28 (15.0)	0.686#
Severe/mild Injury	13 (26.0)	16 (8.0)	0.001*#
Initial GCS×	13±3	14±2	0.010*
Systolic BP (mmHg) ×	126±23	127±29	0.720
Diastolic BP (mmHg)×	71±20	72±16	0.900
Presence of hypotension	5(10.0)	10(5.0)	0.220

**= significant p-value; ° median (interquartile range); + fisher's exact test; x mean ± standard deviation; # univariate logistic regression, BP- blood pressure; GCS- Glasgow coma score*

Table 3: Laboratory characteristics of alltrauma patients assessed at presentation and during hospitalization

Variables	Acute Kidney Injury (median (IQR)) Yes	No	p-value
Serum Creatinine (µmol/l)			
Day 1	129 (113, 167)	80 (69, 94)	<0.001*
Day 2	135 (101, 199)	80 (71, 90)	<0.001*
Day 3	93 (71, 129.5)	71 (62, 80)	0.001*
Day 14	84.5 (75, 106)	70.5 (62, 76)	0.13
Sodium (mmol/l)			
Day 1	141 (139, 144)	140 (139, 143)	0.67
Day 2	140 (132, 145)	135 (130,141)	0.50
Day 14	145 (138, 148)	139 (138, 145)	0.82
Urea (mmol/L)			
Day 1	5.1(3.8, 7.0)	3.9 (3.1, 4.5)	0.016*
Day 2	5.7 (5.2, 23.7)	2.6 (2.4,3.8)	1
Day 14	3.8 (3.0, 4.5)	3.1 (2.7, 4.0)	1
Potassium (mmol/l)			
Day 1	3.9 (3.4, 4.7)	3.8 (3.5, 4.2)	0.344
Day 2	5.2 (3.4, 7.2)	3.9 (3.6, 5.2)	1
Day 14	3.5 (3.3, 3.8)	3.8 (3.4, 4.1)	1
Bicarbonate (mmol/l)			
Day 1	23 (22, 24.5)	26 (24, 35)	0.74
WBC (x 109/L)			
Day 1	16(13, 20)	10.3(7.6, 16.1)	0.05
Anemia at presentation n (%)			
Yes	10(20.0)	7(4.0)	<0.001*^
No	40(80.0)	182(96.0)	
Urine output (ml/kg/hr.) mean±SD			
Day 1	0.8 ± 0.5	0.8 ± 0.4	0.96+
Day 2	1.1 ± 0.8	1.1 ± 0.7	0.97+
Day 3	1.2 ± 1.1	1.1 ± 0.7	0.79+

**significant; + -T-test; ^fishers exact test, IQR=inter quartile range*

Table 4: Logistic regression for risk factors associated with AKI in trauma patients

Factor	Crude OR	p-value	AdjustedOR	95% CI Lower	Upper	p-value
Age	1.04	0.01	1.04	1	1.09	0.04*
Gender(Male/Female)	5.65	0.02	15.24	0.86	270.31	0.06
Revised Trauma Score	0.65	0.005	0.89	0.45	1.75	0.74
Initial GCS	0.84	0.014	0.96	0.73	1.27	0.77
Length of Hospital Stay	1.06	0.002	1.04	1	1.08	0.04*
ICU Admission	5.65	0.001	4.12	1.1	15.35	0.04*
Abdominal Injury	12.23	<0.001	22.41	6.66	75.36	<0.001*
Multiple injury	2.07	0.023	3.34	1.33	8.4	0.01*
Anemia at presentation	6.50	<0.001	3.46	0.64	18.63	0.15

** significant p value; B- coefficient; CI- confidence interval; E- exponential*

Table 5: Outcomes of patients with AKI by KDIGO clinical staging

AKI Stage	Rapid reversal of AKI	Persistent AKI	AKD	Total
Stage I	19 (50.0)	1 (12.5)	2 (50.0)	22(44.0)
Stage II	13 (34.0)	2 (25.0)	0 (0.0)	15(30.0)
Stage III	6 (16.0)	5 (62.5)	2 (50.0)	13(26.0)
Total	**38 (100.0)**	**8 (100.0)**	**4 (100.0)**	**50(100.0)**

Acute Kidney Injury (AKI); Acute kidney disease (AKD)

DISCUSSION

This study described the incidence, risk factors and outcome of AKI, in trauma patients seen at NHA. Fifty out of 239 patients developed AKI and risk factors observed were older age, admission to intensive care unit, abdominal trauma, multiple injuries, and length of hospital stay. Majority of the AKI patients had rapid reversal of AKI, while 8% had Acute Kidney Disease (AKD) and 16% had persistent AKI.

Majority of the victims of trauma were young adult males and RTA was the predominant mechanism of injury as seen in reports from other parts of the country. A higher rate of assault was observed compared to other studies done in Nigeria [23,24], perhaps the consequence of migration and rapid urbanization with its associated social-ills.

Most studies of AKI among trauma patients report an incidence rate between 15-30% [25,26]. This study found a comparable incidence of 20.9% to 20.4% observed by Haines et al in a systematic review and meta-analysis [11].

Using KDIGO criteria has the inherent advantage of being more sensitive than the RIFLE or AKIN criteria as observed by Eriksson especially in detecting the AKI stage 1 [26].

The early diagnosis of AKI within the first 7 days post-injury is similar to findings made by Perkins et al [27] and this suggests that the pathophysiology causing AKI in our trauma population was mainly from the earlier insults associated with trauma like hypovolaemia, rhabdomyolysis, and direct kidney trauma.

The lack of a significant difference between the mean urine output of the AKI and the non-AKI group could be a reflection of a moderately injured population, as only 6.3% of patients were hypotensive and 3% required emergency blood transfusion in this study. Also, 58% of the patients were transferred from other hospitals where they would have likely received crystalloid infusion and could have been recovering from AKI with SCr lagging behind GFR in recovery.

This study identified a significant relation between older age, abdominal injury, ICU admission, multiple injury, length of hospital stay and AKI. Older patients are at risk of AKI because of the reduction in renal reserve and physiological decline in GFR that occurs with aging [26]. The association between AKI and older age may also be due to the fact that older patients have more comorbidities and underlying CKD that may predispose them to AKI.

A high injury severity score is an indicator of the amount of injured tissue that may trigger systemic inflammatory response to trauma and result in AKI [28]. The Injury severity score used in this study was not an independent predictor of AKI, similar to findings by Skinner et al [29] but in contrast to findings observed in several other studies [1,26,30,31]. The later could be attributed to the small proportion of severely injured persons in this study.

No uniform definition of renal recovery exist, making its evaluation across studies quite challenging [4]. A significant proportion of the trauma patients in this study who had AKI had rapid recovery similar to the findings of Søvik et al [25]. The high renal recovery rate observed in trauma patients with AKI is probably because they are majorly young and healthy patients. This might also suggest that the AKI was due to pre-renal factors. In addition, this recovery rate could also be attributed to the fact that the National Trauma centre is a major regional trauma centre and as such the trauma resuscitation is effective.

The terms persistent AKI and AKD have not become widely used for clinical research on outcome of AKI [22]. The idea of AKD was proposed to describe the period of transition between AKI and

CKD since the acute renal damage may extend beyond AKI diagnosis and influence long term renal function [8]. Although the proportion of patients with persistent AKI and AKD observed is quite low, the proportion of patients with AKD who died in-hospital is noteworthy. This finding validates the concept of AKD as a distinct condition from AKI, with implications for long-term outcome and highlights the need for clinical vigilance to identify potential points of intervention that could alter the long-term sequel of AKI [22].

The in-hospital mortality rate for AKI patients in this study (20%) was similar to the rate found by Beitland et al. in their study of trauma patients with severe AKI requiring dialysis [32]. Despite including less severe stages of AKI, the mortality rate was surprisingly not lower than Beitland's study. However, other studies by Skinner et al. and Zyada et al. found even higher AKI mortality rates (56.9% and 45.3% respectively) in trauma patients admitted to the ICU [29,33]. The high mortality rates in the ICU trauma studies may be attributed to the severity of injuries in those patient cohorts. Overall, the similar or higher mortality rates across these studies highlight the significant risks associated with AKI, even at less severe stages, in hospitalized trauma populations.

Twelve percent of AKI patients in this study required haemodialysis, much higher than the 2% rate found by Søvik et al. in ICU patients [25], and no patients were discharged on long-term dialysis, similar to Beitland *et al*.'s findings [32]. The mortality rate for the haemodialysis group (83.3%) was higher than rates found in some other study [34], but lower than Okunola et al.'s study where no haemodialysis patients died [35]. The high mortality with haemodialysis indicates a possible association between intermittent haemodialysis and worse outcomes in critically ill AKI patients. However, evidence does not clearly support superiority of continuous renal replacement therapy (CRRT) over intermittent haemodialysis, though CRRT is recommended for unstable patients [36].

In conclusion, this study revealed a high incidence of AKI in trauma patients. Most AKI cases were stage 1 and reversed quickly, though some had persistent AKI and AKD. Compared to those without AKI, a significant proportion of patients with AKI died during hospitalization and majority of those who died had received renal replacement therapy.

Deliberate search and appropriate treatment for AKI is recommended irrespective of severity of injury. Further research also is recommended to better identify other etiological factors of AKI at play in trauma patients so to improve outcomes and reduce mortality rates.

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