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The incidence and outcomes of acute kidney injury amongst patients admitted to a level I trauma unit

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A B S T R A C T

Purpose: This study aimed to identify the incidence and outcomes of patients with trauma related acute kidney injury (AKI), as defined by RIFLE criteria, at a single level I trauma centre and trauma ICU.
Methods: We performed a retrospective observational study of 666 patients admitted to a trauma ICU from a level I trauma unit from March 2008 to March 2011. We conducted multivariable logistic regression to identify independent predictors for AKI and mortality.
Results: The overall incidence of AKI was 15% (n = 102). Median injury severity score (ISS) was 25 (inter quartile range [IQR] 16–34) and mean age was 39 (SD 16.3) in the AKI group. Thirteen patients (13%) were referred with rhabdomyolysis associated renal Failure. Overall mortality in the AKI group was 57% (n = 58) but was significantly lower in the rhabdomyolysis Failure group (23% versus 64%; p = 0.012). AKI was independently associated with older age, base excess (BE) < -12 (odd ratio [OR] 22.9, 95% confidence interval [CI] 1.89–276.16), IV contrast administration (OR 2.7 95% CI 1.39–5.11) and blunt trauma (OR 2.2 95% CI 1.04–4.71). AKI was an independent predictor of mortality (OR 8.5, 95% CI 4.51–15.95). Thirty-nine (38%) patients required renal replacement therapy.
Conclusions: AKI in critically ill trauma patients is an independent risk factor for mortality and is independently associated with increasing age and low BE. Renal replacement therapy utilisation is high in this group and represents a significant health care cost burden.

Introduction

Acute kidney injury (AKI) is common in critically ill patients and has a profound impact on survival with mortality ranging from 15% to 57% [1,2]. The critically ill trauma patient sustains multiple insults to the kidney which include hypovolemic shock, hypothermia, direct urological organ injury, rhabdomyolysis [3], abdominal compartment syndrome, sepsis [4,5], and exposure to nephrotoxins such as contrast material [6] and antimicrobials. In South Africa a common cause of renal dysfunction is myoglobin release following beatings with a heavy leather whip called a *sjambok*. These patients often develop severe renal dysfunction requiring renal replacement therapy (RRT) [3].

Although it has long been recognised that trauma patients are at risk for renal dysfunction [7] recent studies consider trauma related AKI to be a distinct subpopulation [8–12]. The previous lack of a consensus definition of AKI has made determining the incidence of trauma related AKI difficult. The RIFLE criteria consist of three levels of severity in AKI; Risk, Injury and Failure, which are determined by changes in creatinine, glomerular filtration rate (GFR) or urine output, and with two clinical outcomes, Loss and End Stage Kidney Disease (ESKD) [13]. Although the RIFLE criteria have gained widespread acceptance in critical illness for risk stratification of AKI [1,14–17] few studies have evaluated the incidence and risk factors for trauma related AKI using RIFLE criteria [8,10,11,18].

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In this study we describe the incidence and outcomes of patients with trauma related AKI who were managed in the Trauma Intensive Care Unit (TICU) at Inkosi Albert Luthuli Central Hospital (IALCH) in Durban, South Africa.

Methods

We conducted a retrospective observational study of patients admitted to the TICU at IALCH from March 2008 to March 2011. This 10-bedded ICU is dedicated for critically injured patients and serves a drainage area of approximately eleven million people. Admissions to this unit are either direct referral from scene, or as inter-hospital transfer from a facility lacking either RRT facilities, or the necessary surgical, or intensive care expertise to manage the patient. All patients presenting to the unit were included in the study irrespective of age. Patients who died during resuscitation or in the operating theatre directly after admission were excluded.

The trauma unit database and hospital information systems (Medicom® and Soarian®) were used to retrieve patient data for this analysis. We extracted:

1) patient demographics: age, sex, mechanism of injury, injury severity score (ISS), and site of referral;
2) temperature, pH, base excess (BE), lactate, haemoglobin (Hb), blood pressure, and heart rate as recorded at time of presentation to the unit;
3) drug administration: inotropes, loop diuretics, intravenous contrast, aminoglycosides, glycopeptides, and non-steroidal anti-inflammatories.

Study outcomes

The primary study outcome was the in-hospital incidence of organ failure, duration of ventilation, length of ICU stay and mortality in patients with AKI. For the secondary outcomes we aimed to identify independent predictors for the development of trauma related AKI and in-hospital mortality. In addition we wished to describe RRT utilisation in patients with AKI.

We recorded the Sequential Organ Failure Assessment (SOFA) scores at day 3 and day 7, number of days ventilated, ICU length of stay and in-hospital mortality. AKI was defined using the Acute Dialysis Quality Initiative criteria [13]. Serum creatinine measurements were used to stratify patients into the categories of Risk, Injury, or Failure. Where no baseline serum creatinine was available we estimated the baseline using the Modification of Diet in Renal Disease (MDRD) equation and presumed a low normal GFR of 75 ml/min per 1.73 m^2 body surface area [13].

Hypotension was defined as a systolic blood pressure <90 mmHg or mean arterial pressure <65 mmHg. ISS was calculated according to the American Association for the Surgery of Trauma (AAST) grading of injury [19]. SOFA score was calculated at day 3 and day 7 according to points awarded to respiratory, cardiovascular, hepatic, renal, coagulation and neurological system assessment [20]. Mortality was defined as death in ICU.

Slow Low Efficiency Dialysis (SLED) was the only RRT used in this study. The decision for the need and duration of RRT was left to the attending physician's discretion.

Patients were grouped according to their RIFLE score and sjambok victims were grouped separately. These patients are often referred specifically for RRT with established renal failure.

Statistical analysis

Means and standard deviations are reported for normally distributed data; median and inter-quartile range for data not normally distributed. Range is reported for all ages. The χ^2 test and Fisher's exact test were used for categorical data, and Student's *t*-test and one-way ANOVA for continuous data where appropriate.

We conducted multivariable logistic regression to identity independent predictors for AKI and mortality. In the mortality prediction model we evaluated the following 6 risk factors: age, mechanism of injury (blunt vs. penetrating), referral from scene, ISS, base excess (BE) on admission, and AKI. In the AKI prediction model we evaluated the following eight risk factors: age, sex, blunt vs. penetrating injury, scene referral, ISS, first haemoglobin measurement on admission, BE measurement on admission, and the administration of intra-venous (IV) contrast during computed tomography angiography (CTA). We categorised: age as <30 (reference category), 30–50, and >50 years old; BE as >4 (reference category), 4–0, 0 to −4, −4 to −12, and <−12 mEq/l; ISS as <30 (reference category); 30–45; >45. AKI was categorised into Risk, Injury, and Failure, with patients without AKI being the reference category. As a sensitivity analysis we repeated our analyses after excluding patients who were primarily referred to the unit for dialysis after being sjamboked.

All *p*-values are reported to three decimal places and statistical significance was defined as a two-sided $p\text{-value} \leq 0.05$. All data analyses were performed using SPSS 19.0 for Windows (SPSS, Chicago, IL).

Results

During the 3-year study, 666 patients were admitted to the TICU. The mean age of these patients was 29 (SD 15.5, range 2–82) years, with a median ISS of 22 (IQR 16–32). Fifteen percent (102/666) of these patients fulfilled the definition of AKI. Of these, 58 (57%) were diagnosed with AKI at the time of admission and 44 (43%) developed AKI during their time in TICU. Twenty five percent

Table 1
Demographics of patients admitted to the TICU at IALCH stratified by the presence of AKI.

		Total population (*n* = 666)	No AKI (*n* = 564)	AKI (*n* = 102)	*p* value
Age (SD)		29.3 (15.5)	27.7 (14.8)	39.0 (16.3)	<0.001*
Male (%)		494 (74.2)	415 (73.6)	79 (77.5)	0.462
Mechanism of injury	Blunt (%)	502 (75.4)	422 (74.8)	80 (78.4)	0.532
	Penetrating (%)	164 (24.6)	142 (25.1)	22 (21.6)	
Referral from scene (%)		169 (25.8)	149 (26.4)	20 (19.6)	0.139
ISS (median (IQR))		22 (16–32)	22 (16–29)	25 (16–34)	0.665

TICU = trauma intensive care unit; IALCH = Inkosi Albert Luthuli Central Hospital; SD = standard deviation; ISS = injury severity score, AKI = acute kidney injury and IQR = interquartile range.
* $p \leq 0.05$.

Table 2
Distribution of AKI patients according to severity of renal dysfunction.

		Total AKI population (n = 102)	Risk (n = 25)	Injury (n = 19)	Failure (n = 58)	p value
Age (SD)		39.0 (15.9)	40.8 (15.6)	44.1 (16.0)	36.1 (16.3)	0.138
Male (%)		79 (78)	19 (76)	14 (74)	46 (79)	0.861
Mechanism of injury	Blunt (%)	80 (78)	21 (84)	15 (79)	44 (76)	0.709
	Penetrating (%)	22 (22)	4 (16)	4 (21)	14 (24)	
Referral from scene (%)		20 (20)	9 (36)	3 (16)	8 (14)	0.058
ISS (median (IQR))		25 (16–34)	27 (20–34)	34 (26–39.5)	19 (9–25)	<0.001*

AKI–acute kidney injury; SD = standard deviation; ISS = injury severity score.
* $p \leq 0.05$.

(25/102) of patients were categorised as Risk, 19% (19/102) as Injury, and 57% (58/102) as Failure. Eighty percent (82/102) were received as an inter-hospital transfer.

In patients presenting with or developing AKI the mean age was 39 (SD 16.3, range 2–80), median ISS was 25 (IQR 34–16), and males predominated with 79 (78%) admissions. Most patients sustained blunt injury (80/102, 78%), of whom 13 (13%) were referred following sjambok beatings (Table 1).

Twenty (20%) patients were referred from scene and had similar ISS, mortality, inotrope use, length of ICU stay and length of ventilation as compared to those referred via inter-hospital transfer. Scene referrals had lower SOFA scores on day 7 (mean 5.5 SD [3.1] vs. 8.1 [3.3], $p = 0.025$).

Table 2 shows the distribution of AKI patients according to the severity of renal dysfunction. One patient was diagnosed with ESKD after an admission for acute on chronic renal failure. No patients fell into the Loss outcome category.

Table 3 documents the day 3 and day 7 SOFA scores, the length of ventilation, and length of ICU stay in patients with AKI. The overall mortality rate was 57% (58/102) in the entire group, with patients in the Injury group having the highest mortality rate (79%). Patients classified as having sustained Injury had higher SOFA scores on day 3 and day 7.

The independent predictors for in-hospital mortality were an ISS > 45 ([OR] 37.1, 95% [CI] 13.27–103.82), AKI (OR 8.5, 95% CI 4.51–15.95), ISS 30–45 (OR 4.6, 95% CI 2.46–8.47), and age > 50 years (OR 95% CI 1.34–6.9) (Table 4).

The independent predictors for AKI were BE > −12 (OR 22.9, 95% CI 1.89–276.15); age > 50 (OR 9.4, 95% CI 4.4–20.3), IV contrast (OR 2.7, 95% CI 1.39–5.11), age 30–50 years (OR 2.6, 95% CI 1.46–4.5) and blunt trauma (OR 2.2, 95% CI 1.04–4.71). Referral from scene was protective (OR 0.5, 95% CI 0.26–1) (Table 5).

The sensitivity analysis identified the same independent predictors for in-hospital mortality: ISS > 45 (OR 35.4, 95% CI 12.62–99.46); AKI (OR 9.8, 95% CI 5.1–19); ISS 30–45 (OR 4.1, 95% CI 2.2–7.73); and age > 50 years (OR 2.7, 95% CI 1.18–6.28). In the AKI model the sensitivity analysis found that only BE > −12 (OR 15.2, 95% CI 1.32–174.4); age > 50 (OR 10.2, 95% CI 4.48–21.75), and age 30–50 years (OR 2.7, 95% CI 1.49–4.88) remained predictive. Blunt trauma (OR 1.3, 95% CI 0.58–2.86), referral from scene (OR 0.6, 95% CI 0.3–1.15), and receiving CT contrast (OR 0.6, 95% CI 0.29–1.12) were no longer significant after excluding patients referred for dialysis after sjambok injury.

Table 6 illustrates the two groups of patients with and without sjambok injuries within the Failure group. The sjambok group showed lower mortality, inotrope use and ISS.

The mean temperature on presentation was 36.3 (SD 1.3) with no statistically significant difference between the three groups of AKI ($p = 0.405$). Seventeen patients (90%) in the Injury group required inotropic support versus 33 (57%) in the Failure and 18 (72%) in the Risk group.

Dialysis was required in 39 (38%) patients; 2 (11%) in Injury patients and 37 (64%) in Failure patients. All 13 patients with sjambok injury were dialysed on the day of admission while the remaining 26 patients were dialysed on average at day 3.6 (SD 4.6). There was no statistically significant difference between the duration of dialysis required between sjambok and general trauma patients (11.2 days, SD 8.6 vs. 10 days, SD 9.5; $p = 0.507$)

Discussion

Our primary objective was to evaluate the incidence and outcomes of AKI as defined by the RIFLE criteria in our patient population. Previous attempts to identify the incidence of AKI in trauma have been hampered by the lack of an AKI consensus definition [7,21,22]. We chose to use the RIFLE criteria to define AKI as these have been validated in acutely ill populations [1,4,16], and have been successfully used to examine the incidence of AKI in the trauma population with varying results [8,9,12,18,23].

The incidence of AKI in this study was 15%. Bagshaw et al. studied a similar cohort of critically ill trauma patients and showed a similar incidence of early AKI in trauma at 18% [11]. Other studies that used RIFLE criteria in trauma patients have shown a wide incidence of AKI, ranging from 10.7% to 50% [8,9,12,18,23]. This wide range reflects variation in injury severity scores, age, and mechanism of injury in the study populations all of which are risk

Table 3
Primary study outcomes in patients with trauma associated AKI stratified according to renal dysfunction.

Outcomes	Total AKI population (n = 102)	Risk (n = 25)	Injury (n = 19)	Failure (n = 58)	p value
Mortality (n, %)	58 (57)	11 (44)	15 (79)	32 (55)	0.063
SOFA D3 (mean, SD)	7.8 (4.1)	7.3 (4.1)	8.3 (4.3)	7.9 (5.4)	0.782
SOFA D7 (mean, SD)	5.0 (3.3)	5.0 (3.3)	6.4 (5.1)	5.5 (4.7)	0.673
Length of ventilation (mean, SD)	10.9 (11.4)	10.0 (6.4)	12.4 (8.3)	12.1 (13.5)	0.852
Length of ICU stay (mean, SD)	16.5 (15.4)	16.4 (14.1)	14.4 (11.0)	17.6 (17.0)	0.550

AKI = Acute Kidney Injury; SD = standard deviation; SOFA = Sequential Organ Failure Assessment score; D3 = day 3; D7 = day 7.

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Table 4
Independent predictors for in-hospital mortality.

Predictor variable		OR	95% CI	p value
Age	<30 (reference)	–	–	–
	30–50	1	0.56–1.90	0.906
	>50	3	1.34–6.90	0.008*
Blunt injury		1.3	0.65–2.54	0.470
Referral from scene		1.5	0.78–2.73	0.237
ISS	<30 (reference)	–	–	–
	30–45	4.6	2.46–8.47	<0.001*
	>45	37.1	13.27–103.82	<0.001*
BE	>4 (reference)	–	–	–
	4–0	0.6	0.05–8.22	0.738
	<0 to −4	0.9	0.08–10.22	0.935
	<−4 to −12	1.6	0.15–18.37	0.685
	<−12	3.8	0.32–45.88	0.290
AKI		8.5	4.51–15.95	<0.001*

OR = odds ratio; CI = confidence interval; ISS = injury severity score; BE = base excess; AKI = acute kidney injury.
* $p \leq 0.05$.

factors for AKI. In our study, more patients were found to have Failure (56.9%) than has been reported in other studies. This is largely due to referral of patients with established renal failure to our trauma unit for RRT.

The mortality rate amongst patients with AKI was high (56.9%) with the greatest being in those with renal Injury (78.9%). This is surprising and in contrast to other published reports that demonstrate an expected increased mortality rate in the more severe AKI categories in both trauma and non-trauma critical illness [8,11,24,25]. In our population the Injury group were older, had higher ISS, higher use of inotropes and subsequently the highest group SOFA scores; all of which explain the increased mortality. Further care was considered futile in eight (42%) of the Injury group which may imply that these patients demised prior to developing Failure with AKI rather than from AKI.

RRT use was high in the AKI group (38%) as was expected. In a resource restricted environment, this represents a large burden on the healthcare system. Other studies on critically ill trauma patients have found varying RRT utilisation ranging from none [18] to 36.5% [9]. Many of our patients were referred for RRT due to the lack of facilities in other centres explaining our higher utilisation. Of these patients, only one went on to require long-term dialysis. That patient was admitted with a diagnosis of acute on chronic renal failure. Renal recovery following AKI in critical illness varies greatly from 57% to 100% [26–28]. Beitland et al. examined renal recovery following AKI in trauma and showed similar results to our study, with no patients requiring long term RRT [10]. This may imply a better prognosis for renal recovery in trauma associated AKI than other mechanisms.

A small number of sjambok injuries that were referred only for dialysis were included in our study. They all presented with Failure and mortality was significantly lower in this group than in those with non-sjambok Failure. Both ISS and inotropic/vasopressor use were significantly lower in the sjambok Failure group. As the injuries sustained from a sjambok are mostly skin abrasions or contusions, most patients were awarded an ISS of 1. This group also tended towards lower SOFA scores on D3 and D7 even taking into account the renal component of this scoring system. This suggests less organ dysfunction, helping to explain the lower mortality. The pathophysiology of AKI in sjambok injuries is often due to the single renal insult of myoglobinuria whereas AKI in other forms of trauma involves multiple insults to the kidney such as sepsis, hypotension and IV contrast administration. AKI that occurs after sjambok beatings needs to be studied in a large group to assess their natural evolution and to make stronger recommendations for therapy.

We showed a relationship between AKI and age, administration of IV contrast, BE <−12 and blunt trauma. Advancing age is a known risk factor for AKI in critical illness and its identification as a risk factor in this cohort is unsurprising [8,24,29]. Intravenous contrast is also a known risk factor for AKI and careful consideration must be given to the amount, type and indication

Table 5
Independent predictors for AKI.

Predictor variable		OR	95% CI	p value
Age	<30 (reference)	–	–	–
	30–50	2.6	1.46–4.50	0.001*
	>50	9.4	4.40–20.30	<0.001*
Male sex		1.2	0.66–2.29	0.509
Blunt injury		2.2	1.04–4.71	0.040*
Referral from scene		0.5	0.26–1.00	0.050*
ISS	<30 (reference)	–	–	–
	30–45	0.8	0.26–2.38	0.673
	>45	1.5	0.81–2.85	0.190
Admission haemoglobin		0.9	0.85–1.05	0.266
BE	>4 (reference)	–	–	–
	4–0	0.8	0.06–12.00	0.900
	<0 to −4	2.8	0.24–32.32	0.421
	<−4 to −12	7.6	0.67–87.10	0.102
	<−12	22.9	1.89–276.15	0.014*
IV CT contrast		2.7	1.39–5.11	0.003*

OR = odds ratio; CI = confidence interval; ISS = injury severity score; BE = base excess; AKI = acute kidney injury; IV = intravenous; CT = computer tomography.
* $p \leq 0.05$.

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Table 6
Sjambok Failure vs. Non-sjambok Failure groups.

	Total AKI population ($n = 102$)	Sjambok Failure ($n = 13$)	Non-sjambok Failure ($n = 45$)	p value
ISS (median, IQR)	24.5 (14.3)	1 (1–1)	25 (17–29)	<0.001*
Mortality (n, %)	58 (57%)	3 (23%)	29 (64%)	0.012*
SOFA D3 (mean, SD)	7.8 (4.1)	8.5 (2.6)	10.5 (4.1)	0.117
SOFA D7 (mean, SD)	5 (3.3)	6.8 (2.6)	8.8 (3.3)	0.099
Inotrope use		2 (15%)	29 (64%)	0.003*
Length of ventilation (mean, SD)		8.4 (7.1)	12.2 (14.3)	0.364
Length of ICU stay (mean, SD)		18.3 (10.5)	16.7 (17.8)	0.064

IQR = interquartile range; SD = standard deviation; ISS = injury severity score; SOFA = Sequential Organ Failure Assessment score; D3 = Day 3; D3; Day 7 = 7; ICU = Intensive Care Unit.
* $p \leq 0.05$.

for contrast assisted imaging [30]. Whole body CT scanning with IV contrast in the polytrauma patient is commonly used, especially in the high risk patient [31]. Although some studies have shown no correlation between IV contrast administration and AKI in even high risk trauma patients [32,33], and despite the fact that this risk factor fell away in the sensitivity analysis, the utilisation of CT angiography in the critically ill trauma patient needs to be appraised. Up to 7.8% of patients will receive unnecessary CT scans [34] and the benefit of diagnosing clinically relevant but undetectable injuries versus causing AKI must be evaluated on an individual basis.

Limitations

This is a single centre retrospective study in a level 1 trauma unit that accepts a heterogeneous group of critically ill trauma patients. The large number of trauma patients referred to our unit for RRT is a unique feature of this study population and may not be representative of a general trauma population. However, sensitivity analysis demonstrates that our primary results remain even after excluding these patients. In addition, no significant outcome difference could be seen in patients referred from scene as compared to those admitted via inter-hospital transfer.

We used the MDRD equation to estimate baseline GFR in this population. As the patient's true baseline creatinine is unknown, it is possible that patients with AKI may have been missed. We were also unable to estimate the prevalence of chronic kidney disease in our population, which would affect the RIFLE classification. The indications for and duration of dialysis were decided upon by the attending physician and hence there may be some variability between practitioners.

We designed this study to identify the early risk factors for the development of AKI and we did not examine risk factors such as septic shock for the development of late onset AKI in critically ill trauma patients. We decided to focus on the early risk factors for the development of AKI and used BE as a surrogate marker for shock, which revealed a significant finding. The other markers of shock (blood pressure, pulse and pH) were not included in the model to avoid overfitting. We were unable to extract a complete data set to analyse the role of lactate or hypothermia as a marker for the development of AKI and we were unable to include these in our analysis. The SOFA scores were composite scores and it may have been of benefit to examine individual organ failure scores in order to examine association between specific organ dysfunction and AKI.

Conclusion

AKI associated with trauma is an independent risk factor for mortality in this study and occurs more commonly in older patients and patients with low BE. RRT utilisation among these patients is high resulting in a significant healthcare cost burden. Preventing and reducing the progression of AKI is essential and strategies for this require early identification of patients at risk for renal dysfunction. The natural evolution of AKI in trauma and the risk of long term renal dysfunction, RRT, and mortality following discharge from hospital are areas for future research.

Conflict of interest statement

All authors declare that there is no conflict of interest noted for the submitted paper.

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Ethical approval

The study protocol for the paper was submitted to and accepted by the Biomedical Research Ethics Committee at the University of KwaZulu-Natal.

This study has been approved by the appropriate ethics committee and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Reference BE091/11.

The authors have full control over the data presented.

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