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Acute Kidney Injury in Severe Trauma Patients; a Record-Based Retrospective Study

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Abstract

Introduction: Acute kidney injury (AKI) is a common and devastating clinical issue in the community associated with high rates of morbidity and mortality.

Objective: We aimed at estimating the frequency and levels of severity of AKI in trauma patients requiring hospital admission using the RIFLE criteria and assess their outcome.

Method: Our retrospective record based study enrolled data of 80 participants aged 18-59 years who presented to the emergency department of KIMS hospital following an acute traumatic event. Participants with pre-existing renal dysfunction, chronic heart failure and chronic liver disease were excluded. Tests of significance were Chi square and independent sample t test, a $p<0.05$ was considered statistically significant.

Results: Participants with AKI had significantly lower age ($p=0.02$) and lower revised trauma score (RTS) ($p=0.01$). Significant association of AKI with hypotension ($p=0.01$) and Glasgow coma scale (GCS) ($p=0.008$) was observed. No association of AKI with gender was observed ($p=0.6$). None of the AKI patients required renal replacement therapy and all participants attained normal renal function at discharge. Significantly longer mean duration of hospital stay (14.4 days) was observed among AKI patients ($p=0.02$). Totally, 6.3 % mortality was observed among both participants with and without AKI.

Conclusion: Forty percent of acute trauma patients had AKI (in risk and injury category); but none were in failure, loss or end stage renal disease. No association of AKI and mortality was observed. AKI was associated with age, RTS, hypotension and GCS.

Key words: Acute Kidney Injury; Glasgow Coma Scale; Hypotension; Multiple Trauma; Trauma Severity Indices

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INTRODUCTION

Acute kidney injury (AKI) is a common and devastating clinical issue in the community, especially in critically ill patients where it is associated with higher rates of morbidity and mortality (1). AKI is defined as an abrupt reduction in renal function which manifests within hours and encompasses both injury (structural damage) and impairment (loss of function) leading to accumulation of end products of nitrogen metabolism primarily blood urea nitrogen (BUN) and serum creatinine (2). Recently the term AKI has been replaced by acute renal failure (ARF) due to the significant re-examination of various aspects of this entity (2). It is difficult to point a sole etiology for majority of AKI and is thought to be due to the focal mismatch between oxygen and nutrient delivery to the nephrons and increased demand owing to cellular stress. The etiological factors for AKI has been classified as pre-renal, intrinsic acute kidney disease and acute post renal obstructive nephropathy with multiple etiological factors in each class (3). Of these only intrinsic acute kidney disease truly represents renal disease, whereas pre-renal and post renal AKI are consequences of extra-renal disorders reducing glomerular filtration rate (GFR). The presence of multiple etiological factors and co-existence of sepsis, ischemia and nephrotoxicity complicate the recognition and treatment of the patients with AKI. AKI affects 5-7% of all hospitalized patients and an incidence of 1-25% has been reported from in-hospital patients (4, 5). The incidence of community-acquired AKI in India was reported to be 4.14 per 1000 hospital admissions in 1996–2008 and ~11% mortality was observed among these patients. The incidence and mortality associated with AKI among critically ill patients were reported to be 15-50% and 45-50% respectively (6, 7). Critically ill patients who develop AKI requires higher rates of dialysis, has

lower quality of life and will face financial impoverishment over a short period of time. The incidence and prevalence of AKI varies widely between developing and developed countries, hospital acquired infections is the primary cause of AKI in developed nations and community acquired infections is the commonest etiological factor in developing countries (2). Though some of these reports are not standardized, with the advent of criterions which classify AKI as risk, injury, failure, loss, end stage (RIFLE), and Acute Kidney Injury Network (AKIN) have provided some standardization to reports (8). These criteria have an advantage of providing diagnostic definitions for stages where kidney injury can still be prevented, and have been tested in clinical practice and seems to be relevant with the outcome of a patient with AKI. The signs and symptoms of AKI range from minimal elevation of serum creatinine to anuric renal failure. The current diagnosis of AKI is done with the help of estimated GFR (eGFR) and serum creatinine where a reduction in eGFR accompanied with elevation of serum creatinine is indicative of renal injury. Serum creatinine is not a biomarker for AKI but a marker for eGFR and whether to use serum creatinine and eGFR as sole biomarkers for determining AKI is a matter of debate since serum creatinine can vary with a wide range of characteristics such as age, gender, muscle mass, medication and hydration status and eGFR is dependent on serum creatinine. Whether or not multiple diagnostic parameters are required for diagnosing AKI is unclear since many proposed biomarkers are under development and validation for their use as predictors of renal injury (2). The absence of a true standardized baseline value of serum creatinine also makes the current diagnostic parameter an imperfect gold standard for diagnosis of AKI (9).

The RIFLE classification has been evaluated and validated in numerous clinical studies enrolling critically ill patients namely post-operative patients and burns patients, and had been found to be a valid tool for the diagnosis and staging AKI and can be utilized for predicting mortality (10). Studies that applied RIFLE criteria to characterize AKI in a population of patients with trauma show an incidence of renal failure in trauma patients between 0.1-18%, with an associated mortality of 7-83% (11-14). Keeping the relevance of this issue in mind and data available in the literature, we aimed to characterize AKI in trauma patients using the RIFLE classification and relate it to hospital in-patient length of stay (LOS) and mortality in severe trauma patients who required intensive care. The aim of the study is to estimate the frequency and levels of severity of AKI in trauma patients requiring hospital admission using the RIFLE criteria and assess their outcome.

Methods

Our retrospective record based study enrolled data of 80 participants aged 18-59 years who presented to the Emergency Department of KIMS hospital with acute trauma who had revised trauma score (RTS) (15) of less than 4 and grade 2 or higher hemorrhagic loss (16) during the time period between June 2012 and July 2014. Participants with pre-existing renal dysfunction, chronic cardiac failure and chronic liver disease were excluded from the study. Data was collected in structured case record form and collected data included age, gender, mechanism of injury, RTS at presentation, presence of hypotension at presentation, Glasgow coma scale (GCS) at presentation and length of in-hospital stay. Vital signs, systemic examination findings and laboratory parameters such as blood urea nitrogen (BUN) and serum creatinine were collected at baseline and at 24 hours of presentation. Participants were categorized based on RIFLE criteria (17) during in-hospital stay. Outcomes were measured using duration of hospital stay, renal replacement therapy and mortality in-hospital. Mortality post discharge and during extra institutional transport were not taken into consideration. Study commenced after obtaining approval from Institutional Ethics Committee and waiver of consent was obtained since the study is retrospective record based and identifying details of participants were not collected. Sample size was calculated as 80 assuming α as 0.05 and β as 0.2 with 95% power. Values are expressed as frequencies and as mean ± standard deviation (SD) and are rounded off to nearest decimal. Chi square test was used to estimate the association of categorical variables and independent sample t test for detecting significant difference between groups of numerical variables. All statistical analysis was performed using free software R® and a $p < 0.05$ was considered statistically significant.

Results

Our retrospective study collected data from medical records of 80 participants with acute trauma presenting to Emergency medicine department of KIMS hospital, Trivandrum. 85% (n=68) participants were males and 15% (n=12) were females. AKI occurred in 40% (n=32) participants of which 93.8% (n=30) participants

Table 1: Association between patients' characteristics and AKI in studied population

	AKI (n=32)	Non AKI (n=48)	P
Age (mean ± SD)	32.0 ±10.7	39.3 ± 14.8	0.02
Gender [N (%)]			
Male	28 (87.5)	40 (83.3)	0.6
Female	4 (12.5)	8 (16.7)	
RTS (mean ± SD)	9.7 ± 1.4	10.6 ± 1.8	0.01
Hypotension [N (%)]			
Yes	21 (65.6)	39 (81.3)	0.01
No	11 (34.4)	9 (18.7)	
GCS [N (%)]			
≥10	10 (71.4)	4 (28.6)	0.008
<10	22 (33.3)	44 (66.7)	

AKI: acute kidney injury; GCS: Glasgow coma scale; RTS: revised trauma score

were in the risk category and 6.2% (n=2) participants in the category injury according to serum creatinine, eGFR and RIFLE criteria. None of the participants were in the RIFLE categories failure, loss and end stage renal disease.

The association between patients' characteristics and AKI in studied population are demonstrated in table 1. Based on the findings, there was significant difference between groups regarding their age probably indicating lower mean age among participants with AKI; No association was observed between groups regarding their gender. There was significant difference between groups regarding RTS, probably indicating lower RTS among participants with AKI. Significant association was observed between groups regarding blood pressure, probably indicating the higher proportion of participants with hypotension without AKI. Significant association was observed between groups regarding their GCS, probably indicating higher proportion of participants with AKI who had GCS ≥ 10.

None of the participants who were diagnosed with AKI required renal replacement therapy and all participants attained normal renal function in terms of urine output and serum creatinine levels. Participants with AKI were having significantly longer mean duration of hospital stay, 14.4 days compared to participants without AKI, 10.8 days (p=0.02). Mortality among participants with AKI was 6.3% (n=2) and among participants without AKI was 6.3% (n=3). Mortality among participants without AKI within 2 days of injury was 4.2% (n=2) and after 2 days was 2.1% (n=1).

Discussion

Eighty-five percent of study participants were males which was higher than previous reports of 50-60% of trauma victims being males. Males are at a higher risk of traumatic events owing to high risk behaviours such as drunken driving, rash driving etc. (18-20). Among males especially Keralites exposing them to higher frequencies of trauma. India was reported to have the highest number of road traffic accidents in the world and 2-33% had history of alcohol consumption prior to driving and 6-48% fatalities also had history of alcohol consumption (21). AKI was observed among 40% participants with acute trauma which is lower than previous reports of 50% AKI among acute trauma (22). Participants with AKI had lower mean age compared to previous reports which had reported a higher incidence of AKI associated with trauma among elderly (23). Advancing age results in decline in renal function thus predisposing these individuals to renal injury during acute trauma. Our finding, since a contradicting one requires further evaluation as to whether AKI is common among younger trauma victims and to establish the association of age and AKI among urban Keralites. Whether this finding is due to the high incidence of renal dysfunction among young Keralites owing to early development of lifestyle disorders such as diabetes mellitus and hypertension is to be evaluated (24). No association was observed between gender and AKI though males have been reported to be at higher risk of developing AKI (24). The exact reason for gender difference in AKI has not been understood clearly, though testosterone has been implicated as a causative factor for this increase in risk among males (25). Further studies demonstrating association of gender and acute kidney injury in trauma patients are required to demonstrate this association. The mean RTS among participants with AKI was significantly lower, this is a contrasting finding since AKI is usually associated with severe injuries and with higher RTS (23). In acute trauma many factors contribute towards AKI, hypovolemia and rhabdomyolysis cause damage to kidneys initially, the use of fluids (crystalloids or colloids) in patients with acute trauma worsens the existing

injury produced by hypovolemia and rhabdomyolysis. Crystalloids produce compartment abdominal or renal syndrome while colloids cause injury to the kidneys directly (23). Trauma via tissue injury produce systemic inflammation leading to increased renal oxidative stress. This is also produced by the ischemia reperfusion associated with haemorrhage and rhabdomyolysis. Renal oxidative stress results in production of superoxide anion which triggers renal cell apoptosis. Inducible nitric oxide synthase catalyses nitric oxide production which combines with superoxide to form peroxynitrate which produces structural alteration of mitochondria. Ischemia reperfusion also lead to expression of intracellular adhesion molecule 1 and E-selectin which mediate leukocyte adhesion, rolling and transmigration which develops into a pro-inflammatory state. Haemorrhage and blood loss reduces renal perfusion pressure, coupled with loss of erythrocytes and reduction in serum haemoglobin cause renal hypoxia. Hypovolemia and renal hypoxia activates sympathetic nervous system and renin angiotensin aldosterone system that result in further intrarenal vasoconstriction. These compensatory mechanisms increase renal perfusion but complicates renal ischemia by virtue of the increased demand of ATP for sodium reabsorption. Renal oxidative stress leads to renal inflammation and subsequent migration of renal inflammatory cells causing acute kidney injury. The use of iodinated contrast materials in patients with acute trauma cause direct injury to the kidneys by direct toxic effect of contrast materials. Haemorrhage also reduces blood volume and lead to renal hypo perfusion and hypoxia causing AKI. Myoglobin released as a result of rhabdomyolysis cause injury by producing hypovolemia due to swelling of muscles and by renal vasoconstriction both directly and by accentuating the vasopressor action of Angiotensin II which worsen renal ischemia and hypoxia (26). Myoglobin also increase the concentration of superoxide anion which in turn reduce the nitric oxide in vessel wall of afferent arterioles which lead to subsequent vasoconstriction (26). Myoglobin being a small molecule is filtered via glomerular capillaries produce damage to renal tubular epithelium due to oxidative ability of the end product of myoglobin breakdown, haeme (27). Myoglobin accumulation in renal tubules due to the acidic environment in haemorrhage and this accentuates the damage to renal tubules. Myoglobin also activates renal inflammation by activation of NF-kB and interleukin-6 leading to monocyte migration and also myoglobin catalyses the conversion of monocytes to macrophages. M1 macrophages secrete interleukin 1 and 12 which results in renal fibrosis and cause subsequent damage to renal tubules. Abdominal compartment syndrome cause mechanical constriction of blood vessels (arteries and veins) causing renal ischemia. Renal ischemia in acute trauma can also be a resultant of direct pressure and compression on the abdomen can directly lower the renal perfusion and produce ischemia. Renal interstitial oedema due to fluid resuscitation and inflammation could be considered as another etiological factor for AKI in acute trauma patients. Excessive use of crystalloids cause renal parenchymal oedema and renal hypo perfusion.

Our study also demonstrated significantly higher proportion of participants with hypotension who did not develop AKI. This is a new observation since studies evaluating the association of hypotension and AKI are scarce though many studies demonstrating pathophysiological changes are available as published literature. Higher proportion of participants with AKI had GCS ≥ 10, which has not been described in literature. There are reports of AKI among patients with traumatic head injury and had been detected to 9.2% of head injury patients (28). Different criteria for classification of patients according to GCS was used in the above mentioned study.

None of the participants required renal replacement therapy. Early initiation of renal replacement therapy has been advocated by many studies though methodological flaws limit the use of this recommendation (29). Renal replacement therapy is also associated with catheter related complications from insertion and infection, mechanical complications associated with extracorporeal circuit which includes severe blood loss, electrolyte disturbance, haemodynamic compromise, activation of humoral and cell mediated immune response and dialysis associated hypotension. These factors are considered to delay the recovery of renal injury in AKI (30, 31). All participants recovered completely from AKI at discharge. AKI patients were having significantly longer duration of hospital stay compared to participants without AKI. This is an established fact since AKI is associated with severe injuries, the hospital stay will be longer in these patients. Studies have demonstrated that the longer the persistence of AKI the higher the risk of mortality, heart failure and incident chronic kidney disease (32). The mortality among participants with AKI was 6.3% and this has not been reported in

previous studies from our setting.

Limitations

Small sample size and study design being a record based retrospective study are the major limitations of our study.

Conclusions

Forty percent of the acute trauma patients had AKI of which 93.8% of patients were in risk category and 6.2% of patients were in injury category according to RIFLE criteria. Surprisingly no patients of categories failure, loss and end stage renal disease were encountered. This could be due to timely arrival and intervention by protocol based care. No association of AKI and mortality was observed probably due to lower rates of mortality encountered in our study. AKI was associated with age, RTS, hypotension and GCS. No association of AKI with gender was observed. None of the patients required renal replacement therapy and the renal function of all patients returned to normal at the time of discharge.

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Authors' contribution

All the authors met the standards of authorship based on the recommendations of the International Committee of Medical Journal Editors.

Conflict of interest

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