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Incidence, Risk Factors and Short Term Outcome of Acute Kidney Injury among Patients with Acute Coronary Syndrome

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Abstract

Background: Cardio-renal syndrome is the leading cause of death globally. Acute kidney injury (AKI) is a major complication among patients admitted in Coronary Care Unit (CCU) with acute coronary syndrome (ACS). AKI in ACS patients is associated with higher morbidity, mortality and prolong hospital stay. **Objective:** To determine the incidence, risk factors and short term outcome of acute kidney injury (AKI) among the patients admitted in CCU with ACS. **Methods:** This cross sectional study was conducted at Department of Nephrology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh from January 2013 to December 2013. Following selection criteria a total of two hundred (200) patients with ACS were studied. AKI was defined according to the KDIGO guideline and further categorized by RIFLE criteria. Data of patients with AKI and those without AKI were analyzed and compared by statistical tests. **Results:** Majority of the study patients were male (79.5%). AKI was developed in 40 of the 200 study patients (20.0%). The mean (±SD) age of the study patients was 60.1 ± 11.1 years in patients with AKI and 55.9 ± 10.1 years in patients without AKI. Our data analysis showed that older age (>65 years), diabetes mellitus, dyslipidemia and smoking were significantly correlated to the development of AKI. Mortality was significantly high in AKI group (7.15%) compared to no AKI group (1.25%). Out of 27 patients who achieved renal recovery most (80.8%) belonged to risk class. Severity of AKI showed significant effect on renal recovery and final outcome.

Conclusion: This study demonstrated that, incidence of AKI among patients with ACS was 20%. Elderly patients, diabetes mellitus, dyslipidemia, and exposure to smoking were significantly associated with development of AKI in ACS.

Keywords

Acute Kidney Injury (AKI), Acute Coronary Syndrome (ACS), Cardio-Renal Syndrome

1. Introduction

Acute kidney injury (AKI) is a major complication in patients with acute coronary syndrome (ACS) and its ultimate expression is the cardio-renal syndrome. It is associated with prolonged hospital stay and higher morbidity and mortality. The prevalence of renal disease was found between 30% - 60% in patients with major cardiac events [1]. The incidence of acute kidney injury (AKI) is high (ranging from 10% to 25%) in patients those hospitalized with acute myocardial infarction (AMI) [2]. The development of AKI is associated with unfavorable outcomes and higher mortality after an AMI [2]. Contrast-induced nephropathy may occur up to 25% of patients undergoing coronary intervention [3] [4]. The occurrence of contrast induced acute kidney injury (CI-AKI) has been associated with poor short and long-term outcomes [4].

Acute coronary syndrome (ACS) may induce AKI through various mechanisms; including impaired cardiac output, use of contrast media in percutaneous coronary intervention (PCI) and the nephrotoxic effect of drugs. It has been suggested that AKI is not only a marker of severity of the illness but is also a causal factor for acceleration of cardiovascular injury through the activation of neurohormonal, immunological and inflammatory pathways [5]. In ACS patients, the most crucial mechanism causing AKI includes hemodynamic changes due to reduced cardiac output, ultimately decreasing glomerular filtration rate (GFR). Of note, factors reflecting cardio-circulatory impairment such as reduced left ventricular ejection fraction, left anterior descending coronary artery lesion and high end-diastolic pulmonary arterial blood pressure are independently associated with AKI in ACS [6]. Furthermore, changes in volume status, medical therapies, athero-embolism (during PCI or intra-aortic balloon pump insertion) and bleeding are involved in the pathogenesis of AKI. Additionally, in ACS patients, enhanced inflammatory response, increased oxidative stress and activation of the sympathetic nervous system synergistically accelerated the development of AKI, causing a vicious cycle amplifying the progression of the ongoing renal injury [7]. Finally, metabolic factors, including acidosis and acute hyperglycemia may favor the development of AKI [8] [9] [10].

The relationship between AKI and short term outcomes remains unclear. Understanding the impact of AKI on short term and long term outcomes will have a marked impact on treatment and risk stratification during hospitalization and will assist with guiding follow-up care after discharge from hospital. AKI may serve as a pathogenic factor in the development of other renal sequelae such as proteinuria, hypertension, and chronic kidney disease (CKD), which will compound cardiovascular risk over time. It has been reported that about 13% - 20% patients developed AKI after acute coronary syndrome and was associated with increase in hospital morbidity and mortality [11] [12] [13].

In many hospitals, most patients admitted in the CCU with acute coronary syndrome (ACS) are not investigated for renal disease with prime importance. If renal impairment was screened at admission and diagnosed earlier, both cardiac and renal outcomes would be better at discharge of these patients. There is scarce evidence addressing incidence of acute kidney injury, its risk factors and short term outcome among patients with acute coronary syndrome in Bangladesh. Therefore the purpose of the current study was to evaluate the acute kidney injury in patients with acute coronary syndrome admitted in coronary care unit (CCU), BSMMU, Dhaka, Bangladesh. This study could be helpful in estimating the morbidity and mortality of these patients and hence to develop effective preventive strategies to prevent AKI and thereby reduce the burden of the individual and the society.

2. Methodology

This cross sectional study was conducted in Department of Nephrology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh form January 2013 to December 2013. This study was approved by the Ethical Review Committee, BSMMU, Dhaka, Bangladesh. Sample size was estimated by using, $n = z^2pq/d^2$ formula; where allowable error 5% with 95% confidence level. Assuming a 20% prevalence of renal involvement in ACS [2], the required sample size was 245. It was a single centre study and time constraints, therefore a total of 200 patients were studied. Total 200 patients admitted with acute coronary syndrome in coronary care unit (CCU), Department of Cardiology, BSMMU, during the study period were included in this study purposively. Informed written consent was taken from each participant prior to enrollment. Inclusion criteria were adult patients (age > 18 years) of both sexes with any variety of ACS (Unstable angina, ST elevation MI or non-ST elevation MI). Patient with clinical picture or investigations suggesting chronic kidney disease (CKD), patients undergoing intervention (PCI) and patients with malignancy were excluded from the study.

Participants' demographic profile, clinical examination findings and relevant investigation reports were recorded in a data collection sheet. Each patient was assessed by following investigations-serum creatinine, urine-routine microscopic examination (R/M/E), urinary albumin creatinine ratio (ACR), serum electrolytes, complete blood count (CBC), random blood sugar (RBS), ultrasonogram of KUB (kidney ureter and bladder) region, electrocardiography (ECG), electrocardiogram (ECHO-color doppler) and serum Troponin-I level. Patients' serum creatinine was measured at hospital presentation, everyday during CCU stay and at the time of discharge from hospital. In hospital mortality rate were also recorded. All patients were followed up regularly till their discharge from hospital or death. The study population was divided initially into two groups (AKI group = patient admitted with acute coronary syndrome in CCU developing AKI and No AKI group = patient admitted with acute coronary syndrome in CCU but did not develop AKI) then sub grouped of AKI group into: risk, injury and failure. All AKI cases were categorized in 3 stages/classes based on RIFLE criteria [14]. The differences within outcome variables between the groups were analyzed and compared; these were: age, gender, smoking, diabetes mellitus (DM), hypertension, dyslipidemia, duration of CCU stay and final outcome.

In this study short term outcome of AKI refers to patient outcomes that had occurred during hospital (CCU) stay; these were: partial or complete recovery from AKI or death. On the other hand, long term outcome of AKI refers to the outcomes that developed after discharged from the hospital.

2.1. Acute Kidney Injury (AKI)

According to KDIGO* guideline acute kidney injury is currently defined as an absolute increase in serum creatinine ≥ 0.3 mg/dl (≥26.4 μmol/l), a percentage increase in serum creatinine ≥ 50% (1.5-fold from baseline), or a reduction in urine output (documented oliguria < 0.5 ml/kg/hour for >6 hours). Or in whom who do not have any previous records, AKI is defined as the increase of serum creatinine by 0.5 mg/dl and/or by 50% over baseline, with:

- Previously normal renal function;
- There is no haematuria or proteinuria on routine examination;
- Ultra-sonogram (USG) shows no structural abnormality.

[*KDIGO = Kidney Disease Improving Global Outcomes]

2.2. Different Classifications of Acute Kidney Injury (AKI) [14]

RIFLE	
an acute ↑ in sCr over 7 days	
Risk	↑ in sCr ≥ 1.5 × baseline
Injury	↑ in sCr ≥ 2.0 × baseline
Failure	↑ in sCr ≥ 3.0 × baseline or ↑ in sCr ≥ 0.5 mg/dL if baseline sCr ≥ 4.0 mg/dL
Loss	Complete loss of kidney function > 4 weeks
ESRD	End-stage renal disease > 3 months
AKIN	
an acute ↑ in sCr within 48 h	
Stage 1	↑ in sCr ≥ 1.5 - 2.0 × baseline or ↑ in sCr ≥ 0.3 mg/dL

Continued

Stage 2	↑ in sCr > 2.0 - 3.0 × baseline
Stage 3	↑ in sCr >3.0 × baseline or sCr ≥ 4.0 mg/dL with an acute ↑ ≥ 0.5 mg/dL or initiation of RRT
KDIGO	
an acute ↑ in sCr within 48 h	
Stage 1	↑ in sCr ≥ 1.5 - 1.9 × baseline or ↑ in sCr ≥ 0.3 mg/dL
Stage 2	↑ in sCr ≥ 2.0 - 2.9 × baseline
Stage 3	↑ in sCr ≥ 3.0 × baseline or sCr ≥ 4.0 mg/dL with an acute ↑ ≥ 0.5 mg/dL or initiation of RRT

AKIN = acute kidney injury network; ESKD = end-stage kidney disease; KDIGO = Kidney Disease Improving Global Outcomes; RIFLE = Risk, Injury, Failure, Loss, and End-stage renal disease; RRT = renal replacement therapy; sCr = serum creatinine; ↑ = increase; ↓ = decrease.

2.3. Acute Coronary Syndrome (ACS) [15]

Acute coronary syndrome (ACS) is a syndrome that occurs due to decreased blood flow in the coronary arteries of heart and comprises the following varieties:

ST elevation MI (STEMI):

- Typical chest pain.
- ECG change: New or presumed new ST-segment elevation at the J point in 2 or more contiguous leads with the cut-off points of ≥2 mm in chest leads (V1-V6) and ≥1 mm in other leads.
- Cardiac marker: raised troponin-I and creatine kinase-MB (CKMB).

Non-ST elevation MI (NSTEMI):

- Typical chest pain.
- Acute ST depression on the initial ECG.
- Raised cardiac troponin T or I concentration.

Unstable Angina (UA):

It is a clinical syndrome that is characterized by new onset or rapidly worsening angina, angina on minimal exertion or angina at rest.

2.4. Cardio-Renal Syndrome

The cardio-renal syndrome (CRS) defined "as an acute worsening of heart function leading to AKI or dysfunction" that is a complication of "acute heart failure and/or acute coronary syndrome (ACS)", associated with a high risk mortality and longer hospital stay [15]. A newly describe syndrome of inter-dependency. Each dysfunctional organ can initiate and maintain disease in the other through common haemodynamic, neurohormonal and immunological pathways.

2.5. Statistical Analysis

Data cleaning validation and analysis was performed using the SPSS (Statistical

Package for Social Science) software. Categorical data were presented as frequency/percentage and continuous variable was expressed as mean ± SD (standard deviation). The statistics used to analyze the data were descriptive statistics and the tests done were Student's "*t*" test and Chi-square test. The level of significance was set at 0.05 and p value < 0.05 was considered significant.

3. Results

A total of 200 patients with acute coronary syndrome (ACS), who had got admitted in the coronary care unit (CCU), Department of Cardiology, BSMMU were included in this study. The study population was divided initially into two group: AKI group (ACS patients with AKI; n = 40, male = 33, female = 7) and No AKI group (ACS patients without AKI; n = 160, male = 126, female = 34) and AKI group then sub grouped into: risk, injury and failure classes.

Among total 200 ACS patients; AKI was found in 40 (20%) patients and remaining 160 (80%) patients had no AKI. Incidence of AKI was 20.0%. Out of 40 (20%) AKI patients; 26 (13.0%) were in risk class, 7 (3.5%) were in injury class and 7 (3.5%) were in failure class of RIFLE criteria as displaying in **Figure 1**.

It was observed that among 40 patients of AKI; 20 (50.0%) patients had ST segment elevated myocardial infarction (STEMI), 19 (47.5%) patients had non-ST segment elevated myocardial infarction (NSTEMI) and 1 (2.5%) patient had unstable angina (UA). On the other hand among 160 patients of no AKI group; 83 (51.9%) patients had ST segment elevated myocardial infarction (STEMI), 64 (40.0%) patients had non-ST segment elevated myocardial infarction (NSTEMI) and 13 (8.1%) patient had unstable angina (UA). There was no significant difference (p = 0.386) in different types of ACS among the groups (**Table 1**).

Majority of the study patients were male (79.5%). Mean (±SD) age of the AKI group patients was 60.1 ± 11.1 years and patients in no AKI group that was 55.9 ± 10.1 years. Our data analysis showed that age > 65 years, duration of CCU stay, diabetes mellitus, dyslipidemia and smoking were significantly correlated to the development of AKI. Mortality was significantly high in AKI group (7.15%) compared to no AKI group (1.25%). Other variables did not show any significant association with the development of AKI (**Table 2**).

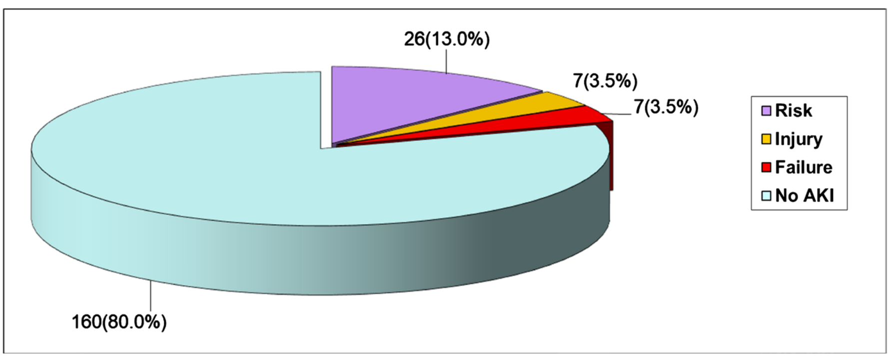

Figure 1. Overall incidence of acute kidney injury (AKI) among acute coronary syndrome (ACS) patients (n = 200).

Table 1. Types of ACS in study patients (n = 200).

Types of ACS	AKI (n = 40) No. (%)	No AKI (n = 160) No. (%)	p value
NSTEMI	19 (47.5%)	64 (40.0%)	
STEMI	20 (50.0%)	83 (51.9%)	0.386^{ns}
UA	1 (2.5%)	13 (8.1%)	

Chi-square test was performed to compare between groups. n = Number of subjects; ns = Not significant.

Table 2. Risk factors for development of AKI in patients with ACS (n = 200).

Parameters	AKI (n = 40) No. (%)	No AKI (n = 160) No. (%)	p value	Odds ratio	95% CI
Age					
<65 yrs	31 (77.50%)	139 (86.9%)	0.025*		
>65 yrs	9 (22.50%)	21 (13.1%)			
Mean ± SD	60.1 ± 11.1	55.9 ± 10.1			
Gender					
Male	33 (82.50%)	126 (78.75%)	0.599	1.272	0.518 - 3.127
Female	7 (17.50%)	34 (21.25%)			
Diabetes mellitus					
Yes	25 (62.5%)	52 (32.5%)	<0.001*	3.462	1.684 - 7.115
No	15 (37.5%)	108 (67.5%)			
Hypertension					
Yes	28 (70.0%)	116 (72.5%)	0.753^{ns}	0.885	0.414 - 1.893
No	12 (30.0%)	44 (27.5%)			
Dyslipidemia					
Yes	16 (40.0%)	38 (23.7%)	0.038*	2.14	1.032 - 4.441
No	24 (60.0%)	122 (76.3%)			
Smoking					
Yes	22 (55.0%)	54 (33.7%)	0.013*	2.399	1.187 - 4.850
No	18 (45.0%)	106 (66.3%)			
CCU stay (days)	10.71 ± 1.91	5.86 ± 0.84	<0.001*		
Final outcome					
Survived	37 (92.5%)	158 (98.75%)	0.02*	0.16	0.02 - 1.20
Expired	3 (7.5%)	2 (1.25%)			

Chi-square test for qualitative data and Unpaired *t*-test for quantitative data were performed; n = Number of subjects; * = Significant; ns = Not significant.

Among total 40 ACS patients who developed AKI; 26 patients were in risk class, 7 patients were in injury class and 7 patients were in failure class. Out of 27 patients who achieved renal recovery, maximum [21 (80.8%)] belonged to risk class. An analysis of final outcome revealed that all patients of risk class (26) and injury class (7) were survived while out of 7 patients of failure class 3 patients were expired. Among 40 AKI patients; 37 patients were managed conservatively and survived while 3 patients expired despite receiving hemodialysis. Therefore renal recovery, management and mortality were found to be significantly affected by severity of AKI. Besides these, no other variables were found to be significantly correlated with the RIFLE classification of AKI severity (Table 3).

4. Discussion

Cardio-renal syndrome is the leading cause of death globally. Acute kidney injury (AKI) has a known catastrophic impact on critically ill patients like acute coronary syndrome (ACS) patients in coronary care unit (CCU) [5] [16]. The relationship between AKI and ACS remains unclear and its pathogenesis is multifactorial. This hospital based study was conducted among 200 patients with ACS to determine the incidence, risk factors and short term outcome of acute kidney injury. Patients with ACS admitted in our coronary care unit and fulfilled the selection criteria were studied.

Table 3. Demographic factors, ACS types and outcomes in relation to AKI severity (n = 40).

Parameters	Risk (n = 26) No. (%)	Injury (n = 7) No. (%)	Failure (n = 7) No. (%)	Total (n = 40)	p value
Age					
<65 yrs	20 (76.9%)	5 (71.4%)	6 (85.7%)	31	0.571^{ns}
>65 yrs	6 (23.1%)	2 (28.6%)	1 (14.3%)	9	
Mean ± SD	58.69 ± 12.01	62.42 ± 9.32	62.85 ± 9.23		
Gender					
Male	22 (84.6%)	7 (100.0%)	4 (57.1%)	33	0.09^{ns}
Female	4 (15.4%)	0 (0.0%)	3 (42.9%)	7	
Types of ACS					
NSTEMI	11 (42.3%)	4 (57.1%)	4 (57.1%)	19	0.88^{ns}
STEMI	14 (53.8%)	3 (42.9%)	3 (42.9%)	20	
UA	1 (3.8%)	0 (0.0%)	0 (0.0%)	1	
CCU stay (days)	9.85 ± 1.22	10.57 ± 0.98	11.71 ± 3.55		0.06^{ns}
Renal recovery					
Yes	21 (80.8%)	3 (42.9%)	3 (42.9%)	27	0.05*
No	5 (19.2%)	4 (57.1%)	4 (57.1%)	13	
Final outcome					
Survived	26 (100.0%)	7 (100.0%)	4 (57.1%)	37	<0.001*
Expired	0 (0.0%)	0 (0.0%)	3 (42.9%)	3	
Management					
Conservative	26 (100.0%)	7 (100.0%)	4 (57.1%)	37	<0.001*
Hemodialysis	0 (0.0%)	0 (0.0%)	3 (42.9%)	3	

Chi-square test for qualitative data and unpaired *t*-test for quantitative data were performed. n = Number of subjects; * = Significant; ns = Not significant.

The study population was divided initially into two groups (AKI group and No AKI group) then sub grouped into risk, injury and failure classes according to the severity of renal impairment. In our study AKI occurred in 40 of the 200 ACS patients during their CCU stay. Therefore the overall incidence of AKI in ACS patients was 20.0%, which was consistent with other studies as reported that prevalence of AKI among patients admitted with acute coronary syndrome in CCUs was 13% - 20% [1] [2] [13]. The mean age of the study patients in AKI group was 60.1 ± 11.1 years, while in no AKI group that was 55.9 ± 10.1 years. The mean age difference between two groups was found statistically significant ($p = 0.025$) and this finding was accordant with a previous study which showed that ACS patients with AKI were older (61.6 ± 15 years) than the non-AKI group (54.7 ± 13 years, $p = 0.031$) [17]. It was found that; in AKI group 82.50% patients were male and 17.50% were female, while in no AKI group 78.75% were male and 21.25% were female patients. Among total study population majority of the patients were male (79.5%). Similar findings were observed in previous studies [15] [17]. Mean (±SD) duration of CCU stay was significantly higher ($p < 0.001$) among patients with AKI (10.71 ± 1.91 days) compared to patients without AKI (5.86 ± 0.84 days) and this was also a finding in the previous study as well [17].

Patients with no AKI (98.75%) had significantly higher ($p = 0.02$) chance of survival compared to patients with AKI (92.5%). In accordance Buargub M and Elmokhtar ZO reported that the CCU mortality among the AKI patients was 25.7% compared with 6.12% in the non-AKI patients, and the mortality worsened with increasing severity of AKI [17].

The risk of developing AKI was significantly high in patients associated with diabetes mellitus ($p < 0.001$), dyslipidemia ($p = 0.038$) and smoking ($p = 0.013$) while there was no significant association in patients with hypertension ($p = 0.753$). These results were statistically significant and supported by a few previous studies [18] [19].

In this study, out of 40 patients who had developed AKI 37 (92.5%) survived; while out of 160 patients who did not developed AKI 158 (98.75%) survived. AKI severity had significant effect ($p = 0.05$) on renal recovery. Out of 27 patients who achieved renal recovery, 21 (77.8%) belonged to the "risk" class, followed by the "injury" 3 (11.1%) and "failure" 3 (11.1%) classes. Out of 37 patients who survived, 26 (70.3%) allocated to "risk", 7 (18.9%) to "injury" and 4 (10.8%) to "failure" classes of the RIFLE classification of AKI severity. It was observed that although 5 (19.2%) patients with mild renal impairment (i.e. the risk class) and 4 (57.1%) of those with moderate renal impairment (i.e. the injury class) did not fully regain their previously normal renal function; all of the patients in these two groups survived and received conservative management. The 3 (42.9%) patients who expired belonged to only the "failure" class and none of their renal functional parameters improved despite hemodialysis. Within this class, the other patients were managed conservatively and among the 4 (57.1%) patients who survived, 3 (42.9%) had AKI (resolved) and 1 (14.2%) was discharged with renal functional impairment possibly leading to CKD. The final outcome was thus found to be significantly influenced ($p < 0.001$) by the severity of AKI. These findings were consistent with previous studies as reported that ACS patients with AKI compared to non-AKI patients demonstrated greater risk of poorer outcomes [20] [21].

AKI was detected in 20% of ACS cases among total 200 CCU patients which was most often hospital acquired and probably due to hemodynamic causes. Despite much progress and increased recognition of AKI, it still remains an underestimated and unnoticed entity in patients with ACS. Although there is a high mortality rate in these patients, there were a significant number of survivors. In this study we aimed to provide a framework of knowledge to increase physicians' awareness of AKI among patients with ACS, with the goal of improving the outcome of these patients.

5. Conclusion

This study demonstrated that, incidence of AKI after ACS was 20%. We conclude that elderly patient, diabetes mellitus, dyslipidemia, exposure to smoking were significantly associated with development of AKI in ACS. Morbidity and mortality were significantly high in AKI compared to no AKI group among patients with ACS. Appropriate intervention in early stages of AKI may have a positive impact on patient outcomes.

Limitations of Study

It was a single centre study with a relatively small sample size.

Recommendations

Acute kidney injury (AKI) has a known catastrophic impact on critically ill patients. Morbidity and mortality are significantly high in AKI patients with ACS. A large scale, multi-center study will be needed to assess the long term survival of these patients.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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