Associated Biochemical Changes and Outcome of Acute Kidney Injury in ICU Patients and Impact on Rifle Classes

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Abstract

Background: Acute Kidney Injury (AKI) has an independent impact on outcome, even after correction of all other variables in critically ill patients . AKI in ICU is often associated with different biochemical metabolic derrangements as a result of sepsis and non-renal organ system failure. Adequate informations are essential to develop effective measures to prevent and control morbidity and mortality. This study was done to detect AKI with their associated biochemical abnormalities and outcome among admitted patients in intensive care unit of BSMMU.

Materials and methods: This prospective observational study was carried out in the Department of Nephrology, Bangabandhu Sheikh Mujib Medical University (BSMMU) Dhaka, during the period of September 2015 to October 2016. A total of 105 patients who were admitted in the Department of Anesthesia, Analgesia and intensive care medicine, BSMMU were included in this study. Patients who had pre-existing CKD, those on maintenance dialysis, with history of renal transplantation, Feature suggestive of chronic kidney disease were excluded. Baseline data were recorded accordingly. The study population was divided initially into two group (No AKI and AKI) then sub groups into risk, injury, failure and followed up till discharge or death.

Results: Incidence of AKI was 37.14%. Mean increase in Serum creatinine was 64.53%, 132.87% and 375.01% from baseline for risk, injury and failure respectively. Subgroup analysis revealed risk (20%) injury (6.67%) and failure (10.47%). Associated acid base disorder, electrolytes imbalance, hepatic dysfunction, haemotogical disorder and hypoalbuminemia were found statistically significant between two groups. Logistic regression analysis showed that associated haematological abnormalities were positively correlated to the development of AKI. But among these no variables showed significant effect on RIFLE class population. Our study revealed overall morality is (53.8%). Mortality was highest in Failure class and most patients from risk class achieved renal recovery.

Conclusion: The incidence of AKI in critically ill patient is high. Associated biochemical changes should be addressed properly to minimize fatality. RIFLE classification for AKI might help in recruitment of patients for predicting prognosis.

Key words : Acute Kidney Injury (AKI); Biochemical abnormalities; Morbidity and mortality; RIFLE.

Introduction

Acute kidney injury has a known catastrophic impact on critically ill patients in ICU.[1] It is common clinical problem and mostly multifactorial. AKI may progress to renal failure, preventing the kidneys to play their most important role, homeostasis.[2] AKI is characterized by sudden and generally reversible renal function impairment, failing to maintain the homeostasis and may or not be accompanied by reduced urine output for a certain period.[3] Recent evidence suggests that acute dysfunction of kidney manifest by changes in urine output and blood chemistries results in serious clinical consequences, even death.[4] The incidence of Acute Kidney Injury (AKI) in hospitalized patient is 5-7% and One to twenty five percent of critically ill patients who are admitted to Intensive Care Unit (ICU) develop acute kidney injury, depending on the definition used.[5-7]. AKI in this setting is associated with mortality rates of 50 to 70 %.[8]

Usually AKI may be categorized as pre-renal, related to reduced blood flow for inappropriate cardiac output or intravascular volume, intrinsic renal disease, from an insult to the renal parencyhma including ischemic, vasular, tubular or glomerular disorders and post renal, due to urinary tract obstruction either in single kidney or both kidney.[9,10] Recent epidemiological studies have demonstrated wide variation in etiologies and associated abnormalities with AKI and increased Hospital mortality following AKI. The

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cause of AKI in critically ill patients is often multifactorial though Sepsis is highly prevalent and results in a wide range of biochemical abnormalities.[11] Yet there is no consensus on the mount of dysfunction that defines acute kidney injury, with than 30 definitions is use in the literature today.[12] The variety of definitions used in clinical studies may be partly responsible for the large variation in the reported incidence (1-31%) and associated mortality (19-83%) of acute kidney injury.[13,14,15] To establish a uniform definition for acute kidney injury, ADQI has recently published a consensus definition of ARE, using a set of criteria called RIFLE (Risk, injury, failure, loss and end stage) criteria.[16] The RIFLE criteria classify ARF into three groups (Risk, Injury and failure) according to relative changes of serum creatinine and urine output. The last two groups, classed as loss and end stage renal disease were the outcome of kidney dysfunction. The first step of which is to estimates the patient risk for acute kidney injury. During the last few years the number of ICU is increasing in Bangladesh. But there is limited data regarding the incidence of AKI with their associated biochemical characteristics and the outcome in ICU admitted patients.

Materials and methods

A prospective observational study was done in the Department of Nephrology, Bangabandhu Sheikh Medical University, Dhaka Bangladesh. This study was carried out at Department of Anesthesia, Analgesia and intensive care medicine. BSMMU, Dhaka, Bangladesh. From September 2015- October 2016. total 105 patients who were admitted in ICU. On the basis of resource constraint only 105 respondents taken by purposive sampling. Case was selected according to selection criteria. The need for informed consent was waived because most of the studied population were unconscious or was on ventilation. Informed consent were taken from patients legal guardian. Data were collected by using structured questionnaire. The data collected from their medical charts according to a protocol and the RIFLE classification rated during the ICU stay. Each patient was followed-up to the final outcome, either death or discharge from ICU.

Data collection was performed on a daily basis. Demographic profile, clinical examination and relevant investigation reports were recorded in pre-designed data with collection sheet. Fluid status of the patient monitored by CVP, fluid chart and urine output. Patient assessed by baseline and serial routine chemistry, electrolytes, renal function test including B. Urea and S.creatinine. Investigation performed to determine the cause of renal failure when needed. lnvestigations done relevant to cause of ICU admission. And all the patients were followed up till their discharge or death. Statistical analysis was conducted using SPSS (Statistical Package for Social Science) 13.0 for windows software. Categorical data were expressed as frequencies and corresponding percentages. Parametric data were expressed in mean ± SD. Parametric data were evaluated by independent sample't' test. Categorical data were evaluated by chi-square test as needed. Level of significance for all analytical test were set at 0.05 and p Value <0.05 is considered significant. Approval to perform the study was obtained from ethical committee, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.

Results

A total of one hundread five patients (Male 75 and female 30) fulfilled the inclusion criteria were studied over a period of one year (September 2009 to October 2010). Patients were initially divided in two groups AKI and no AKI. Then the AKI group is further divided into three groups (Risk, Injury and failure).the incidence of AKI was. (Figure:1). Mean baseline serum creatinine level in no AKI was (0.89+0.11 mg/dl) and AKI was (0.93+0.15 mg/dl). This is almost similar in two groups.

The associated biochemical anomalies such as acid base disorder, electrolytes imbalance, hepatic dysfuntion (LFT) haematological disorder and hypoalbuminaemia were the major abnormalities were found significant (p<0.01) in patients of AKI (Table I). But no variable was significant for subclass of RIFLE criteria of AKI. (Table III).The outcome was significantly varied with sub groups of AKI by RIFLE criteria.

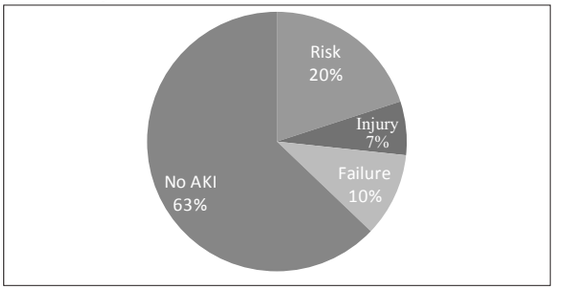

Fig 1 Incidence of AKI (n=105)

Figure 1 shows incidence of AKI among ICU admitted patients. Out of 105 ICU admitted patients, 66(62.86%) developed no AKI, 21(20%) developed risk',7(6.67%) injury' and 11 (10.47%) failure' class of AKI.

Table I Associated metabolic abnormalities in the patient of AKI

Parameters **Associated abnormalities**	No AKI (n=66) No. (%)	AKI (n=39) No. (%)	p value
Acidbase disorder			
Present	32 (48.5)	32 (82.1)	
Absent	34 (51.5)	7 (17.9)	0.001**
Electrolytes imbalance			
Present	33 (50.0)	35 (89.7)	
Absent	33 (50.0)	13 (10.3)	0.0001***
Hepatic (LFT) dysfunction			
Present	2 (3.0)	9 (23.1)	
Absent	64 (97.0)	30 (76.9)	0.001**
Haematological disorder			
Present	7 (10.6)	31(79.5)	
Absent	59 (89.4)	8 (20.5)	0.0001***
Cardiac enzyme elevation			
Present	0	1 (2.6)	
Absent	66 (100.0)	38 (97.4)	0.191ns
Hypoalbuminaemia			
Present	0	6 (15.4)	
Absent	66 (100.0)	33(84.6)	0.001**

Univariate analysis (Chi-square test) ns= Not significant ,*= Significant (p<0.01), **:((p<0.001).

Table I shows major associated abnormalities in the patient of AKI. Associate abnormalities . All were significantly associated with group of patients with AKI except cardiac enzyme elevation.

Table II Impact of baseline biochemical characteristics on the occurrence of AKI (Logistic regression)

Parameters	Coefficient	SE	Wald	Sig	Odds ratio	95% CI for Odds ratio Lower	Upper
Acid base	-1.4451	1.4635	0.9749	0.324	0.2357	0.0134	4.1512
Electrolytes	0.8371	1.4460	0.3351	0.563	2.3096	0.1357	39.2954
Hepatic	-0.9323	2.1525	0.1876	0.665	0.3937	0.0058	26.7493
Haematological	4.6016	1.7528	6.8916	0.009**	0.0100	0.0003	0.3116
Hypo-albuminaemia	-13.1331	30.7975	0.1818	0.670	0.0000	0.0000	0.0003
Constant	47.6087	62.3041	0.5839	0.445			

[a]Odds ratio expressed for a 10 unit change

Logistic regression analysis

*= Significant at (p<0.05)

**= Significant at (p<0.01)

***= Significant at (p<0.001)

Table II shows logistic regression analysis. Except haematological abnormality (p<0.01), no other parameter showed any significant risk in the development of AKI during ICU stay.

Table III Effect of associated abnormalities on AKI class

Associated abnormalities	Risk No.(%)	Injury No. (%)	Failure No. (%)	Total	p value
Acidbase disorder					
Yes	15 (46.9)	7 (21.9)	10 (31.3)	32	0.155ns
No	6 (85.7)	0	1 (14.3)	7	
Electrolytes imbalance					
Yes	18 (51.4)	6 (17.1)	11 (31.4)	35	0.417ns
No	3 (75.0)	1 (25.0)	0	4	
Hepatic (LFT) dysfunction					
Yes	3 (33.3)	1 (11.1)	5 (55.6)	9	0.115ns
No	18 (60.0)	6 (20.0)	6 (20.0)	30	
Haematological disorder					
Yes	19 (61.3)	4 (12.9)	8 (25.8)	31	0.135ns
No	2 (25.0)	3 (37.5)	3 (37.5)	8	
Cardiac enzyme elevation					
Yes	0	0	1 (100.0)	1	0.271ns
No	21 (55.3)	7 (18.4)	10 (26.3)	38	
Hypoalbuminaemia					
Yes	2 (33.3)	1 (16.7)	3 (50.0)	6	0.416ns
No	19 (57.5)	6 (18.2)	8 (24.2)	33	

Chi-square test

ns= Not significant.

Table III shows effect of associated abnormalities on AKI class. None of the parameters showed any significant effect on AKI class.

Our study revealed overall morality is (53.8%).

Table IV Final outcome of the patients with AKI according to RIFLE classes.

Parameters	Risk N% (n=21)	Injury N% (n=7)	Failure N% (n=11)	Total (n=39)	p value
Renal recovery at time of death/ discharge					
Yes	15 (78.9%)	3 (15.8%)	1 (4.3%)	19	0.003*
No	6 (30%)	4(20.0%)	10 (50.0%)	20	
Final outcome					
Survived	15 (83%)	22 (11.1%)	1(5.6%)	18	0.002*
Expired	6 (28.6%)	5 (23.8%)	10 (47.6%)	21	

Table IV shows that renal recovery at time death or discharge and final outcome in terms of survival varies significantly according to RIFLE sub classes and outcome is worse in failure group.

Discussion

The definition we used for the diagnosis of AKI is RIFLE criteria,Where three grades of acute kidney Injury-Risk (Class R) Injury (ClassI) and Failure (Class F) based on serum Creatinine is evaluated. We did not evaluate the outcome classes (Loss-Class L and end-stage kidney disease- class E). In Risk class-increased serum Creatinine X 1.5 from baseline, injury class-increased serum Creatinine x 2 from baseline and Failure class-increased serum creatinine x 3 from baseline or serum creatinine > 4 mg/dL. In our study AKI occurred in 39 of the 105 patients (37.14%) during their ICU stay with maximum RIFLE-R.l.F in 20%, 6.67% and 10.4% respectively. Other study reported that the incidence of AKI was 36.1%.[17] In a retrospective study in ICU demonstrated incidence of AKI was 41.3%, incidence of AKI was 40.3%, in a prospective multicenter study demonstrate 10.8% incidence and incidence of AKI was 35.8%[8,18-20]. Our study the overall incidence in 37.14% which is consistent with other study conducted abroad.

AKI may progress to renal failure, preventing the kidneys to play their most important role, homeostasis. Thus AKI is associated with various metabolic and biochemical disturbance especially those caused by sepsis mostly and other contributory factors.[1] During the time of AKI diagnosis acid base disorder (82.1%) electrolytes imbalance (89.7%) hepatic dysfunction (23.1%) hematological disorder (79.5%) and hypoalbuminaemia (15.4%) were the major abnormalities in patient of AKI ($p < 0.01$, $p < 0.001$, $p < 0.01$ and < 0.01 respectively).

Studies in different areas found sepsis (57%) as a contributory factor and associated with these biochemical abnormalities.[15,21] Associated abnormalities is patient with AKI in our study is acid base disorder, electrolytes imbalance, hepatic dysfunction, Haematological disorder and hypoalbuminaemia which is almost consistent with study by Dinna N. Cruz et al.[8,22]

In this study logistic regression analysis found that hematologic abnormality showed significant risk in the development of AKI along with age >65 years, exposureto ACEi/ARB, Aminoglycosides, direct ICU admission and transfer from medical ward, diabetes, sepsis and cardiogenic sock. Hospital stay (Not shown in result). This findings also similar to findings by De Mendonca et al and joao F.P. Oliveira et al.[23,24]

During Analysis of AKI in risk, injury and failure group we found that, associated abnormalities has no significant effect on AKI class. Most probably this may be due to small sample size in each group. And the effect of associated abnormalities is patient with AKI in our study is almost consistent with study performed.[8] Our study revealed overall morality is (53.8%). Among RIFLE class highest (47.6%) in Failure class. Other study showed similar pattern of mortality rate among RIFLE class.[25,26] Final outcome showed significant effect ($P<0.05$) . In our study renal Recovery at the time of death/discharge showed significant effect on class of AKI ($P<0.05$). Maximum patients (78.9%) belonged to risk class achieved renal recovery. Review of study showed similar type of result.[7]

Limitations

i) This was a single centre study and small sample size, so conclusion may not be consistent with similar large studies.

ii) A longer follow-up could provide a larger sample and possible more robust analysis.

iii) To diagnose AKI, we used only serum creatinine criteria. This compromised this study. It is possible that urine output and creatinine taken together could provide complementary information.

iv) Patient outcome in our study was evaluated at exit from the ICU, which underestimates the impact of AKI on outcome.

Conclusion

In this study the incidence of AKI in critically ill patient is high. Associated biochemical changes should be addressed properly to minimize fatality. Until serum and urine biomarkers for AKI become widely available for clinical use, a simple and clinically applicable method for identifying these patients across different centers, such as the RIFLE classification would help in recruitment of patients for predicting prognosis.

Recommendations

- To know the correct incidence of AKI and risk factors, in Bangladeshi population, a large scale, multicenter study will likely to be needed.

- Even small changes in renal function carry significant risk for the affected patients, making the prevention of AKI of paramount importance, if possible, the associated factors should be corrected.
- Regular and close attention should be paid on critically ill patient admitted in ICU to detected early AKI and manage as early as possible in an ICU setting because it is an independent risk factor for death.

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Contribution of authors
SMUI-Conception, acquisition of data, interpretation of data, drafting and final approval.
MA-Data analysis, critical revision & final approval.
NH-Conception, drafting, critical revision & final approval.
RBK-Design, drafting & final approval.
MSH-Data analysis, interpretation of data, critical revision & final approval.
AM-Data analysis, critical revision & final approval.

Disclosure
All the authors declared no competing interest.

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