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A STUDY OF ACUTE KIDNEY INJURY IN INTENSIVE CARE UNIT

Nephrology

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ABSTRACT

Introduction: Acute kidney injury (AKI) is major global public health problem. AKI is defined as a functional or structural abnormality of the kidney as determined by blood, urine or tissue tests or by imaging studies. AKI complicates upto 30% of admissions to intensive care units (ICU). AKI is associated with very high rates of morbidity and mortality.

Materials and Methods: This is a prospective observational cohort study conducted in department of Nephrology in Christian Medical College and Hospital, Ludhiana over a period of one year. Patients admitted in ICU fulfilling inclusion criteria were studied for the prevalence, risk factors, etiology, outcomes of AKI and to compare for early diagnosis of AKI using RIFLE(risk, injury, failure, loss and end stage renal disease and AKIN (acute kidney injury network) criteria. Independent unpaired t-test , Mann-Whitney U test and Chi-Square test were used for statistical analysis.

Results: A total of 360 patients were enrolled, 65.1% were male and 34.9% were females. The prevalence of AKI in ICU was 85.5% by AKIN and 80.7% by RIFLE criteria. Sepsis was the most common cause of AKI seen in 61.8% and 63.1% of patients by AKIN and RIFLE criteria. Mortality was 22.3% and 23.2% by AKIN and RIFLE criteria respectively. RRT was required by 29.8% and 31.4% of AKI patients diagnosed by AKIN and RIFLE criteria. Mortality rate of patients receiving RRT was 65.5%. Hypotension resulted in AKI in 56.3% and 58.4% of patients by AKIN and RIFLE criteria and RRT was required in 39.4% and 40.3% of these patients respectively.

Conclusion: Prevalence of AKI in ICU is high. The AKIN criteria helps in early and more diagnosis of AKI compared to RIFLE criteria. Hypotension and sepsis were the most common causes of AKI. Mortality was higher in AKI compared to non-AKI patients.

KEYWORDS

Acute kidney injury, ICU, AKIN, RIFLE

INTRODUCTION

Acute kidney injury (AKI) is defined as a functional or structural abnormality of the kidney as determined by blood, urine or tissue tests or by imaging studies. [1] AKI is often under-recognized disorder, which is associated with a high risk for mortality, development of chronic kidney disease (CKD) and other organ dysfunction. AKI complicates approximately 5% of hospital admissions and upto 30% of admissions to intensive care units (ICU). AKI is associated with a markedly increased risk of death in hospitalized individuals, particularly in those admitted to the ICU where in-hospital mortality rates may exceed 50%.[2]

The epidemiology of AKI differs tremendously between developed and developing countries, owing to differences in demographics, economics, geography, and co morbid disease burden. The lack of a uniform definition for AKI is considered to be one of several reasons for conflicting epidemiological data of AKI. It has resulted in a broad range of estimated prevalence of AKI in the ICU.

The etiology of AKI is multifactorial, and among all causal factors, septic shock is the one most commonly associated with the onset of AKI [3]. The risk factors for AKI in ICU patients described in the literature include old age, previous renal disease, sepsis, obesity, hypovolemia, surgery, history of hypertension, and cardiovascular disease [4].

In patients who recover from AKI after variable periods of renal replacement therapy, renal insufficiency is observed in 41% and five year survival is about 50% [5]. This puts an additional burden on health infrastructure and economy.

AIMS AND OBJECTIVES

1. To determine the clinical characteristics, risk factors, etiology and outcomes of acute kidney injury (AKI) in patients presenting in intensive care unit.
2. To determine the prevalence and to compare for early diagnosis of AKI in critically ill patients according to RIFLE and AKIN criteria.

MATERIALS AND METHODS

Study Design: This is a prospective observational cohort study conducted in department of Nephrology in Christian Medical College and Hospital, Ludhiana.

Inclusion criteria:

All patient admitted in ICU with wide variety of medical & surgical disorders necessitating ICU care during the one year period from 1st June 2015 to 31st May 2016 were included, after obtaining due consent.

Exclusion Criteria:

Age less than 18 years, chronic kidney disease (CKD), patients with ICU stay less than 48 hours and patients unwilling to participate in the study or to give informed consent.

METHODOLOGY:

All patients admitted to the ICU fulfilling the inclusion criteria during the study period were recruited and evaluated for AKI as per standard work up in the ICU. Demographic data was collected according to the study protocol. History, clinical examination and laboratory samples were collected as per protocol. All patients were evaluated with a hemogram, blood urea, creatinine, arterial blood gas, electrolytes and urinalysis. Blood, urine or other fluid cultures and relevant serological tests were done for patients whenever indicated.

These patients were followed up during ICU stay and till discharge from hospital. Accrued data reviewed after discharge to establish an etiology and analyse their presentation, management as well as complications, intervention with hemodialysis and outcome at discharge was collected.

The prevalence of AKI in ICU was determined by using RIFLE & AKIN criteria. AKI after ICU admission was diagnosed by using the RIFLE and AKIN criteria.

For AKIN criteria, the ICU admission creatinine was used as the baseline, and a rolling baseline was also used over the course of 48 hours. Severity of AKI based on AKIN was staged over the course of 7 days by change in creatinine.

Statistical Analysis

In the descriptive analysis, continuous variables were expressed as mean ± standard deviation and categorical variables were expressed as count (percentages). Univariate analysis was performed using independent unpaired t-test for normally distributed variables to determine presence or absence of CAC and Mann-Whitney U test for non-normally distributed continuous variables. ANOVA test was used to analyse class of CCS and the differences among group means with three or more categories. For categorical variables Chi-Square test was used. Fisher's exact test was used when there were one or more of cells with an expected frequency less than five. Multinomial and binary logistic regression analysis was done. A two-tailed P value ≤

0.05 was considered significant. All statistical analysis was performed using SPSS, version 21.0. Armonk, NY: IBM corp.

RESULTS

A total of 583 patients got admitted in ICU, out of these 223 patients were excluded (58 patients had underlying CKD, 5 patients were less than 18 years of age and 160 patients had ICU stay of less than 48 hours) and a total of 360 patients were included in the study.Out of 360 subjects, 65.1% were male and 34.9% were females; 69.4% were medical vs 30.6% surgical patients. 85.8% subjects by AKIN and 81.4% by RIFLE criteria were diagnosed to have AKI. Actual death was 25% and 29.7% of subjects left against medical advice in sick condition. The total assumed mortality was calculated taking actual death and subjects who left against medical advice (as these were assumed to have expired at home or at other center) and it was 54.7%.

Table 1: Co- morbidities and Risk factors

Co-morbidities	Percent
Coronary artery disease	15.0
Diabetic Mellitus Type2	17.8
Hypertension	20.5
Lungs(COPD)	11.4
Liver(Cirrhosis)	1.7
Risk Factors	
Trauma	9.4
Poison	3.17
Nephrotoxic Drug exposure	23.8
Hypotension	52.9
Sepsis	52.4
Dehydration	7.8

Table 1 show that the hypertension, Type 2 diabetes mellitus, coronary artery disease and lung diseases were the common pre-existing co-morbidities. Hypotension and sepsis were the most common risk factors seen.

Prevalence of AKI in ICU

Table 2: Distribution of subjects according to the RIFLE and AKIN criterion

RIFLE Criterion	No.	%age	AKIN	No.	%age
No AKI	67	18.61	**No AKI**	51	14.17
Risk	68	18.89	**Stage 1**	97	26.94
Injury	92	25.56	**Stage 2**	81	22.50
Failure	133	36.94	**Stage 3**	131	36.39
All Categories AKI	293	81.39	**All Stages**	309	85.83

AKI occurred in 81.4% of patients as per the RIFLE criteria- risk in 18.9%, injury in 25.6% and failure in 36.9%. According to AKIN criteria, AKI occurred in 85.8% of patients - 26.9% in Stage 1; 22.5% in Stage 2 and 36.4% in Stage 3. AKIN criteria allowed the identification of more patients as having AKI and classified more patients in Stage 1 (risk in RIFLE).

Table 3: Causes of AKI among subjects

Causes of AKI	AKIN (N=309)		RIFLE (N=293)	
	No.	%age	No.	%age
Cardiorenal syndrome	22	7.12	19	6.48
Trauma/Rhabdomyolysis	20	6.47	19	6.48
Hepatorenal syndrome	8	2.59	7	2.39
Obstetrical causes	7	2.27	7	2.39
Acute pancreatitis	11	3.56	10	3.41
Drugs/poison	13	4.21	13	4.44
MAHA	2	0.65	2	0.68
Multifactorial	26	8.41	26	8.87
Sepsis	191	61.81	185	63.14
Others	14	4.53	12	4.10

Sepsis was the most common cause of AKI followed by cardiac, surgical (trauma & acute pancreatitis), hepatic and drugs/poison. Obstetrical diseases, Dengue, Scrub typhus, leptospirosis, snake bite, H1N1 influenza, multiple myeloma, MAHA (microangiopathic haemolytic anemia) were the other less common causes of AKI.

Table 4: Renal outcome of the subjects: RIFLE

Stage	No Recovery		Improving		Death		Total
	No.	%age	No.	%age	No.	%age	
Risk	13	19.12	45	66.18	10	14.71	68
Injury	26	28.26	53	57.61	13	14.13	92
Failure	44	33.08	44	33.08	45	33.83	133
Total	83	28.33	142	48.46	68	23.21	293

Table 5: Renal outcome of the subjects: AKIN

Stage	No Recovery		Improving		Death		Total
	No.	%age	No.	%age	No.	%age	
Stage-I	27	27.84	57	58.76	13	13.40	97
Stage-II	16	19.75	55	67.90	10	12.35	81
Stage-III	45	34.35	40	30.53	46	35.11	131
Total	88	28.48	152	49.19	69	22.33	309

Both table 4 and 5 shows that with worsening renal function there were fewer chances of renal recovery and higher mortality. AKIN criterion diagnosed more AKI patients compared to RIFLE criterion but total mortality and morbidity in both criteria were comparable.

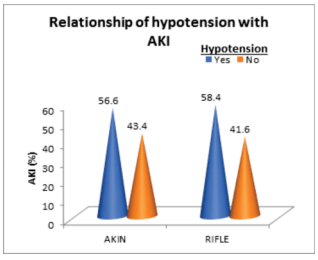

Figure 1

Subjects with hypotension who were diagnosed to have AKI by AKIN criteria were 56.6% (n=175) and by RIFLE were 58.4% (n=171). Hypotension and AKI had statistically significant correlation by both RIFLE (p- 0.006) and AKIN criteria (p=0.008).

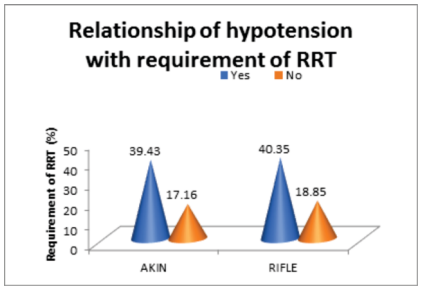

Figure 2

Figure 2 shows that 39.43% (n=69) and 40.35% (n=69) of patients required RRT who had hypotension and developed AKI by AKIN and RIFLE criteria respectively. Statistically significant correlation was seen between hypotension and the need for RRT.

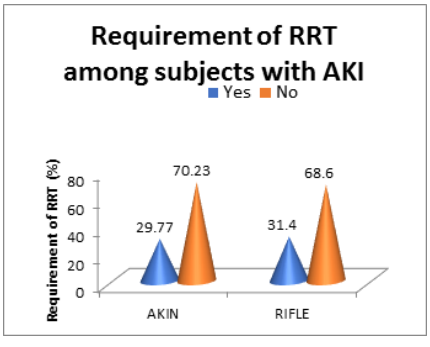

Figure 3

Figure 3 shows that by AKIN criterion 309 subjects were diagnosed to have AKI out of which 92 (29.8%) required RRT. By RIFLE criterion out of 293 diagnosed AKI patients about 92(31.4%) required RRT. In RIFLE criterion slightly more percentage of AKI patients required RRT, but this was not statistically significant.

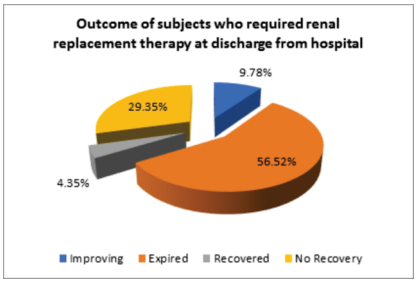

Figure 4

Figure 4 shows that 56.5% of patient expired and 29.4 % showed no recovery among subjects who required RRT which was statistically significant.

Table 6: Relationship of AKI/Non AKI with mortality: AKIN and RIFLE

Renal Failure	AKIN: Mortality		RIFLE: Mortality	
	No.	% age	No.	% age
Yes (309, 293)	90	29.13	89	30.38
No (51, 67)	3	5.88	4	5.97
p-value	0.007		0.006	

Table 6 shows relationship of AKI vs non AKI subjects with in-hospital mortality. The AKI subjects showed statistically significant mortality compared to patients who did not have AKI according to both AKIN and RIFLE criterion.

DISCUSSION:

Among our patients studied, male to female ratio was 1.8:1 and mean age was 49.4 years. The youngest and oldest patient enrolled were 18 years and 94 years respectively. A study based in United Kingdom showed 16% of the AKI patients were older than 65 years while a study in United States showed that 12.4% of the patients were above the age of 65 [6]. Our study had 25.6% of the AKI patients older than 65 years of age.

69.6% were medical patients, 85.9% required mechanical ventilation and mean length of stay in ICU was 7.6 days. In a large multinational, multicenter prospective study of acute kidney injury in critically ill patients (BEST Kidney investigators) found 60% medical patients and mean length of stay in ICU was 16 days [7]. There is no data from Indian subcontinent currently.

We had majority of medical patients (69.6%) but the prevalence of AKI was comparable among surgical and medical patients. Patients with AKI had a longer ICU length of stay compared to patients without AKI. Patients with Failure/Stage 3 AKI had even a shorter length of stay than patients with Risk/Stage 1 AKI when defined by both the RIFLE and AKIN. This probably can be explained by the higher mortality associated with Failure/Stage III AKI.

Diabetes mellitus type 2, hypertension, coronary artery disease and lung diseases were the common pre-existing co-morbid illnesses. The common risk factors observed were hypotension (52.9%), sepsis (52.4%) and nephrotoxic drug exposure (23.8%) [Table 1]. Our findings were in agreement with a review study by Rodrigo *et al*., which demonstrated a significantly increased risk of AKI in critically ill patients with older age, diabetes, hypertension, heart failure, sepsis/systemic inflammatory response syndrome, use of nephrotoxic drugs, disease scores, use of vasopressors/inotropes, high risk surgery [8].

Hypotension showed statistically significant relation with AKI (p-0.006) and requirement of RRT (p-0.007) [Figure 1 & 2]. Probable cause of AKI requiring RRT in these subjects was development of ATN (acute tubular necrosis) after prolonged ischemia.

We found an overall AKI prevalence of 81.4% by RIFLE and 85.8% by AKIN criteria. The AKIN criteria identified 4.4% (n=16) more patients with AKI than the RIFLE criteria [Table 2]. In a study by Hoste *et al.* [9] in 5,383 ICU patients, AKI occurred in 67% of the patients.

The prevalence of AKI in our study was high compared to the older studies. Several reasons could be found to explain this difference. Firstly this was a different patient cohort. Secondly the urine output criteria were not included in previous studies. Thirdly there was a different method of estimating baseline creatinine. In our study, the lowest creatinine value among the hospital admission creatinine, the ICU admission creatinine or the MDRD creatinine value was used as the baseline value when there was no baseline available. This was also suggested by Zavada et al. [10]. They stated that the use of the 4-variable MDRD equation to calculate baseline creatinine may over- or underestimate some mild AKI cases, but does not misclassify patients in Injury and Failure. In a big cross-sectional analysis, the CKD-EPI creatinine equation proved to be better than the MDRD equation, especially at higher GFR, and could replace it for routine clinical use [11].

Sepsis (61.8%) was the most common cause of AKI accounting for more than one half of the cases as shown in Table 3. The role of sepsis in AKI has been well documented in western literature, causing nearly 50% of the AKI cases in few studies [13]. Jha *et al*., evaluated AKI irrespective of ICU setting had shown that nephrotoxic drugs were the most common cause of AKI.[14] Drugs/poison which were consider to be nephrotoxic accounted for only 3.6% of the cases, which is lower than the previous studies. This might suggest that increasing knowledge of precautions regarding nephrotoxic drugs have helped to reduce the incidence of drug induced AKI. The higher number of sepsis might be attributed to the fact that our institution is a tertiary care center and patients referred after developing sepsis and renal complications. Trauma (Road side and rail-track accident), acute pancreatitis, cardiac failure, hepatic and obstetrical diseases constitute other causes of AKI. Dengue, Scrub typhus, leptospirosis, snake bite, H1N1, Multiple myeloma, MAHA were also reported as the cause of AKI, although less common.

In our study, 81.4% of the subjects were diagnosed to have AKI according to RIFLE criteria, with 18.9% in the risk class, 25.5% in the injury class and 36.9 % in the failure class [Table 2]. Among AKI subjects about 48.5% of the patients showed improvement in renal function. Excluding the patients who expired about 28.3% showed no recovery during ICU stay [Table 4]. The observed mortality rates were highest in the failure class, followed by injury and risk class.

There was slight mortality difference between RIFLE and AKIN which was not statistically significant as mentioned in Table 4 and 5. So whether this small increase in the mortality of these patients, identified by AKIN but missed by RIFLE, is of high risk requires further research.

Mortality was significantly higher for AKI patients as compared with non-AKI patients [Table 6]. AKI defined by the RIFLE criteria (30.4% versus 5.9%, *P* -0.006) or AKIN criteria (29.1% versus 5.8%, P-0.007). Joaniddis *et al*., in their study of ICU patients showed that the mortality rate among patients classified to have AKI by RIFLE criteria was 36.5%.[15]

A study by Bagshaw *et al*.[12] included 1,20,123 critically ill patients, found that 36.1% of the patients had AKI according to RIFLE criteria, with 16.2% in the risk class, 13.6% in the injury class and 6.3% in the failure class. They also reported that the mortality rates were 17.9% in the risk group, 27.7% in injury group and 33.2% in failure group.

RRT was required in 29.8% (n=92) of subjects diagnosed by AKIN and in 31.4% (n=92) diagnosed by RIFLE criterion [Figure 3]. An Indian study by Singh et al (2013) reported 20.5% of cases required RRT. Intermittent haemodialysis and slow low efficiency dialysis were the most commonly used modalities of RRT. 42 patients received intermittent haemodialysis and 50 patients received slow low efficiency dialysis. Mortality rate was higher among patients receiving RRT (56.5%) and about 29.4% of these subjects showed no recovery [Figure 4]. The requirement of RRT and mortality showed statistically significant correlation. Chertow et al (1995) previously demonstrated that among critically ill patients AKI requiring RRT is an omnious condition with a high risk of in-hospital mortality.

CONCLUSION

Our study showed overall prevalence of AKI in ICU of 81.4% by RIFLE and 85.8% by AKIN criteria. The AKIN criteria helps in early and more diagnosis of AKI compared to RIFLE criteria. The AKIN criteria identified 4.4% more patients with AKI. Hypotension showed statistically significant correlation with AKI and requirement of RRT. Sepsis was the most common cause of AKI. Mortality was higher in AKI compared to non AKI patients and it increased with severity of AKI.

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