A study on the causes of Acute Kidney Injury in ICU in a Tertiary care centre and comparison of prognostic scoring systems (SOFA score and APACHE score) to predict mortality and renal outcome

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Abstract

Introduction: Acute kidney injury (AKI) is a complex clinical disorder that is associated with severe morbidity and mortality, which in spite of technological advances in Renal replacement therapy (RRT), continues to be associated with poor outcomes. AKI is a syndrome of sudden loss of kidney's excretory function, often associated with oliguria, occurring over hours to days seen commonly in hospitalised patients who are critically ill. Subjects and Methods: A prospective and observational study was conducted at Sapthagiri Institute of Medical Sciences & Research Centre from January 2020 to December 2020. Patients with Acute Kidney Injury satisfying inclusion and exclusion criteria, admitted in the medical Intensive care unit (ICU), were selected after obtaining informed consent. Results: The mean age of the population was $64.51 \pm$ 14.29 years. 65% patients were males. Most common age group was older age group (65 to 75 years) for both males and females. In the younger age group (18-44 years) most of them were males. In the elderly age group (85-100 years) females exceeded males. The mean duration of hospital stay was 10.78 \pm 8.39 days and the median duration of hospital stay was 9 days. The mean duration of ICU stay was 6.15 \pm 5.31 days and the median duration of ICU stay was 4 days. In our study some patients had AKI on day 1 of ICU admission and the others developed AKI later during the course of ICU stay. The median day of ICU admission on which patients presented with AKI in our study was on the day 1. RRT was initiated in majority of the patients (53%) on the 1st day of ICU admission itself. Remaining patients (25.6%) received RRT on day 2 of ICU admission. Only a few patients (21%) received RRT after 2 days. Conclusion: Elderly males are at higher risk for developing AKI. Sepsis with pneumonia is the leading cause of AKI in ICU. Pre-existing Chronic Kidney disease (CKD)has worse renal outcome. Kidney Disease Improving Global outcomes(KDIGO) staging is an independent predictor of ICU mortality, RRT requirement and ventilatory support. In the setting of acute kidney injury, Acute Physiology and Chronic Health Evaluation (APACHE) III is superior to Sequential Organ Failure Assessment (SOFA) and APACHE II for predicting in-hospital mortality. Patients with AKI have 2.33 times more risk of mortality compared to those without AKI. AKI is an independent predictor of mortality in ICU.

Keywords: Acute kidney injury, SOFA score, APACHE score, Renal outcome

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Introduction		mild loss of kidney function to co usually occurs as a complication	· ·
Acute kidney injury (AKI) is that is associated with severe m in spite of technological adv be associated with poor outco sudden loss of kidney's excrete with oliguria, occurring over hospitalised patients who are cr	norbidity and mortality, which ances in RRT, continues to omes. AKI is a syndrome of ory function, often associated hours to days, commonly in	It has only been in the past few yo kidney function has been recogni- risk factor for mortality, in the co- on contrast induced nephropati- continues to remain a significa- patients and has a high morta	ized as potentially important ritically ill, ^[3] and in studies hy ⁽⁴⁾ .Acute Kidney Injury ant problem in hospitalized

incidence of AKI continues to increase and currently there is no definitive therapy for it.

Acute Kidney Injury (AKI) affects over 13 million people per year globally, and results in 1.7 million deaths.^[4–6] AKI is diagnosed in up to 20% of hospitalized patients and in 30–60% of critically ill patients.^[7–10] It is the most frequent cause of organ dysfunction in intensive care units (ICUs) and the occurrence of even mild AKI is associated with a 50% higher risk of death.^[11] AKI results in a significant burden for the society in terms of health resource use during the acute phase, and the potential long-term sequelae including development of chronic kidney disease (CKD) and kidney failure.^[12–14] The effect of AKI on an individual patient and the resulting social burden that ensues from the longterm effects of the disease, including development of chronic kidney disease (CKD) and end-stage renal disease (ESRD), is attracting increasing scrutiny.

Acute Kidney Injury is not a single disease but rather a syndrome comprising multiple clinical conditions. Outcomes from AKI depend on the underlying disease, the severity and duration of renal impairment, and the patient's baseline renal function. The development of AKI is the consequence of complex interactions between the actual insult and subsequent activation of inflammation and coagulation. AKI can also lead to problems that are not readily appreciated at the bedside and can extend well beyond the ICU stay, including progression of CKD and impaired innate immunity. Experimental and small observational studies provide evidence that AKI impairs innate immunity and is associated with higher infection rates.^[9]

Multiple definitions of AKI has led to great disparity in the reported incidence of AKI making it difficult to compare various published studies focusing on AKI.^[12,15–19] In 2011 the KDIGO work group combined the RIFLE and AKIN classifications of AKI to establish one classification of AKI for practice, research and public health. Due to the rising incidence and mortality in patients with AKI, it is important to evaluate the causes of acute kidney injury. There have been several studies concentrating on the prediction of mortality in critically ill patients using several scoring systems like SOFA score, APACHE score, MODS score, SAP score etc. Literatures on classification and prognostication of AKI in critically ill based on KDIGO guidelines in Indian population are limited . Also studies on predicting mortality in critically ill patients with acute kidney injury using APACHE III is also limited.

This study is done to determine the causes of acute kidney injury in critically ill patients and to predict their mortality using SOFA score, APACHE II and APACHE III scoring systems.

Subjects and Methods

A prospective and observational study conducted at Sapthagiri Institute of Medical Sciences & Research Centrefrom January 2020 to December 2020. Patients with Acute Kidney Injury satisfying inclusion and exclusion criteria, admitted in the medical ICU, were selected after obtaining informed consent.

Sample size: The sample size was calculated assuming the expected proportion of any particular cause of AKI as 34.25% as per the study by Chih-Hsiang Chang et al. The other parameters considered for sample size calculation were 95% confidence level and 5% precision. As per the previous year statistics, the monthly ICU admission is about 250 patients per month. Hence, the total number of ICU admissions expected is about 3000 during 12-month data collection period. Considering the reported proportion of AKI subjects are likely to get admitted during data collection period. Hence a finite population correction factor for 900 subjects was added in sample size calculation.

Inclusion criteria

- 1. Patients with Acute Kidney Injury diagnosed based on the KDIGO guidelines.
- 2. Patients aged more than 18 years.

Exclusion criteria

- 1. Patients with End Stage Renal Disease (ESRD) on maintenance Renal Replacement Therapy.
- 2. Patients aged less than 18 years.
- 3. Patients who underwent renal transplantation.

Statistical Methods

The data was entered in Excel and the software used for statistical analysis was SPSS version 22 (Statistical Package for Social Science).

Descriptive analysis: Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. Data was also represented using appropriate diagrams like bar diagram, pie diagram and box plots.

The association between categorical explanatory variables and quantitative outcome was assessed by comparing the mean values, Independent t test, ANOVA was used to assess statistical significance. The association between explanatory variables and categorical outcomes was assessed by cross tabulation and comparison of percentages. Chi square test was used to test statistical significance.

Results

During the study period, 218 patients diagnosed to have acute kidney injury (KDIGO criteria), fulfilling the inclusion and exclusion criteria were admitted in the medical ICU. Their data was collected and analysed. Another 100 patients without kidney injury admitted to the ICU was studied for comparison with the AKI patients. Results of this study are as follows:

Demographic Data of the Study Population

There were 218 patients recruited for study. Age group taken was adults more than 18 years of age. The mean age of the population was 64.51 ± 14.29 years. 65% patients were males. Most common age group was older age group (65 to 75 years) for both males and females. In the younger age group (18-44 years) most of them were males. In the elderly age group (85-100 years) females exceeded males.

Patients were followed up from admission to discharge/ death from the hospital. The mean duration of hospital stay was 10.78 ± 8.39 days and the median duration of hospital stay was 9 days. The mean duration of ICU stay was 6.15 ± 5.31 days and the median duration of ICU stay was 4 days. In our study some patients had AKI on day 1 of ICU admission and the others developed AKI later during the course of ICU stay. The median day of ICU admission on which patients presented with AKI in our study was on the day 1.

RRT was initiated in majority of the patients (53%) on the 1^{st} day of ICU admission itself. Remaining patients (25.6%) received RRT on day 2 of ICU admission. Only a few patients (21%) received RRT after 2 days.

[Table 7] The mean SOFA score in the study population was 7.04 \pm 3.83. The mean APACHE II and APACHE III scores in the study population were 20.96 \pm 7.65. and 73.02 \pm 25.1 respectively.

All the 218 patients were followed up until discharge from the hospital or in hospital death. For all the patients who survived following AKI, status at discharge was assessed by recording serum creatinine at discharge and this was compared with the baseline creatinine and degree of recovery was assessed. 33% patients recovered completely; 35% expired during the course of treatment and 1% patients became dialysis dependent. Of the remaining patients who survived 21% recovered only partially and 8% patients did not recover at all.

Discussion

AKI is common in ICUs and has been associated with increased mortality, length of ICU stay, and medical costs for critically ill patients. Reliable and comparable data about the clinical spectrum of AKI is necessary for optimizing management. This study is done to describe the etiologies of AKI, prognostication and outcome of AKI. In our study

we recruited 218 patients in ICU who presented with Acute Kidney Injury and those who developed AKI during the course of ICU stay. The KDIGO guidelines were applied to diagnose AKI. The baseline serum creatinine value of the patients was collected. In those patients whose baseline creatinine was not known serum creatinine on the day of admission to the hospital was taken as baseline. We also grouped the patients according to the severity of Acute Kidney Injury based on the KDIGO severity staging. Mortality in critically ill patients was usually due to multisystem involvement, and renal failure plays a very important role in prognosis. Mortality prediction for patients in intensive care units (ICU) remains an important challenge. Many severity scores are used but none of these individually outperform all others regardless of the context. In this study we tried to predict mortality in patients admitted to the ICU using three scoring systems (SOFA, APACHE II, APACHE III scores) and to find out which score had the maximum ability to predicted mortality.

Until recently AKI had several definitions, in several literatures AKI was still diagnosed based on old definitions (RIFLE criteria, AKIN classification). Though the KDIGO group put forward the KDIGO guidelines for diagnosis and staging of AKI in 2011, literatures on KDIGO criteria were limited. So we used the KDIGO guidelines to diagnose and assess the severity of AKI in our study population.

In our study there were 42(19.3%) patients with pre-existing CKD and 172(78.8%) had AKI without pre-existing renal impairment. On analysis we have found that there was statistically significant increase in age for CKD patients (p=0.05). There was no significant difference in the duration of hospital stay between these two groups. Analysis of our data showed the prevalence of diabetes, hypertension and coronary artery disease is significantly higher in CKD when compared to patients with AKI without pre-existing CKD (p< 0.05).

In our study mean duration of ICU stay was 6.15 ± 5.31 days which was in concordance with the study done by Eswarappa et al where mean duration of ICU stay was 5.6 days and median ICU length of 7 days as in study of Piccini et al.^[20,21] The mean duration of hospital stay was 10.78 \pm 8.39 days. In our study, we observed the day of ICU admission on which the patient developed AKI. In this the minimum was on day 1 of ICU admission and maximum was 16 days after ICU admission. The median day of ICU admission on which AKI occurred was on Day 1.

In the AKI population (218 patients), three prognostic scoring systems SOFA, APACHE II, APACHE III scores were calculated within 24 hours of ICU admission and were compared to find which score had the best ability to predict mortality. The mean SOFA score was 7.04 ± 3.83 . Mean APACHE II and APACHE III were20.96 \pm 7.65 and 73.02 \pm 25.1 respectively.

Paul et al; Acute Kidney Injury in ICU

Table 1: S ex distribution		
Gender	Frequency	Percentages
Male	142	65.10%
Females	76	34.90%

Table 2: Sex distribution in different age groups.				
Age group	Females	Males		
15-24	0	3		
25-34	0	6		
35-44	2	7		
45-54	8	24		
55-64	16	31		
65-74	23	38		
75-84	17	27		
85-94	10	5		
95-104	0	1		

Table 3: Age characteristics						
Parameter	$\mathbf{Mean} \pm \mathbf{SD}$	Median	Min	Max	95% C.I	
					Lower	Upper
AGE	64.51 ± 14.29	66.50	18.00	99.00	62.60	66.42

Table 4: Length of hospital stay/ length of ICU stay/ day of occurrence of AKI in ICU (n=218)						
Parameter	$\mathbf{Mean} \pm \mathbf{SD}$	Median	Min	Max	95% C.I	
					Lower	Upper
Number of days in hospital	10.78 ± 8.39	9.00	1.00	53.00	9.66	11.90
No of days in ICU	6.15 ± 5.31	4.00	1.00	38.00	5.44	6.86
AKI on day of ICU	1.43 ± 1.62	1.00	1.00	16.00	1.21	1.64

Table 5: Day of ICU stay on which R	RT was started (n=43)	
ICU Day	Frequency (%)	
1st	23 (53%)	
2nd	11 (25.6%)	
3rd	2 (4.6%)	
4th	2 (4.6%)	
>5 Days	5 (12%)	

Table 6: Survival outcome			
Characteristics	Alive (n=140)	Dead (78)	p value (independent t test)
SOFA score	5.71±3.087	9.42±3.890	0.279*
APACHE II score	18.27±6.287	25.78±7.529	0.0001
APACHE III score	62.62±19.302	91.68±23.530	0.0001
Age	63.46±15.110	66.40±12.568	0.146
Days in ICU	5.91±5.181	6.59±5.551	0.964*
Days in hospital	12.63±8.736	7.46±6.570	0.0001*
GCS	13.84±2.585	11.74±3.812	0.0001
MAP	89.90±27.208	76.64±27.901	0.001
Creatinine	3.44±2.696	3.72±2.357	0.036*
НСО3	19.59±8.421	17.64±6.892	0.082*
Potassium	4.38±.917	4.58±.905	0.126
Sodium	132.50±6.873	134.04±9.004	0.159
Sugar- RBS	203.92±127.635	185.87±113.741	0.290*
Albumin	3.12±.754	2.87±.745	0.019
Haemoglobin	11.24±2.518	$11.54{\pm}2.891$	0.421
Platelets	205.89±122.416	202.60 ± 140.046	0.606*
No of patients required rrt	19	31	0.0001\$
No of patient required ventilation	17	35	0.0001 ^{\$}
No of patient on inotropes	28	39	0.0001 ^{\$}

*Mann whitney u test, \$ chi-square test To assess the factors affecting mortality the above mentioned characteristics were compared in survivors and non survivors. There was statistically significant difference in the APACHE II and III scores between these two groups (p=0.001) with higher scores in non survivors. There was no significant difference in SOFA score. There was statistically significant increase in duration of hospital stay, requirement of RRT, inotropic support and mechanical ventilation among non survivors (p=0.001). Among the non survivors there was significant decreased in GCS, albumin, mean arterial pressure and increase in creatinine levels(p<0.05).

Table 7: ICU scoring systems with mean value.						
Parameter	$\mathbf{Mean} \pm \mathbf{SD}$	Median	Min	Max	95% C.I	
					Lower	Upper
Sofa	7.04 ± 3.83	6.00	1.00	21.00	6.53	7.55
Apache II	20.96 ± 7.65	20.00	6.00	45.00	19.94	21.98
Apache III	73.02 ± 25.1	68.50	20.00	166.00	69.67	76.37

Table 8: Renal outcome			
Renal outcome	Frequency	Percent	
Complete recovery	71	32.50%	
Partial recovery	46	21.10%	
No recovery	17	8%	
Dialysis dependent	2	1%	
Death	78	35.7%	
Discharge against advice	4	2%	

There was statistically significant difference in the SOFA, APACHE II and APACHE III scores between the 3 stages of AKI (0.0001), with maximum scores in patients belonging to KDIGO stage 3. When comparing AKI versus AKI with CKD, it was found that only APACHE II has a statistically significant difference, with higher scores in CKD.

All the 218 AKI patients were followed up until discharge or in hospital death. Renal outcome was assessed based on the serum creatinine at discharge. Out of 218 AKI patients, 32.5% recovered completely, 35.7% patients expired, 1% became dialysis dependent at discharge, 21% had partial recovery while 8% had no recovery at the time of discharge. In study by Yang et al the recovery rate was 21% and the mortality rate was 19.6%.^[22-25]The scores were also used to predict the renal outcome. Patients with higher ICU scores did not have complete recovery, they either had no recovery or they expired. There was statistically significant difference in the SOFA, APACHE II, APACHE III scores of patients who completely recovered and those who died during treatment or those without complete recovery. (p,0.05) Higher the scores of SOFA, APACHE II and APACHE III, poorer the renal outcome. So high scores are an indicator of poor renal outcome or mortality.

Conclusion

Elderly males are at higher risk for developing AKI. Sepsis with pneumonia is the leading cause of AKI in ICU. Preexisting CKD has poorer renal outcome. KDIGO staging is an independent predictor of ICU mortality, RRT requirement and ventilatory support. In the setting of acute kidney injury, APACHE III is superior to SOFA and APACHE II for predicting in-hospital mortality. Patients with AKI have 2.33 times more risk of mortality compared to those without AKI. AKI is an independent predictor of mortality in ICU.

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