A Prospective Observational Study on Incidence, Risk Factors. Etiology and Outcomes Associated with Acute Kidney Injury.

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ABSTRACT:

Acute kidney injury (AKI) is a common clinical condition among patients admitted in the hospital.The condition associated with both increased short term and longterm mortality ,with the development of a standerdised definition for AKI and the acknowledgement of the impat of AKI on patient outcomes there has been increased recognition of AKI . two advances from past decades ,the usage of computer decision support and the discovery of AKI biomarkers ,have the ability to advance the diagnostic method to and further management of AKI .

Acute kidney injury(AKI) Increases in critically ill patients morbidity ,mortality ,length of ICU stay ,and long term risk chronic kidney disease.

Studies with a comprehensive analysis of the epidemiology of acute kidney injury in intensive care units are still limited in developing countries .

The aim of this study is to asses the incidence of acute kidney injury at the study site and to compare etiology ,risk factors to predict the AKI enhanced outcome based on the SOFA score among critically ill patients ..we include 150 patients .the incidence of AKI was 45% and the AKI dialysis rate was 45 (30%) on comparision of SOFA with outcome (ie,mortality) the AUC was observed to be 0.805.which suggests that SOFA could predict the mortality significantly with excellent predictability.

At the best cutoff 11.5, SOFA could predict the mortality with sensitivity of 80 % and specificity of 92.7% .among the study population 51-65 age group was observed as highest frequency of AKI ie.,56 (37%). Based on gender wise distribution highest frequency of AKI observed in males (70%) we analyse AKI cases from different departments .Highest frequency observed in nephrology then cardiology and neurology. By comparing etiology in relation to ICU stay , sepsis AKI is one of the etiology present in ICU in comparision to 65.4% of caes who did not have ICU stay still have sepsis AKI .there is no significant difference in the etiology in admission in ICU and NON ICU.Sepsis AKI is the most common etiology for mortality patients who receive RRT there is no mortality was observed . patients who did not receive dialysis was observed as died.

Key Words: Acute kidney injury, chronic kidney injury, intensive care unit, renal replacement therapy, sequential or sepsis related organ failure assessment score, dialysis.

INTRODUCTION:

AKI is defined as reduction in kidney function, including diminished GFR and kidney failure. Staging of AKI is appropriate because, with increased stage of AKI, the imminence for death and need for RRT increases.

According to International society of nephrology(2021) Every year, there are around13.3 million cases of AKI. A burden that's on the increase in emerging countries where the annual incidence is estimated to be11.3 million Out of1.7 million global deaths per year caused by AKI, around1.4 million come down in low and middle income countries[1].

A prospective observational study conducted in 100 critically ill cases by Eswarappa M etal.(2018), in Indian population, it was set up that incidence of AKI was17.3 cases/ 1000 persons[2].

Knowledge of incidence and risk factors is pivotal because it drives local and international works on finding and treatment.

In hospitalized cases perioperative risk factors promoting AKI postoperatively. A previous knowledge of risk factors contributing to a planned preventative management and prognostication[3]. AKI occurs due to pre-renal, renal, and post renal aetiologies.

The sequential organ failure assessment score(SOFA score) [4]. preliminarily known as the sepsis related organ failure assessment score, is used to track a person's status during the stay in Intensive care unit(ICU) to determine the extent of person's organ function or rate of failure[5].

The score is predicated on six discriminative scores, one each for the respiratory, cardiovascular, hepatic, coagulation, renal and neurological systems.

The SOFA scoring system is useful in prognosticating the clinical outcomes of critically ill patients[6].

METHODOLOGY :

A prospective observational study on incidence ,riskfactors ,etiology and outcomes associated with acute kidney injury . the study was conducted in tertiary care hospital with different specialized department such as nephrology ,cardiology ,neurology ,pulmonology ,general medicine ,gastroenterology ,for a period of six months and this study was included the patients of all ages the data was collected from casesheets ,patient reports who are admitting in different departments apart from nephrology with AKI .collected data from laboratory reports and dialysis notes, and also collected data for calculating SOFA score in critically ill patients .the study was conducted in santhiram medical collage and general hospital ,nandyal .after the approval of institution human ethics committee ,at santhiram medical collage and general hospital ,nandyal.this study was initiated during the study period of 6 months of this study the total sample size was 150 patients . we included all age group people from different departments who are diagnosed with acute kidney injury apart from nephrology department . patients followup was done to identify their outcomes. The results were analyzed and tabulated stastically by spss (statistically package for social sciences) association between continuous variable was assessed using independent T test .probability value (p- value) was used to determine the level of significance p- value ,< 0.05 was considered as highly significant . comparision of etiology in relation to outcome the value 0.49 is statistically taken as non significant . By comparing co morbidity in relation to ICU stay the P-value obtained as non ststistically significant . by comparing comorbidity in relation to outcome the P- value obtained as non statistically significant .by comparing all three criterias (AKIN,KDIGO,RIFLE)in relation to outcome ,the P- value obtained as 0.375,0.313,and 0.313 is taken as non statistically significant . By comparing creatinine and uric acid in relation to ICU stay the mean creatinine is 3.77 ± 3.30 SD when compared to non ICU stay the mean creatinine is 3.17 ± 2.39 SD. Likewise uric acid in relation to ICU stay the mean uric acid is 8.41 ± 3.15 SD when compared to non ICU stay the mean uric acid is 8.57 ± 10.10 ,are statistically not significant.except oliguria , with p-value 0.027 is statistically significant remaining all laboratory parameters obtained as statistically non significant . by comparing ICU patients who underwent dialysis in relation to outcome the P- value obtained as 0.02 is taken as statistically significant asymptotic 95% confidence interval obtained with lower bound 0.502 and upper bound 1. At the best cutoff 11.5 ,the SOFA could predict mortality with sensitivity of 80% and specificity of 92.7 %.

RESULTS:

Table.No-1 Incidence of Acute Kidney Injury

| Age (years)	Total No. Of patients hospitalized	Patients diagnosed with AKI	Incidence (%)
1-9'	67	0	0
1O-20	121	5	4.1%
21-30	215	8	3.7%
31-40	341	11	3.2%
41-50	575	24	4.1%
51-60	614	36	5.8%
61-70	678	41	6%
71-80	357	19	5.3%
81-90	68	4	5.8%
91-100	4	2	50%

Figure.No-1 INCIDENCE OF AKI
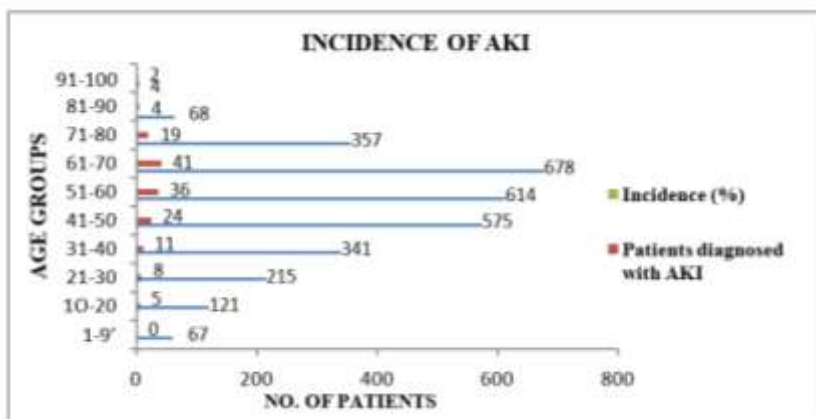
Incidence of AKI was observed to be 4.9% per 6 months .

Table.No-2 : Distribution of patients based on Age group

Age Group	Frequency	Percent
<= 20	5	3.3
21 - 35	13	8.7
36 - 50	30	20.0
51 - 65	56	37.3
66 - 80	40	26.7
81+	6	4.0
Total	150	100.0

	Mean	SD
age	56.49	16.60

Figure.No-2 Distribution of Patients based on Age
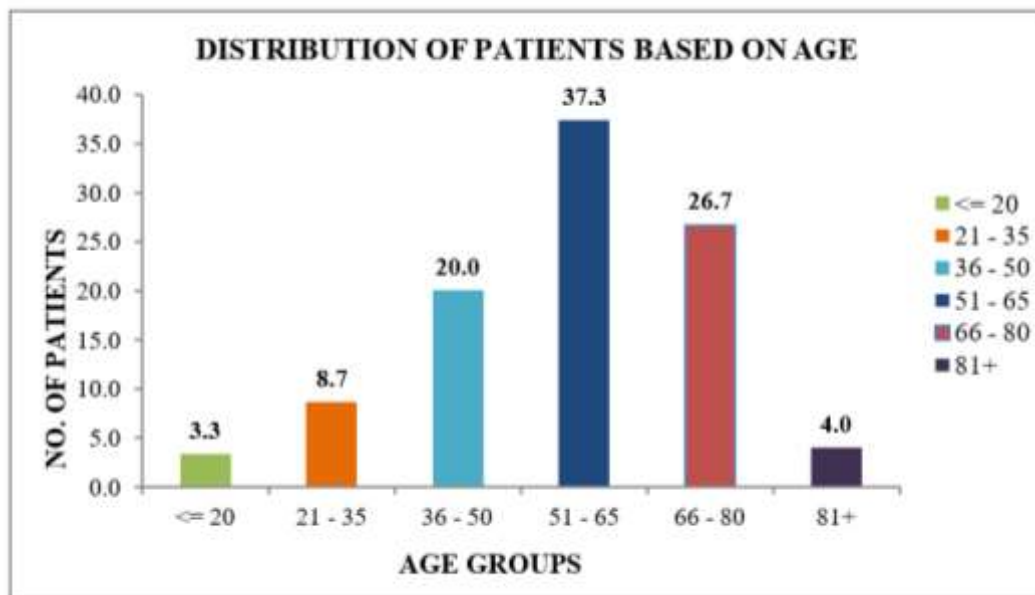
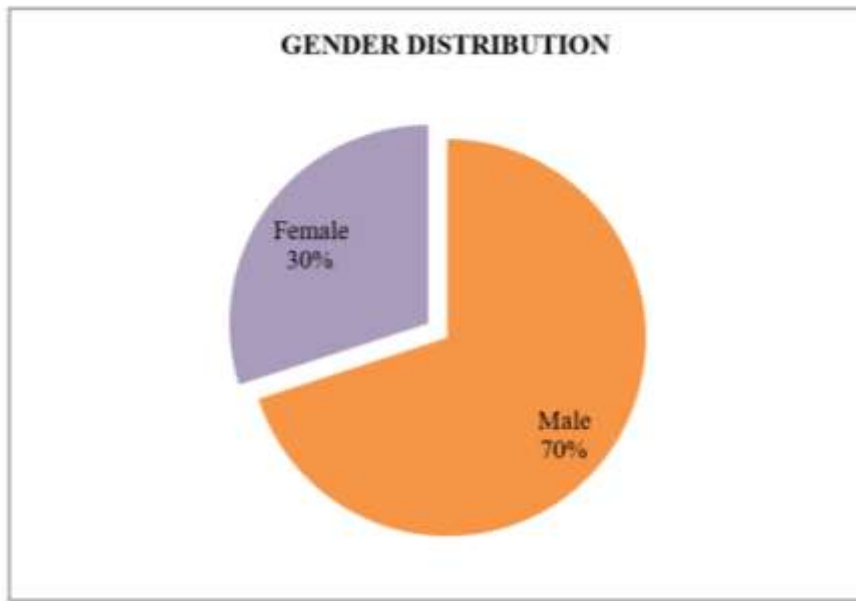
In our study include 150 cases, minimum age developed AKI was observed to be 10 and maximum age developed AKI was observed to be 95 with mean 56.5± 16.6 standard deviation.

Table.No-3 Distribution Of Patients Based On Gender.

|	Frequency	Percent
Male	105	70.0
Female	45	30.0
Total	150	100.0

Figure.No-3 Gender Distribution

Based on gender wise distribution highest frequency of AKI observed in males (70%) when compared to females have lowest frequency of AKI (30%).

Table.No-4 Departments

Departments	Frequency	Percent
cardiology	32	21.3
General medicine	18	12.0
general surgery	2	1.3
nephrology	68	45.3
neurology	24	16.0
pulmonology	5	3.3
surgical gastro	1	.7
Total	150	100.0

**Figure.No-4 Department wise Distribution**
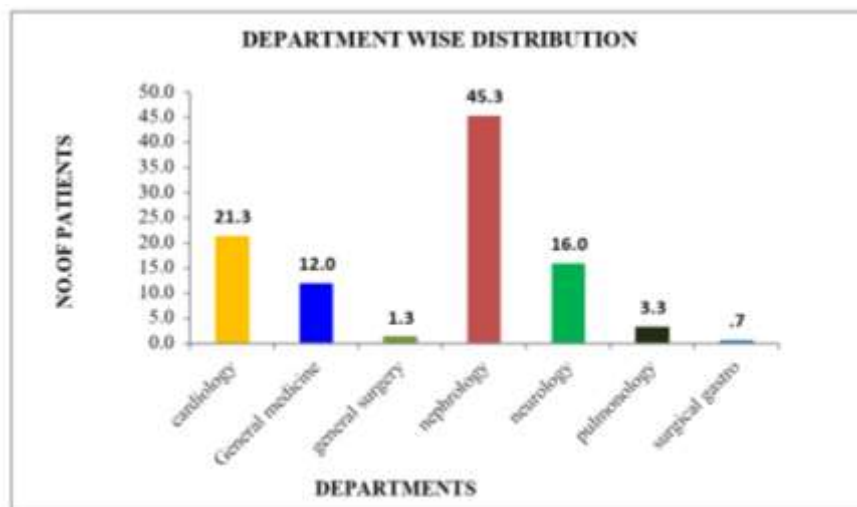
we have AKI cases from different departments in that highest frequency of AKI observed in nephrology (45.3%) followed by cardiology (21.3%) and neurology (16%).

Table.No-5 Comparison between Etiology and ICU stay

Etiology	ICU stay		Non ICU Stay	
	No.	%	No.	%
Acute over CKD	1	2.2%	5	4.8%
Cardio renal AKI	3	6.5%	18	17.3%
RPRF	1	2.2%	11	10.6%
sepsis AKI	38	82.6%	68	65.4%
Toxic AKI	3	6.5%	2	1.9%
Total	46	100.0%	104	100.0%

Chi square = 9.381, p value = 0.05

**Figure.No-5 Comparison Between Etiology and ICU stay**
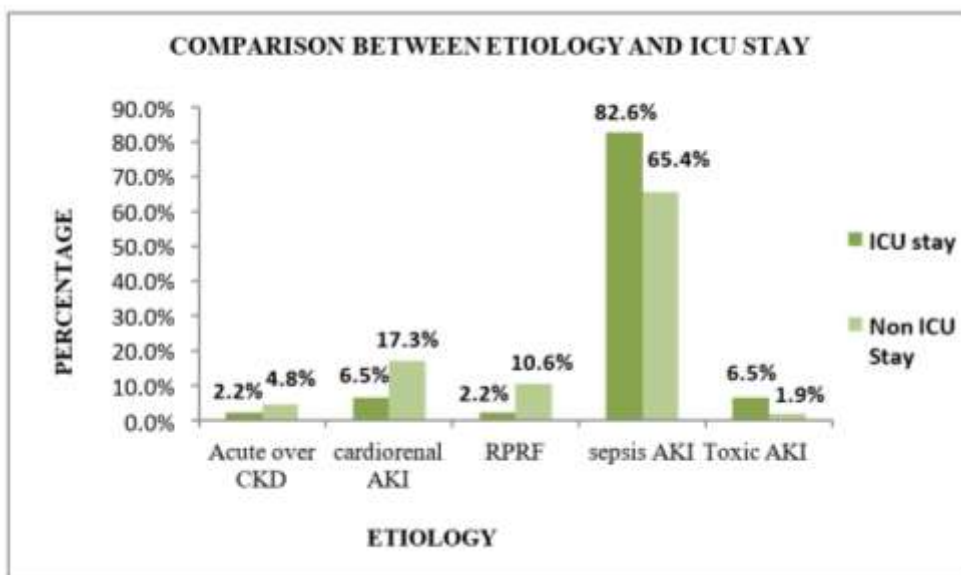
82.6% of cases who were in ICU had sepsis AKI is one of the etiology in comparison to 65.4% of cases who did not have ICU stay still have sepsis AKI.

Table.No-6 Comparison between Etiology and Outcomes

Etiology	Alive		Dead	
	No.	%	No.	%
Acute over CKD	5	3.6%	1	10.0%
Cardio renal AKI	20	14.3%	1	10.0%
RPRF	12	8.6%	0	0.0%
sepsis AKI	99	70.7%	7	70.0%
Toxic AKI	4	2.9%	1	10.0%
Total	140	100.0%	10	100.0%

Chi square = 3.373, p value = 0.497

**Figure.No-6 Comparison Between Etiology and Outcomes**
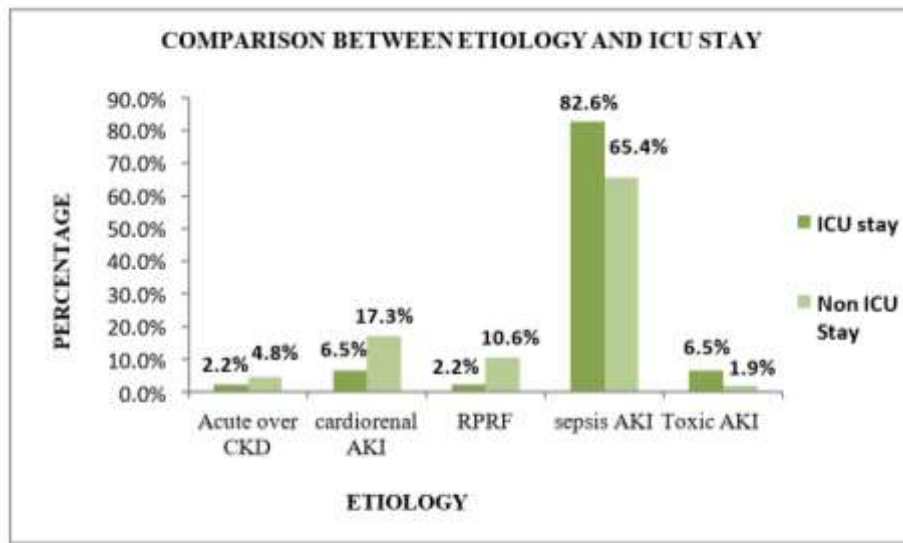
Though sepsis AKI has more deaths but it is not statistically significant with P-value of 0.49. sepsis AKI is the most common etiology for mortality (70%) followed by AKI over CKD (10%), Cardiorenal(10%), ,and toxic AKI(10%).

Table.No-7 Comparison of co morbidities in relation to ICU stay

Co morbidities	ICU stay		Non ICU Stay		p value
	No.	Percent	No.	Percent	
DM	21	45.7%	53	51.0%	0.549
HTN	28	60.9%	74	71.2%	0.213
CAD	5	10.9%	18	17.3%	0.313
CVA	2	4.3%	14	13.5%	0.672

**Figure.No-7 Comparison of co- morbidities in relation to ICU stay**
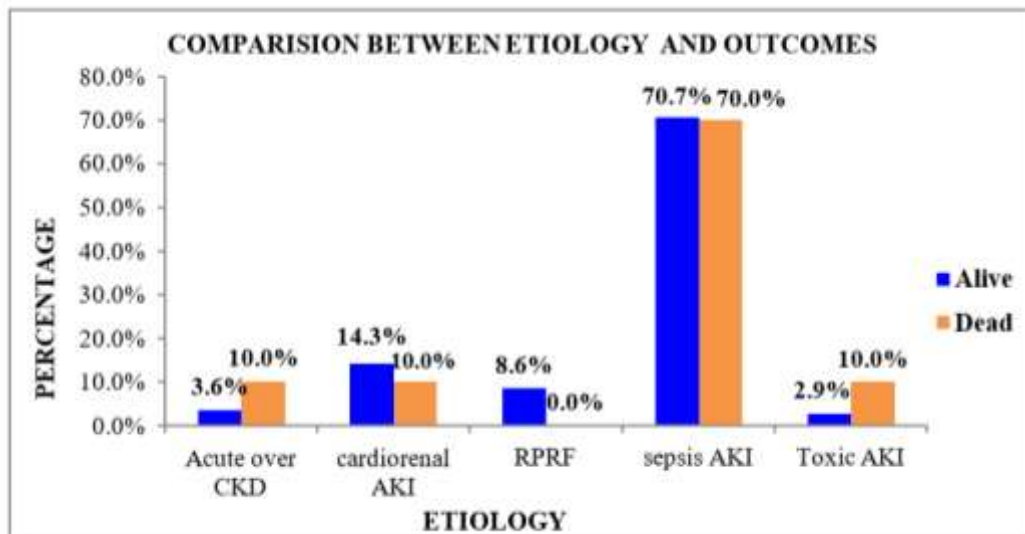
Patients with comorbidities such as hypertension, diabetes, stroke and heart diseases present with high percentage in non-ICU when compared to ICU stay patients, because critically ill patient present with comorbidities and also applicable with highest sequential organ failure assessment score.

Table.No-8 Comparison of comorbidities in relation to outcome

Co morbidities	Alive		Dead		P value
	No.	Percent	No.	Percent	
DM	69	49.3%	5	50.0%	0.965
HTN	98	70.0%	4	40.0%	0.05
CAD	21	15.0%	2	20.0%	0.672
CVA	13	9.3%	3	30.0%	0.04

Figure.No-8 Comparison of comorbidities in relation to outcome
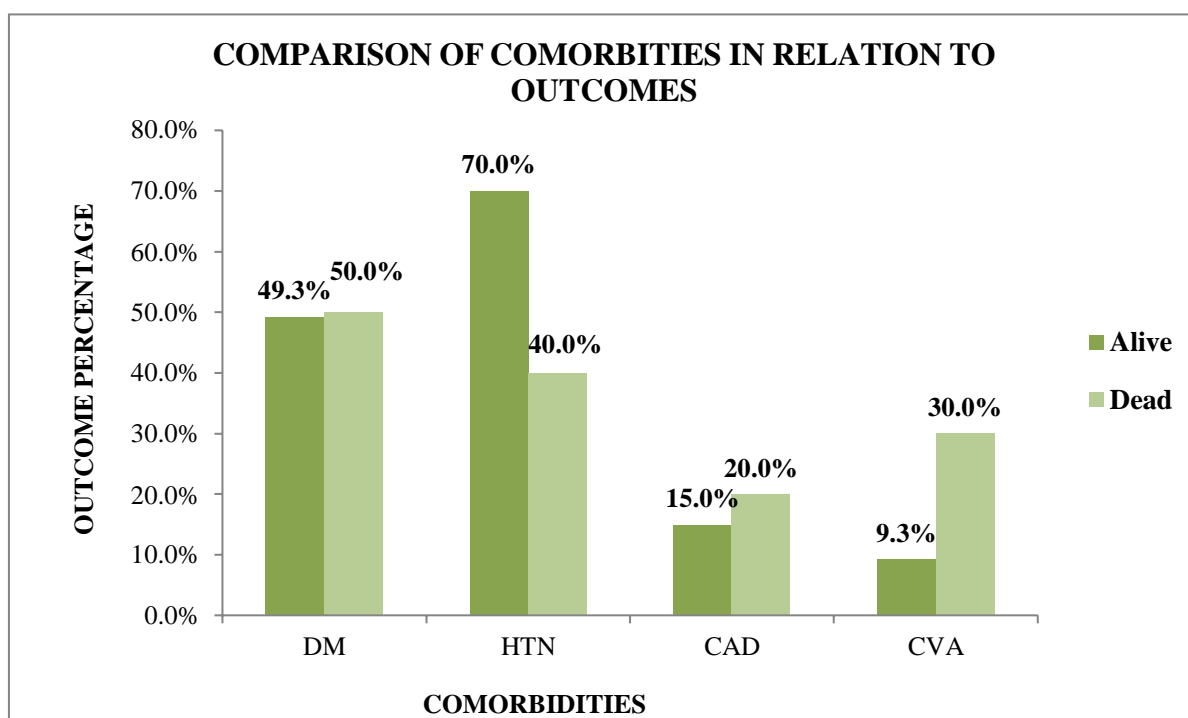
Among the patients who died, 60% of patients did not have hypertension and 40% of patients had hypertension. patients who did not have stroke those are 90% of survival compared to patients with stroke those are 9.3% survival

Table.No-9 Comparison of ICU patient who underwent dialysis in relation to outcome

Dialysis	Alive		Dead	
	No.	Percent	No.	Percent
Yes	21	51.2%	0	0.0%
No	20	48.8%	5	100.0%
Total	41	100.0%	5	100.0%

Figure.No-9 Comparison of ICU patient who underwent dialysis in relation to outcome
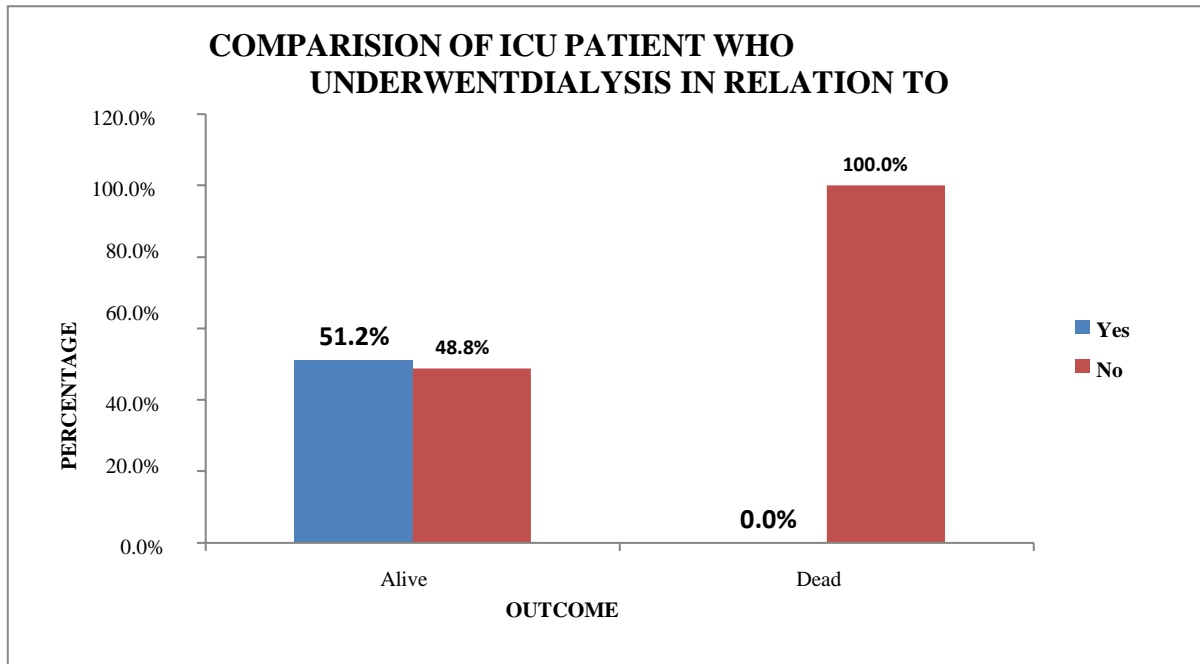
There is no mortality rate observed in patients who receive renal replacement therapy when compared to 20 patients who did not receive renal replacement therapy 5 patients were died.

Table.No-10 Comparison of SOFA in relation to outcome

Outcome	SOFA		t value	p value	95% CI
	Mean	SD			
Alive	8.63	2.56	2.86	0.006	7.85 - 9.42
Dead	12.60	5.37			11.82 - 13.38

Figure.No-10 Comparison of SOFA in relation to outcome
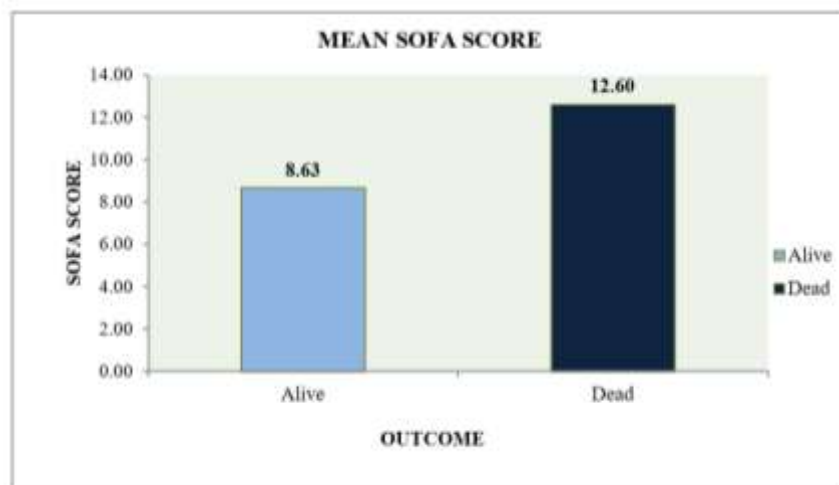
The mean SOFA score indicates the average degree of organ failure over time. We correlated the mean score with mortality. The mean SOFA score in survivors was 8.63±2.56 and in non- survivors was 12.6± 5.37 and the difference was statistically significant (P<0.006).

Area	P value	Asymptotic 95% Confidence Interval	
		Lower Bound	Upper Bound
.805	0.027	0.502	1

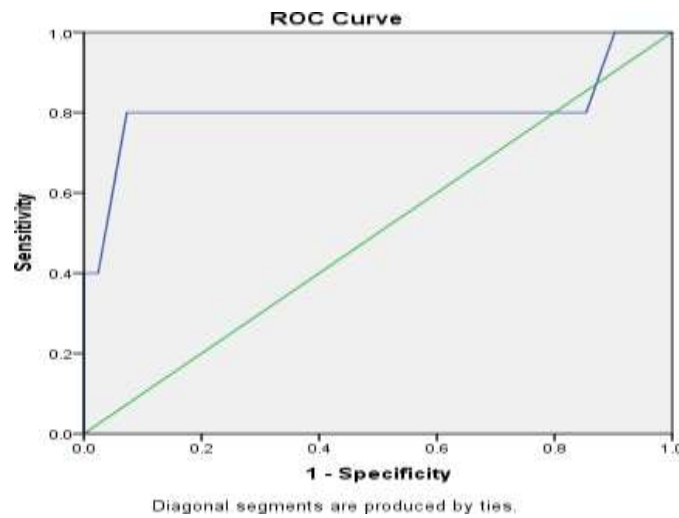| Best cut off	Sensitivity	specificity
11.5	80	92.7

ROC curve analysis

Diagonal segments are produced by ties.

AUC is an effective way to summarize the overall diagnostic accuracy of the test. It takes values from 0 to 1, where a value of 0 indicates a perfectly inaccurate test and a value of 1 reflects a perfectly accurate test. AUC of 0.5 suggests no discrimination ability to predict the disease or mortality, 0.7 to 0.8 is considered acceptable, 0.8 to 0.9 is considered excellent ability to predict disease.On comparison of SOFA with outcome (i.e. mortality) the AUC was observed to be 0.805, which suggests that SOFA could predict the mortality significantly with excellent predictability.At the best cut off of 11.5, SOFA could predict mortality with sensitivity of 80 % and Specificity of 92.7%

Table.No-11 SOFA Score and Mortality Percentage

SOFA Score	Mortality %
0 - 6	20.0%
7 - 9	0.0%
10 - 12	40.0%
13 - 14	20.0%
15 -24	20.0%
Total	100.0%

Figure.No-11 SOFA Score and Mortality Percentage
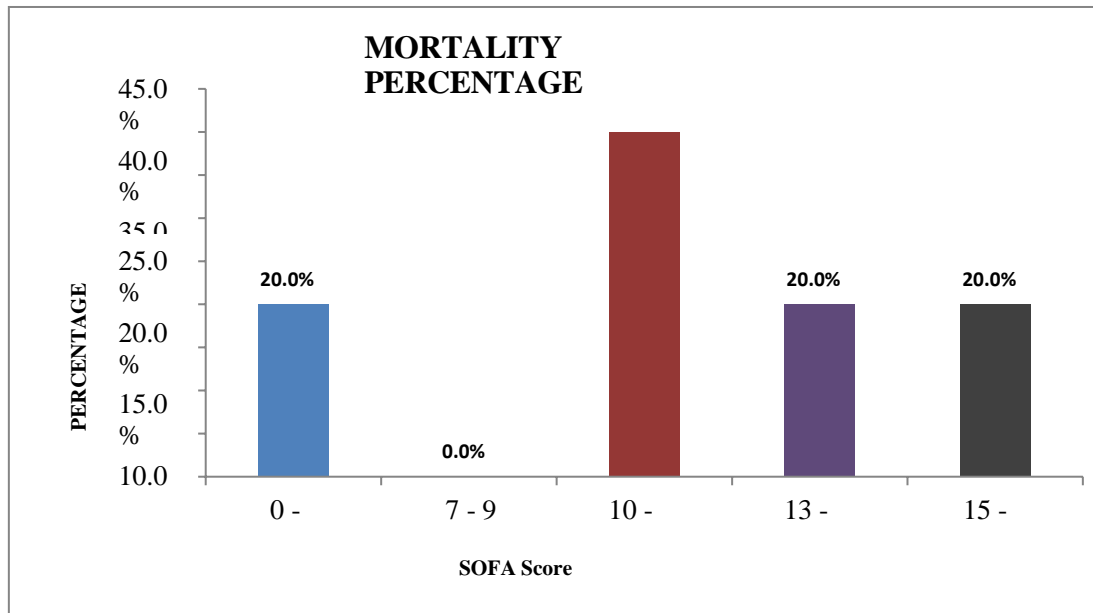
Highest SOFA score(10-12) seen in 40% of patients.

Table.No-12 Comparison between Age group and outcome

Age Grp	Completely Recovered		Patients who receive RRT		CKD		Dead	
	No.	%	No.	%	No.	%	No.	%
<= 20	1	1.1%	3	6.7%	0	0.0%	1	10.0%
21 - 35	9	10.0%	3	6.7%	0	0.0%	1	10.0%
36 - 50	15	16.7%	11	24.4%	0	0.0%	4	40.0%
51 - 65	37	41.1%	15	33.3%	3	75.0%	1	10.0%
66 - 80	25	27.8%	10	22.2%	1	25.0%	3	30.0%
81+	3	3.3%	3	6.7%	0	0.0%	0	0.0%
Total	90	100.0%	45	100.0%	4	100.0%	10	100.0%

Figure.No-12 Comparison between Age group and outcome
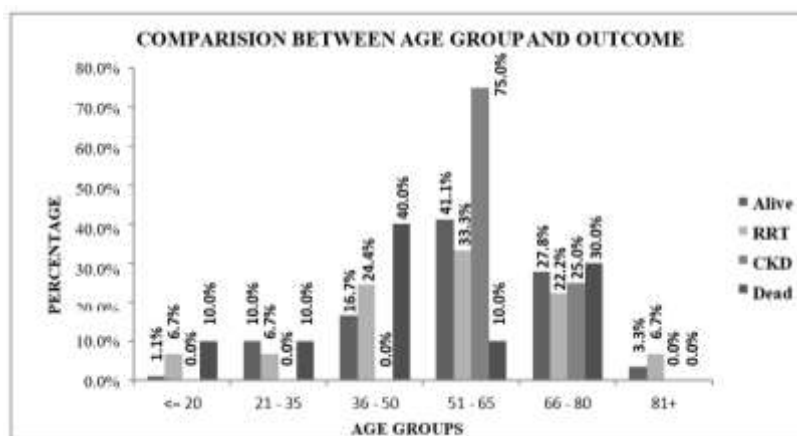
In our study out of 150 patients ,90 patients were recovered. Among 90 patients the possible highest recovery observed in 51-60 age group with 41.1%.

7. DISCUSSION

☐ The total number of patients hospitalized due to various diseases and disorders during the study period was observed to be 3,040, which was mentioned in table.no-1. Among them 150 patients were observed to be admitted with AKI with an incidence of 4.9% per 6months. In our study 91-100 age group with highest incidence of 50%, followed by 51-60 age group and 81-90 age group people with the same incidence of 5.8% per 6 months period.

☐ In our study include 150 cases, minimum age developed AKI was observed to be 10 and maximum age developed AKI was observed to be 95 with mean age of 56±16.6 years from table.no-2, and majority were men seen in table.no-6.3. **Sanjayvikrant et al (2018)** study described that mean age developed AKI was observed to be 49±18.1 years, 86 (27.3%) patients were of age 60 years or above out of 309 study population and majority were men[7].

☐ From table.no-4 we have AKI cases from different departments in that highest frequency of AKI observed in nephrology (45.3%) followed by cardiology (21.3%) and neurology (16%). **XiaoJing Tang et al (2017)** findings suggested that ICU and medical departments are major affected departments with a large number of AKI cases[8].

☐ From table.no-5 82.6% of cases who were in ICU had sepsis AKI is one of the etiology in comparision to 65.4% of cases who did not have ICU stay still have sepsis AKI. **Peerapornratanas et al(2019)** study suggested that for patients in the intensive care unit sepsis is found in about 40% to 50% of patients with AKI in the ICU(P<.0001)[9]. **Vandenberghe W et.al (2016)** study concluded that of all included cardio renal syndrome patients in their study almost one quarter developed AKI and approximately 3% needed renal replacement therapy . Acute heart failure patients experienced the highest occurrence of AKI their study[10]. In our study coronary artery disease patients experienced the highest occurrence of AKI. of all study population 28% had CAD in that 10.9% admitted in ICU for renal replacement therapy. **Jiang F et al (2019)** study concluded that among 479 stroke patients ,the incidence of AKI development was 30.18%(P<.0001) in patients with stroke admitted to the ICU and other risk factor include hypertension in ICU admitted patients(P<0.001)[11].

☐ By comparing with our study the incidence of AKI development seen in 17.8% stroke patients in that 4.3% patients admitted in ICU for renal replacement therapy.

☐ Sepsis AKI is the most common etiology for mortality (70%) followed by AKI over CKD (10%), Cardiorenal (10%), and toxic AKI (10%), which is seen in table.no-6. There is no significant difference between alive (70.7%) and dead patients (70%) with sepsis in our study. **Saxena et .al (2018)** study reported that sepsis was the most common cause of AKI and also had the highest in hospital mortality (P<.001)[12].

☐ Patients with comorbidities such as hypertension, diabetes, stroke and heart diseases present with high percentage in non-ICU when compared to ICU stay patients, because critically ill patients present with comorbidities and also applicable with highest sequential organ failure assessment score.

☐ Among the patients who died, 60% of patients did not have hypertension and 40% of patients had hypertension which is statistically significant (P0.05) **.MLC Rigonatto et al (2018)** study reported that hypertension and diabetes evolved with impaired renal function or increase risk for kidney injury (p<0.05)[13]. Among 10 patients died in overall study population 50% of patients had diabetes. Out of 140 patients who survived 49.3% had diabetes (P value 0.96)[14].

☐ patients who did not have stroke those are 90% of survival compared to patients with stroke those are 9.3% survival . **Haung y et . al (2020)** suggested that acute kidney injury appears to be a common complication after stroke and it is related to increased mortality and disability in stroke. Additionally high NIHSS(stroke score) on admission and history of hypertension were the the critical risk factors for the AKI after stroke(p<0.001)[15].

☐ Among 10 patients who died, 20% of patients with caronary artery disease had developed acute kidney injury,**Evaschonen Berger MD et . al (2019)** study reported that AKI was more common after cardiac catheterization than after CT angiography in their prospective randomized study of patients suspected of having caronary artery disease (p0.005)[16]. In our study it was found as statistically not significant from table.no-7.

☐ Creatinine in ICU stay with mean 3.77±3.3 SD and in non-ICU stay with mean 3.17± 2.39 SD, this shows that the mean creatinine was no different if the patient was in the ICU or not in the ICU. Uric acid in ICU stay with mean 8.14± 2.39 SD and in non-ICU stay mean 8.57± 1010 SD was found non statistically significant P-value of 0.13 shown in table.no-8.

☐ In our study individual parameters statistically not significant but these parameters when combined with SOFA score it was found statistically significant (P<0.002) in table.no-9. We should not compare individual parameters ,we should depend on SOFA score for ICU admissions and mortality rate explanation. Though creatinine and thrombocytopenia both individually doesn't give statistically significant but they are a part of SOFA score.

☐ There is no mortality rate observed in patients who receive renal replacement therapy when compared to 20 patients who did not receive renal replacement therapy 5 patients were died seen in table. No-10. **Fieghen H. et al (2009)** study concluded that when severe enough to renal replacement therapy mortality in critically ill patients with AKI is increasing[17]. In our study no mortality rate observed in patients who receive

renal replacement therapy. **Lin WT .et. al (2019)**study concluded that early RRT doesnot improve the survival rate ,renal function recovery of critically ill patients with AKI in comparison with late RRT(P<0.0001)[18]which is contrast in our study.

☐ Highest SOFA score(10-12) seen in 40% of patients. The mean SOFA score indicates the average degree of organ failure over time. We correlated the mean score with mortality. The mean SOFA score in survivors was 8.63±2.56 and in non-survivors was 12.6± 5.37 and the difference was statistically significant (P<0.006). **Jain A et. al (2016)** study described that the mean SOFA score indicates the average degree of organ failure over time. They correlated the mean score with mortality. The mean SOFA score in survivors was 3.48±2.238 and in non-survivors was 8.9±3.45 and the difference was statistically significant (P<0.002)[19]. Studies such as **Flavolopes ferriera et.al (2001)** concluded that both mean and highest sofa score are particularly useful predictors of outcome[20], this was also observed in our study.

☐ At the best cut off of 11.5, SOFA could predict mortality with sensitivity of 80 % and Specificity of 92.7%.Our study shows that the SOFA score show good discrimination (AUC 0.805) for predicting the prognosis of the patients hospitalized in the ICU. AUC is an effective way to summarize the overall diagnostic accuracy of the test.

☐ It takes values from 0 to 1, where a value of 0 indicates a perfectly inaccurate test and a value of 1 reflects a perfectly accurate test. AUC of 0.5 suggests no discrimination ability to predict the disease or mortality, 0.7 to 0.8 is considered acceptable, 0.8 to 0.9 is considered excellent ability to predict disease. **Fuchs PA et al.(2020)** study shows that the SOFA score show good discrimination (AUC 0.788) for predicting the prognosis of the patients hospitalized in the ICU[21] .

☐ Table.no-11 shown comparison between Age group and outcome. In our study out of 150 patients ,90 patients were recovered. Among 90 patients the possible highest recovery observed in 51-60 age group with 41.1%. 45 patients receive RRT, among them 51-60 age group was observed as highest percentage of 33.3%. among 4 patients who progress to CKD , in that 51-65 age group was observed as highest percentage of 75%. Among 10 patients who died , in that highest mortality rate 45% observed in 36-50 age group. This was found to be statistically not significant (P- value of 0.47).

8. CONCLUSION

Incidence of AKI is 4.9% among hospital admissions in 6 months period. Highest incidence of AKI seen in elderly patients.

Despite of sepsis present in non-ICU admitted AKI patients, it is the most common etiology in critically ill AKI patients.

Only presence of comorbities cannot decide the patient's stay in intensive care unit, patient's ICU stay will be decided by the applicability of SOFA score, need of renal replacement therapy, presence or absence of multi organ failure and baseline severity of illness. Hypertension, diabetes, cerebrovascular accident were the most common risk factors for development of AKI.

All laboratory parameters which included in this study was statistically not significant when compared individually in relation to outcome, but few parameters was statistically significant when combined in SOFA score prediction of outcome .

Mean and highest sofa score are particularly useful predictors of outcome and show good discrimination for predicting the prognosis of the patients hospitalized in the ICU.

Recovery rate of patients from AKI is higher than mortality rate.

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