# Clinical Profile, Need for Dialysis and Mortality of Community Acquired versus Hospital Acquired Acute Kidney Injury

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# ABSTRACT

**Introduction:** Occurrence of Acute Kidney Injury (AKI) is high in hospitalised and critically ill patients. Most of the cases reported by the developed countries are Hospital Acquired Acute Kidney Injury (HA-AKI). AKI is a major medical complication in the developing world also and is due to predominantly community acquired causes, where the epidemiology differs from that in developed countries. Many studies have reported that Community Acquired Acute Kidney Injury (CA-AKI) and HA-AKI differ in mortality, need for renal replacement and residual renal injury.

**Aim:** To know the difference in need for renal replacement therapy and in-hospital mortality between patients diagnosed with CA-AKI and HA-AKI using Kidney Disease: Improving Global Outcomes (KDIGO) criteria.

**Materials and Methods:** A prospective cohort study was conducted from January 2018-December 2018 after obtaining Institutional Ethical Clearance by comparing 50 cases of CA-AKI and 50 cases of HA-AKI admitted by the General Medicine Department as per the inclusion and exclusion criteria. Serum Creatinine (S.Cr) at admission, after 48 hours and at the time of discharge were measured. Serial urine output measurements were done. Need for dialysis was noted in both the groups. Both groups were compared based on need for dialysis, difference in mortality and residual renal injury at the time of discharge. Chi-square and student t-tests were applied respectively and p-value  $\leq 0.05$  was considered as significant. Statistical Package for Social Sciences (SPSS) version 17.0 was used for data entry and analysis.

Results: The CA-AKI and HA-AKI groups were comparable in age and gender but differed in some co-morbidities. CA-AKI group had underlying hepatobiliary disorders and Non steroidal Anti-Inflammatory Drug (NSAID) abuse more often than HA-AKI group. There was a significant reduction in S.Cr over the duration of hospital stay in CA-AKI (mean S.Cr at admission was 4.85 mg/dL, at 48 hours 2.05 mg/dL and at discharge 1.20 mg/dL). S.Cr increased after 48 hours of admission from baseline and declined later in HA-AKI but did not reach baseline in many patients in comparison to CA-AKI group (mean S.Cr at admission was 1.10 mg/dL, at 48 hours 2.38 mg/dL, at discharge 1.57 mg/dL). The highest stage of AKI was stage 3 in CA-AKI group (22 vs 11 of HA-AKI). HA-AKI group had more number of patients in stage 2 AKI (26 vs 18 of CA-AKI). There was no significant difference in mortality and requirement of haemodialysis between CA-AKI and HA-AKI groups.

**Conclusion:** There was no difference between the two groups in terms of mortality and need for renal replacement therapy but there was significant residual renal injury in HA-AKI group.

#### Keywords: Hospital mortality, Renal replacement, Residual renal injury, Risk factors, Serum creatinine

# INTRODUCTION

The AKI is a disease presenting with a range of disorders from asymptomatic with transient changes in laboratory parameters to derangements in intravascular volume, electrolyte and acidbase composition of the plasma often causing persistent renal dysfunction or deaths [1]. It is defined and staged by three systems: Risk, Injury, Failure, Loss and End-stage definition (the RIFLE), Acute Kidney Injury Network (AKIN), KDIGO the last being accepted since 2012 [2-4].

The AKI comprises of 5-7% of acute care hospital admissions and up to 30% intensive care admissions. It is associated with increased risk of death in hospitalised individuals, particularly in those admitted to the ICU with mortality rates exceeding 50% [1]. It is a risk factor for the development of Chronic Kidney Disease (CKD). Severity of illness is directly proportional to the number of co-morbidities [5]. Even stage 1 and 2 AKI can result in CKD, high socio-economic burden for the family and mortality. Even such small increase in S.Cr as 0.5 mg/dL is associated with 6.5-fold increase in odds of death, 3.5-days increase in length of hospital stay and \$7500 in excess hospital cost [6].

Most of the cases reported by the developed countries are HA-AKI. HA-AKI is defined as AKI developing in 48 hours following hospital admission [4,7]. The HA-AKI is that group of patients in whom S.Creatinine increases by atleast 1.5 times above admission value during hospitalisation. HA-AKI is usually associated with one or more of three renal insults that includes prerenal events, exposure to nephrotoxins and sepsis. The causes of HA-AKI reported in Spain and France were prerenal (17-21%), acute tubular necrosis (53-78%) and obstructive (5-10%) [8,9].

Risk factors for HA-AKI include postoperative state, advanced cardiovascular disease, nephrotoxic drugs, neoplastic disease, hospital acquired infection, multiple organ failure, sepsis and solid organ transplantation. Patients with impaired left ventricular systolic function, advanced age commonly defined as >75 years of age, diabetes and dehydration are at particularly high risk of AKI. In addition, specific surgery-related factors including time spent on heart-lung machine, the use of an intra-aortic balloon pump, need for blood transfusions and haemodilution are associated with AKI [7,10].

In the developing countries; incidence, clinical features and outcome of AKI are influenced by environmental, economic and aetiological factors besides healthcare seeking behaviour [11,12]. AKI is reported in 7% of hospitalised patients and 36-67% of critically ill patients. The causes for AKI in a tropical country like India are a variety of illness like malaria, gastroenteritis, snakebites, toxins and sepsis [1]. CA-AKI is that group of patients in whom S.Cr is elevated at the time of admission. Many studies have reported that incidence of CA-AKI was two to three times more than HA-AKI but carried same prognostic significance as HA-AKI in terms on mortality, longer length of stay and higher healthcare cost [7,13,14]. So, this study was conducted to know the difference in need for renal replacement therapy and in-hospital mortality between patients diagnosed with CA-AKI and HA-AKI using KDIGO criteria in patients admitted to general medicine wards.

# **MATERIALS AND METHODS**

A prospective cohort study was conducted from January 2018-December 2018 after obtaining Institutional ethical clearance at General Medicine Department of Shri Dharmasthala Manjunatheshwara College of Medical Sciences and Hospital, Dharwad, Karnataka, India. Informed consent was obtained from all the study participants.

**Sample size calculation:** Hundred patients above 18 years of age with AKI as defined by KDIGO criteria were enrolled by convenience sampling [4]. Prevalence of AKI in the department was 33.5% during 2017. The formula  $n=z^2pq/d^2$  was applied, where z=1.96, with 95% confidence interval and d=20 was considered. So, the sample size was estimated at 96 and rounded up to 100.

**Inclusion and Exclusion criteria:** Fifty patients of CA-AKI and 50 patients of HA-AKI were selected by convenience sampling for describing the clinical profile. The patients who received renal transplant or dialysis within a year of admission or patients with CKD were excluded.

#### **Study Procedure**

Demographic data, history, prior co-morbidities, clinical examination, investigations undertaken to arrive at the diagnosis, provisional diagnosis, need for renal replacement therapy and in-hospital mortality were recorded. AKI was diagnosed as per KDIGO criteria [4]. S.Cr measurements were made at admission, 48 hours and discharge in milligrams per decilitre. Urine output measurements in millilitres were noted.

#### STATISTICAL ANALYSIS

Numerical data were represented as proportions and percentages and continuous data as mean±standard deviation. Chi-square and student t-tests were applied for significance. The p-value ≤0.05 was considered as significant. S.Cr and urine output were compared between HA-AKI and CA-AKI groups using independent t-test. Time trends comparison in each group was done by dependent t-test. Mortality rate and need for dialysis were compared between HA-AKI and CA-AKI by using Chisquare test. The SPSS version 17.0 was used for data entry and analysis.

# RESULTS

The baseline characteristics of the patients are depicted in [Table/ Fig-1,2]. Mean age±standard deviation was 58.98±15.52 years in CA-AKI and 52.22±16.32 years in HA-AKI group.

Age (years)	CA-AKI n (%)	HA-AKI n (%)	Total	Chi- square	p- value	
18-29	2 (4)	3 (6)	5			
30-59	20 (40)	27 (54)	47	2.58	0.28	
≥60	28 (56)	20 (40)	48			
Total	50 (100)	50 (100)	100			
[Table/Fig-1]: Comparison of CA-AKI and HA-AKI with age groups.						

The CA-AKI and HA-AKI were comparable in age and gender, but differed in co-morbidities (type 2 diabetes mellitus and ischemic

Baseline characteristics	CA-AKI	HA-AKI	Significance			
Male: female	38:12	30:20	Chi-square=2.94 (p=0.08)			
With Type 2 DM: without Type 2 DM	20:30	11:39	Chi-square=3.79 (p=0.05*)			
With hypertension: without hypertension	22:28	13:37	Chi-square=3.56 (p=0.06)			
With Ischemic heart disease: without Ischemic heart disease	4:46	1:49	Chi-square=4.35 (p=0.04*)			
[Table/Fig-2]: Baseline characteristics.						

heart disease) which were more often seen in CA-AKI patients. CA-AKI and HA-AKI differed at admission in their diagnosis significantly (p=0.002) as shown in [Table/Fig-3].

Variables	CA-AKI n (%)	HA-AKI n (%)	Total (n)
Chronic alcoholic liver disease	1 (2)	1 (2)	2
Hepatitis B positive chronic alcoholic liver disease	1 (2)	O (O)	1
Non alcoholic steatohepatitis	1 (2)	0 (0)	1
Infected haemorrhoids	1 (2)	O (O)	1
Status post cholecystectomy	1 (2)	0 (0)	1
Dilated cardiomyopathy with reduced ejection fraction	1 (2)	O (O)	1
Old pulmonary TB	0 (0)	1 (2)	1
HIV AIDS	0 (0)	1 (2)	1
Non Steroidal Anti-Inflammatory Drug (NSAID) abuse	2 (4)	0 (0)	2
Myeloproliferative disease	1 (2)	0 (0)	1
Recurrent urinary tract infection	1 (2)	0 (0)	1
Rheumatoid arthritis	2 (4)	1 (2)	3
Chronic obstructive airway disease	4 (8)	1 (2)	5
Hypothyroidism	3 (6)	3 (6)	6
Seizure disorder	1 (2)	0 (0)	1
Cerebrovascular accident	2 (4)	1 (2)	3
Parkinson's disease	1 (2)	1 (2)	2
None of the above co-morbidities	27 (54)	40 (80)	67
Total	50	50	100

[rable/rig-3]: Diagnosis at the time of admission in CA-AA and PA-AA groups Difference between primary diagnosis at admission as listed above was significant Chi-square=9.333 p=0.002\*

There was higher S.Cr in CA-AKI at admission in comparison to HA-AKI (statistically insignificant) whereas it was similar at 48 hours of admission. But at the time of discharge the S.Cr persisted at higher levels in HA-AKI in comparison to CA-AKI [Table/Fig-4].

Time points	Groups	Mean	SD	SE	t-value	p-value	
Baseline	CA-AKI	4.85	13.80	1.95	1.9210	0.0576	
	HA-AKI	1.10	0.19	0.03	1.9210	0.0576	
48 hours	CA-AKI	2.05	1.26	0.18	-1.4772	0.1428	
	HA-AKI	2.38	0.92	0.13	-1.4772		
At discharge	CA-AKI	1.20	0.42	0.06	-2.0163	0.0465*	
At discharge	HA-AKI	1.57	1.20	0.17	-2.0103	0.0400	

**[Table/Fig-4]:** Comparison of CA-AKI and HA-AKI by mean S.Cr in milligrams per decilitre at baseline, 48 hours and at discharge by independent t-test (\*p<0.05 significant).

There was a significant reduction (p<0.05) in S.Cr over the duration of hospital stay in CA-AKI. S.Cr increased after 48 hours of admission from baseline and declined later in HA-AKI as shown in [Table/Fig-5].

Groups	Time points	Mean	Standard deviation	Mean Diff.	% of change	Paired t	p- value
	Baseline	4.85	13.80	2.80	57.71	1.4311	0.4507
	48 hours	2.05	1.26	2.80	57.71	1.4311	0.1587
	Baseline	4.85	13.80	0.05	75 47	F 0577	0.0041
CA-AKI	At discharge	1.20	0.42	3.65	75.17	5.8577	<0.001*
	48 hours	2.05	1.26	0.05	41.30	1.8674	0.0070
	At discharge	1.20	0.42	0.85			0.0678
	Baseline	1.10	0.19	1.00	-116.32	0.0100	<0.001*
	48 hours	2.38	0.92	-1.28		-9.2186	
HA-AKI	Baseline	1.10	0.19	0.47	10.01	0 7055	0.0094*
	At discharge	1.57	1.20	-0.47	-42.61	-2.7055	
	48 hours	2.38	0.92	0.01	04.00		
	At discharge	1.57	1.20	0.81	34.08	8.0942	<0.001*
<b>[Table/Fig-5]:</b> Trends at baseline, 48 hours and at discharge in mean S.Cr in CA- AKI and HA-AKI by dependent t-test.							

There was a significant difference in urine output between CA-AKI and HA-AKI at admission with CA-AKI having lower urine output not amounting to oliguria. At 48 hours of admission, HA-AKI patients had lower urine output. In both the groups, the urine output improved at discharge [Table/Fig-6].

Time points	Groups	Mean	SD	SE	t-value	p-value
At	CA-AKI	559.80	290.65	41.10	-7.3176	0.0001*
admission	HA-AKI	1027.80	346.46	49.00		
40 hours	CA-AKI	832.60	270.51	38.26	3.8536	0.0002*
48 hours	HA-AKI	633.40	245.82	34.76		
At	CA-AKI	1125.90	244.26	34.54	1.8459	0.0679
discharge	HA-AKI	1022.40	312.30	44.17	1.0459	0.0079
[Table/Fig-6]: Comparison of CA-AKI and HA-AKI with mean urine output (mL) at						

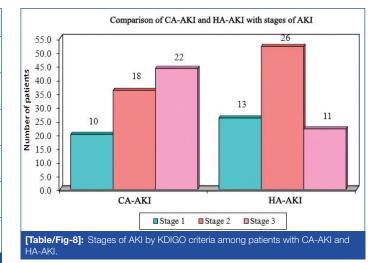
[Iable/Fig-6]: Companson of CA-AKI and HA-AKI with mean urine output (mL) at baseline, 48 hours and at discharge by independent t-test.

There was a trend of increasing urine output among CA-AKI patients till discharge. However, HA-AKI patients had a dip in urine output at 48 hours that improved subsequently [Table/Fig-7]. There was a significant difference between all time points in CA AKI group, however there was no significant difference between the baseline and the discharge in HA-AKI group [Table/Fig-7].

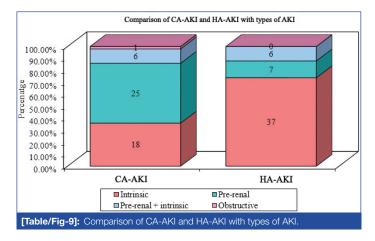
There were more cases of stage 3 in CA-AKI group in comparison to HA-AKI whereas HA-AKI group had more number of patients in stage 2 as shown in [Table/Fig-8].

Groups	Time points	Mean	Std. Dv.	Mean Diff.	% of change	Paired t	p-value
	At admission	559.80	290.65	-272.80	-48.73	0.0007	0.0001*
	48 hours	832.60	270.51	-272.00	-40.73	-9.9667	0.0001*
CA-AKI	At admission	559.80	290.65	-566.10	-101.13	15 4000	0.0001*
CA-ARI	At discharge	1125.90	244.26	-300.10	-101.13	-15.4299	0.0001*
	48 hours	832.60	270.51	-293.30	-35.23	-11.9268	0.0001*
	At discharge	1125.90	244.26	-293.30			
	Baseline	1027.80	346.46	004.40	38.37	9.0959	0.0001*
	48 hours	633.40	245.82	394.40			
HA-AKI	Baseline	1027.80	346.46	5.40	0.50	0.1000	0.0100
	At discharge	1022.40	312.30	5.40	0.53	0.1030	0.9183
	48 hours	633.40	245.82	200.00	389.00 -61.41	-61.41 -10.6353	0.0001*
	At discharge	1022.40	312.30	-369.00			0.0001
[Table/Fig-7]: Trends in mean urine output (mL) at baseline, 48 hours and at							

[Iable/Fig-7]: Irends in mean urine output (mL) at baseline, 48 nours and discharge with in CA-AKI and HA-AKI by dependent t-test.



More number of patients with CA-AKI had prerenal AKI and intrinsic causes of AKI were more in HA-AKI [Table/Fig-9]. This difference was statistically significant (Chi-square=17.6890, p-value 0.0010).



There was no significant difference in requirement of haemodialysis [Table/Fig-10] and mortality [Table/Fig-11] between CA-AKI and HA-AKI groups.

Dialysis	CA-AKI n (%)	HA-AKI n (%)	Total	Chi- square	p- value
No	43 (86)	45 (90)	88		
Yes	7 (14)	5 (10)	12	0.3790	0.5380
Total	50 (100)	50 (100)	100		
[Table/Fig-10]: Comparison of CA-AKI and HA-AKI with need for renal replacement					

Mortality	CA-AKI n (%)	HA-AKI n (%)	Total	Chi-square yates	p-value	
Expired	1 (2)	5 (10)	6			
Improved	49 (98)	45 (90)	94	1.5960	0.2070	
Total	50 (100)	50 (100)	100			

[Table/Fig-11]: Comparison of CA-AKI and HA-AKI with mortality

# DISCUSSION

The CA-AKI occurs in younger patients due to tropical infectious diseases, diarrhoeal disorders or complicated pregnancies in developing countries even before arrival to the hospital where as HA-AKI occurs in older patients due to sepsis, nephrotoxic drugs and hospital acquired infections in developed countries after admission to hospital [15,16].

The pattern of age distribution, co-morbidities and aetiology contrary to expectations in CA-AKI in our study may be attributed

to the fact that ours is a medical college hospital situated in urban area receiving referred cases from many districts of North Karnataka. There is also ease of availability of NSAIDs over the counter contributing to CA-AKI cases contrary to other studies [17-19].

Patients with CA-AKI had high S.Cr at admission which were comparable to those of HA-AKI and reached normal range at the end of hospital stay. This may be related to the diagnostic criteria for CA-AKI. None of the CA-AKI patients had baseline S.Cr values prior to admission. In contrast, HA-AKI patients had persistent and residual increased S.Cr at the end of hospital stay.

The normalisation of S.Cr may be attributed to the prerenal azotemia in CA-AKI and its persistent increased values reflect intrinsic renal injuries in HA-AKI. This was similar to study done by Der Mesropian PJ et al., which concluded that CA-AKI had better glomerular filtration rate (71.3 vs 61.1 mL/min/1.73 m<sup>2</sup>) and lower prevalence of CKD (43.8 vs 29.1) at baseline and had similar long-term consequences to HA-AKI [20].

The urine output was lower in CA-AKI patients at admission, improved at 48 hours and continued to improve till the end of hospital stay. The urine output reduced from previously normal values at 48 hours in HA-AKI patients. At the end of hospital stay both the groups had similar urine output. The mismatch between urine output and S.Cr among patients of HA-AKI at the end of hospital stay is explained as change in S.Cr follows improvement in urine output in patients with intrinsic renal disease.

There were more cases of stage 3 in CA-AKI group in comparison to HA-AKI whereas HA-AKI group had more number of patients in stage 2. This may be because of early recognition of AKI among HA-AKI patients and preventive measures undertaken in hospital. The number of CA-AKI patients in stage 3 was more than in stage 1. This was different from another study conducted in south India where both stage 1 and stage 3 were 37% and stage 2 were 24%. In the present study increase in number of patient in stage 3 is due to late healthcare seeking behaviours as as the present was the private hospital is private hospital [7].

There was no statistically significant difference between the two groups in mortality and requirement of renal replacement therapy in the present study. According to study done by Hsu CN et al., HA-AKI had more severe outcomes than CA-AKI in the form of increased mortality, longer duration of hospital stay and need for dialysis [11].

Wonacott A et al., conducted a prospective study in United States of America in which patients with CA-AKI had better survival than patients with HA-AKI. Mortality in CA-AKI was 45% as compared to 62.9% in HA-AKI, however renal outcomes were similar in both CA-AKI and HA-AKI (39.4% vs 33.6%) in developing CKD or progression of pre-existing CKD within 14 months [21].

In a study conducted by Priyamvada PS et al., the mortality was not different between CA-AKI and HA-AKI (56% vs 48%). Bhadade R et al., reported high mortality in ICUs due to tropical illnesses and multiorgan failure (51.9%) though the present mortality rates were lower (2% vs 10%). This difference in mortality rates in comparison to the study by Priyamvada PS et al., may be due to early referral to nephrologists, early initiation of volume resuscitation and sepsis bundle of care as discussed by

Yang L although convenience sampling could also have biased the results [7,22,23].

#### Limitation(s)

The present study could have been influenced by small sample size and convenience sampling. The follow-up of the patients only up to discharge was done. Further studies with larger sample size can be conducted in future.

## CONCLUSION(S)

The differences between CA-AKI and HA-AKI in need for renal replacement and mortality during hospital stay are influenced by underlying co-morbidities and diagnosis at admission. However the long-term outcomes are likely to be different as there is a significant residual renal injury in HA-AKI.

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