ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 12 | December - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

STUDY OF CLINICAL PROFILE, OUTCOME AND ASSESSMENT OF RISK FACTORS FOR MORTALITY IN AKI (ACUTE KIDNEY INJURY) PATIENTS IN MEDICAL INTENSIVE CARE UNIT

General Medicine

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ABSTRACT

Background: Acute kidney injury (AKI) is characterized by the sudden impairment of kidney function resulting in the retention of nitrogenous and other waste products. It 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%. The present study was aimed to analyse the clinical spectrum, final outcome and risk factors for mortality among AKI patients in the ICU. **Methodology:** The present Prospective observational study was conducted on 100 patients aged > 18 years, with diagnosis of AKI (fulfilling the KDIGO definition of AKI) admitted in MICU of tertiary care centre over a period of 18 months. Detailed history taking, general physical examination, systemic examination and routine and specific lab investigations, was done to find out the underlying etiology, clinical features and outcome of AKI. Data was analysed using appropriate statistical tests. **Results:** 57% patients belonged to age group 51 to 60 years with mean age 49.69±9.5 years with median (25th-75th percentile) of 53.5 (44.5-55.25). In the study, 59% were males. 29% patients had dengue followed by sepsis (19%) and AGE 13%. In majority 65%, type of AKI was intrinsic followed by pre renal (32%). In majority (63%) of patients, KDGIO stage was 2 followed by stage 3 (22(22%)). Majority (61%) of patients survived. Proportion of died patients was significantly higher in fulminant hepatitis, sepsis, comorbidities (58.54%), U/RM - sediment positive (75.68%), hypotension (60.47%) as compared to patients without hypotension (22.81%), ventilatory support (67.57%), in patients who required inotropic support (87.50%), in KDGIO stage 3(63.64%) as compared. **Conclusion:** The most common cause of acute kidney injury is dengue hemorrhagic fever. Significant risk factors associated with mortality was seen with co-morbidities like diabetes mellitus and hypertension, requirement of inotropic supports, KDIGO stage 3 patients and occurrence of hypotension.

KEYWORDS

Acute Kidney Injury, Medical Intensive Care Unit, Clinical Profile, Risk Factors, Outcome

INTRODUCTION

Acute kidney injury (AKI), previously known as acute renal failure is characterized by the sudden impairment of kidney function resulting in the retention of nitrogenous and other waste products normally cleared by the kidneys[1]. KDIGO- AKI guidelines[2] has defined by parameters like Sr. Creatinine and urine volume. AKI complicates 5–7% of acute care hospital admissions and up to 30% of admissions to the intensive care unit[3] and is a major medical complication in the developing world, particularly in the setting of diarrheal illnesses, infectious diseases like malaria and leptospirosis, snake bites and natural disasters[1]. AKI may complicate a wide range of diseases.

Acute kidney injury (AKI) has been reported in up to 25% of critically-ill patients with SARS-CoV- 2 infection, especially in those with underlying comorbidities. AKI is associated with high mortality rates in this setting, especially when renal replacement therapy is required. Acute kidney injury (AKI) during SARS-CoV-2 infection is associated with high mortality rates in ICU[4].

For the purpose of diagnosis and management, it is divided into three categories[5] as prerenal, renal and postrenal AKI with varied causes for each type. AKI can range in severity from asymptomatic and transient changes in laboratory parameters of glomerular filtration rate (GFR), to overwhelming and rapidly fatal derangements in effective circulating volume regulation and electrolytes, acid-base composition of the plasma. The initial care of patients with acute kidney injury is focused on reversing the underlying cause and correcting fluid and electrolyte imbalance. Dialysis is used as an extension of the supportive measure.

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%[6]. Morbidity depends on severity of injury and underlying disease. Other factors[7] influencing patient survival in acute kidney injury include age, number and severity of coexistent illnesses and associated complications. The present study was aimed to analyse the clinical spectrum, final outcome and risk factors for mortality among AKI patients in the ICU.

OBJECTIVE:

To analyse the clinical spectrum, final outcome and to identify risk factors for mortality among AKI patients in the ICU.

MATERIALS AND METHODS:

The present study was started after getting approval from Institutional Ethical Committee. The Prospective observational study was conducted on 100 patients aged > 18 years, with diagnosis of AKI (fulfilling the KDIGO definition of AKI) admitted in Medical Intensive Care Unit of tertiary care centre over a period of 18 months. Patients with known case of CKD(chronic kidney disease) will be excluded. Data collection was started after taking written informed consent in language that the patient best understands. Detailed thorough history taking, general physical examination, systemic examination and routine and specific lab investigations, was done to find out the underlying etiology, clinical features and outcome of AKI. All the patients were followed clinically and biochemically till the time of discharge

Standardized data collection form was used to collect the information pertaining to demographic, clinical and laboratory parameters of the study subjects.

Statistical analysis:

The presentation of the Categorical variables was done in the form of number and percentage (%). On the other hand, the quantitative data were presented as the means ±SD and as median with 25th and 75th percentiles (interquartile range). The association of the variables which were quantitative in nature were analysed using independent t test. The association of the variables which were qualitative in nature were analysed using Chi-Square test. If any cell had an expected value of less than 5 then Fisher's exact test was used. Multivariate logistic regression was used to find out independent significant risk factors of mortality. For statistical significance, p value of less than 0.05 was considered statistically significant.

RESULTS:

Table 1: Demographic Profile of the Patients:

Demographic Parameters		Frequency	Percentage
Age(years)	19 to 20	1	1%
	21 to 30	3	3%
	31 to 40	20	20%
	41 to 50	15	15%
	51 to 60	57	57%
	61 to 70	4	4%

Gender	Female	41	41%
	Male	59	59%

Demographic and Clinical Profile of the Patients:

In the present study, 57(57%) patients belonged to age group 51 to 60 years followed by 31 to 40 years 20%. Mean age (years) of study subjects was 49.69±9.5 with median (25th-75th percentile) of 53.5 (44.5-55.25). In the study, 59(59%) patients were males and 41(41%) patients were females.

29% patients had dengue followed by sepsis (19%), AGE 13%, CVD 9%, leptospirosis 9% and malaria 5%. Comorbidity was present in only 41 out of 100 patients (41%). In 27% patients, diabetes mellitus was present. Hypertension was present in only 26% patients.

Table 2: Clinical Profile of the Patients:

Clinical Parameters		Frequency	Percentage
Diagnosis	AGE	13	13%
	BPH	1	1%
	CVD	9	9%
	Dengue	29	29%
	Fulminant Hepatitis	4	4%
	Leptospirosis	9	9%
	Malaria	5	5%
	Malignancy	2	2%
	Nephrolithiasis	3	3%
	OP poisoning	3	3%
	Sepsis	19	19%
	Snake Bite	3	3%
Comorbidities	No	59	59%
	Yes	41	41%
Type of Comorbidities	Diabetes mellitus	27	27%
	Hypertension	26	26%
U/RM - sediment		37	37%
Oliguria		77	77%
Hypotension		43	43%

In majority (63%) of patients, U/RM - sediment was negative. 77% had oliguria and in 44% of patients, hypotension was present.

Table 3: Parameters of the patients after admission:

Clinical Parameters after admission		Frequency	Percentage
Type of AKI	Pre renal	32	32%
	Intrinsic renal	65	65%
	Post renal	3	3%
Urine Output (mL/Kg/hr)	<0.5 for 6-12 hrs	21	21%
	<0.5 for >12hrs	25	25%
	Anuria > 12 hrs	20	20%
	<0.3 for >24 hrs	34	34%
Ventilatory support		37	37%
Hemodialysis		37	37%
Inotropic support		32	32%
Initial serum creatinine (mg/dL)	Mean 2.66±0.27	Median 2.6(2.4-2.9)	Range 2.2-3.1
Peak serum creatinine (mg/dL)	Mean 4.8±0.64	Median 4.8(4.175-5.4)	Range 3.8-5.9
ICU stay (days)	Mean 7.96±2.48	Median 8(6.5-9)	Range 3-17

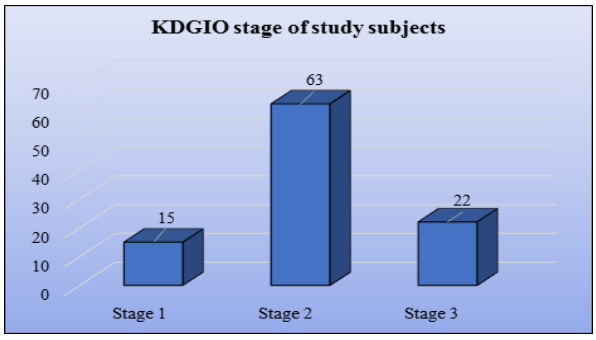
Ventilatory support was required in only 37% patients. In majority (65%) of patients, type of AKI was intrinsic renal followed by pre renal (32%). Type of AKI was post renal in only 3 out of 100 patients (3%). Hemodialysis was done in 37 out of 100 patients (37%). Inotropic support was required in only 32% patients.

In 34(34%) patients, urine output in mL/Kg/hr was <0.3 for >24 hours followed by <0.5 for >12hours 25% and <0.5 for 6-12 hours 21%. Urine output in mL/Kg/hr was anuria > 12 hours in only 20 out of 100 patients (20%).

Mean value of initial serum creatinine(mg/dL) and peak serum creatinine(mg/dL) of study subjects was 2.66±0.27 and 4.8±0.64 with median(25th-75th percentile) of 2.6(2.4-2.9) and 4.8(4.175-5.4) respectively. Mean value of ICU stay (days) of study subjects was 7.96±2.48 with median(25th-75th percentile) of 8(6.5-9).

Distribution of KDGIO stage of study subjects:

In majority (63%) of patients, KDGIO stage was 2 followed by stage 3 (22(22%)). KDGIO stage was 1 in only 15 out of 100 patients (15%). (Figure 1)



Outcome of study subjects:

Majority (61%) of patients survived. Only 39 out of 100 patients (39%) died. (Figure 2)

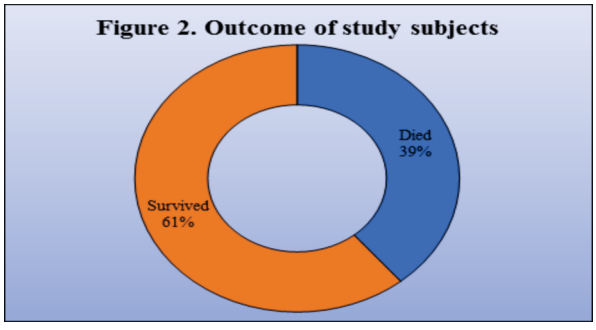


Table 4: Association of Demographic Profile with mortality:

Demographic Profile		Died (n=39)	Survived (n=61)	Total	P value
Age (years)	Mean± SD	50.77± 8.23	49±10.17	49.69±9.46	0.364*
	Median(25th-75th percentile)	55(49-56)	53(40-55)	53.5(44.5-55.25)	
	Range	32-68	19-65	19-68	
Gender	Female	13 (31.71%)	28 (68.29%)	41 (100%)	0.213‡
	Male	26 (44.07%)	33 (55.93%)	59 (100%)	

* **Independent t test,** ‡ **Chi square test**

Mean± SD of age(years) of died was 50.77±8.23 and survived was 49±10.17 with no significant association between them. (p value=0.364). Distribution of mortality was comparable between gender. (Female 31.71% vs Male 44.07%) (p value=0.213).

Table 5:-Association of Clinical Profile with mortality.

Clinical Profile		Died (n=39)	Survived (n=61)	Total	P value
Diagnosis	AGE	0 (0%)	13 (100%)	13 (100%)	<0.0001†
	BPH	0 (0%)	1 (100%)	1 (100%)	
	CVD	1 (11.11%)	8 (88.89%)	9 100%)	
	Dengue	11(37.93%)	18 (62.07%)	29 (100%)	
	Fulminant Hepatitis	3 (75%)	1 (25%)	4 (100%)	
	Leptospirosis	3 (33.33%)	6 (66.67%)	9 (100%)	
	Malaria	0 (0%)	5 (100%)	5 (100%)	
	Malignancy	1 (50%)	1 (50%)	2 (100%)	
	Nephrolithiasis	1 (33.33%)	2 (66.67%)	3 (100%)	

	OP poisoning	2 (66.67%)	1 (33.33%)	3 (100%)	
	Sepsis	16(84.21%)	3 (15.79%)	19 (100%)	
	Snake Bite	1 (33.33%)	2 (66.67%)	3 (100%)	
Comorbidities	No	15(25.42%)	44 (74.58%)	59 (100%)	0.0008 ‡
	Yes	24(58.54%)	17 (41.46%)	41 (100%)	
Diabetes mellitus	No	23(31.51%)	50 (68.49%)	73 (100%)	0.012‡
	Yes	16(59.26%)	11 (40.74%)	27 (100%)	
Hypertension	No	23(31.08%)	51 (68.92%)	74 (100%)	0.006‡
	Yes	16(61.54%)	10 (38.46%)	26 (100%)	

† **Fisher's exact test,** ‡ **Chi square test**

Proportion of died patients was significantly higher in fulminant hepatitis (75%), sepsis (84.21%), OP poisoning (66.67%) as compared to AGE (0%), BPH(0%), CVD (11.11%), dengue (37.93%), leptospirosis (33.33%), malaria (0%), malignancy (50%), nephrolithiasis (33.33%), snake bite (33.33%). (p value <0.0001).

Proportion of died patients was significantly higher in patients with comorbidities (58.54%) as compared to patients without comorbidities (25.42%). (p value=0.0008). Proportion of died patients was significantly higher in patients with diabetes mellitus (59.26%) as compared to patients without diabetes mellitus (31.51%). (p value=0.012). Proportion of died patients was significantly higher in patients with hypertension (61.54%) as compared to patients without hypertension (31.08%). (p value=0.006)

Table 6:-Association of U Parameters of the patients after admission with mortality.

Clinical Parameters after admission		Died(n=39)	Survived(n=61)	Total	P value
U/RM - sediment	Negative	11 (17.46%)	52 (82.54%)	63 (100%)	<0.0001‡
	Positive	28 (75.68%)	9 (24.32%)	37 (100%)	
Oliguria	Absent	6 (26.09%)	17 (73.91%)	23 (100%)	0.148‡
	Present	33 (42.86%)	44 (57.14%)	77 (100%)	
Hypotension	Absent	13 (22.81%)	44 (77.19%)	57 (100%)	0.0001 ‡
	Present	26 (60.47%)	17 (39.53%)	43 (100%)	
Ventilatory support	No	14 (22.22%)	49 (77.78%)	63 (100%)	<0.0001‡
	Yes	25 (67.57%)	12 (32.43%)	37 (100%)	
Type of AKI	Pre renal	12 (37.50%)	20 (62.50%)	32 (100%)	1‡
	Intrinsic renal	26 (40%)	39 (60%)	65 (100%)	
	Post renal	1 (33.33%)	2 (66.67%)	3 (100%)	
Hemodialysis	No	27(42.86%)	36(57.14%)	63(100%)	0.302‡
	Yes	12(32.43%)	25(67.57%)	37(100%)	
Inotropic support	No	11 (16.18%)	57 (83.82%)	68 (100%)	<0.0001†
	Yes	28 (87.50%)	4 (12.50%)	32 (100%)	
KDGIO stage	Stage 1	0 (0%)	15 (100%)	15 (100%)	0.0005 ‡
	Stage 2	25 (39.68%)	38 (60.32%)	63 (100%)	
	Stage 3	14 (63.64%)	8 (36.36%)	22 (100%)	

† **Fisher's exact test,** ‡ **Chi square test**

Proportion of died patients was significantly higher in U/RM - sediment positive (75.68%) as compared to U/RM - sediment negative (17.46%). (p value <0.0001). Distribution of mortality was comparable between patients without and with oliguria. (Absent(26.09%) vs Present(42.86%)). (p value=0.148). Proportion of died patients was significantly higher in patients with hypotension (60.47%) as compared to patients without hypotension (22.81%). (p value=0.0001)

Proportion of died patients was significantly higher in patients who required ventilatory support (67.57%) as compared to patients who did not require ventilatory support (22.22%). (p value <0.01). Distribution of mortality was comparable with type of AKI. (Pre renal(37.50%) vs Intrinsic renal(40%) vs Post renal(33.33%)). (p value=1)

Distribution of mortality was comparable with hemodialysis. (No(42.86%) vs Yes(32.43%)). (p value=0.302). Proportion of died patients was significantly higher in patients who required inotropic support (87.50%) as compared to patients who did not require inotropic support (16.18%). (p value <0.0001). Proportion of died patients was significantly higher in KDGIO stage 3(63.64%) as compared to stage 1(0%), stage 2(39.68%). (p value=0.0005)

Mean ±SD of ICU stay (days) in died patients was 8.15±3.48 and survived was 7.84±1.56 with no significant association between them. (p value=0.593)

On performing multivariate regression, requirement of inotropic support was significant independent risk factor of mortality after adjusting for confounding factors. Patients who required inotropic support had significantly high risk of mortality with adjusted odds ratio of 6.465(1.53 to 27.318).

DISCUSSION

In our study, in majority 57% patients belonged to age group 51 to 60 years with mean age was 49.69±9.5 years with median of 53.5 years. Study done by **Bagasha et al[8],** shows that the average age was 37 years in study participants. (range18–90 years). Study done by **Igiraneza G et al[9],** shows that median age of patients studied was 38 years (IQR 28–57 years) mostly including young population. So, median in this study is lower than median age in our study. This finding is unlike reports from Western countries where the most frequently affected people are the elderly as per study done by **Cerda et al[10].**

In our study, 59(59%) patients were males, showing male predominance. Study done by **Igiraneza G et al[9],** shows that there were 51% males and 49% females, leading to slight male predominance. Study done by **Bagasha et al[10],** shows that there were 55.6% males and 44.4% females in the study leading to male predominance which is consistent with our study outcome.

In our study, accordingly, 29% patients had dengue followed by sepsis (19%), AGE (13%), CVD (9%), leptospirosis (9%). The World Health Organization (WHO) estimates that malaria may result in AKI in 1% of cases[11], but can be as high as 4% in some malaria endemic regions, being more prevalent in adults and older children as per study done by **Prakash et al[12]** and **Maheshwari et al[13].** In spite of 82% of Rwandan households owning at least one long lasting insecticide treated mosquito net, 1.9 million malaria cases occurred in 2015 as demonstrated in a study by **Igiraneza G et al[9].**

In our study, in 27(27%) patients, diabetes mellitus was present. Hypertension was present in only 26 out of 100 patients (26%). Study done by **Igiraneza G et al[9],** shows that severe hypertension was observed in 23.2% of the cohort and hyperkalemia >6.6 mmol/L in 40.2%.

In our study, mean value of initial serum creatinine (mg/dL) and peak serum creatinine (mg/dL) of study subjects was 2.66±0.27 and 4.8±0.64 with median (25th-75th percentile) of 2.6 (2.4-2.9) and 4.8(4.175-5.4) respectively. Study done by **Wang et al[14],** shows that maximum peak sr. creatinine in patients with AKI was 2.4±2.4 mg/dl.

In our study, in 34% patients, urine output in mL/Kg/hr was <0.3 for >24 hours followed by <0.5 for >12hours (25%) and <0.5 for 6-12 hours (21%). Study done by **Bagasha et al[8],** shows that at age adjusted analysis however, AKI was more commonly associated with a a urine output of 0.6–2.4 mL/kg (*p*=08). In patients with AKI, urine output was <0.5 L/ 24hrs in 26.98% patients, 0.6 to 2.4 L/ 24 hr in 68.25% patients and >2.4 L/24 Hrs in 4.76% patients.

In our study, majority (61%) of patients survived. Only 39 out of 100 patients (39%) expired. So, mortality rate in our study was 39%. Study done by **Wang et al**[14], shows that mortality rate in patients with AKI was 10.8%. This value is less than mortality rate of our study. Study done by **Bagasha et al**[8], shows that in-hospital mortality among patients with AKI was 21% (13/63). So, mortality rate of this study is less than our study. Of the 13 patients who died 12 (92%) had AKIN stage 3 AKI and were eligible for ICU admission and dialysis which were not available. Patients were considered eligible for ICU admission if they had single or multiple organ failure refractory to conservative management, while all patients with renal failure refractory to conservative management were considered eligible for dialysis. AKIN Stage 2 and 3 in this study were more likely to die or have persistently elevated creatinine than resolved kidney injury at discharge.

Pregnancy-related AKI is one of top causes of mortality among young women in low- and middle-income countries, while the condition is uncommon in the developed world as per study done by **Naicker et al**[15]**.** These include conditions such as post-caesarian section peritonitis, post- and antepartum hemorrhage, septic abortion, preeclampsia, and eclampsia. In alignment with our findings, previous studies on AKI in sub-Saharan Africa have reported obstetric complications as an important cause of AKI as per study done by **Naicker et al**[15] and **Cerda et al**[10]**.** In South Africa, pregnancy-related disorders, most notably septic abortion and preeclampsia, were responsible for 15% of AKI requiring dialysis.

In our study, proportion of died patients was significantly higher in U/RM - sediment positive (75.68%) as compared to U/RM - sediment negative (17.46%). (p value <01). Study done by **Wang et al**[14], shows that Larger increases in Sr. Creatinine were associated with higher mortality rates: stage 1, 6.3%; stage 2, 16.5%, and stage 3, 23.7%.

In our study, distribution of mortality was comparable between patients without and with oliguria. Mortality rate in patients with oliguria and without oliguria was 42.86% and 26.09% respectively. (p value=0.148). In the bivariable analysis for clinical patterns AKI was less common in patients with a urine output of 0.6-2.4 ml/kg/min (p=01) and more than 2.4 ml/kg/minute (p=0.036) as per study done by **Bagasha et al**[8]**.**

In our study, on performing multivariate regression, requirement of inotropic support was significant independent risk factor of mortality after adjusting for confounding factors. Patients who required inotropic support had significantly high risk of mortality with adjusted odds ratio of 6.465(1.53 to 27.318). In study done by **Bagasha et al**[8], of admissions to the casualty department and medical wards, the prevalence of sepsis-related AKI was 16.3%, which similar to the prevalence of 24% found by **Rayner et al**[16] in their study of acute renal failure in community-acquired bacteremia. They also found that persistence of AKI resulted in a higher mortality when compared to bacteremic patients in whom AKI resolved upon treatment of the bacteremia. Sixty-one percent of patients in study done by **Bagasha et al**[8] were HIV positive with multiple co-morbidities. HIV infection is associated with pre-existing renal damage from other co-morbid conditions, which may occur independently of sepsis as per study done by **Xue et al**[17]**.**

The high incidence of AKI observed in study done by **Wang et al**[14] is also consistent with other epidemiologic studies of AKI in the hospital setting. Creatinine-based studies of AKI in hospitalized patients in Austin, Australia, and Chicago, USA utilized data that were more than 10 years old as per study done by **Uchino et al**[18] and **Nash et al**[19]**. Liangos et al**[20] and **Waikar et al**[21] used national hospital discharge data to characterize the incidence of AKI but defined AKI using ICD-9 discharge diagnoses – not changes in serial Sr. Creatinine measurements. **LaFrance and Miller et al**[22] analyzed 1.2 million patient records from the Department of Veteran's Affairs (VA) Health Care System, identifying AKI rates ranging from 7.8 to 11%.

CONCLUSION

We concluded that most common cause of acute kidney injury is dengue hemorrhagic fever followed by sepsis. Most common system involved in sepsis was urinary system followed by lower respiratory tract infection. Hemodialysis is required in 37% patients. Sr. creatinine is an important marker of prognosis. Mortality rate in our study is 39%. Significant risk factors associated with mortality was seen with co-morbidities like diabetes mellitus and hypertension, requirement of inotropic supports, KDIGO stage 3 patients and occurrence of hypotension. Early diagnosis and intervention may decrease morbidity and mortality in acute kidney injury.

Acknowledgement:

I wish to acknowledge Hon. Dean of TN Medical College and BYL Nair Charitable Hospital for immense help, guidance and suggestions at every step in carrying out this study.

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