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"TO STUDY THE OUTCOME OF ACUTE KIDNEY INJURY (AKI) AND ITS ASSOCIATED FEATURES FOR ALL-CAUSE MORTALITY AND MORBIDITY IN A TERTIARY CARE HOSPITAL"

Nephrology

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ABSTRACT

Background & Aims: Acute kidney injury (AKI) is leading cause of all-cause mortality in community and hospitals. AKI represents heterogeneous syndrome characterized by an abrupt reduction in the glomerular filtration rate, is often complication of acute illnesses and associated with adverse sequelae in short and long-term. [1–2] It is common complication in patients admitted to hospitals with prevalence of 10–15% of all hospitalizations (3) and in intensive care unit (ICU) patients, its prevalence can sometimes exceed 50%. (4) **Material & Methods:** After getting approval from institutional ethics committee and written informed consent, a cross-sectional observational study was conducted at Nephrology department of a tertiary care hospital on 150 patients presenting at OPD, admitted in ward and ICU fulfilling inclusion criteria. All patients were subjected to detailed history, clinical examination with complete general and systemic examination with special reference to AKI with laboratory investigations and radiological imaging. Daily follow-up has been done until discharge or death and follow-up for 3 months. ICU support, treatment with dialysis, survival at discharge and in-hospital mortality have been studied. **Results:** Old age, male-gender and co-morbid conditions like diabetes & hypertension were significantly associated with higher incidence of mortality ($p<0.05$). The most frequently reported symptom was breathlessness, occurring in 62 cases (34.1%). The most common etiology was sepsis occurring in 43 cases (23.62%) followed by acute gastroenteritis in 21 patients (11.53%). Compared to all stages, KDIGO stage-3 had significantly higher mortality ($P<0.001$). The observed difference in survival rates reached statistical significance when compared to the control or alternative treatment group ($p<0.001$). **Conclusion:** We observed that most common cause for AKI was sepsis followed by cardiorenal and acute gastroenteritis. Higher the KDIGO stage higher was the mortality. AKI due to glomerulopathies was most commonly associated with partial recovery and dialysis dependency after 3 months.

KEYWORDS

AKI (Acute kidney injury), KDIGO stagging, all-cause morbidity & mortality. (https://meshb.nlm.nih.gov/MeSHonDemand).

INTRODUCTION:

Acute kidney injury (AKI) is a leading cause of all-cause mortality in the community and hospitals. AKI represents a heterogeneous syndrome, characterised by an abrupt reduction in the glomerular filtration rate, is often a complication of acute illnesses and associated with adverse sequelae in short and long-term. [1–2]

AKI is a common complication in patients admitted to hospitals with prevalence of 10–15% of all hospitalizations [3] and >50% in patients of intensive care unit (ICU).[4] In 2012, Kidney Disease Improving Global Outcomes (KDIGO) described its new definition of AKI as a 7-day loss of kidney function characterised by elevated blood creatinine levels and/or decreased urinary output. [5]

AKI is traditionally seen as a single disease or classified according to semi-anatomical categories as pre-renal, intrinsic, and post-renal AKI, now developing into more specific syndromes, including cardiorenal, hepatorenal, nephrotoxic, sepsis-associated AKI, etc. [6] This has posed a major challenge to AKI diagnosis and treatment as specific syndromes often co-exist, which themselves cause substantial morbidity and mortality.

AKI is easily overlooked as a significant independent marker for both disease severity and a determinant of short-term and long-term morbidity and mortality outcomes.[7] Recently, studies have shown that even small changes in renal function are associated with a substantial increase in mortality. [8] On the other hand, AKI from insults to the kidney from offending agents often leads to significant structural damage to the kidney and loss of kidney function. [9]

According to available literature, the incidence of AKI varies from 1% to 53%, depending on the definition used. The overall data from India is very low, and there are no systematic studies from the north western region. In this context, this study was carried out in a tertiary care hospital to study the aetiology, clinical profile, complications, short-term prognosis, and progress of kidney diseases.

AKI is a critical concern in healthcare, with diverse outcomes ranging from recovery to chronic kidney disease (CKD) or death. The study presented here investigates the association between sociodemographic factors, clinical characteristics, and the three outcomes of AKI. By categorizing patients based on their recovery status, we aim to identify patterns and prognostic indicators that could inform treatment approaches and improve patient outcomes.

MATERIAL & METHODS:

After getting approval from **institutional ethics committee** and **a written informed consent**, a cross-sectional observational study was conducted at Nephrology department of a tertiary care hospital, on 150 patients belonging to age group of above 18 years, having uremic symptoms or oliguria or anuria of recent onset and having AKI stage-1, 2 & 3 according to KDIGO criteria.

Patients below the age of 18 years, not giving consent, having all chronic kidney disease and suffering from AKI on CKD were excluded from the study. CKD was excluded from the study based on KDIGO criteria for CKD which includes GFR, albuminuria, structural abnormality in imaging, urinary sediments, etc., retrieved from previous records of patients.

Sample size calculation was done using $N = (Z\alpha/2)\ 2 * (PQ) / d2\ Z\alpha/2 = 1.96$ formula at 5% level of significance, where p = prevalence of sepsis causing AKI- 38.6% (Based on Eswarappa et al [133] on spectrum of AKI in critically-ill patients q = 100 – p, d = absolute precision taken. 8 (4x38.6x61.4)/8x8=148. Minimum required sample size was 150.

All patients presenting at OPD, admitted in ward and ICU, fulfilling inclusion criteria have been included in the study. All patients have been subjected to a detailed history, clinical examination with complete general and systemic examination with special reference to AKI with laboratory investigations and radiological imaging of the kidneys. Patients who have AKI on admission according to KDIGO have been considered in this study. Patients have been provided supportive care and given dialysis as per standard hospital protocol. Daily follow-up was done until discharge or death and until 3 months post-discharge.

Patients remaining oligo-anuric or whose serum creatinine did not

decrease satisfactorily to baseline at the end of four weeks of treatment or unexplained AKI was classified as partial recovery, and those with features suggestive of systemic and glomerular disease, were subjected to kidney biopsy which was examined with light and immunofluorescence-microscopy. Outcomes of requirement of vasopressor drugs and ICU support, treatment with dialysis, survival at-discharge, and in-hospital mortality have been studied. The survival and non-survival were compared to see difference in clinical characteristics and laboratory features between two groups.

Statical Analysis:
Qualitative Data have been presented using frequency, percentage and Quantitative Data have been presented using descriptive statistics such as Mean, SD, and SEM for proportion and chi-square test for association. Level of significance will be set at 5%. All p- values <0.05 will be treated as significant.

RESULTS:
Acute kidney injury (AKI) is a critical concern in healthcare, with diverse outcomes ranging from recovery to chronic kidney disease (CKD) or death. The study presented here investigates association between sociodemographic factors, clinical characteristics, and three outcomes of AKI. By categorizing patients based on their recovery status, we aim to identify patterns and prognostic indicators that could inform treatment approaches and improve patient outcomes.

Our analysis delves into the relationships between patient demographics, existing comorbidities, initial clinical presentations, detailed laboratory and imaging findings. This approach allows us to determine how these variables might influence the trajectory of AKI in patients. The ensuing data provides a clear depiction of the factors at play in AKI progression and recovery, offering valuable insights for clinical practice and future research.

In the present study, 54.95 % of the patients were males (n=100) and 45.05 % (n=82) were females with no significant difference in mortality between the two genders (p value = 0.588).

In the analysis of patient outcomes by age, 82 individuals (45.0%) aged <60 years were survived, whereas 19 individuals (10.4%) did not. In contrast, among patients aged >60 years, 54 (29.6%) survived and 27 (14.8%) died. A statistically significant difference in survival rates between the two age groups (P = 0.0258) was found indicating age may be an influential factor in the likelihood of survival. Mean age was 53.9 and 58 in survival v/s non survival group.

In our study, diabetes mellitus (DM) was present in 46 survivors (25.27%) and 25 non-survivors (14%), with the difference reaching statistical significance (P = 0.01). Patients without DM showed a survival count of 90 (49.4%) versus 21 (11.5%) who died. Hypertension (HTN) was documented in 50 survivors (27.4%) and 26 non-survivors (14.2%), with a significant P value of <0.05. In contrast, the presence of chronic liver disease (CLD), ischemic heart disease (IHD) and stroke did not significantly affect survival outcomes, with P values of 0.3, 0.9 and 0.08 respectively.

Table-1: Demographic Distribution Of Study Population

Patients	Total	Survived	Mortality	Chi-square (p value)
Male	100	73	27	0.5
Female	82	63	19	
Age <60	101	82	19	0.025
Age>60	81	54	27	
Diabetic	71	46	25	0.01
Non-diabetic	111	90	21	
Hypertensive	76	50	26	<0.05
Non-hypertensive	106	86	20	
CLD +	14	9	5	0.3
CLD -	168	127	41	
IHD	39	29	10	0.9
No h/o IHD	143	107	36	
H/o stroke +	29	18	11	0.08
H/o stroke -	153	118	35	

The most frequently reported symptom among the patients was breathlessness, occurring in 62 cases, which constitutes 34.1% of the reported symptoms. Oliguria was most common, presenting in 71 patients (39.0%). Fever was noted in 33 patients (18.1%). Pedal edema was observed in 17 patients (9.3%), and diarrhea was reported by 16 patients (8.8%). Notably, chest pain was experienced by 27 patients (14.8%), indicating a revision from the previously stated number. Similarly, vomiting was noted in 15 patients (8.2%). Blurring of vision, hematuria, weakness, and right groin pain each were reported in 5 patients (2.7%). Symptoms reported less frequently included altered mental status, cough, anasarca, and weight loss, each in 4 patients (2.2%). Other complaints like bleeding gums, facial puffiness with abdominal fullness, flank pain, oral ulcers, and oliguria/anuria affected 3 patients each (1.6%). The list continues with several symptoms such as constipation, fatigue, left flank pain, peripheral edema, burning micturition, fever with chills, and pain abdomen occurring 77 in 2 patients (1.1%).

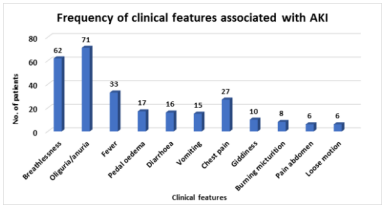

Figure-1: Frequency of clinical features associated with AKI

The most common etiology among patients was Sepsis, occurring in 43 cases (23.62%). Acute gastroenteritis was also common, presenting in 21 patients (11.53%). Cardio renal was noted in 27 patients, representing 14.83% of cases. Less commoner aetiologies are hepato-renal, contrast, obstructive uropathy, post-partum AKI, poisoning, etc.

Highest mortality was seen in Sepsis related AKI patients with total of 22 patients were expired out of 43 cases. Cardio-renal causes were secondary to sepsis in terms to AKI related mortality. No mortality was seen in acute gastro-enteritis, post-partum, drug and contrast induced AKI patients, making them higher survival groups.

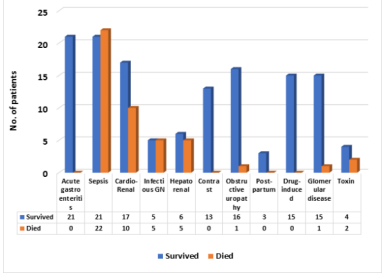

Figure 2: Etiology associated with AKI and mortality

Table 2: - Association of mortality with treatment of the patients HD

	Survived	Died	Total	p-value (chi-square test)
On dialysis	24	22	46	P<0.001
On conservative treatment (No dialysis)	112	24	136	
Total	136	46	182	

In the conservative treatment group, 112 patients survived, while 24 patients succumbed to the condition. The observed difference in survival rates reached statistical significance when compared to the control or alternative treatment group (p<0.001). Total 46 patients require dialysis, out of which 22 died. Patient who did not underwent dialysis and died were 24 out of 112.

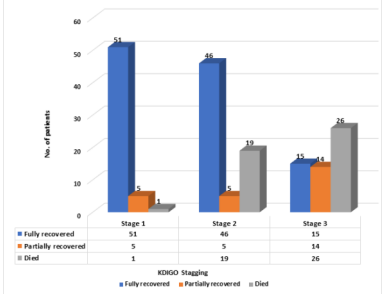

Figure 3: Association of KDIGO Staging with mortality and recovery of patients.

Compared to all-stages, KDIGO stage-3 had highest mortality of 26 patients with statically significant value P<0.001. They are highest risk for mortality. Stage-2 had slightly better outcome and stage-1 has good prognosis. On contrary, KDIGO stage-1 had highest recovery followed by stage-2. Only 15 patients (8.2%) were fully recovered in KDIGO stage-3 group with having least survival of all 3 groups.

DISCUSSION:

In the analysis of patient outcomes by age, it was found that of those aged less than 60, 82 individuals (45%) survived, whereas 19 individuals (10.4%) did not. In contrast, among patients aged more than 60, 54 (29.6%) survived and 27 (14.8%) died. A statistically significant difference in survival rates between two age groups was observed (P = 0.0258). Although incidence of AKI was higher in younger groups, mortality was higher in elderly population. Similar results were observed by M. Ram Prabakar et al. [14] and Prakash et al. [15]

We observed that the mean age of the patients was 56 years. Liano F et al. [13] mean age was 63.5, and in our study, it was 56. Also, in M. Ram Prabakar et al. [14], the mean age group was 33, with higher mortality in the older age group. Also, in Prakash et al. [15], older age was a risk factor for developing AKI. This has been corroborated with other studies in both Indian and Western cohorts [16][17].

The reason age is linked to AKI could be due to reduced physiological reserve or increasing co-morbidities with increasing age. [16]

In the present study, the study population included a majority of male patients (54.94%, n = 100) and the rest were females (45.05%, n = 82). The mortality of the patients was not significantly different between the two genders (p value = 0.588). However, males had a higher incidence of AKI as compared to females. This is similar to Ram Prabakar et al.'s [14], where there are 60.8% males. In Singh et al.'s [11] research, over two-thirds of the 120 patients (67.5%) were male. In Ranganatha et al. [18], 65% were male and 35% were female, with a male-to-female ratio of 1.29:1. All these studies have concordance with our study of males with a higher number of AKI.

In our study, diabetes mellitus (DM) was present in 46 survivors (25.27%) and 25 nonsurvivors (14%), with the difference reaching statistical significance (P = 0.01). Similarly, hypertension (HTN) was documented in 50 survivors (27.4%) and 26 nonsurvivors (14.2%), with a significant P value of <0.05. In contrast, presence of chronic liver disease (CLD) and ischemic heart disease (IHD) did not significantly affect survival outcomes, with P values of 0.3 and 0.9, respectively.

Indian and Western centres have found diabetes to be a significant factor commonly seen in association with AKI. [19][20] In the research by Satri et al., [12] 65 (33.7%) of 193 patients were diabetic, and 80 (41.5%) were hypertensive. According to Ranganatha et al. [18], 33% of AKI patients had diabetes, which was the most common co-morbid condition, followed by HTN (28%), CAD (8%), and COPD (5%). According to Bhattacharjee et al. [10], type 2 diabetes was the most frequent comorbidity, followed by hypertension and coronary artery disease.

In our study, oliguria and anuria were statistically significant for mortality. Singh et al. (140) discovered that the most prevalent presentation was feverish illness (n = 61), followed by dehydration (n = 33) and dyspnoea (n = 17). Other less frequent manifestations were urinary retention (n = 9) and abdominal discomfort (n = 7), with only three participants presenting with multiple injuries. Singh et al. [11] discovered that the most prevalent presentation was feverish illness (n = 61), followed by dehydration (n = 33) and dyspnoea (n = 17). Other less frequent manifestations were urinary retention (n = 9) and abdominal discomfort (n = 7), with only three participants presenting with multiple injuries. According to Yousuf et al., [17] vomiting (92%) was the most common cause, followed by oliguria (40%), fatigue (72%), fever (70%), and loose stools (32%). According to Ranganatha et al., [18] oliguria was noted in 64%, vomiting in 66%, and breathlessness in 10%, followed by loose motion, burning maturation, and 103 edema.

The most common aetiology among the patients was sepsis, occurring in 43 cases, which constitutes 23.62% of all etiologies. Cardio-renal disease and acute gastroenteritis was also common, presenting in 27 patients (14.43%) and 21 patients (11.53%), respectively. Less common aetiologies are hepato-renal, contrast, obstructive uropathy, post-partum AKI, poisoning, etc. Chugh et al. [20] ranked RPGN (rapidly progressive glomerulonephritis) at 11%, Sepsis at 10%, post-diarrhoea at 5%, followed by other illnesses. According to Zabiuddin [21] et al., sepsis was the major cause of AKI (49%), followed by UTI, gastroenteritis, and glomerulonephritis. According to Ranganatha [18] et al., Sepsis is the most common cause of AKI, followed by gastroenteritis (16%), cardiorenal (10%), chronic liver disease (8%), nephrotoxic medication (9%), poisoning (8%), snake bite (8%), post-surgery AKI (6%), obstructive uropathy (6%), malaria (2.6%).

In our study, 112 patients belonging to the conservative treatment group were survived, while 24 patients succumbed to the condition. Total 46 patients require dialysis, out of which 22 died. Patient who did not underwent dialysis and died were 24 out of 112. The observed difference was statistically significant (p= 0.001). Only 25 % of our patients required haemodialysis for recovery. Remaining was treated with non-dialysis. Mortality was around 25% mainly due to co morbid conditions sepsis, cardiac, liver and CNS disorder rather than due to renal failure itself.

In Ranganatha [18] et al. 20 % required haemodialysis and mortality was 25%. Also, in Saxena et al there was 28 % mortality with AKI and same with Liano et al. [13] In a study by Mathew et al [22] ICU mortality with AKI was 41% and 45% had undergone dialysis.

In study by Mathew et al [22] 45% of the patients in the study group required dialysis, among which 24% underwent CRRT and the 76% underwent haemodialysis. In a study conducted by Bernieh b et al. [23] 58% of patients were managed conservatively and 42% patient were managed with dialysis.

A total of 46 patient died and from survival 24 patient partially recovered and 112 fully recovered. Most patient who died were of KDIGO stage 3 and requiring dialysis. Significant association was found between the staging by KDIGO and the mortality of the AKI patients in our study. A total of 46 patient died and from survival group, 24 patients partially recovered and 112 fully recovered. Most common cause of partial recovery was Glomerulonephritis in our study. Most patient who died were of KDIGO stage 3 and requiring dialysis. In Lopez et al [24] which classified AKI according to AKIN criteria, AKI occurred in 50.4% of patients – 21.1% with Stage 1, 10.1% with Stage 2 and 19.2% with Stage 3. Most mortality was associated with stage 3 AKI as also seen in our study which reached statically significance. Hence, AKI stages based on serum creatinine criteria predicted mortality as in a study by Lopez et al. [24] which can also be seen in our study with KDIGO classification.

There are some limitations to our study that the findings may not be generalizable to other geographic locations because this was single-centre research with a relatively small sample size. Secondly, biomarkers were not used to make an early diagnosis of acute kidney injury due to financial constraints of the patients admitted at the tertiary health care centre. We have not compared general examination findings and laboratory investigations. CRRT and Peritoneal dialysis was not done in this study due to financial constraint.

CONCLUSION:

In our study, we observed that most common cause for AKI was sepsis followed by cardiorenal and acute gastroenteritis. Old age, male gender and co-morbid conditions like diabetes & hypertension were associated with higher incidence of mortality. Higher the KDIGO stage higher was the mortality. AKI due to glomerulopathies was most commonly associated with Partial recovery and dialysis dependency at the end of 3 months.

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