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# Clinical profile and determinants of short-term outcome of acute kidney injury: A hospital-based prospective study from Northeastern India

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## Abstract:

**CONTEXT:** Acute kidney injury (AKI) is an outcome of multiple etiologies and is mostly reversible. Data on its incidence and outcome, particularly from India, are limited.

**AIMS:** To study the etiology, clinical profile, and short-term prognosis in AKI.

**SETTINGS AND DESIGN:** A hospital-based prospective observational study on AKI.

**SUBJECTS AND METHODS:** Seventy-five AKI patients diagnosed by Acute Kidney Injury network criteria were selected. Patients with preexisting chronic kidney disease were excluded.

**STATISTICAL ANALYSIS USED:** Data were compiled using the Statistical Package for the Social Sciences version 17. Regression analysis was done for determining the association of various variables for mortality.  $P < 0.05$  was considered statistically significant.

**RESULTS:** The mean age of patients was  $41.09 \pm 16.17$  years with a male:female ratio of 1.42:1. Comorbidities were present in 37.3%, with diabetes mellitus (10.6%) and chronic liver disease (10.6%) being the most common. Fever was the most common (40%) presenting symptom, followed by oliguria (25.8%). Infection was the most common cause of AKI (56%), with sepsis in 26.7% followed by acute gastroenteritis in 17.3%. Pneumonia was the primary focus in 50% of cases with sepsis. Mean serum creatinine and urea at admission were  $2.37 \pm 0.90$  and  $92.44 \pm 39.67$  mg/dl, respectively. Serum creatinine rose progressively to  $2.96 \pm 1.18$  and  $3.26 \pm 1.56$  mg/dl at 24 and 48 h, respectively, since hospitalization. Majority of the cases (73.3%) were nonoliguric. Hemodialysis was necessary in 24% of cases. Mean hospital stay was 8.16 days. In-hospital mortality was 24%. Among survivors, 92.9% had complete renal recovery on discharge. Sepsis, need for hemodialysis, urea  $>100$  mg/dl, and peak serum creatinine  $>3$  mg/dl were contributors to mortality ( $P < 0.01$ ).

**CONCLUSIONS:** Infections, especially sepsis, were the most common cause of AKI. Hemodialysis was required in one-quarter of the patients. Sepsis, need for hemodialysis, and high creatinine were associated with a significantly higher mortality.

## Key words:

Acute kidney injury, hemodialysis, mortality, sepsis, short-term outcome

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## Introduction

Acute kidney injury (AKI) is caused by multiple etiologies, is basically preventable to a large extent, and is

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potentially reversible if diagnosed and treated early. Failure to detect and treat timely and/or adequately usually leads to significant untoward consequences. It is associated with a high morbidity and permanent loss of kidney function.<sup>[1]</sup> All stages of AKI are associated with significantly

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high short- and long-term mortality.<sup>[2]</sup> However, early detection and treatment leads to partial or total reversal of renal damages caused by AKI.

The exact incidence of AKI has been a subject of significant debate because of the rapid change in criteria for the definition of AKI. According to available literature, the incidence varies from 1% to 31%, depending on the definition used.<sup>[3]</sup> The overall data from India are sparse, and there are no systematic studies from the northeastern region of the country. In this background, this study was carried out in a tertiary care hospital to study the etiology, clinical profile, and short-term prognosis of patients with AKI.

## Subjects and Methods

A prospective, hospital-based, observational study was conducted on all cases of AKI admitted to the department of general medicine in a tertiary care hospital, from January to December 2015. Cases were selected by consecutive sampling after due ethical clearance and informed consent.

### Inclusion criteria

All patients, aged above 18 years, with the diagnosis of AKI as per the AKIN criteria<sup>[4]</sup> suggested by Kidney Disease Improving Global Outcomes Clinical Practice Guideline for AKI were selected as follows:

1. Patients with increase in serum creatinine by  $\geq 0.3$  mg/dl within 48 h; or
2. Increase in serum creatinine to  $\geq 1.5$  times baseline, which is known or presumed to have occurred within the prior 7 days; or
3. Urine volume  $\leq 0.5$  ml/kg/h for 6 h.

### Exclusion criteria

Patients with preexisting chronic kidney disease.

Further staging of AKI into Stages 1, 2, and 3 was done as per the AKIN criteria as follows:

- Stage 1: An abrupt (within 48 h) reduction in kidney function defined as an absolute increase in serum creatinine of more than or equal to 0.3 mg/dl ( $\geq 26.4$   $\mu\text{mol/L}$ ), a percentage increase in serum creatinine of more than or equal to 50% (1.5-fold from baseline), or a reduction in urine output (documented oliguria of  $<0.5$  ml/kg/h for more than 6 h)
- Stage 2: Increase in serum creatinine (2–3 times from baseline) or a urinary output lower than 0.5 ml/kg/h for 12 h
- Stage 3: Increase in serum creatinine (three times or more from baseline) or a serum creatinine higher than 4 mg/dl if there is an acute rise in serum creatinine of at least 0.5 mg/dl, or a urinary output lower than 0.3 ml/kg/h for 24 h, or anuria for 12 h. Stage 3

also includes patients who need renal replacement therapy, irrespective of the stage they are in, at the time of renal replacement therapy.

In all selected patients, a thorough history was taken followed by clinical examination. Laboratory investigations including complete blood counts, urine analysis, blood urea, serum creatinine, blood glucose, liver function tests, chest X-ray, and ultrasonography of abdomen were done. Additional investigations were done as and when required. All the results of each patient were recorded in a structured pro forma. For serum urea and creatinine, samples were taken at admission, at 24 and 48 h and repeated daily until death or discharge. All patients were put on an indwelling Foley's catheter, and urine output was measured through the same. Sepsis was diagnosed using the International Sepsis Definitions Conference criteria 2003,<sup>[5]</sup> and cases of sepsis were further subdivided into sepsis, severe sepsis, and septic shock. Patients requiring renal replacement therapy were put on intermittent hemodialysis either in the dialysis unit or in the intensive care unit (ICU). Ethical clearance was taken from the Institutional Ethical Committee, and written informed consent was taken from all the patients included in the study. Statistical analyses were done using the IBM SPSS (Statistical Package for the Social Sciences software) Statistics for Windows, version 17.0, (IBM corporation, New York, United states of America). The results were tabulated and graphically represented using Microsoft Office for Windows 2010. Multivariate regression analysis was done for determining the association of various variables for mortality.  $P < 0.05$  was considered statistically significant.

## Results

Of the 75 patients with AKI in the present study, 44 (58.67%) were male and 31 (41.33%) were female, with a male-to-female ratio of 1.42:1. The age of the patients ranged from 18 to 75 years, with a mean age of  $41.09 \pm 16.17$  years and a median age of 37 years, with a majority of the patients (58.6%) in the age group between 18 and 40 years [Table 1]. Medical comorbidities were present in 28 (37.33%) patients of which diabetes mellitus and chronic liver disease were the most common [Table 2]. Fever (40%) was the most common

**Table 1: Age and sex distributions of patients with acute kidney injury**

Age group	Male	Female	Total (%)
18-30	18	7	25 (33.33)
31-40	8	11	19 (25.33)
41-50	4	8	12 (16)
51-60	4	2	6 (8)
61-70	8	3	11 (14.67)
71-80	2	0	2 (2.67)

presenting symptom followed by oliguria (25.83%), diarrhea (17.33%), and anasarca (10.67%). The other presenting symptoms were leg swelling, altered sensorium, gastrointestinal bleeding, jaundice, dyspnea, abdominal pain, and cellulitis [Table 3].

Among the acute clinical conditions leading to AKI, sepsis was the most common, found in 26.67% of patients, followed by acute gastro-enteritis (17.33%), cardio-renal syndrome (10.67%), hepatorenal syndrome (10.67%), and scrub typhus (8%). The other conditions associated with AKI were lupus nephritis, acute glomerulonephritis, severe malaria, mushroom poisoning, gastrointestinal bleeding, acute pancreatitis, snake bite, and contrast-induced nephropathy [Table 4]. Of the 20 AKI patients due to sepsis, pneumonia was the primary focus of sepsis in 10 (50%), genito-urinary tract infection in 8 (40%), while no localization of sepsis was found in the remaining 2 (10%) cases. Overall, 56% of the AKI patients had an infective etiology. Hypotension (38.67%) was the most common physical finding in AKI, followed by tachycardia (28%), tachypnea (22.67%), edema (14.67%), and ascites (10.67%) [Table 5]. Urine analysis showed pyuria in 14.67% of patients, while hematuria, tubular epithelial cells, and renal casts were present in 9.33%, 12%, and 5.33% of cases, respectively. No urinary abnormalities were seen in 66.67% of patients.

At admission, serum creatinine of the patients ranged from 1 to 7.8 mg/dl, with a mean of  $2.37 \pm 0.90$  mg/dl. Serum urea ranged from 49 to 202 mg/dl, with a mean of  $92.44 \pm 39.67$  mg/dl. Mean serum creatinine rose to  $2.96 \pm 1.18$  and  $3.26 \pm 1.56$  mg/dl at 24 h and at 48 h, respectively, since hospitalization. Further, 26.67% of the patients had an oliguric renal failure. Majority of the patients (54.67%) were in AKI Stage 1, with the remaining 16.0% and 29.33%, respectively, in AKI Stages 2 and 3. Eighteen (24%) patients required hemodialysis during the course of treatment.

Eighteen (24%) of the 75 patients expired during the course of hospital stay. Of the 57 survivors, 53 had complete renal recovery, while 4 had partial renal recovery at discharge. The average length of hospital stay was 8.16 days; however, the average length of hospital stay varied with the stage of AKI; patients in Stages 1, 2, and 3 AKI had an average length of hospital stay of 6.95 days, 9 days, and 10.04 days, respectively. Further, the average length of hospital stay was significantly longer in AKI Stages 2 and 3 compared to Stage 1 ( $P = 0.04$ ). On regression analysis to find the association of variables to mortality, presence of sepsis [Table 6], peak serum creatinine  $>3$  mg/dl, peak serum urea  $>100$  mg/dl, severe metabolic acidosis, hyperkalemia [Table 7], and need for renal replacement therapy [Table 8] were significantly associated with

mortality ( $P < 0.01$ ). However, age above 40 years, presence of comorbidities, and oliguria were higher in nonsurvivors, but the results were statistically not significant.

## Discussion

In the present study, the mean age of the patients with AKI was  $41.09 \pm 16.17$  years, and the median age was 37 years. Overall, the most common age group was

**Table 2: Existing medical comorbidities in patients with acute kidney injury**

Presence/absence of comorbidity	Number of patients (%)
Comorbidity	28 (37.34)
Chronic liver disease	8 (10.67)
Chronic obstructive pulmonary disease	4 (5.33)
Diabetes mellitus	8 (10.67)
Diabetes mellitus + hypertension	5 (6.67)
Heart failure	4 (5.33)
Hypertension	4 (5.33)
Hypothyroidism	1 (1.33)
No comorbidities	47 (62.66)

**Table 3: Presenting symptom of patients with acute kidney injury**

Presenting symptom	Number of patients (%)
Fever	30 (40.00)
Oliguria	19 (25.83)
Diarrhea	13 (17.33)
Anasarca	8 (10.67)
Leg swelling	4 (5.33)
Altered sensorium	4 (5.33)
Gastrointestinal bleed	3 (4.00)
Jaundice	3 (4.00)
Dyspnea	3 (4.00)
Abdominal pain	1 (4.00)
Cellulitis	1 (1.33)

**Table 4: Acute clinical conditions associated with acute kidney injury**

Acute clinical conditions associated with AKI	Number of patients (%)
Sepsis	20 (26.67)
Acute gastroenteritis	13 (17.33)
Cardiorenal syndrome	8 (10.67)
Hepatorenal syndrome	8 (10.67)
Scrub typhus	6 (8.00)
Acute glomerulonephritis	4 (5.33)
Lupus nephritis	4 (5.33)
Malaria	3 (4.00)
Mushroom poisoning	3 (4.00)
Upper gastrointestinal bleed	3 (4.00)
Acute pancreatitis	1 (1.33)
Snake bite	1 (1.33)
Contrast-induced nephropathy	1 (1.33)

AKI=Acute kidney injury

18–40 years. Other studies from India<sup>[6,7]</sup> found the respective age to be between 41 and 48 years. However, a review of large pooled data of AKI in the ICU setting from five American teaching universities (the PICARD group) in 618 patients found the mean age of patients to be higher at 59.5 years.<sup>[8]</sup> A possible reason for a comparatively younger age group being affected by AKI in the present study is the higher number of infection-related AKI observed in the study compared to the American data.

**Table 5: Physical findings in patients with acute kidney injury**

Physical finding	Number of patients (%)
Hypotension (SBP ≤90 mmHg/DBP ≤60 mmHg)	29 (38.67)
Tachycardia	21 (28.00)
Tachypnea	17 (22.67)
Edema	11 (14.67)
Ascitis	8 (10.67)
Encephalopathy	4 (5.33)
Jaundice	3 (4.00)
Pleural effusion	3 (4.00)
Pallor	2 (2.67)
Pericardial effusion	2 (2.67)
Pericardial rub	2 (2.67)
Raised jugular venous pressure	1 (1.33)

SBP=Systolic blood pressure, DBP=Diastolic blood pressure

In the present study, comorbidities were associated with higher in-hospital mortality although it was not statistically significant. Existing medical comorbidities have been shown to be associated with adverse renal outcomes, particularly in the elderly age group.<sup>[9]</sup> The PICARD group<sup>[8]</sup> reported extensive comorbidities in patients with AKI, with 37% having coronary artery disease, 29% having diabetes mellitus, and 21% having chronic liver disease. Our data did not reach statistical significance, probably due to smaller sample size.

In the present study, fever (40%) was the most common presenting symptom followed by oliguria (25.83%), diarrhea (17.33%), and anasarca (10.67%). A previous Indian study had shown similar results, with fever being the most common presenting symptom of AKI being present in 58% of the cases.<sup>[6]</sup> Oliguria has also been shown to be one of the common symptoms of AKI in a study from the North Indian state of Uttar Pradesh in 607 patients reporting oliguria in 85.2% of the cases with AKI.<sup>[10]</sup>

In the present study, sepsis was the most common acute clinical condition associated with AKI which was present in 26.67% of the patients. Sepsis remains one of the major contributors of AKI worldwide. In a population-based study with 1811 AKI patients, sepsis was the most

**Table 6: Sepsis as predictor of mortality in patients with acute kidney injury**

Sepsis	Survivors	Nonsurvivors	OR (95% CI)	Z statistic	P
Present	10	10	4.6250 (1.4457-14.7964)	2.581	0.01
Absent	37	8			

OR = Odds ratio, CI = Confidence interval

**Table 7: Metabolic parameters as predictors of mortality in acute kidney injury**

Parameters	Survivors	Nonsurvivors	OR (95% CI)	Z statistic	P
Peak serum creatinine (>3 mg/dl)					
Present	16	17	43.5625 (5.3455-355.0086)	3.526	<0.01
Absent	41	1			
Peak serum urea (100 mg/dl)					
>100	14	15	15.3571 (3.8692-60.9542)	3.884	<0.01
<100	43	3			
Hyperkalemia					
Present	4	10	16.5625 (4.1776-65.6637)	3.994	<0.01
Absent	53	8			
Metabolic acidosis					
Present	6	10	10.6250 (3.0230-37.3440)	3.685	<0.01
Absent	51	8			

OR = Odds ratio, CI = Confidence interval

**Table 8: Need for renal replacement therapy (hemodialysis) as predictor of mortality in patients with acute kidney injury**

Renal replacement therapy	Survivors	Nonsurvivors	OR (95% CI)	Z statistic	P
Required	7	11	11.2245 (3.2665-38.5697)	3.840	<0.01
Did not require	50	7			

OR = Odds ratio, CI = Confidence interval

frequent precipitating factor being present in 47% of the cases.<sup>[11]</sup> In a multicentric study conducted in 81 centers in Australia, sepsis and septic shock accounted for 45.0% of the cases of AKI.<sup>[12]</sup> Similarly, in another study from India, sepsis was reported to be the most common cause of AKI.<sup>[7]</sup> Acute gastro-enteritis has also been reported as a common cause of AKI. Cardiorenal syndrome and hepatorenal syndrome also contributed to AKI in a significant number of patients in the present study. These entities have also been documented to be the important causes of AKI, especially in critically ill patients in a study of 2017 patients from Korea.<sup>[13]</sup> Tropical infections including scrub typhus and malaria were also responsible for many AKI cases in the present study. In another Indian study from the southern state of Tamil Nadu, AKI was seen in 41.1% of patients with tropical acute febrile illness, with the most common causes being scrub typhus, malaria, salmonellosis, dengue, and leptospirosis.<sup>[14]</sup>

In the present study, the mean serum creatinine of patients with AKI was  $2.37 \pm 0.90$  mg/dl and the mean serum urea was  $92.44 \pm 39.67$  mg/dl. A previous study from Nepal showed higher admission values of serum creatinine in patients with AKI ( $4.35 \pm 2.72$  mg/dl), whereas serum urea levels were similar to those reported in the present study ( $101.78 \pm 57.56$  mg/dl).<sup>[15]</sup>

In the present study, around three-fourths of the patients (73.33%) had nonoliguric AKI, while the remaining 26.67% had an oliguric renal failure. On classification of AKI as per the AKIN criteria, more than half of the patients with AKI (54.67%) were in Stage 1, whereas 16% and 29.33% were in Stage 2 and Stage 3, respectively. These results are consistent with results from a large retrospective cohort study from seven American ICUs enrolling 14,524 patients with AKI which showed that AKI Stage 1 was the most frequent (38.5%) followed by AKI Stage 2 (14.1%) and AKI Stage 3 (4.3%).<sup>[16]</sup>

In the present study, 24% of the patients required hemodialysis. Other studies from India<sup>[6,17]</sup> showed requirement of hemodialysis in AKI to vary from 28% to 51.6%.

In the present study, the in-hospital mortality was 24%. A previous Indian study from the state of Uttar Pradesh has shown the overall in-hospital mortality in AKI as 26.2%.<sup>[18]</sup> The mortality in AKI reported from the PICARD group was 37%.<sup>[8]</sup> Pooled data from the Madrid Acute Renal Failure Study Group also stated that the overall mortality in patients with AKI remains high and has not materially improved. The rates of complications associated with AKI also show an upward trend.<sup>[19]</sup>

Overall, patients with AKI had an average length of hospital stay of 8.16 days. Patients in Stages 1, 2, and 3 AKI had an individual average length of stay of 6.95 days, 9 days, and 10.04 days, respectively. The Madrid Acute Renal Failure Study Group has shown a comparatively higher length of hospital stay of 25 days.<sup>[19]</sup> However, the study had a greater number of patients admitted in the intensive care setting. In the present study also, the duration of hospital stay was also significantly higher in patients in the higher AKIN stage.

Among the predictors of mortality, age above 40 years was found to be associated with an increased risk of mortality in patients with AKI; however, the result was not statistically significant. A previous Austrian study reported that older age is a risk factor for the occurrence of AKI, nonrecovery of renal function, and higher mortality rate in patients with AKI.<sup>[20]</sup> In a meta-analysis of studies of AKI in the elderly by Schmitt *et al.*, it was found that recovery from AKI was 28% lower in patients older than 65 years.<sup>[21]</sup>

Sepsis was found to be a predictor of mortality in patients with AKI, with a significant number of cases due to sepsis-related AKI having a fatal outcome (odds ratio = 4.6250,  $P = 0.01$ ). An Egyptian study of 532 patients found that sepsis is the most common cause of AKI and is a predictor of nonrecovery and increased mortality among those patients.<sup>[22]</sup> The multicentric European Sepsis Occurrence in Acutely Ill Patients study found that 51% of septic patients with Sequential Organ Failure Score above 2 developed AKI, and sepsis was an independent predictor of mortality.<sup>[23]</sup> Lastly, large retrospective data from the UPHS-AKI cohort of 6119 patients also found sepsis to be an independent predictor of mortality in AKI.<sup>[24]</sup>

Among metabolic parameters, peak serum creatinine and urea  $>3$  and  $>100$  mg/dl respectively, hyperkalemia ( $>5.5$  mEq/L), and severe metabolic acidosis ( $\text{pH} < 7.20$ ) were all significantly associated with increased mortality in patients with AKI in the present study. Serum creatinine  $>4$  mg/dL was found to be associated with an increased mortality by others.<sup>[18]</sup>

In the present study, need for hemodialysis was significantly associated with increased mortality. The results are similar to previous Indian works<sup>[7,18]</sup> which are in agreement with other large studies.<sup>[8,19,24]</sup>

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### Conflicts of interest

There are no conflicts of interest.

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