



## Factors Predicting Length of Hospital Stay in Acute Kidney Injury Patients Admitted in a Rural Tertiary Care Hospital

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### Abstract

**Background:** Acute kidney injury (AKI) is a major medical complication in the developing world, particularly in the setting of infectious diseases, diarrheal illnesses, venomous snake bites and natural disasters. AKI in ICU is associated with high mortality, longer hospital stays, increased health resource utilization and greater costs especially in patients requiring haemodialysis.

**Materials and Methods:** A hospital based prospective observational study was conducted in patients of AKI admitted in ICU of department of Medicine of a rural tertiary care hospital located in a town in central India. Data of all consecutive AKI inpatients related to demographic variables (age, gender), clinical profile, clinical diagnosis on admission, comorbidities, presence of hypotension, use of mechanical ventilator, presence of sepsis, need for haemodialysis during hospitalisation, urine output (oliguria or normal), staging of AKI, length of stay (LOS) in hospital, APACHE 2, GCS scores and laboratory investigations were collected from patients' medical records.

**Results:** Of the total 188 AKI patients enrolled, 95 (50.5%) patients had LOS in hospital > 7 days. Presence of hypotension, GCS and APACHE 2 score, staging of AKI, peak rise in serum creatinine and blood urea levels within 48 hours of diagnosis of AKI, leucocytosis, use of invasive mechanical ventilator and haemodialysis in AKI patients were found to be significantly associated with hospital LOS ( $P < 0.05$ ).

**Conclusion:** Sepsis was the commonest cause of AKI (19.1%) in this study. Presence of hypotension, GCS and APACHE 2 score, advanced AKI stage, peak rise in serum creatinine and blood urea levels within 48 hours of diagnosis of AKI, leucocytosis, use of mechanical ventilator and haemodialysis were associated with prolonged hospital LOS in AKI patients.

**Keywords:** Acute Kidney Injury; Incidence; Predictors; Length of Stay; Etiology

### Introduction

Acute kidney injury (AKI) is characterized by abrupt decline in kidney function over a period of hours to days irrespective of the underlying etiology [1]. AKI is a challenging problem in low resource settings because of high burden of infectious diseases such as malaria and leptospirosis, diarrhoeal illnesses, the over the counter availability of potentially nephrotoxic drugs and medicinal herbs, snake bites, late presentation of patients to healthcare services.

AKI complicates 5 - 7 % of acute care hospital admissions and 25% to 30 % of admissions to intensive care unit (ICU), with 5% to 6% of the ICU population requiring renal replacement therapy after developing AKI [2-4]. AKI in ICU is associated with high mortality, longer hospital stays, increased health resource utilization and greater costs especially in patients requiring haemodialysis [5,6]. In addition, AKI increases the risk of incident and progressive CKD and is associated with reduced long-term survival [7,8]. Small fluctuations in serum creatinine have been included in the spectrum of AKI as they have an adverse effect on the overall outcome of the

patient [5]. Prolonged hospital stay adds to the financial burden of healthcare and poses a great challenge to the already under-resourced countries of the world [9].

The identification of factors associated with hospital length of stay (LOS) among patients hospitalized for AKI could help in establishing interventions or preventive measures that could reduce hospital LOS in AKI patients. In view of the limited data on hospitalized AKI patients from India and its likely importance, there is a need to understand the clinical profile and factors affecting the hospital LOS in AKI patients in our setting i.e. a rural tertiary care hospital.

**Materials and Methods**

A prospective observational study was conducted in patients of AKI admitted in ICU of department of Medicine of a rural tertiary care hospital located in a town in central India over a period of sixteen months from 1<sup>st</sup> December 2014 to 31<sup>st</sup> March 2016.

**Inclusion Criteria:** All consecutive patients of AKI 18 years of age or older admitted with AKI or developed AKI after hospitalization and fulfil the Kidney Disease Improving Global Outcomes (KDIGO) definition and admitted in Medicine ICU [10]. For the purpose of this study AKI is defined as an acute increase in serum creatinine by  $\geq 0.3$  mg/dl within 48 hours or an increase of 1.5-fold or more in baseline serum creatinine level within the prior 7 days or reduction in urine output  $< 0.5$  ml/kg/hour for at least 6 hours.

**Exclusion Criteria:** Patients with CKD or ESRD, patients with age  $< 18$  years, withdrawal of therapy during ICU stay, AKI patients with incomplete data, AKI patients who died during hospital stay and who did not wish to participate were not included in this study.

Data related to demographic variables (age, gender), clinical profile, reason for hospitalization in the ICU based on the clinical diagnosis on admission, comorbidities [hypertension(HTN), diabetes mellitus(DM), ischemic heart disease(IHD)], alcohol intake, smoking history, presence of hypotension, use of mechanical ventilator, presence of sepsis, need for haemodialysis during hospitalisation, urine output (oliguria or normal), LOS in hospital and laboratory investigations - serum creatinine at the time of diagnosis of AKI (Cr1), blood urea at the time of diagnosis of AKI (Urea1), difference between peak rise in serum creatinine (within 48 hours of diagnosis of AKI) and serum creatinine at diagnosis of AKI [Diff. Cr], difference between peak rise in blood urea (within 48 hours of diagnosis of AKI) and blood urea at diagnosis of AKI [Diff. Urea], sodium, po-

tassium, haemoglobin, total leukocyte count (TLC) and presence of metabolic acidosis were collected from medical records of the patients. Oliguria was considered to be present when the urinary volume was less than 400 ml/day. LOS was measured in days and calculated from the date of admission until the date of discharge. ICU scores - Acute Physiologic Assessment and Chronic Health Evaluation (APACHE 2) score and Glasgow Coma Scale (GCS) scores of the AKI patients were also recorded.

AKI was further classified into 3 stages according to severity of kidney injury.

- AKI stage 1-increase in serum creatinine by  $\geq 0.3$  mg/dl or 1.5 - 1.9 times baseline
- AKI stage 2- increase in serum creatinine by 2.0 - 2.9 times baseline
- AKI stage 3-increase in serum creatinine of  $\geq 3.0$  times baseline or increase in serum creatinine to  $\geq 4$ mg/dl or initiation of renal replacement therapy.

The AKI patients were prospectively monitored up to hospital discharge on a regular basis.

**Statistical Analysis**

Statistical analysis was done by using descriptive and inferential statistics. Variables (demographic, clinical and biochemical variables) were compared using bivariate analysis. Continuous variables were presented as mean  $\pm$  standard deviation (SD) and compared using students t-test. Categorical variables were presented as proportions and compared using chi-square test. Data was analysed using SPSS 17.0 version. P value  $< 0.05$  is regarded as being statistically significant.

**Results**

We enrolled a total of 188 patients of AKI over a 16 months period. The mean age was  $50.5 \pm 17.2$  years ranging from 18 to 92 years. There were 29(15.4%) AKI patients below the age of 30 years, 96 (51.1%) AKI patients were between 30 and 60 years and 63 (33.5%) AKI patients were above the age of 60 years (Table 1). Of the total 188 patients of AKI, 55 (29%) were males and 133 (71%) were females. Ninety three (49.5%) of 188 AKI patients had LOS in hospital  $\leq 7$  days and 95 (50.5%) patients had LOS in hospital  $> 7$  days (Table 1).

| Demographic variables |               | LOS $\leq 7$ days (n = 93) | LOS $> 7$ days (n = 95) | Total (n = 188) | P value |
|-----------------------|---------------|----------------------------|-------------------------|-----------------|---------|
| Age-groups (years)    | < 30 years    | 13 (44.8%)                 | 16 (55.2%)              | 29 (15.4%)      | 0.65    |
|                       | 30 - 60 years | 46 (47.9%)                 | 50 (52.1%)              | 96 (51.1%)      |         |
|                       | > 60 years    | 34 (54%)                   | 29 (46%)                | 63 (33.5%)      |         |
| Gender                | Male          | 23 (41.8%)                 | 32 (58.2%)              | 55 (29.3%)      | 0.25    |
|                       | Female        | 70 (52.7%)                 | 63 (47.3%)              | 133 (70.7%)     |         |

**Table 1:** Distribution of Demographic Variables among AKI Patients with LOS in Hospital.

Figures in Parenthesis in Column 3 and 4 Represent the Row Percentage. Figures in Parenthesis in Column 5 Represent the Column Percentage.

The association of age of the patient ( $< 30$  years, 30 - 60 years, and  $> 60$  years) and gender of the patient with the LOS in hospital was not statistically significant ( $P > 0.05$ ) (Table 1).

Of the 188 AKI patients, 75 (40%) had HTN, 54 (29%) had DM and 39 (21 %) had IHD (Table 2). The association of co-morbidities (HTN, DM and IHD) with hospital LOS was not statistically significant. There were 27 (14%) current smokers and 36 (19%) alcohol drinkers of the total 188 AKI patients (Table 2).

| Co-morbidities/ habitual history |         | LOS ≤ 7 days<br>(n = 93) (%) | LOS > 7days<br>(n = 95) (%) | Total<br>(n = 188) (%) | P value |
|----------------------------------|---------|------------------------------|-----------------------------|------------------------|---------|
| HTN                              | Present | 33(55.9%)                    | 26(44.1%)                   | 59(31.4%)              | 0.272   |
|                                  | Absent  | 60 (46.5%)                   | 69(53.5%)                   | 129(68.6%)             |         |
| DM                               | Present | 21(55.3%)                    | 17(44.7%)                   | 38(20.2%)              | 0.47    |
|                                  | Absent  | 72(48%)                      | 78(52%)                     | 150(79.8%)             |         |
| IHD                              | Present | 18(62.1%)                    | 11(37.9%)                   | 29(15.4%)              | 0.16    |
|                                  | Absent  | 75(47.2%)                    | 84(52.8%)                   | 159(84.6%)             |         |
| Alcohol intake                   | Present | 20(55.6%)                    | 16(44.4%)                   | 36(19.1%)              | 0.462   |
|                                  | Absent  | 73(78.5%)                    | 79(83.2%)                   | 152(80.9%)             |         |
| Current Smokers                  | Present | 13(48.1%)                    | 14(51.9%)                   | 27(14.4%)              | 1.000   |
|                                  | Absent  | 80(49.7%)                    | 81(50.3%)                   | 161(85.6%)             |         |

**Table 2:** Distribution of Co-Morbidities/ Habitual History among AKI Patients with LOS in Hospital.

Figures in Parenthesis in Column 2 and 3 Represent the Row Percentage. Figures in Parenthesis in Column 4 Represent the Column Percentage.

The association of hospital LOS with either current smoking or alcohol drinking was not statistically significant.

Of the 188 AKI patients, 72 (38%) had stage 1 AKI, 67 (36%) had stage 2 AKI and 49 (26%) had stage 3 AKI (Table 3). The association of staging of AKI patients (severity) with the hospital LOS was found to be statistically significant (P < 0.05).

| Stages of AKI | LOS ≤ 7 days (n = 93) (%) | LOS > 7days (n = 95) (%) | Total(n = 188) (%) | (P value)             |
|---------------|---------------------------|--------------------------|--------------------|-----------------------|
| Stage 1       | 45(62.5%)                 | 27(37.5%)                | 72(38.3%)          | 11.862<br>(P = 0.003) |
| Stage 2       | 33(49.3%)                 | 34(50.7%)                | 67(35.6%)          |                       |
| Stage 3       | 15(30.6%)                 | 34(69.4%)                | 49(26.1%)          |                       |

**Table 3:** Distribution of Staging of AKI (Severity) among AKI Patients with LOS in Hospital.

Figures in Parenthesis in Column 2 and 3 Represent the Row Percentage. Figures in Parenthesis in Column 4 Represent the Column Percentage.

Ninety-one (48 %) of 188 patients had oliguria, Hypotension was present in 61(32%) AKI patients. One hundred forty-two (75 %) had metabolic acidosis. Invasive mechanical ventilator was used in

40 (31%) AKI patients. Haemodialysis was done in 61 (32%) AKI patients (Table 4).

| Clinical variables/ interventions used |           | LOS ≤ 7 days(n = 93) (%) | LOS > 7days(n = 95) (%) | Total (n = 188) (%) | P value |
|--|-----------|--------------------------|-------------------------|---------------------|---------|
| Urine output (UO)                      | Oliguria  | 40(44%)                  | 51 (56%)                | 91 (48.4%)          | 0.265   |
|  | Normal UO | 53 (54.6%)               | 44 (45.4%)              | 97 (51.6%)          |         |
| Hypotension                            | Present   | 19 (31.1%)               | 42(68.9%)               | 61(32.45%)          | 0.00001 |
|  | Absent    | 74(58.3%)                | 53(61%)                 | 127(67.6%)          |         |
| Metabolic acidosis                     | Present   | 65(45.8%)                | 77(54.2%)               | 142(75.5%)          | 0.090   |
|  | Absent    | 28(60.9%)                | 18(39.1%)               | 46(24.5%)           |         |
| Invasive mechanical ventilator         | Used      | 5(12.5%)                 | 35(87.5%)               | 40(31.3%)           | 0.0001  |
|  | Not used  | 88(59.5%)                | 60(40.5%)               | 148(78.7%)          |         |
| Haemodialysis                          | Used      | 17(27.9%)                | 44(72.1%)               | 61(32.4%)           | 0.0001  |
|  | Not used  | 76(59.8%)                | 51(40.2%)               | 127(67.6%)          |         |

**Table 4:** Distribution of Clinical Variables/ Interventions used among AKI Patients with LOS in Hospital.

Figures in Parenthesis in Column 2 and 3 Represent the Row Percentage. Figures in Parenthesis in Column 4 Represent the Column Percentage.

The association of urine output and presence of metabolic acidosis in AKI patients with hospital LOS was not statistically significant (P > 0.05) (Table 4). Presence of hypotension, use of invasive mechanical ventilator and use of haemodialysis in AKI patients were found to be significantly associated with hospital LOS (P < 0.05) (Table 4). Thirty-six (19 %) of the 188 AKI patients had GCS < 10 and 152 (81 %) had GCS >10 (Table 5). Forty-three patients (23%) had APACHE 2 score ≤ 15, 110 patients (58%) had APACHE 2 score between 16 and 30 and 35 patients (19%) had APACHE 2 score ≥ 31. Both GCS and APACHE 2 score were found to be significantly associated with hospital LOS (P < 0.05) (Table 5).

The mean serum creatinine value was 3.69 ± 1.53 mg/dl and 3.83 ± 2.13 among AKI patients with LOS ≤ 7days and LOS > 7days, respectively. The mean blood urea was 113.6 ± 66.2 mg/dl and 124.9 ± 71.8 mg/dl among AKI patients with LOS ≤ 7days and LOS > 7days respectively (Table 6). The mean haemoglobin was 10.7 ± 3.07 gm% and 11.26 ± 3.41 gm% among AKI patients with LOS ≤ 7days and LOS > 7days, respectively (Table 6).

Diff. Creatinine and Diff. Urea were found to be significantly associated with hospital LOS (P < 0.05) (Table 6). Serum creatinine level at diagnosis of AKI, blood urea level at diagnosis of AKI, serum sodium and haemoglobin level in AKI patients were not related to hospital LOS (P > 0.05) (Table 6).

| ICU scores     |         | LOS ≤ 7 days(n = 93)(%) | LOS > 7days(n = 95) (%) | Total (n = 188) (%) | P value |
|----------------|---------|-------------------------|-------------------------|---------------------|---------|
| GCS score      | < 10    | 11(30.6%)               | 25(69.4%)               | 36(19.1%)           | 0.015   |
|                | 11 - 15 | 82(53.9%)               | 70(46.1%)               | 152(80.9%)          |         |
| APACHE 2 score | 0 -15   | 28(65.1%)               | 15(34.9%)               | 43(22.9%)           | 0.001   |
|                | 16 - 30 | 57(51.8%)               | 53(48.2%)               | 110(58.5%)          |         |
|                | > 31    | 8(22.9%)                | 27(77.1%)               | 35(18.6%)           |         |

**Table 5:** Distribution of ICU Scores among AKI Patients with LOS in Hospital.

Figures in Parenthesis in Column 2 and 3 Represent the Row Percentage. Figures in Parenthesis in Column 4 Represent the Column Percentage.

| Laboratory Parameters | LOS in hospital | N  | Mean   | Standard Deviation | Standard Error Mean | t-value | P-value |
|-----------------------|-----------------|----|--------|--------------------|---------------------|---------|---------|
| Sr. Creatinine        | LOS ≤ 7 days    | 93 | 3.689  | 1.531              | 0.158               | 0.525   | 0.6     |
|                       | LOS > 7days     | 95 | 3.832  | 3.832              | 0.218               |         |         |
| Blood Urea            | LOS ≤ 7days     | 93 | 113.6  | 66.2               | 6.86                | 1.12    | 0.263   |
|                       | LOS > 7days     | 95 | 124.9  | 71.8               | 1.37                |         |         |
| Sr. Sodium            | LOS ≤ 7days     | 93 | 132.03 | 9.99               | 1.036               | 0.24    | 0.675   |
|                       | LOS > 7days     | 95 | 131.69 | 9.24               | 0.948               |         |         |
| Hemoglobin            | LOS ≤ 7days     | 93 | 10.7   | 3.07               | 0.319               | 1.17    | 0.244   |
|                       | LOS > 7days     | 95 | 11.26  | 3.41               | 0.350               |         |         |

**Table 6:** Association of Laboratory Parameters with LOS in Hospital.

N = Number of AKI Patients

Hyperkalaemia and leucocytosis were present in 54 (29%) and 123 (65%) AKI patients, respectively. Leucocytosis was significantly associated with hospital LOS (P < 0.05) (Table 7).

| Lab parameters |         | LOS ≤ 7 days (n = 93) (%) | LOS > 7days (n = 95) (%) | Total (n = 188) (%) | P value |
|----------------|---------|---------------------------|--------------------------|---------------------|---------|
| Hyper-kalemia  | Present | 21(38.9%)                 | 33(61.1%)                | 54(28.7%)           | 0.086   |
|                | Absent  | 72(53.7%)                 | 62(46.3%)                | 134(71.3%)          |         |
| Leuko-cytosis  | Present | 71(57.7%)                 | 52(42.3%)                | 123(65.4%)          | 0.009   |
|                | Absent  | 24(36.9%)                 | 41(63.1%)                | 65(34.6%)           |         |

**Table 7:** Distribution of Laboratory Parameters among AKI Patients with LOS in Hospital.

Figures in Parenthesis in Column 2 and 3 Represent the Row Percentage. Figures in Parenthesis in Column 4 Represent the Column Percentage.

The most common cause of AKI in our medicine ICU patients was sepsis (19.1%) followed by snake bite (16.5%), acute gastroenteritis (15.4%), cirrhosis (8%), congestive cardiac failure (CCF) (6.4%), malaria(5.3%), CV stroke (4.3%), acute respiratory distress syndrome(ARDS) (3.7%), sickle cell disease (3.7%), obstructive uropathy (3.7%), dengue (3.2%), organophosphorus poisoning (OPP) (2.6%), contrast induced AKI (1.6%), acute pancreatitis (1.6%), scrub typhus (1.1%), bee sting (1.1%), HELLP syndrome (1.1%), haemolytic uremic syndrome (HUS) (1.1%) and eclampsia (0.5%) (Table 8).

**Discussion**

In our study, the mean hospital LOS of AKI patients was 8.84 ± 5.5 days. Ninety-three (49.5%) of 188 AKI patients had hospital LOS ≤ 7days and 95 (50.5%) AKI patients had hospital LOS > 7days. In PICARD study done by Mehta., *et al.* a median hospital LOS of 25 days was found in AKI patients admitted in ICUs [11]. Apart from the medical diagnosis, patients were also having malignancy, immune-compromised status and surgical background in the PICARD

| S.No. | Etiology              | Frequency (N) (%) |
|-------|-----------------------|-------------------|
| 1     | Sepsis                | 36 (19.1%)        |
| 2     | Snake Bite            | 31 (16.5%)        |
| 3     | Acute gastroenteritis | 29 (15.4%)        |
| 4     | Cirrhosis             | 15 (8%)           |
| 5     | CCF                   | 12 (6.4%)         |
| 6     | Malaria               | 10 (5.3%)         |
| 7     | CV Stroke             | 8 (4.3%)          |
| 8     | ARDS                  | 7 (3.7%)          |
| 9     | Sickle cell disease   | 7 (3.7%)          |
| 10    | Obstructive uropathy  | 7 (3.7%)          |
| 11    | Dengue                | 6 (3.2%)          |
| 12    | OPP                   | 5 (2.6%)          |
| 13    | Acute Pancreatitis    | 3 (1.6%)          |
| 14    | Contrast - induced    | 3 (1.6%)          |
| 15    | Scrub Typhus          | 2 (1.1%)          |
| 16    | HELLP                 | 2 (1.1%)          |
| 17    | HUS                   | 2 (1.1%)          |
| 18    | Bee sting             | 2 (1.1%)          |
| 19    | Eclampsia             | 1 (0.5%)          |

**Table 8:** Etiology Wise Distribution of AKI Patients.

N= Number of AKI Patients

study representing more critically-ill patients with advanced AKI. It might be the explanation for a longer median hospital LOS in PICARD study. A median LOS of 13 days (2 - 21) and 11 days (1 - 81) in ≤ 80 years and > 80 years elderly AKI patients, respectively was found in a study done by Funk., *et al.* [12]. Bagshaw., *et al.* reported a mean LOS of 16 days in AKI patients in ICU and Gurjar., *et al.* observed a mean LOS of 22 days [13,14].

The age and gender of the patients, presence of comorbidities (HTN, DM or IHD), smoking, alcohol intake, urine output, presence of metabolic acidosis, haemoglobin, serum creatinine and blood urea levels at the time of diagnosis of AKI were not associated with prolonged hospital LOS (≥ 7 days). Chao., *et al.* found in their study that the presence of comorbidity (heart failure) was associated with longer hospital length of stay [15].

Presence of hypotension, the use of invasive mechanical ventilator, GCS and APACHE 2 score, staging of AKI patients (severity), peak rise in serum creatinine and blood urea levels within 48 hours of diagnosis of AKI (Diff. Creatinine and Diff. Urea), use of haemodialysis and leucocytosis were found to be significantly associated with prolonged hospital LOS ( $\geq 7$  days). Advanced AKI staging (stage 3), presence of hypotension, use of invasive mechanical ventilator, use of haemodialysis and higher GCS and APACHE 2 scores in AKI patients might denote seriously severely ill patients who can potentially have more morbidity and multi-organ dysfunction resulting in increased hospital stay. Similar to our results, Chertow, *et al.* also found that modest increase in serum creatinine were significantly associated with prolonged hospital stay [5]. Bedford, *et al.* observed that length of hospital stay was increased in AKI patients with severity of AKI [16]. Hoste, *et al.* also found that AKI patients with advanced stage had significantly increased LOS [17].

The most common cause of AKI in our medicine ICU patients was sepsis (19.1 %) followed by snake bite (16.5 %) and acute gastroenteritis (16.5 %). Similarly, Bagshaw, *et al.* found sepsis as the most common cause of AKI in ICU patients (47.5%). Kaul, *et al.* found acute diarrheal disease as the most common cause of community-acquired AKI (29%), followed by malaria (18.8%) and sepsis (13.9%). Nephrotoxic drugs were the commonest cause responsible for hospital-acquired AKI (29%) followed by decreased renal perfusion (21%) and sepsis (17%) in a study done by Jha, *et al.* [18]. Soliman, *et al.* found pre-renal azotaemia and acute tubular necrosis due to acute cardiovascular diseases (19.6%) as the commonest cause of AKI [19].

Our study has several strengths. Our patients represent typical rural Indian patients from central India. By including every consecutive AKI inpatients in Medicine ICU, we avoided the selection bias. We made a blind assessment (GCS, APACHE 2 score assessment and data collection) of the patients.

We acknowledge that there are few limitations in our study. The criteria for discharges may have been variable among various clinicians taking care of our AKI patients and could interfere with the results of our findings. This study is also limited to one hospital and may not be representative of the population as a whole.

## Conclusion

Sepsis was the commonest cause of AKI (19.1%) in this study. Presence of hypotension, GCS and APACHE 2 score, advanced AKI stage, peak rise in serum creatinine and blood urea levels within 48 hours of diagnosis of AKI, leucocytosis, use of mechanical ventilator and haemodialysis were associated with prolonged hospital LOS in AKI patients.

## Sources of Support

Nil.

## Conflicts of Interest

None declared.

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