Profile of Community-Acquired Acute Kidney Injury Defined Using RIFLE Criteria Among Medical In-Patients: A Prospective Descriptive Single Centre Study

Sahil Bagai†, Anupam Prakash‡*, Aparna Agrawal§

Abstract

Aim: To determine the proportion of patients who have Acute Kidney Injury (AKI), identify severity of AKI using RIFLE criteria and to identify associated factors with AKI.

Methods: One thousand consecutive medical in-patients were screened for AKI and severity assessed using RIFLE criteria in tertiary care hospital in Northern India. Patients with medical renal disease and obstructive uropathy were excluded. Serum creatinine of all patients were done on days 0, 3, 7 and 14. CKD cases were also excluded. AKI patients were followed at 4 weeks and 3 months.

Results: Amongst 1000 patients screened, 65 had AKI. 27(41.5%), 15(23.0%) and 23(35.38%) patients belonged to risk, injury and failure classes of AKI respectively as per RIFLE criteria, and there was incremental risk of mortality (25.92%, 46.33% and 86.95%, p<0.001). In-patients with pneumonia, chronic liver disease and acute gastroenteritis have greater odds of developing AKI, with chronic liver disease having a high mortality (90%). Hypotension (OR- 5.5:1, p=0.002) or leucocytosis at presentation (OR-2.8:1, p=0.002) or leucocytosis at presentation (OR-2.8:1, p<0.001), smokers (OR-2.2:1, p=0.03) and alcoholics (OR-2.5:1, p=0.047) had greater odds of developing AKI. 33(50.7%) patients with AKI died and 27(41.5%) recovered before day 28. Five (7.7%) were seen in class L who had persistently elevated creatinine at day 90 i.e. progressed to ESRD, class E.

Conclusion: The incidence of AKI among medical in-patients was 6.5%, with an incremental risk of mortality in risk, injury and failure classes. Pneumonia and acute gastroenteritis among infections and chronic liver disease have greater odds of developing AKI. Hypotension, leucocytosis, smoking, alcohol and aetiology are independent risk factors for AKI.

Introduction

Acute kidney Injury (AKI) is a common clinical problem, defined by an abrupt (< 48 hours) increase in serum creatinine resulting from an injury that causes a functional or structural change in the kidney.1 Epidemiological studies have demonstrated wide variations in the aetiologies and risk factors associated with AKI, especially in the tropical countries vis-à-vis countries in the temperate climes. The already high in-hospital mortality following AKI further worsens if dialysis is required. There is emerging recognition that even minor short-term changes in serum creatinine are associated with increased mortality; only other important consequences of AKI are progression of pre-existing CKD and even development of end-stage renal disease (ESRD).2 Diagnosis of renal disease is often missed or discovered too late, which contributes to the increased morbidity and mortality associated with renal diseases. Besides, patients of acute kidney injury, especially when they are diagnosed late, have a greater propensity to develop CKD.

In 2004, Acute Dialysis Quality Initiative (ADQI) proposed a classification system for AKI, known as RIFLE classification. Here (R stands for renal dysfunction, I for Injury to parenchyma, F for failure of organ, L for loss of organ and E for ESRD). The Risk, Injury, Failure, Loss of function and End stage (RIFLE) criteria unified the definition and classification of AKI.3 The RIFLE criteria provide a uniform definition of AKI and has now been validated in numerous studies.4

However, there is a dearth of studies from tropical countries including India outlining the profile of AKI and development of CKD. The causes of AKI in the tropics are peculiar and the few studies that have dealt with this issue are either retrospective in nature or are conducted at apex referral centres with dedicated nephrology set-ups. The present study aimed to determine the aetiological and clinical profile of AKI in medical in-patients and identify the sub-set of patients who go on to develop CKD.

Material and Methods

This was a Descriptive study conducted in a tertiary care centre in Northern India over a 12-month period. The study was approved by the Institutional Ethics Committee and subjects were included only after obtaining an informed consent. One thousand patients who got admitted to the medical units were enrolled and screened for presence of AKI using RIFLE criteria and staged accordingly. Patients with cystic kidney disease, obstructive uropathy and known CKD were excluded.

Demographic profile was noted, a detailed history and clinical examination was conducted for all patients. A

---

†Consultant Nephrologist, Department of Nephrology, MAX Saket, New Delhi; ‡Professor, ¶Department of Medicine, Lady Hardinge Medical College and Associated Hospitals, New Delhi; *Corresponding Author
Received: 02.10.2018; Accepted: 12.06.2019
standard set of investigations including complete blood counts, liver function tests, serum creatinine, urea and electrolytes were done for all. Serum creatinine values were used alone to stage a patient as per RIFLE criteria.

**Staging Criteria**

A pilot study was done on 80 consecutive subjects reporting to medical out-patient for routine health check-up or medical examination. Maximum serum creatinine value observed in these subjects was 1.1 mg/dL and hence, 1.65 mg/dL (1.5 times*1.1 mg/dL) was taken as cut-off for a patient to be classified as AKI according to RIFLE criteria. Groups B, C and D constituted AKI group.

Serum creatinine at admission was taken to classify patients according to RIFLE criteria into 4 groups-

a. **Group A (non-AKI group)** - Included people with serum creatinine <1.65mg/dL.

b. **Group B- At risk** (serum creatinine values between 1.65-2.2mg/dL) i.e. serum creatinine became 1.5 times of baseline (R of RIFLE).

c. **Group C- Renal injury** (serum creatinine values between 2.2-3.3mg/dL) i.e. serum creatinine became more than double (I of RIFLE).

   **Group D- Renal failure** (serum creatinine values ≥3.3mg/dL) i.e. serum creatinine became three times of the baseline (F of RIFLE).

Groups B, C and D together constituted the AKI study group.

In patients whose serum creatinine values were ≥ 1.65mg/dL on day of admission, creatinine was repeated on days 3, 7 and 14 and if variation was < 10% then patients were excluded as were considered to be having chronic kidney disease (CKD), which was undiagnosed and asymptomatic till this presentation.

AKI patients were followed up to look for recovery/progression. Also, the factors leading to AKI were ascertained. Follow-up was done at 4 weeks and 12 weeks of patients in groups B, C, D to look for L and E class of RIFLE Criteria

L – Loss of Renal Function (serum creatinine ≥ 1.65mg/dL for > 4 weeks).

E – End stage renal disease (serum creatinine ≥ 1.65mg/dL for > 3months).

Various variables were outlined in the AKI vs Non-AKI groups and AKI survivors vs AKI non-survivors, and then compared.

**Results**

**Demography**

One thousand patients were screened for AKI. Average age was 42.3±17.13 years, with 427 males and 573 females. Sixty five patients had AKI as per RIFLE criteria (M:F- 0.96:1). Patients in either group were divided into different age groups- 18-30, 31-45, 46-60 and > 60 years (Table 1). 5.8% patients in the 18-30 years age group, pneumonia (21.05%), chronic liver disease (20%), acute gastroenteritis (15.1%), chronic heart failure (14%) and COPD (11.1%) dominated (Table 2).

Significant odds ratio of developing AKI was observed for the following diseases- (i) chronic liver disease (OR=4.1:1, p=0.001), (ii) acute gastroenteritis (OR=2.8:1, p=0.035) and (iii) pneumonia (OR=4.2:1, p=0.002).

**Associated factors**

Average age of AKI group was 45.6±16.8 years comparable to non-AKI group 42.1±17.1 years. Haemoglobin levels were lower in the AKI group (10.9±2.5 vs 10.2±2.7, p=0.02) while leucocyte counts were higher (9568.6±5133 vs. 13252.3±7791.1, p<0.001). Serum total bilirubin, transaminase levels, alkaline phosphatase levels and blood urea and serum creatinine levels were also higher in the AKI group. Liver functions were elevated because of a greater proportion of chronic liver disease patients in the AKI group, while kidney functions were elevated because of the inherent nature of the AKI group. Rest of the parameters viz. plasma sugar and serum lipids were comparable between the two groups.

There was a significantly high odds of patients developing AKI, if

**Table 1: Age distribution of study population**

<table>
<thead>
<tr>
<th>Age group</th>
<th>Total patients (n=1000)</th>
<th>Non-AKI (n=935)</th>
<th>AKI (n=65)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-30 years</td>
<td>330 (33%)</td>
<td>311 (33.2%)</td>
<td>19 (29.2%)</td>
</tr>
<tr>
<td>31-45 years</td>
<td>279 (27.9%)</td>
<td>262 (28.0%)</td>
<td>17 (26.5%)</td>
</tr>
<tr>
<td>46-60 years</td>
<td>225 (22.5%)</td>
<td>211 (22.5%)</td>
<td>14 (21.5%)</td>
</tr>
<tr>
<td>&gt;60 years</td>
<td>166 (16.6%)</td>
<td>151 (16.1%)</td>
<td>15 (23.07%)</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>42.30±17.13</td>
<td>42.06±17.14</td>
<td>45.63±16.83</td>
</tr>
</tbody>
</table>

**Table 2: Aetiological correlation in Non-AKI and AKI groups**

<table>
<thead>
<tr>
<th>Aetiology</th>
<th>Non-AKI (n=935)</th>
<th>AKI (n=65)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus</td>
<td>87 (9.3%)</td>
<td>4 (6.15%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>78 (8.3%)</td>
<td>6 (9.2%)</td>
</tr>
<tr>
<td>CNS</td>
<td>75 (8.01%)</td>
<td>0</td>
</tr>
<tr>
<td>COPD</td>
<td>71 (7.5%)</td>
<td>9 (13.8%)</td>
</tr>
<tr>
<td>Malaria</td>
<td>62 (6.63%)</td>
<td>6 (9.2%)</td>
</tr>
<tr>
<td>Liver abscess</td>
<td>50 (5.3%)</td>
<td>1 (1.5%)</td>
</tr>
<tr>
<td>Dengue fever</td>
<td>49 (5.2%)</td>
<td>2 (3.07%)</td>
</tr>
<tr>
<td>Complicated UTI</td>
<td>44 (4.7%)</td>
<td>5 (7.6%)</td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>40 (4.2%)</td>
<td>10 (15.3%)</td>
</tr>
<tr>
<td>Enteric fever</td>
<td>39 (4.1%)</td>
<td>1 (1.5%)</td>
</tr>
<tr>
<td>Acute gastroenteritis</td>
<td>33 (3.5%)</td>
<td>6 (9.2%)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>30 (3.2%)</td>
<td>8 (12.3%)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>18 (1.9%)</td>
<td>3 (4.6%)</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>330 (35.2%)</td>
<td>12 (21.5%)</td>
</tr>
</tbody>
</table>

*Out of the 12 aetiologies, sepsis-3, tubercular lymphadenitis-1, abdominal tuberculosis-3, unknown poisoning-1, anaemia-2, unstable angina-1, aortic stenosis-1, N.B.- The cumulative total in both AKI and Non-AKI groups is more than 65 and 935, since there were patients in both the groups having more than one disease aetiologies; p significant <0.05

(9.1%), Hypertension (8.4%), chronic obstructive pulmonary disease (8%), central nervous system disorders (7.5%), and Malaria (6.8%). In the AKI group, pneumonia (21.05%), chronic liver disease (20%), acute gastroenteritis (15.1%), chronic heart failure (14%) and COPD (11.1%) dominated (Table 2).
they had hypotension at presentation (OR- 5.5:1, p=0.002), leucocytosis at presentation (OR-2.8:1, p=0.001), were smokers (OR-2.2:1, p=0.03) or alcoholics (OR-2.5:1, p=0.047). No relation to age, gender, body mass index, hypertension, hypertriglyceridemia or hypercholesterolemia was observed.

Mortality

The mortality among the AKI patients was 50.7% (n=33). 90% of chronic liver disease patients who developed AKI died; two-thirds of COPD and CHF patients died. 60% of complicated UTI with AKI died. Mortality was 50% among patients who had pneumonia or hypertension or diabetes, and developed AKI. However, AKI related to malaria and acute gastroenteritis did not have any mortality in the present study. AKI associated with Dengue, amoebic liver abscess and enteric fever, in the present study, was associated with full recovery of renal function.

The mean serum bilirubin and alkaline phosphatase levels analyzed in the AKI group excluding CLD cases significantly dropped from 3.6±5.18 to 2.1±3.65 and 244.70±264.07 to 225.66±295.83, respectively and the result was not significantly associated with mortality. This could be attributed to the high predominance of cases of CLD in the AKI mortality group.

AKI follow-up

Patients enrolled in AKI group were followed up at day 28. Out of total 65 patients in AKI group, 33 patients had died, while serum creatinine reverted to normal range before the 28th day in 27 (41.5%) patients. The remaining 5 (7.7%) patients (who had not recovered on Day 7) were followed up at day 28. Three of the 5 patients (4.6%) were found to be in L class of RIFLE criteria. Out of these 5 patients, one had alcoholic liver disease with portal hypertension, second had pyelonephritis, third had hypertension with pulmonary tuberculosis and remaining two had only hypertension. The patients, who were in L class of RIFLE at day 28, were followed up on day 90, and were found to have persistently elevated serum creatinine values, i.e. were in Class 5 of RIFLE criteria i.e. End stage renal disease.

Discussion

Community-acquired AKI encompasses medical causes, surgical or obstructive AKI causes and obstetric AKI. The present study has focussed only on medical causes of AKI, since the aetiological factors and management principles that govern obstructive/post-surgical AKI and obstetric AKI are entirely different from medical causes of AKI. The profile of medical causes of AKI in the tropics also differs from the AKI profile in other geographical areas, with infections and dehydration predominating in the tropics. There have been very few studies on profile of AKI since the RIFLE criteria were enunciated, and to the best of our knowledge, no study actually tried to follow these cases for residual kidney dysfunction (Stage L and E of RIFLE classification). The studies on profile of AKI have been far and few with some limitations viz. retrospective nature of studies; profiling medical, surgical and obstetric causes of AKI together; studying only a subset of causes of medical AKI such as profiling only fever cases; and being conducted in nephrology set-ups only. The present study obviated all these limitations.

Demography

In the present study, average age of AKI group was 45.6±16.83 years with an almost equal gender distribution (0.96:1). This was similar to other studies in the region, with average age in AKI patients reported from Himachal Pradesh (hill state in northern part of India) as 48.96±18.3 years,6 39.7±16.9 years from CMC, Vellore (southern part of India)8  and 39.8±14.48 years from SGPGI, Lucknow, India.2 However, gender distribution was 1.5:1 in CMC Vellore (southern part of India) where only febrile causes of AKI were studied, and 1.7:1 in a study from Bokaro, Jharkhand (eastern part of India).7

AKI is known to complicate 5-7% of hospital admissions, and up to 30% of admissions in critical care units.6 The prevalence of AKI was 6.5% in the present study. A study in U.K. showed AKI prevalence around 4.6%.4 However, an Indian study done in Himachal Pradesh reported an AKI prevalence of only 0.53% where 84.3% patients developed community-acquired AKI and 15.7% had hospital-acquired AKI.1 A retrospective study from SGPGI, Lucknow reported 2.5% prevalence of community-acquired AKI.7 In one study 603 patients admitted in ICU were evaluated and 161 (26.7%) developed AKI.10 However, as earlier stated, these studies do not accurately depict community-acquired AKI, as these have been carried out in nephrology set-ups which by-and-large receive referred cases.

Staging of AKI

Patients in AKI group were staged using RIFLE criteria. In the present study, patients in R, I and F stage of RIFLE were 27 (41.50%), 15 (23%) and 23 (35.38%). This was comparable to CMC, Vellore study6 where total AKI incidence was 41.1% (R= 17.4%, I=9.3%, F=14.4%). A study conducted in Seoul, Korea8 reported hospital-acquired AKI in 1.2% patients with 29.2% in stage R, 36.5% were in stage I and 34.4% were in stage F. The studies exclusively carried out in intensive care unit patients had AKI prevalence and RIFLE staging different from our study, which may be due to the critical illness setting. In a tertiary care setup in USA, AKI occurred in 67% of intensive care unit admissions with class R, class I and class F in 12%, 27% and 28% with incremental mortality rates.12

Aetiological distribution

The causes of AKI vary in accordance with the geographical area. The causes of AKI in tropics are different than in the western world.13 Febrile illness and infections predominate as the cause of AKI in the tropics.14 In the present study, AKI group had Pneumonia (21.05%), CLD (20%), acute gastroenteritis (15.1%), CHF (14%) and COPD (11.1%) as the commonest causes. One study reported that 18% of pneumonia patients developed AKI.15 Twenty percent of all CLD patients in the present study developed AKI which is comparable to data in another study.16 In a study from Canada, 82 episodes of AKI occurred in 49 patients of cirrhosis with 9 patients showing no recovery.17 The most common causes of AKI in cirrhosis are pre-renal azotemia, hepatorenal syndrome and acute tubular necrosis. In a Nepalese study, out of 45 AKI patients, 10 (22%) had acute gastroenteritis,18 while in the present study out of 65 AKI patients, only 6 had acute gastroenteritis.

Association of clinico-biochemical parameters with AKI and non-AKI groups

There is a distinct lack of studies which have compared various clinico-biochemical parameters in between the AKI and non-AKI subjects. Proportion of
subjects having Hypertension, diabetes mellitus, COPD, CHF and infections like malaria, Dengue, enteric fever and complicated UTI were statistically similar in the AKI group and the non-AKI group, without any increased odds of patients getting admitted with these diagnoses developing AKI, in the present study. However, hypertension did seem to correlate with greater extent of residual renal dysfunction, with three out of five patients who reached ‘L’ RIFLE stage having hypertension. Infections do stand out as an important cause of AKI in tropics, as evidenced from Table 2 wherein 36 out of the 70 enlisted causes are infectious aetiologies. However, only pneumonia and acute gastroenteritis had greater odds of developing AKI, vis-à-vis other infectious aetiologies. The high prevalence of chronic liver disease could be the only potential bias, because of the proximity of the New Delhi railway station, around which area many addicts do reside.

There is a usual impression obtained from studies from the tropics that infections stand out as an important cause of AKI, however it is noteworthy that the other studies in the region were primarily having nephrology set-ups, wherein patients requiring nephrology services are likely to seek referrals. The present study was conducted in a general hospital, situated in the heart of the city, with easy access to the general public, and is more representative of the community scenario.

In the present study, hypotension (systolic blood pressure <90mm Hg) and leukocytosis, both were associated with greater chances of developing AKI. Volume depletion was found to be an important cause of AKI in an Indian study, and leukocytosis in a Canadian study. Septis, in India, has been reported to be an important cause of AKI, which can also partly explain the relation of leukocytosis with AKI in the present study. Relation of glyceremia and BMI with AKI has been reported, although not obvious in the present study.

Smoking causes an increase in renovascular resistance leading to a decrease in glomerular filtration rate (GFR), and is a known risk factor for chronic kidney disease. However, there are no studies showing direct correlation of smoking with AKI, although smoking as well as alcohol were significant associates of AKI patients in the present study. The latter association could be spurious since chronic liver disease was significantly associated with development of AKI, and many of the chronic liver disease cases were alcohol-related.

In the present study, lower hemoglobin was observed in AKI subjects as compared to non-AKI subjects. This was in line with a previous study. In the present study significant correlation was seen between occurrence of AKI and serum bilirubin. This is in accordance with a previous study where the toxic effects of bilirubin and bile salts have been established with renal dysfunction.

**Correlates of AKI mortality**

The mortality among the AKI patients was 50.7% (n=33), and 90% of chronic liver disease subjects who developed AKI died. High rates of mortality (65.5%) have also been reported in Taiwan. Also in the present study, two-thirds of COPD, CHF and 50% of pneumonia patients died. Leucocytosis and hypotension were significantly higher among AKI non-survivors. This is in line with previous studies. In the present study high bilirubin levels and high alkaline phosphatase levels were associated with mortality in the AKI group.

In the present study, 41.05% patients’ serum creatinine normalized within 4 weeks while 50.7% patients of AKI had died during the same period. In accordance with RIFLE criteria 7 (25.92%) patients out of 27 in class ‘R’, 7 (46.33%) patients out of 15 in class ‘I’ and 20 (86.95%) patients out of 23 in class ‘F’ expired. This shows that higher stage in RIFLE criteria is associated with higher mortality rates. This is consistent with previous studies. In Korea, a study reported high mortality for patients in class 3 AKI as compared to patients in class 1 or 2.

Five patients progressed to stage ‘L’ of RIFLE criteria and also had persistently elevated serum creatinine at day 90, i.e. belonged to class ‘E’ of RIFLE criteria (ESRD). Also, there are no studies available where follow-up of patients has been done to look for sequel of acute kidney injury. Because of the small number of patients in ‘L’ and ‘E’ categories in the present study, it is not possible to comment on the correlates or associates of AKI which contribute to development of CKD or residual renal dysfunction (partial recovery).

The present study was unique in being a prospective study from developing country which highlights disease conditions which cause AKI and diseases which carry increased mortality. In diseases such as pneumonia and CLD timely intervention can prevent AKI. No deaths in AKI group was noted secondary to tropical fever and acute gastroenteritis which shows that if adequate hydration, antimicrobial therapy and supportive management is provided in these diseases, AKI is reversible. Study duration was over 1 year so seasonal bias was eliminated and a composite profile of diseases occurring throughout the year was reflected.

The present study was a single centre study so sample size was a limitation. Also, the AKI causes are dependent on the epidemiology of the area so the causes in tropical countries are different from other non-tropical countries; and hence, these results cannot be extrapolated to non-tropical countries.

**References**

11. Kwon SH, Noh H, Joos JS, Kim Y, Han DC. An assessment of
Introduction

Etiopathological Study of Crescentic Glomerulonephritis and its proliferating cells between the visceral

Abstract

Introduction:


