Clinical profile and outcome of acute kidney injury in a tertiary care center of eastern Nepal [version 1; peer review: awaiting peer review]

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Abstract

Background
Acute kidney injury (AKI) is a global problem and it is encountered both in community and in-hospital patients. AKI has caused very significant damage to the health sector with high morbidity and mortality rates as well as a financial burden to the family. AKI contributes to a 3% incidence of end-stage renal disease (ESRD). Sepsis and hypovolemia-associated ischemia is the most common cause of AKI. AKI has various risk factors, modes of presentation and outcomes. Also, the prevalence varies across the different populations. There is a paucity of data about the clinical profile of AKI in the eastern part of Nepal. This study aims to assess the age, comorbid conditions, the severity of AKI, mode of treatment, and outcome of patients with AKI admitted to the Nobel Medical College and Teaching Hospital, Biratnagar, Nepal.

Methods
This is a cross-sectional analytical study conducted at a Nobel Medical College Teaching Hospital, Biratnagar, Nepal from July 2018 to June 2019 AD.

Results
In this study, 192 patients diagnosed with AKI were included. Male patients accounted for 52.7%. The mean age was 48.6±18.73 years. Most of the patients (74.5%) were below <60 years of age. The average duration of hospital stay was 8 days. The common cause of AKI was sepsis in 71.9%. Diabetes mellitus (DM) was seen in 52.6% of patients. Most of the patients (41%) were at stage III AKI at the time of
admission. Hemodialysis was done in 14.6% and 85.4% were managed conservatively. Average sessions of hemodialysis were 3.61. Complete recovery was seen in 69.8% of the patients.

Conclusions
We observed that early diagnosis, avoidance of nephrotoxic agents, and early, aggressive, and appropriate interventions result in improved patient outcomes. However late presentations of AKI have a higher hospital mortality rate.

Keywords
Acute kidney injury, qSOFA, Hemodyalysis, sepsis, renal, creatinine, urea
Introduction
The abrupt and usually reversible decline in glomerular filtration rate (GFR) over days to weeks is defined as acute kidney injury (AKI). This term also highlights that injury to the kidney that does not result in “failure” is also of great clinical significance. The definition has evolved from the Risk, Injury, Failure, Loss, End-stage (RIFLE) criteria in 2004 to the AKI Network (AKIN) classification in 2007. In 2012, both were merged resulting in the Kidney Disease Improving Global Outcomes (KDIGO) classification. Accordingly, AKI is diagnosed if serum creatinine increases by ≥0.3 mg/dl within 48 hours or rises ≥1.5 times from the baseline within 7 days, and urine volume <0.5 mL/kg/hr for 6 hours. AKI stages are defined by the maximum serum creatinine or urine output change.

The epidemiology and outcome of AKI differ significantly across the industrialized and underdeveloped worlds. Developing countries account for more than 85% of the worldwide burden of AKI. In Nepal higher burden of community acquired AKI is seen in younger age group. Even a modest type of AKI is linked to higher long-term mortality in ICU survivors, as well as an elevated risk of chronic and end-stage kidney disease and significant cardiovascular events. Specific organ system failures occur at varying rates among AKI patients admitted to the ICU, with varying degrees of correlation between individual organ system failures and ICU mortality. qSOFA is very useful tool to access the extent of organ dysfunction seen in critically ill patient with AKI. Sequential (Sepsis-related) Organ Failure Assessment score (SOFA) is modified to form qSOFA score. Components of qSOFA comprises of respiratory rate>22 bpm, SBP<100 mmHg, altered Glasgow coma scale (GCS) and one point is allocated to each component. To indicate organ dysfunction, qSOFA score must be ≥2.

qSOFA ≥2 was highly specific for identifying organ dysfunction and mortality (96.1% and 91.3% respectively), but sensitivity was poor (29.7% and 49.1% respectively). Low-and middle income like Nepal lack adequate information, healthcare resources, and patient adherence to the treatment protocol. Additionally, data on AKI is not sufficiently available in the literature. Therefore, this study aimed to assess the clinical profile and short-term outcomes of acute kidney injury in single-center hospitalized patients.

Methods
Ethics and consent
Ethical clearance (ref. no. 171/2018) was granted from the ethics and research committee of Nobel Medical College Teaching Hospital, Biratnagar, Nepal on 22nd June 2018. Written informed consent was obtained from participants and from parents for the participants who were <18 years for the publication of their clinical details.

Procedure
This is a cross-sectional analytical study conducted at Nobel Medical College Teaching Hospital, Biratnagar, Nepal from July 2018 to June 2019 AD. The study population was all patients admitted at Nobel Medical College with a diagnosis of AKI. Non-probability convenient sampling method was used. The research team approached all the admitted patients with the diagnosis of AKI. Patients meeting the inclusion and exclusion criteria were recruited.

Inclusion criteria include age >15 years, and all patients admitted in the ICU and ward with a diagnosis of AKI meeting criteria as per KDIGO guidelines 2012.

Exclusion criteria include preexisting chronic kidney disease (CKD) with baseline CKD EPI (chronic kidney disease epidemiology collaboration) eGFR (estimated glomerular filtration rate) <60 ml/min/1.73 m² before the onset of illness or dialysis-dependent, suspected or biopsy-proven glomerulonephritis as a cause of AKI and suspected or diagnosed case of heart failure with functional class 3 or 4. eGFR was calculated at time of study to determine if participants were suitable to take part.

Variables assessed in this study were age, gender, duration of hospital stay, comorbidities, cause of AKI, mode of management, and qSOFA score.

As per the hospital data, around 160 patients were annually admitted with the diagnosis of AKI. So, with 20 allowable error, minimum of 140 cases were selected over the study duration.

Continuous variables were expressed as means±standard deviation (SD). Categorical variables were expressed as proportions and compared with the chi-squared test at 95% confident interval where level of significance considered at p≤0.05. Statistical Package for Social Sciences (SPSS) 25th version was used for analysis.
AKI is defined as any of the following:

- An absolute increase in serum creatinine of 0.3 mg/dl or more (26.4 micro-mol/L or more) within 48 hours, or
- Increase in serum creatinine to 1.5 times or more from baseline, which is known or presumed to have occurred within the prior 7 days, or
- Urine output of less than 0.5 ml/kg per hour for more than 6 hours.

qSOFA scoring includes:

- Low blood pressure (SBP $\leq$ 100 mmHg)
- High respiratory rate ($\geq$ 22 breaths/min)
- Altered mentation (GCS $< 15$)

**Results**

The study was carried out on 192 patients who were admitted with the diagnosis of AKI. The demographic and clinical profiles of the patients are shown in Table 1.

The mean duration of hospital stays (ICU and ward) of the patients was 8.91±4.38 days. Almost 88% of patients had hospital stays of $\leq$ 2 weeks. Comorbidities were seen in 76 (39.5%) patients. Among patients with comorbidities, 40 (52.6%) had diabetes mellitus, 21 (27.6%) patients had chronic obstructive pulmonary disease (COPD), and 15 (19.8%) patients had hypertension. The common cause of AKI was sepsis in 138 patients (71.9%), hypovolemia in 30 patients (15.6%), obstructive uropathy in 17 patients (8.9%), surgical cause in 4 (2.1%), and drug-related in 3 (1.6%). Most of the patients (79; 41.1%) were at stage III of AKI at the time of admission as shown in Table 2.

**Table 1. Patients’ demographic and clinical profile.**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Variable</th>
<th>Number</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (in years.)</td>
<td>Mean±SD</td>
<td>48.60±18.73</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
<td>101</td>
<td>52.7</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>91</td>
<td>47.4</td>
</tr>
<tr>
<td>Age group (in years)</td>
<td>15-30</td>
<td>44</td>
<td>22.9</td>
</tr>
<tr>
<td></td>
<td>31-45</td>
<td>41</td>
<td>21.4</td>
</tr>
<tr>
<td></td>
<td>46-60</td>
<td>58</td>
<td>30.2</td>
</tr>
<tr>
<td></td>
<td>61-75</td>
<td>37</td>
<td>19.3</td>
</tr>
<tr>
<td></td>
<td>&gt;76</td>
<td>12</td>
<td>6.3</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>Mean±SD</td>
<td>11.18±2.43 g/dl</td>
<td></td>
</tr>
<tr>
<td>Baseline serum creatinine</td>
<td>Mean±SD</td>
<td>0.99±0.14 mg/dl</td>
<td></td>
</tr>
<tr>
<td>Serum creatinine at admission</td>
<td>Mean±SD</td>
<td>3.87±2.07 mg/dl</td>
<td></td>
</tr>
</tbody>
</table>

**Table 2. Stage of AKI (acute kidney injury) at admission and maximum stage of AKI during a hospital stay.**

<table>
<thead>
<tr>
<th>Stage of AKI at admission</th>
<th>Maximum stage during a hospital stay</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I (40.7%)</td>
<td>II (46.3%)</td>
</tr>
<tr>
<td>I</td>
<td>22</td>
<td>25</td>
</tr>
<tr>
<td>II</td>
<td>0</td>
<td>48</td>
</tr>
<tr>
<td>III</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>22 (11.5%)</td>
<td>73 (38.0%)</td>
</tr>
</tbody>
</table>
At admission, 25 patients had a qSOFA score of 3 as shown in Table 3. 28 patients i.e. 14.60% underwent renal replacement therapy (RRT) in the form of hemodialysis whereas 164 patients i.e. 85.4% were conservatively managed. The average number of sessions of hemodialysis was 3.61 (1-8) sessions. Out of all patients, 90 were managed in the ICU and among those 23 (25.56%) who had partial recovery and 6 patients (3.1%) died during the hospital stay.

Among 138 patients with sepsis, 18 patients (13.0%) were ventilated and 120 patients (87.0%) were not ventilated. Among 30 patients with hypovolemia, 3 patients (10.0%) were ventilated, 27 patients (90.0%) were not ventilated. All 17 patients with obstructive uropathy didn’t require ventilatory support. The cause of AKI was insignificantly (χ²=8.46, df=4, p=0.076) associated with the need to use ventilatory support for the patient.

Among 106 patients with a qSOFA score of 0, 8 patients (7.5%) underwent hemodialysis, and 98 patients (92.5%) were managed conservatively. Among the 31 patients who had a qSOFA score of 1, 3 patients (9.7%) underwent hemodialysis and 28 patients (90.0%) were managed conservatively. Among 30 patients with a qSOFA score of 2, 5 patients (16.7%) underwent hemodialysis, 25 patients (83.3%) were managed conservatively. Also, among the 106 patients with a qSOFA score of 3, 12 patients (48.0%) underwent hemodialysis, and 13 patients (52.0%) were managed conservatively. The score of qSOFA was significantly (χ²=24, df=6, p=0.01) associated with the outcome of the patient.

28 patients underwent hemodialysis out of which 3 patients (10.7%) died, 13 patients (46.4%) had partial recovery, and 12 patients (42.9%) had a complete recovery. In the 164 patients under conservative treatment, 3 patients (1.8%) died, 39 patients (23.8%) had partial recovery, 122 patients (74.4%) had a complete recovery. Chi-square statistics were used to examine the association between categorical variables (mode of treatment and outcome). There is a significant association at a 5% significance level between mode of treatment and outcome (χ²=13.97, df=2, p=0.01).

Among 138 patients with sepsis, 22 patients (15.90%) underwent RRT in the form of hemodialysis. 3 patients (10%) with hypovolemia and 3 patients (17.6%) with obstructive uropathy also received hemodialysis, whereas 164 patients were conservatively managed. There is an insignificant association at a 5% significance level between the cause of AKI and outcomes (χ²=14.83, df=8, p=0.062).

Discussion
In our study, the mean age at presentation was 48.60±18.73 years ranging from 16 years to 89 years. Mean age varies in different studies. In the study by Vikrant et al. it was 49±18.1, 45 in Khakhurel et al., 32±16.85 in Aggrawal et al. and 65.8±14.1 in a study by Teo et al.

In the present study, 143 (74.5%) patients were 60 years or older, and the remaining 49 (25.5%) patients were below 60 years. This signifies that the younger population is also affected in a big proportion. In the study done by Chhetri PK et al. in Nepal Medical College Teaching Hospital, Kathmandu, 64% of patients belonged to the age group 21-60 years which is different than our study and this might be due to the small study sample of 45 in the study by Chhetri PK et al.

In our study, the mean duration of the patient’s hospital stay was 8.91±4.38. Almost 88% of patients had a hospital stay of ≤2 weeks. In a study by Khakhurel et al. in Bir Hospital Kathmandu, the mean hospital stay was 13.6 days. In a study done by Patel et al. Northern Railway Central Hospital, New Delhi, India, most patients (approximately 81%) required hospitalization for around or <2 weeks. This variation in in-hospital stay may be due to inclusion criteria, sample size, socioeconomic status, and nutritional status of patients.

Table 3. qSOFA score at admission and discharge.

<table>
<thead>
<tr>
<th>qSOFA at admission</th>
<th>qSOFA at discharge</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>106</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>31</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>30</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>25</td>
</tr>
<tr>
<td>Total</td>
<td>176</td>
<td>6</td>
</tr>
</tbody>
</table>

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In our study 70 patients (39.5%) had comorbid conditions, among them 40 patients (52.6%) with DM, 21 patients (27.6%) with COPD, and 15 patients (19.8%) had hypertension (HTN). In a study done by Maskey et al. 19 30 patients (35.7%) had DM, 24 (29.7%) had HTN, 14 patients (16.6%) had COPD, and malignancy was found in 6 patients (7%). In a study done by Rathnamalala et al., 24 patients (35.3%) had DM followed by HTN in 6 patients (8.8%), CLD in 2 patients (2.9%), and other conditions were reported in 2 patients (2.9%). In a study done by Ghimire et al. 21 among co-morbid conditions, 9.4% of subjects had DM, followed by 3% with COPD. Therefore, the findings of our study are consistent with the finding from the above studies.

In the present study, 71.9% of patients had sepsis as the major cause of AKI followed by hypovolemia in 15.6% and obstructive uropathy in 8.9%.

In a study by Ghimire et al. 21 sepsis was seen in 47% of the patients as the cause of AKI. In another study in Sri lanka by Rathnamalala et al., 22 sepsis was also the most common (41.2%) cause of AKI. Above mentioned studies by Ghimire et al. 21 and Rathnamalala et al. 22 are consistent with our findings. Whereas, in studies by Khakurel et al. 14 and Chhetri et al. 17 gastroenteritis was the leading cause of AKI followed by sepsis.

In the present study, 9.4% of subjects had DM, followed by 3% with COPD, and malignancy was found in 6 patients (7%). In a study done by Maskey et al. 19 30 patients (35.7%) had DM, 24 (29.7%) had HTN, 14 patients (16.6%) had COPD, and malignancy was found in 6 patients (7%). In a study done by Rathnamalala et al., 24 patients (35.3%) had DM followed by HTN in 6 patients (8.8%), CLD in 2 patients (2.9%), and other conditions were reported in 2 patients (2.9%). In a study done by Ghimire et al. 21 among co-morbid conditions, 9.4% of subjects had DM, followed by 3% with COPD. Therefore, the findings of our study are consistent with the finding from the above studies.

The result of the maximum stage of AKI during the hospital stay as shown in Table 4 is consistent with the study by Wang et al. 25 whereas it differs from the study by Fuhrman et al. 26 and this variation may be due to the larger study sample in Fuhrman et al.

In the present study, 14.6% of patients underwent renal replacement therapy in the form of hemodialysis and 85.4% were managed conservatively. The average number of sessions of hemodialysis was 3.61. In a study by Maskey et al., 19 15% required hemodialysis with the average number of sessions of hemodialysis being 3.4. Similarly, in a study by Shrestha et al., 27 26.7% of the patients received hemodialysis. Our findings are consistent with these studies.

In the present study, 69.8% of patients had complete recovery, 27.1% had partial recovery, and 3.1% had in-hospital mortality. Our findings are consistent with the study by Maskey et al. 19 where 52% showed complete recovery, 37% had partial and 3% had in-hospital mortality.

The score of qSOFA was significantly (x²=24, df=6, p=0.01) associated with the outcome of the patient. This association shows that with an increase in the score of qSOFA there is an increase in the number of patients who underwent dialysis. So, an increase in qSOFA score at the time of admission increases the requirement for dialysis. A qSOFA score of ≥2 points indicates organ dysfunction. qSOFA ≥2 was highly specific for identifying organ dysfunction and mortality (96.1% and 91.3% respectively). 28

In our study, there is a significant association at a 5% significance level between mode of treatment and outcome (x²=13.97, df=2, p=0.01). This signifies that fewer patients died in conservative treatment compared to hemodialysis. Also, more patients survived with conservative treatment. Our findings are in agreement with two large randomized controlled trials which have also failed to show any significant benefit on mortality even in those with more intensive dialysis. 29 However, our findings need to be interpreted with caution as more deaths in the hemodialysis group may

### Table 4. Maximum stage of AKI during hospital stay compared with other studies.

<table>
<thead>
<tr>
<th>Maximum Stage during a hospital stay</th>
<th>Present study (N=192)</th>
<th>Wang et al. 25 (N=361)</th>
<th>Fuhrman et al. 26 (N=8270)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>22 (11.5%)</td>
<td>75 (20.8%)</td>
<td>2823 (34%)</td>
</tr>
<tr>
<td>Stage II</td>
<td>73 (38%)</td>
<td>92 (25.5%)</td>
<td>3457 (42%)</td>
</tr>
<tr>
<td>Stage III</td>
<td>97 (50.5)</td>
<td>194 (53.7%)</td>
<td>1990 (24%)</td>
</tr>
</tbody>
</table>
simply reflect that they were sicker (i.e. they had a higher AKI stage at the time of admission, had higher qSOFA score, and were more ventilated) than the patients on conservative treatment.

Conclusion
Sepsis is the most common cause of AKI in our study. Most of the patients present late i.e. stage III of AKI. Patients who presented with stage III AKI, had a qSOFA score of 2, and who were ventilated had higher mortality. AKI patients can be treated without doing RRT if the patient’s conditions are detected early with judicial investigations. However late stages in AKI have a poorer prognosis even with RRT. Careful monitoring of urine output, serum creatinine, and blood urea should be done in all patients admitted to the hospital especially in critical care to predict AKI. Timely diagnosis will surely improve the outcome and survival chances of patients drastically.

Data availability
Underlying data

This project contains the following underlying data:
- data.xlsx (raw data sheet)

Extended data

This project contains the following extended data:
- Proforma.pdf (patient details form)
- Consent form nobel pdf.pdf (consent form)
- Data key pdf.pdf (data key for thexlsx file)

Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

References


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