

Clinical Profile and Outcomes of Acute Kidney Injury in Patients with Sepsis Admitted to Medical Wards

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Author's Contribution

All authors contributed significantly to this work, participating in conception, study design, data acquisition, analysis, and interpretation. They were involved in drafting, revising, and critically reviewing the article, ultimately giving their approval for the version to be published

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ABSTRACT

Objective: To assess clinical profile, risk factors, and the outcome of acute kidney injury (AKI) in the patients admitted to medical wards with diagnosed sepsis.

Study Design and Setting: A descriptive cross sectional study was done in the department of medicine in a tertiary care teaching hospital for a span of six months.

Methodology: Consecutive sampling was used in enrolling adult patients who were admitted with sepsis. Diagnosis of AKI was made based on the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines. Data were collected on demographic features, comorbidities, clinical presentations, laboratory investigations, need for intensive care unit stay, hospital stay and mortality that occurred in the hospital. Data was analyzed statistically using SPSS 27. The data from continuous variables were presented as mean with standard deviation and categorical data as frequencies and percentages. The chi-square test was used to compare association between variables with a p-value of <0.05 being considered statistically significant.

Results: Fifteen patients had AKI with a total of 150 patients with sepsis included, of which 58 (38.7%) developed AKI. Patients with AKI were 56.4 ± 14.2 years old with a male predominance of 60.3%. The most prevalent comorbidities were hypertension, diabetes mellitus and chronic liver disease. Factors associated with development of AKI were septic shock, elevated serum creatinine, oliguria and prolonged hospital stay ($p < 0.05$). AKI patients were more likely to be admitted to the ICCU and to die than were non-AKI patients. The mortality for the septic patients who developed AKI was 31.0%.

Conclusion: Acute kidney injury is a common and important complication among septic patients admitted into medical wards, and there is an association with increased morbidity, longer hospital stay and mortality. Sepsis associated AKI may be better managed and have better outcomes if diagnosed early and managed promptly.

keywords: Acute kidney injury, Clinical outcomes, Hospital mortality, KDIGO, Medical wards, Renal dysfunction, Sepsis, Septic shock.

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Introduction

Sepsis is a potentially fatal clinical syndrome that is triggered by an infection and results in acute organ dysfunction and mortality on global scale [1]. It is a significant worldwide health problem, impacting millions of patients every year, and is still a major cause of hospital

admission and in-hospital mortality, despite the improvements in antimicrobial therapy and critical care management [2]. The clinical manifestations of sepsis are very diverse from mild organ dysfunction to septic shock and multiorgan failure and early recognition and prompt management of the disease are critical to outcome.

Acute kidney injury (AKI) is one of the most common and important organ dysfunctions associated with sepsis [3]. Sepsis-associated acute kidney injury (SA-AKI) is a significant component of the cohort of patients with AKI admitted to hospital and critical care and has been linked to significant morbidity, longer hospital stay, and higher healthcare expenditure [4]. Sepsis is estimated to be one of the most common causes of AKI in the intensive care unit (ICU) and the general medical wards and has been reported to occur in one-third to half of all septic patients admitted to the hospital [5].

Sepsis is a major risk factor for the development of AKI and AKI is associated with higher short-term and long-term mortality in sepsis in an independent fashion [6]. Mild cases of AKI have been associated with a risk of progression to chronic kidney disease (CKD) and end-stage renal disease (ESRD), demonstrating the importance of early diagnosis and treatment [7]. Poor outcomes resulting from delayed presentation, availability of diagnostic facilities and monitoring are further contributors to the burden of SA-AKI in resource limited settings.

Acute kidney injury is an acute reduction in renal function leading to the inability to adequately eliminate nitrogenous waste products, fluid and electrolyte disturbances [8]. Kidney Disease: Improving Global Outcomes (KDIGO) has established standardized criteria for the diagnosis and staging of the syndrome of AKI by using serum creatinine and urine output reduction [9]. These criteria have had a major impact in the early detection and standardised reporting of AKI in clinical studies and health care systems. However, in the early stages, AKI is frequently not recognized, especially in general medical wards where 24/7 monitoring may be restricted.

The pathophysiology of SA-AKI is complex and multifactorial and differs from ischemic and nephrotoxic AKIs. This includes cellular level systemic inflammation, endothelial dysfunction, microvascular dysregulation, oxidative stress, and mitochondrial injury [4,10]. Sepsis may lead to endothelial activation and capillary leakiness with inflammatory mediators like cytokines and chemokines involved, leading to reduction of oxygen supply to renal tissues. In contrast to classical hypoperfusion models, RBF in SA-AKI could be normal or elevated, and it has been hypothesized that metabolic dysfunction of the cells is a crucial role in the disease progression [10].

Multiple risk factors were identified in several clinical studies of septic patients who developed AKI. These include advanced age, male gender, pre-existing comorbidities (diabetes mellitus, hypertension and chronic kidney disease), severity of infection and septic shock [5,6]. In addition, septic individuals are at risk of renal injury due to exposure to nephrotoxic drugs, hemodynamic instability, and delayed initiation of appropriate antimicrobial therapy [11]. Early risk stratification and targeted management is essential and requires recognition of these risk factors.

Sepsis-associated AKI is strongly associated with poor clinical outcomes. Septic patients with AKI are more likely to be admitted to intensive care unit, require renal replacement therapy, have longer hospital stays and die of the disease compared to those without AKI [6,12]. Patients with SA-AKI have been reported to have significantly higher mortality rates, especially in patients with septic shock and/or multiorgan failure [2]. Moreover, the cardiovascular and renal complications are observed in SA-AKI survivors for a long-term period, which underlines the long-term effect of the condition [7].

The prevalence of SA-AKI is not equal for all health care facilities. Early detection systems, standardization of sepsis protocols and enhanced critical care support have improved outcomes in high income countries. Sepsis, however, poses a serious public health problem in low and middle income countries like Pakistan because of late hospital presentation, poor infection control, lack of diagnostic facilities, high prevalence of antimicrobial resistance [2,11]. These factors lead to higher rates and poorer outcomes of SA-AKI in these environments.

Importantly, most of the existing literature on SA-AKI comes from populations in intensive care units (ICUs) and relatively few data are available for those admitted to general medical wards. Patients with AKI in medical wards may have different levels of illness severity, and may not be monitored as closely as patients in the ICU, which can result in delayed recognition of AKI and poorer outcomes. This evidence gap is important in resource-limited health systems, where there are limited number of ICU beds and a large percentage of septic patients are being treated in general wards.

In light of this background, it is evident that the clinical profile and outcome of septic patients with AKI in non-ICU settings should be assessed. To ensure optimal early diagnosis, management strategies and minimisation of mortality, it is important to understand the pattern of

disease presentation, associated risk factors, and outcomes in the local setting.

The current study aimed to evaluate the clinical characteristics and outcomes of patients with acute kidney injury admitted to medical wards who had sepsis. This study is to provide locally relevant evidence that can help clinicians in identifying high-risk patients earlier, support clinical decision making and ultimately decrease the incidence of sepsis-associated AKI in our healthcare system.

Methodology

It was a descriptive cross-sectional study which was carried out in the Department of Medicine of a tertiary care teaching hospital. The study was conducted for a six months' period of time from 1st January 2024 till 31st July 2024. The aim of the study was to compare the clinical characteristics and outcomes of acute kidney injury (AKI) in patients admitted to medical wards and who had a diagnosis of sepsis.

All procedures were carried out following the Declaration of Helsinki. Consent was obtained from all participants, or their attendants, before any participant is included in the study.

This was a source population comprising all patients ≥ 18 years admitted to the medical wards with a diagnosis of sepsis during the study period.

Inclusion Criteria

- Patients aged ≥ 18 years
- Septic cases (Sepsis-3 criteria)
- The proportion of students admitted to medical wards during the period of study:
- Patients who were informed and consented

Exclusion Criteria

- Known cases of end-stage renal disease on maintenance dialysis
- Patients with obstructive uropathy as primary cause of renal failure
- Patients discharged or transferred before completion of baseline evaluation
- Pregnant females

Sample Size Calculation

Sample size was determined using the WHO sample size calculator, with a 40% expected prevalence of sepsis associated AKI, a 95% confidence level and a 8% margin of error. The sample size was calculated to be 150 patients.

Consecutive sampling technique was employed as a non-probability sampling technique. All patients who met the study requirements during the study period were enrolled in the study until the required number of study patients were reached.

Operational Definitions

Sepsis: Sepsis-3 criteria: Life-threatening organ dysfunction resulting from a dysregulated host response to infection [1].

Acute Kidney Injury (AKI): Defined and staged based on KDIGO criteria: rise in serum creatinine and/or reduction in urine output [2]. Sepsis-associated AKI: An AKI that occurs in a patient with a diagnosis of sepsis while in the hospital.

The demographic information, such as age, gender, and comorbidities (diabetes mellitus, hypertension, chronic liver disease, and chronic kidney disease) were noted. Fever, hypotension, oliguria and septic shock were recorded as clinical features. Laboratory tests included complete blood count, serum creatinine, blood urea nitrogen, electrolytes and urine output monitoring. The automated biochemical analyzer (Roche Cobas c311, Roche Diagnostics, Mannheim, Germany) was used to measure serum creatinine. The collection of the urine was done with a calibrated urinary catheter collection system.

The outcomes that were evaluated during the patient's hospital stay were:

- Development of AKI
- The need for intensive care unit (ICU) admission.
- The need for renal replacement therapy (RRT)
- The duration of hospital stays. The time spent in hospital.
- In-hospital mortality

No investigational drugs or experimental interventions were administered, but standard treatment for sepsis and AKI was provided as per hospital protocol, using intravenous antibiotics, fluid resuscitation, vasopressors and supportive treatment as needed.

The data were analyzed using Statistical Package for Social Sciences (SPSS) version 27.0 (IBM Corp., Armonk,

NY, USA) and entered. Quantitative variables like age and hospital stay were expressed as mean $\pm$ SD. Qualitative data (gender, comorbidities, admission to ICU, mortality, and occurrence of AKI) were presented as frequencies and percentages.

Chi-square test was used to analyze the association of categorical variables. P values <0.05 were deemed to be significant. Odds ratios (OR) with 95% confidence intervals (CI) were computed when applicable to quantify the association. No post-hoc or subgroup exploratory analyses performed; all analyses were pre-specified.

Results

The data of 150 patients who were admitted to the medical wards with sepsis was analysed. There were no dropouts from the study. Data were analyzed statistically in SPSS version 27.0 (IBM Corp., Armonk, NY, USA). The average age of the patients was 56.4 ± 14.2 years and the ratio of male to female patients was 61.3:38.7. Of the comorbid conditions, 41.3% had hypertension, 36.0% had diabetes mellitus, 14.0% had chronic liver disease, and 12.0% had pre-existing chronic kidney disease (Table 1).

Table 1: Demographic and Clinical Characteristics of Patients (n = 150)	
Variable	Frequency (%)
Mean age (years)	56.4 ± 14.2
Male	92 (61.3%)
Female	58 (38.7%)
Diabetes mellitus	54 (36.0%)
Hypertension	62 (41.3%)
Chronic liver disease	21 (14.0%)
Chronic kidney disease (baseline)	18 (12.0%)

AKI was strongly correlated with more severe clinical characteristics such as septic shock, hypotension, oliguria and higher serum creatinine levels. Septic shock was present in 53.4% of AKI patients compared to 19.6% in non-AKI patients. Oliguria was noted in 62.1% and 13.0% and hypotension was noted in 72.4% and 31.5% respectively. The serum creatinine was elevated in all AKI patient's vs 15.2% of non-AKI patients and all associations were significant ($p < 0.001$) (Table 2).

Table 2: Comparison of Clinical Features in AKI and Non-AKI Patients			
Clinical Feature	AKI (n=58)	Non-AKI (n=92)	p-value
Septic shock	31 (53.4%)	18 (19.6%)	<0.001
Oliguria	36 (62.1%)	12 (13.0%)	<0.001
Hypotension	42 (72.4%)	29 (31.5%)	<0.001

Elevated serum creatinine	58 (100%)	14 (15.2%)	<0.001
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In terms of outcomes, patients with AKI had markedly poorer clinical outcomes. The 50.0% of patients with AKI were admitted to the ICU compared to 18.5% of non-AKI patients ($p < 0.001$). Renal replacement therapy was needed in 20.7% of patients with AKI compared to no dialysis being required for patients without AKI. Hospital stay was significantly longer in patient with AKI (11.8 ± 4.6 days) than the non-AKI patient (7.2 ± 3.1 days). In-hospital mortality was significantly higher in AKI patients (31.0%) compared to non-AKI patients (9.8%) with a statistically significant difference ($p = 0.002$) (Table 3).

Table 3: Outcomes of Patients With and Without AKI			
Outcome	AKI (n=58)	Non-AKI (n=92)	p-value
ICU admission	29 (50.0%)	17 (18.5%)	<0.001
Renal replacement therapy	12 (20.7%)	0 (0%)	<0.001
Mean hospital stay (days)	11.8 ± 4.6	7.2 ± 3.1	<0.001
Mortality	18 (31.0%)	9 (9.8%)	0.002

Acute kidney injury was seen in 38.7% of septic patients, and was significantly related with septic shock, hemodynamic instability, length of hospitalization, higher rates of staying in the ICU and mortality.

Discussion

In the present study, acute kidney injury (AKI) was identified as a clinical phenomenon that is highly prevalent and clinically relevant in medical wards of patients with sepsis, having significant associations with disease severity and adverse outcomes. The results of this study are consistent with the available evidence from around the world that sepsis continues to be the most common cause of AKI in hospitalized patients and that this complication is strongly linked with morbidity and mortality.^{13,14}

These were some indications of serious illness (septic shock, hypotension, oliguria), which were found to be closely associated with AKI. This has been observed in other large multicenter cohort studies, in which hypotension and the need for vasopressors were found to be strong predictors of the onset of AKI in septic patients [15,16]. In modern knowledge though, sepsis-associated AKI is not only caused by hypoperfusion of the kidneys, but is also a result of complicated inflammatory and microcirculatory processes.¹⁷ Although renal blood flow is preserved, there is still significant renal cellular damage due to endothelial injury, cytokines induced inflammation and mitochondrial dysfunction.¹⁸

In the current study, patients who developed AKI had significantly poorer clinical outcomes with higher rates of admission to the intensive care unit, renal replacement therapy use, hospital stay and mortality. These results are in line with previous studies based on a large cohort of septic patients that showed that AKI is independently associated with in-hospital mortality.^{19,20} In addition, SA-AKI has been demonstrated to be related to short- and long-term adverse events such as progression to chronic kidney disease and higher cardiovascular risk after hospital discharge.²¹

The mortality rate in our study is similar to the international data, which shows that mortality in septic patients complicated by AKI is still considerably higher than in septic patients without renal involvement [14,19]. This requirement for renal replacement therapy in a subgroup of patients further demonstrates the severity of renal dysfunction in sepsis and its effects on the utilization of healthcare resources.²⁰

An important feature of this study is that it is an examination of admissions to general wards of hospitals rather than intensive care units. Most literature regarding SA-AKI comes from patients in the ICU, but a significant number of septic patients are first treated in the general ward, especially in LIMC. Delayed recognition of AKI in non-ICU settings has been shown to have worse outcomes which may reflect limited monitoring and delayed escalation of care.^{16,22} This emphasizes the need to use early warning systems and to have regular monitoring of renal function in the ward.

This study also found that common comorbidities were diabetes mellitus, hypertension, and chronic liver disease in these patients with AKI. These are well known risk factors for SA-AKI, due to decreased renal reserve, endothelial dysfunction and impaired immune response.^{15,21} Other studies have found that chronic kidney disease is a risk factor for AKI and is a predictor of poor outcomes in septic cases.¹⁹

The study has implications for clinical practice, highlighting the need for early identification and prevention measures. With the use of KDIGO criteria, AKI can be detected in a timely fashion, which enables early corrective measures like optimization of hemodynamics, avoidance of nephrotoxic agents, as well as appropriate antimicrobial therapy, etc.¹⁷ Early goal-directed sepsis management has been found to be beneficial in high-risk patients for renal outcome and mortality.¹⁸

Limitations: There are a number of limitations to this study. One problem is that it was carried out in a single tertiary care hospital, so it is not generalizable. Second, the observational study design makes it impossible to make causal inferences between the risk factors and the outcomes. Thirdly, there were no severity scoring systems included which might have helped to improve the risk stratification. Fourthly, their long-term renal outcomes were not assessed after discharge, so they only assessed the progression to chronic kidney disease. Long-term follow-up multicenter prospective studies are needed to better elucidate the patterns of disease course and recovery in SA-AKI.

Conclusion

Acute kidney injury is a common and severe complication in patients with sepsis in medical wards. It is closely linked to septic shock, hemodynamic instability, systemic inflammatory response and contributes to poor clinical outcomes (mortality, admission to the intensive care unit (ICU) and hospital stay).

The results of this study highlight the need for early identification of S-AKI, through either use of a standardized criteria, and for timely initiation of appropriate treatment for S-AKI. Improvement of clinical monitoring systems in medical wards and early identification of high risk patients might help to decrease morbidity and mortality related to this condition and lead to better outcomes in patients.

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