

**Analysis of Acute Kidney Injury in Patients with Sepsis Under ICU****Rakesh Roshan**

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Conflict of interest: Nil

**Abstract:****Background:** AKI is a frequent and serious complication in critically ill septic patients in an ICU setting. Progress in the field of critical care has been unable to diminish the association noted between sepsis-associated AKI and prolonged length of stay, morbidity, and mortality.**Aim:** Assess the incidence, risk factors, and clinical implications of AKI in septic critically ill patients in the ICU, using the KDIGO classification.**Methods:** This retrospective observational study was conducted at the Department of Internal Medicine at Gouri Devi Institute of Medical Sciences and Hospital, Durgapur, West Bengal. The study population included 70 adults who were admitted to the ICU with sepsis, based on the Sepsis-3 definitions, and were reviewed for clinical features, comorbidities, laboratory parameters, and outcomes. Acute kidney injury (AKI) was diagnosed and staged according to KDIGO guidelines. Disease severity was determined using the APACHE II score.**Results:** Of the 70 septic patients, 62.9% were male, and most patients were aged between 41 and 60 years old (42.9%). The most prevalent comorbidities included hypertension (42.9%) and diabetes (40%). The most common source of sepsis was respiratory infections (40%). AKI occurred in 60% of patients Stage 1 (25.7%), Stage 2 (20%), and Stage 3 (14.3%). Of the AKI cases, 23.8% required renal replacement therapy. Complete renal recovery was achieved in 47.6%, partial in 19%, and 9.5% had no recovery or died. The mean APACHE II score was  $21.6 \pm 6.4$ , and the mean ICU stay was  $8.5 \pm 3.2$  days.**Conclusion:** Sepsis-related acute kidney injury (AKI) is common and has significant consequences on outcomes for patients in the intensive care unit (ICU). Early identification, hemodynamic optimization, and timely initiation of renal support are essential for improving prognosis.**Keywords:** Sepsis, Acute Kidney Injury, KDIGO Classification, ICU, Renal Replacement Therapy, MortalityThis is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.**Introduction**

Due to the use of a number of definitions and diagnostic criteria, there has been unnecessary confusion and heterogeneity among the clinical and research communities about the diagnosis of acute kidney injury (AKI). AKI is a relatively new term that replaces the former term acute renal failure who is an acute loss of renal function occurring over hours to days. Without a standardized diagnosis, it became impossible to make comparisons between studies, measure outcomes, or make treatment protocols [1]. To try to resolve this, the Acute Dialysis Quality Initiative (ADQI) group devised the RIFLE classification system, which is an important step for standardization of the diagnosis and assigning severity of acute kidney injury.

The RIFLE criteria, which consist of Risk, Injury, Failure, Loss of function, and End-stage kidney disease. The RIFLE criteria represent a classification of AKI characterized by alterations in serum creatinine (Scr) and glomerular function rate (GFR) as well as urine output. This classification aided in identifying

the continuum of renal dysfunction, from mild impairment to complete kidney failure, that a clinician will see [2]. Furthermore, the RIFLE classification has demonstrated good correlation with clinical outcomes-mortality and morbidity during hospitalization-in multiple studies, thereby confirming its prognostic legitimacy in different populations of patients.

Over time, it became evident with clinical experience that the RIFLE criteria had some inherent limitations beginning with, perhaps the largest impetus for change, reference creatinine, which is not often available, or reliable in acutely ill patients. Furthermore, subtle but clinically significant increases in serum creatinine may be missed, ultimately resulting in an underestimation of early or mild AKI. To increase clinical applicability and improve diagnostic accuracy, the Acute Kidney Injury Network (AKIN) developed a neutering staging system in the summer of 2007. The AKIN system was built upon the RIFLE criteria but incorporated some specific

modifications as to how a patient was classified as having AKI [3].

In the updated AKIN classification, AKI was recast as an abrupt (over 48 hours) decrease in kidney function resulting in an absolute increase in serum creatinine of 0.3 mg/dl (26.4  $\mu$ mol/L), a relative increase of at least 50% from baseline (1.5-fold), or a decrease in urine output to <0.5 ml/kg/h for >6 hours. This definition, especially the new emphasis on small increases in serum creatinine, was supported by relationship with higher mortality and adverse outcomes [4]. Unlike RIFLE, the AKIN classification required at least two serum creatinine values to be obtained within the 48-hour assessment time frame that relieved some of the reliance on clinicians' imprecise estimating of baseline values.

"Another significant distinction is the mapping of stages between the two systems. In the AKIN model, "Risk" corresponds to Stage 1, "Injury" to Stage 2, and "Failure" to Stage 3. It is important to note that Stage 3 includes all patients who require renal replacement therapy, regardless of serum creatinine level or urine output at the initiation of RRT [5]. The class "Loss," which appears in the RIFLE classification as well as "End-stage kidney disease" are excluded because they only represent chronic and not acute kidney injury."

This also improved sensitivity and specificity for diagnosing AKI. The recognition of the fact that changes in creatinine reflecting damage to a structure in the kidney, even small changes, can signify meaningful stress to the kidneys; thus, it was critical to get in front of the diagnosis and act. Moreover, the AKIN system also allows for standardization of criteria which will result in better data comparison across studies, allowing for collaborative, evidence-based management initiatives in AKI with this variability in initiation of RRT for clinical decision making, availability of resources, and overall regional benefits to the patients involved. [6].

In a clinical environment, AKIN classification is particularly beneficial to critically ill and septic patients with AKI as this is a common and severe disorder. Sepsis-related AKI is a unique disorder with an identifiable pathophysiological basis related to inflammatory, hemodynamic and microcirculatory derangements that lead to kidney dysfunction [7]. The presence of AKI in sepsis increases the likelihood of multi-organ dysfunction and mortality and therefore, is an important clinical disorder to identify early within clinical care.

In this study, we aimed to evaluate septic AKI clinical aspects through the AKIN classification and to evaluate its effectiveness in predicting in-hospital mortality in a cohort with a sepsis diagnosis. This approach is a clinically relevant model to assess the severity of illness, as well as estimate and predict outcomes in a population where AKI is frequently a

prognostic determinant. In a recent review of the literature, it was noted that AKI occurs in 20-50% of patients with sepsis, with mortality of severe AKI often greater than 50% [8]. For this reason, a standardized classification system like AKIN can be beneficial not only in assisting clinicians in risk stratification but potentially impact therapy to follow.

In summary, the progression from RIFLE to AKIN was a significant step forward in our knowledge of and classification of acute kidney injury. The changes made in the AKIN criteria specifically, the addition of smaller creatinine increases, and a shorter time frame for diagnosis, increases the identification of subclinical renal injury and enhances prognostic capability. In the setting of sepsis-related AKI, this classification has an important role for both clinicians and researchers in improving early identification, uniformity of reporting, as well as management, of a condition that continues to be a major issue in critical care medicine.

### Methodology

**Study Design:** This was a retrospective observational study performed in the Department of Internal Medicine, Gouri Devi Institute of Medical Sciences and Hospital, Durgapur, West Bengal, India for one year. The study aimed to evaluate the occurrence, risk factors, and outcomes of acute kidney injury (AKI) in patients with sepsis who were admitted to the Intensive Care Unit (ICU).

**Study Area:** The research was conducted in the Intensive Care Unit (ICU) of Gouri Devi Institute of Medical Sciences and Hospital, West Bengal, India

### Study Participants

#### Inclusion Criteria

- Adults ( $\geq 18$  years) admitted to the intensive care unit (ICU) with a clinical diagnosis of sepsis using Sepsis-3 criteria.
- Patients with medical records containing complete clinical, biochemical, and renal function data.
- Patients who had been admitted for at least 48 hours have appropriate scrutiny of trends in kidney function.

#### Exclusion Criteria

- Patients with pre-existing chronic kidney disease (CKD) on maintenance dialysis.
- Post-renal causes of acute kidney injury (e.g., obstructive uropathy).
- Renal transplant recipients.
- Patients with incomplete records or missing laboratory data.

**Sample Size:** The study sample included 70 patients.

**Procedure:** In this retrospective study, all patients with a diagnosis of sepsis admitted to the ICU during the study duration were included. Data was gathered from patient medical records, ICU charts, and laboratory databases. We recorded demographic variables, comorbidities, hemodynamic parameters, laboratory results and treatment variables including use of vasopressors, mechanical ventilation, and length of stay in the ICU. Sepsis was classified using the criteria from Sepsis-3, and the patients were further categorized into sepsis, severe sepsis, and septic shock based on clinical and laboratory parameters.

AKI was diagnosed and staged using KDIGO Criteria, which includes serum creatinine change and urine output. Serum creatinine was assessed daily, and hourly urine output was collected during ICU admission. The APACHE II score was calculated based on the most deranged values during the first 24 hours of ICU admission to assess severity of illness. All patients were fluid resuscitated and hemodynamically stabilized before AKI diagnosis. Outcome measures included need for renal replacement therapy (RRT), length of ICU stay and mortality. Renal recovery was defined as complete or partial recovery based on serum creatinine normalization and dialysis dependence at discharge.

**Statistical Analysis:** Data was entered and analyzed using SPSS version 27. Descriptive statistics were calculated to summarize baseline characteristics. Continuous variables were presented as mean  $\pm$  standard deviation (SD) or median (interquartile range) as appropriate, and categorical variables as percentages.

### Result

Table 1 depicts the baseline demographic and clinical features of the 70 patients in the study. Most patients (42.9%) were aged 41-60 years; the second highest was greater than 60 years (35.7%) and 18-40 years was lowest (21.4%). There was a greater percentage of males (62.9%) in the study compared to females (37.1%). The most common comorbidities were hypertension (42.9%) and diabetes mellitus (40.0%), while chronic liver disease (14.3%) and the most common, COPD (8.6%), was less common; 17.1% of patients had no comorbidities. The principal source of sepsis were respiratory infections (40%), followed by abdominal (25.7%) and urinary tract infections (17.1%). The remaining cases, 11.4%, were soft tissue infections, while the remaining 5.7% included central nervous system and catheter infections.

**Table 1: Study Population's Baseline Clinical and Demographic Features (n = 70)**

Parameter	Number of Patients (n)	Percentage (%)
<b>Age Group (years)</b>		
18-40	15	21.4
41-60	30	42.9
>60	25	35.7
<b>Gender</b>		
Male	44	62.9
Female	26	37.1
<b>Comorbidities</b>		
Diabetes Mellitus	28	40
Hypertension	30	42.9
Chronic Liver Disease	10	14.3
COPD	6	8.6
No Comorbidity	12	17.1
<b>Type of Infection</b>		
Respiratory	28	40
Abdominal	18	25.7
Urinary Tract	12	17.1
Soft Tissue	8	11.4
Others (e.g., CNS, catheter-related)	4	5.7

Table 2 shows the distribution of sepsis severity and important ICU clinical parameters for the population of 70 patients. Of the entire population, 37.1% had sepsis, while 31.4% were considered severely septic and 31.4% were classified as septic shock. This indicates a high proportion of overall patients with advanced stages of disease. Vasopressor support was needed in a little over half of patients (57.1%), while mechanical ventilation was needed in approximately half of our population (45.7%) indicative of the

degree of hemodynamic instability and respiratory insufficiency in this cohort. The mean APACHE II score was  $21.6 \pm 6.4$  which is representative of a moderately high severity of illness and risk of mortality. The average ICU length of stay was  $8.5 \pm 3.2$  days which represents a longer than normal hospitalization due to sepsis-related complications. Overall, the data indicate there is a considerable burden of critical illness in patients with septic illness and a substantial need for organ support interventions.

Parameter	Number of Patients (n)	Percentage (%)
<b>Sepsis Category</b>		
<b>Sepsis</b>	26	37.1
<b>Severe Sepsis</b>	22	31.4
<b>Septic Shock</b>	22	31.4
<b>Vasopressor Use</b>	40	57.1
<b>Mechanical Ventilation Required</b>	32	45.7
<b>Mean APACHE II Score (<math>\pm</math>SD)</b>	21.6 $\pm$ 6.4	—
<b>Mean ICU Stay (days)</b>	8.5 $\pm$ 3.2	—

Table 3 shows the occurrence and classification of AKI (acute kidney injury) among septic patients admitted to the ICU according to KDIGO definitions. There were 70 patients in total and 42 (60%) patients who developed AKI and 28 (40%) patients who did not develop AKI. In the AKI group, Stage 1 was the most common AKI stage (18 patients or 25.7%), followed by Stage 2 (14 patients or 20%) and Stage 3 (10 patients or 14.3%). This demonstrates that most

patients delineated to the AKI group fell within mild-moderate (Stages 1 and 2) AKI level classification and fewer patients fell into severe AKI stage (Stage 3) and required renal replacement therapy. To summarize, the data shows a substantial incidence of AKI in septic patients in ICU as well as the need for early recognition and management of AKI to attempt to prevent further worsening to stage 3 AKI.

AKI Stage	Serum Creatinine Criteria	Number of Patients (n)	Percentage (%)
<b>Stage 1</b>	1.5–1.9 $\times$ baseline or $\geq$ 0.3 mg/dL increase	18	25.7
<b>Stage 2</b>	2.0–2.9 $\times$ baseline	14	20
<b>Stage 3</b>	$\geq$ 3.0 $\times$ baseline or initiation of RRT	10	14.3
<b>Total AKI Cases</b>	—	42	60
<b>No AKI</b>	—	28	40

Table 4 illustrates the renal outcomes of 42 patients who were diagnosed with acute kidney injury (AKI). Renal replacement therapy (RRT) was administered to ten patients (23.8%) indicating a considerable number of patients with significant renal dysfunction. There was total recovery of renal function in 20 patients (47.6%), and 8 patients (19%) had partial

recovery indicating persistent renal dysfunction. Four patients (9.5%) had no recovery or died from AKI, indicating the possibly fatal nature of AKI when it is severe. The mean duration of AKI was 6.3  $\pm$  2.8 days, which reflects a short but clinically significant duration of renal injury in a critically ill population.

Outcome	Number of Patients (n)	Percentage (%)
<b>Required Renal Replacement Therapy (RRT)</b>	10	23.8
<b>Complete Renal Recovery</b>	20	47.6
<b>Partial Recovery</b>	8	19
<b>No Recovery / Death with AKI</b>	4	9.5
<b>Mean Duration of AKI (days)</b>	6.3 $\pm$ 2.8	—

## Discussion

In the current research, most sepsis patients who entered the ICU were middle-aged to elderly, mainly ranging from 41–60 years (42.9%) and over 60 years (35.7%). This age presentation is unsurprising, as older age increases the risk for not only sepsis, but also acute kidney injury (AKI) possibly due to reduced physiological reserve and higher probability of comorbidities. Contrary to most prior studies, which often report equal or nearly equal prevalence rates, we identified a significant male proportion

(62.9%) in the population studied, supporting the previous reports, which have reported a male predominance for reported sepsis and AKI due to higher infection, comorbid disease exposure, and lifestyle-related risk factors. Hypertension (42.9%) and diabetes mellitus (40%) were the other comorbidities in the sepsis population, supporting the role of chronic vascular and metabolic disease in predisposing people to sepsis-associated organ dysfunction and renal injury. Pannu et al., 2013 [9] identified a lower potential risk for unfavorable renal outcomes, or mortality, in community- and hospital-based cohorts

who were categorized as having renal recovery during AKI, defined as returning to within 25% of baseline serum creatinine (SCr) levels.

In the present research, respiratory infections represented the primary source of sepsis (40.0%), followed abdominal and urinary infections, which are consistent with extensive epidemiological studies globally that reported respiratory tract infections as the most common source of sepsis, particularly in the ICU setting. The predominance of respiratory infections may be due to pneumonia and ventilator-associated infections in critically ill patients. Abdominal infections and urinary infections, although less frequent, were identified as relevant sources of sepsis due to potential direct systemic inflammation and multiorgan failure with rapid time management. The range of the different sources of infection highlights the importance of identifying sources of infection and early antimicrobial treatment to prevent complications, such as AKI. Omotoso et al., (2016) [10] found that in a study of hospitalized AKI patients, renal recovery was also strongly linked to a decreased risk for cardiovascular events.

In terms of illness severity, a considerable number of patients in this study were diagnosed with advanced stages of sepsis, 31.4% each with severe sepsis and septic shock. Most of these patients needed vasopressor support (57.1%), and nearly half (45.7%) needed mechanical ventilation, illustrating a heavy burden of both hemodynamic instability and respiratory failure. An average APACHE II score of 21.6 ( $\pm 6.4$ ) suggests a moderate severity of disease, consistent with proxies established from previous cohorts of sepsis patients in the intensive care unit (ICU). An average length of stay of 8.5 days in the ICU provides additional confirmation of the extended treatments and consumption of resources associated with the treatment of sepsis. Together, these findings characterize the impact of morbid sepsis at the level of multiple organ systems in the body and emphasize the need for early recognition, ideal resuscitation, and organ support to reduce mortality. Lopes et al., (2018) [11] reported long-term follow-up for acute kidney injury (AKI) for 234 septic patients. The analysis determined AKI was an independent predictor of death at 2 years, differentiated by the RIFLE criteria.

In this study, AKI occurred in 60% of septic ICU patients, which is consistent with previously established range of 40-70% in critically ill patient populations. Among patients with AKI, Stage 1 (25.7%) or Stage 2 (20%) AKI were more common than a patient who progressed to Stage 3 AKI with renal replacement therapy (14.3%). While these data suggest that the early or mild stages of AKI are more common, there remains a subset of patients who still progress to severe renal failure. The high frequency of AKI can be attributed to evidence of combined hemodynamic instability, nephrotoxic medications,

systemic inflammation, and microcirculatory dysfunction that can occur in sepsis. The findings support the potential for clinical use of KDIGO framework to effectively characterize AKI severity while assisting in the direction of therapeutic interventions in a timely manner that have the potential to limit irreversible renal injury. Rubin et al., (2019) [12] demonstrated an elevated risk of chronic kidney disease development in 232 critically sick patients.

The renal outcomes of this study indicated that nearly half of AKI patients had complete recovery (47.6%), 19% had partial recovery, and 9.5% had no recovery and died from complications related to AKI. These findings are like previously published series that reported variable rates of renal recovery from septic AKI that were affected by age, comorbidities, source of infection, and severity of illness. A mean ( $6.3 \pm 2.8$  days) often signifies that in many cases, the insult was rather brief, possibly because these were identified early, as they were able to manage some of the support. Peri-mortality in patients who do not recover signifies that AKI is a major contributing factor for a poor prognosis in sepsis. This reinforces the need for kidney protective strategies, effective hemodynamic management, and avoidance of nephrotoxins in the treatment. In follow-up study of 2208 patients with septic shock, Kim et al., (2018) [13] found AKI was associated with mortality, but not with the development of CKD.

This research ultimately illustrates the burden of AKI in ICU patients with sepsis. The high burden of co-morbid conditions, high rates of severe sepsis or septic shock, and overall burden of organ support illustrates the complexity of caring for patients of this nature. Identification of those at risk through clinical or biomarker scores and consistent hemodynamic and renal monitoring should be emphasized ahead of time to improve outcomes. Future studies should be undertaken with larger cohorts and longer follow-up periods to ascertain the long-term renal outcomes of targeted interventions in patients with sepsis-related AKI, and in similar circumstances.

## Conclusion

Overall, this study provides evidence supporting the role of MRI in early detection and prognosis in multiple sclerosis. The finding of periventricular and juxtacortical lesions, gadolinium enhancing lesions, as well as multiple T2 lesions, were all intuitively associated with likelihood of future progression in the disease process, or clinically conversion to MS. The ability to use MRI findings to detect early demyelinating changes to be able to prognosticate future disease activity, as well as support our therapeutic decision making, has been emphasized in these findings. The potential frequent use of MRI for ongoing monitoring has significant advantage for not only disease monitoring but also indicates dissemination in terms of time, which aids in clinical

diagnosis. In summary, the overall evidence for the role of MRI in diagnosis and monitoring of suspected multiple sclerosis is substantiated, and the degree of accuracy delineated, adds to the overall diagnostic process, supports earlier diagnosis, ongoing monitoring, and characterizes the possible clinically likely outcomes for patients with multiple sclerosis.

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