Bulletin of Environment, Pharmacology and Life Sciences
Bull. Env. Pharmacol. Life Sci., Vol 15 [8] July 2026. 27-32
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Online ISSN 2277-1808
Journal's URL: http://www.bepls.com
CODEN: BEPLAD

ORIGINAL ARTICLE **OPEN ACCESS**

Lactate Dehydrogenase-to-Albumin Ratio as a Predictor of Acute Kidney Injury in Patients with Sepsis: A Prospective Observational Study

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ABSTRACT
Sepsis-associated acute kidney injury (AKI) is a common and life-threatening complication associated with increased morbidity and mortality. The lactate dehydrogenase-to-albumin ratio (LAR) has emerged as a novel biomarker reflecting both cellular injury and systemic inflammation. This study evaluated the association between LAR and the development of AKI in patients with sepsis. To determine the association between baseline LAR and the development of AKI in patients with sepsis and to evaluate its predictive value for AKI. A prospective observational study was conducted among 90 adult patients with sepsis admitted to Government Medical College and Associated Hospitals, Kota, Rajasthan, India, between December 2024 and December 2025. Baseline LDH and serum albumin levels were measured within 24 hours of admission, and LAR was calculated. AKI was diagnosed according to KDIGO criteria. AKI developed in 50 (55.7%) patients. Mean LAR was significantly higher in patients who developed AKI than in those who did not (33.4 ± 11.2 vs. 18.2 ± 7.6; p<0.001). LAR demonstrated good predictive performance for AKI (AUC=0.81), with a cut-off value of ≥19.1 providing 85.3% sensitivity and 74.1% specificity. Higher LAR also correlated positively with SOFA score and was associated with increased in-hospital mortality. Elevated LAR is an inexpensive and readily available biomarker associated with an increased risk of AKI, greater disease severity, and poorer clinical outcomes in patients with sepsis. It may serve as a useful early prognostic marker in routine clinical practice.
Keywords: *Sepsis, acute kidney injury, lactate dehydrogenase, albumin.*

Received 12.05.2026 Revised 27.05.2026 Accepted 30.06.2026

INTRODUCTION

Sepsis is a life-threatening syndrome characterized by organ dysfunction resulting from a dysregulated host response to infection and remains one of the leading causes of morbidity and mortality worldwide. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) define sepsis as suspected or documented infection associated with an acute increase of ≥2 points in the Sequential Organ Failure Assessment (SOFA) score, reflecting the development of organ dysfunction.[1] According to the World Health Organization, sepsis accounts for approximately 48.9 million cases and 11 million deaths annually, representing nearly one fifth of all global deaths.[2] Despite advances in antimicrobial therapy, critical care, and supportive management, the burden of sepsis remains particularly high in low and middle income countries, including India.

Acute kidney injury (AKI) is among the most frequent and devastating complications of sepsis. Based on the Kidney Disease Improving Global Outcomes (KDIGO) criteria, AKI is diagnosed by a rise in serum creatinine, reduction in urine output, or both.[3] Sepsis associated AKI (S-AKI) develops in nearly 40–60% of critically ill patients with sepsis and is associated with prolonged hospitalization, increased need for renal replacement therapy, progression to chronic kidney disease, and significantly higher mortality.[4,5] Unlike ischemic AKI, the pathogenesis of S-AKI involves a complex interplay of systemic inflammation, endothelial dysfunction, microvascular injury, mitochondrial dysfunction, oxidative stress, and immune dysregulation, resulting in impaired renal perfusion and tubular injury even in the absence of overt hypotension.[6]

Early recognition of patients at risk for S-AKI is essential because timely interventions may prevent progression of renal dysfunction and improve clinical outcomes. However, conventional biomarkers such as serum creatinine and urine output are insensitive indicators of early kidney injury, as they often become abnormal only after substantial loss of renal function has occurred. [7] Consequently, there is increasing interest in identifying simple, inexpensive, and readily available biomarkers that can facilitate early risk stratification in septic patients.

Lactate dehydrogenase (LDH) is a cytoplasmic enzyme present in almost all tissues and is released into the circulation following cellular injury, tissue hypoxia, and inflammation. Elevated serum LDH levels have been associated with disease severity, multiple organ dysfunction, and increased mortality in critically ill patients, including those with sepsis and AKI. [8] In contrast, serum albumin is a negative acute-phase reactant whose concentration decreases during systemic inflammation due to reduced hepatic synthesis, increased capillary leakage, and enhanced catabolism. Hypoalbuminemia has consistently been associated with poor clinical outcomes, reflecting the severity of inflammation, endothelial dysfunction, and impaired physiological reserve. [9]

The lactate dehydrogenase-to-albumin ratio (LAR) combines these two routinely measured biochemical parameters into a single index that reflects both cellular injury and systemic inflammatory status. Recent studies have demonstrated that elevated LAR is independently associated with the development of sepsis-associated AKI, higher SOFA scores, prolonged intensive care unit stay, and increased short- and long-term mortality. [10] Compared with novel biomarkers such as neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1), and cystatin C, LAR offers the advantages of being inexpensive, widely available, and easily applicable in routine clinical practice.

Although several international studies have reported the prognostic value of LAR in critically ill patients, prospective evidence from the Indian population remains limited. Considering regional differences in nutritional status, disease profile, and healthcare settings, validation of this biomarker in Indian patients is warranted. Therefore, the present study was undertaken to evaluate the association between baseline lactate dehydrogenase-to-albumin ratio and the development of acute kidney injury in patients with sepsis and to assess its predictive value, along with its relationship to disease severity and in-hospital mortality.

MATERIAL AND METHODS

Type of Study: Prospective observational cohort study.

Study Duration: The study was conducted from December 2024 to December 2025 in the Department of General Medicine, Government Medical College and Associated Hospitals, Kota, Rajasthan, India.

Methodology: A total of 90 consecutive adult patients diagnosed with sepsis according to the Sepsis-3 criteria were enrolled after obtaining informed consent. Baseline demographic details, clinical characteristics, comorbidities, source of infection, and SOFA scores were recorded at admission. Blood samples for serum lactate dehydrogenase (LDH) and serum albumin were collected within 24 hours of admission, and the LDH-to-Albumin Ratio (LAR) was calculated by dividing serum LDH (U/L) by serum albumin (g/dL). Patients were followed throughout their hospital stay for the development of acute kidney injury (AKI), diagnosed according to the kidney disease: Improving Global Outcomes (KDIGO) 2012 criteria. Secondary outcomes included correlation of LAR with SOFA score and in-hospital mortality.

Inclusion Criteria:

- Patients aged 18 years or older.
- Patients diagnosed with sepsis according to Sepsis-3 criteria.
- Admission within 24 hours of sepsis recognition.
- Baseline serum LDH and serum albumin measured within 24 hours of admission.
- Written informed consent obtained from the patient or legally authorized representative.

Exclusion Criteria:

- End-stage renal disease requiring maintenance dialysis
- Patients receiving renal replacement therapy before baseline sample collection
- Decompensated chronic liver disease or acute liver failure
- Hematological malignancy or recent cytotoxic chemotherapy
- Acute hemolysis or grossly hemolyzed blood samples
- Major trauma or major surgery within the preceding 7 days
- Blood transfusion within 24 hours before baseline sampling
- Pregnancy
- Patients expected to die within 24 hours or those with a do-not-resuscitate (DNR) order
- Refusal to provide informed consent

Methodology (Outcome Assessment): Serum creatinine and urine output were monitored daily for 7 days or until discharge/death. AKI was diagnosed and staged according to KDIGO 2012 guidelines. Patients were categorized into AKI and non-AKI groups. The association of baseline LAR with AKI, SOFA score, and in-hospital mortality was evaluated.

Statistical Analysis: Data were analyzed using SPSS version 26.0. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequency and percentage. Comparisons between groups were performed using the independent Student's t-test for continuous variables and the Chi-square test for categorical variables. Receiver operating characteristic (ROC) curve analysis was performed to determine the predictive performance of LAR for AKI, and the area under the curve (AUC), sensitivity, specificity, and optimal cut-off value were calculated. Correlation between LAR and SOFA score was assessed using Spearman's correlation coefficient. Logistic regression analysis was used to evaluate the association of LAR with AKI and in-hospital mortality. A p-value <0.05 was considered statistically significant.

Ethical consideration: The study was approved by Institutional Ethical Committee of Government Medical College, Kota, Rajasthan, India vide order no. Acad/Ethical/clearance/Batch2023/2025/05.

RESULTS

Among 90 patients included in the study, 58 (64.4%) were male and the mean age was 56.8 ± 14.2 years. Diabetes mellitus was present in 36 (40.0%) patients and hypertension in 42 (46.7%) patients. Acute kidney injury developed in 50 (55.7%) patients within 7 days of admission according to KDIGO criteria.

Variable	Overall (n=90)
Age (years)	56.8 ± 14.2
Male sex	58 (64.4%)
Diabetes mellitus	36 (40.0%)
Hypertension	42 (46.7%)
Chronic kidney disease	18 (20.0%)
Chronic liver disease	10 (11.1%)
COPD	14 (15.6%)
ICU admission	52 (57.8%)
Septic shock	28 (31.1%)
LDH (U/L)	412.6 ± 138.5
Albumin (g/dL)	2.9 ± 0.6
LAR	26.7 ± 12.4
Baseline creatinine (mg/dL)	1.3 ± 0.6
Peak creatinine (mg/dL)	2.4 ± 1.1
Total SOFA score	8.6 ± 3.2
RRT required	12 (13.3%)
In-hospital mortality	24 (26.7%)

Table 1: Baseline Characteristics of Study Population

Mean LDH levels were significantly higher among patients who developed AKI compared with those who did not develop AKI (468.2 ± 142.1 vs 348.6 ± 112.4 U/L, $p < 0.001$). Serum albumin levels were significantly lower in the AKI group (2.6 ± 0.5 vs 3.2 ± 0.6 g/dL, $p < 0.001$). Consequently, the lactate dehydrogenase-to-albumin ratio (LAR) was significantly higher in patients with AKI (33.4 ± 11.2 vs 18.2 ± 7.6, $p < 0.001$), suggesting a strong association between elevated LAR and development of renal dysfunction.

Variable	AKI (n=50)	Non-AKI (n=40)
Age (years)	58.2 ± 13.8	54.9 ± 14.6
Male sex	34 (68.0%)	24 (60.0%)
Diabetes mellitus	24 (48.0%)	12 (30.0%)
Hypertension	28 (56.0%)	14 (35.0%)
CKD	14 (28.0%)	4 (10.0%)
CLD	6 (12.0%)	4 (10.0%)
COPD	10 (20.0%)	4 (10.0%)
LDH (U/L)	468.2 ± 142.1	348.6 ± 112.4
Albumin (g/dL)	2.6 ± 0.5	3.2 ± 0.6
LAR	33.4 ± 11.2	18.2 ± 7.6
Total SOFA score	10.2 ± 3.1	6.4 ± 2.3
In-hospital mortality	20 (40.0%)	4 (10.0%)

Table 2: Comparison Between AKI and Non-AKI Groups

The ROC curve analysis demonstrated that LAR had good discriminatory ability for predicting AKI. The area under the curve (AUC) was 0.81, indicating good predictive performance. A LAR cut-off value of ≥19.1 provided a sensitivity of 85.3% and specificity of 74.1% for prediction of AKI.

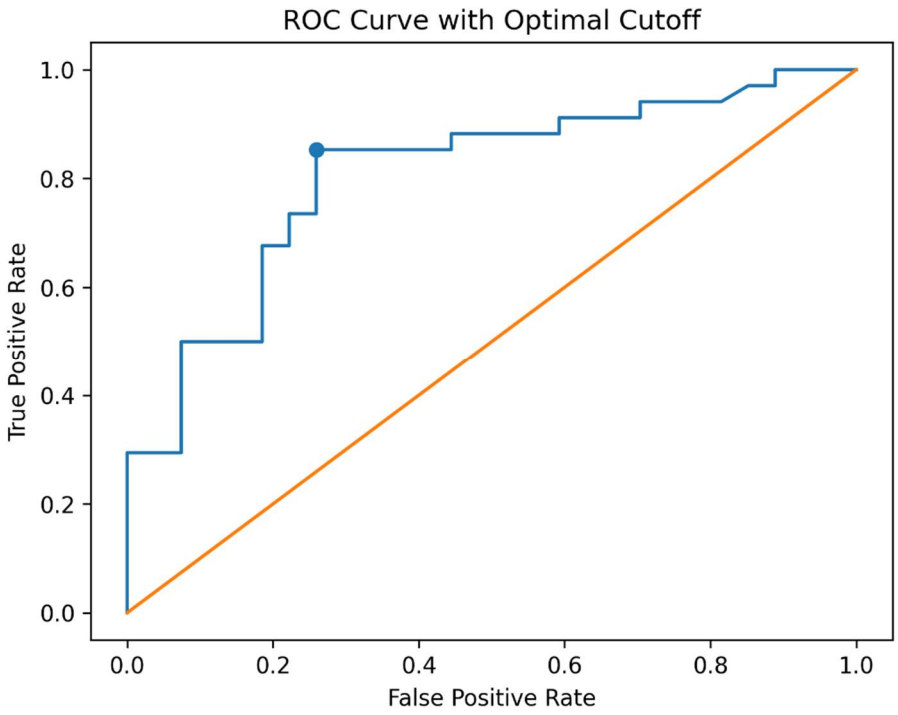

Figure 1: ROC Curve Showing Predictive Ability of LAR for AKI

DISCUSSION

The present study demonstrates that an elevated lactate dehydrogenase-to-albumin ratio is strongly associated with development of AKI in patients with sepsis. The incidence of AKI observed in our study (55.7%) is comparable with previous reports describing sepsis-associated AKI as a common complication in critically ill patients. [11] [12] The significant increase in LDH among AKI patients suggests increased cellular injury, tissue hypoxia, microcirculatory dysfunction, and metabolic disturbance during sepsis. LDH has previously been associated with severity of inflammation, organ dysfunction, and mortality in critically ill patients. [13] [14]

Lower serum albumin levels in AKI patients may reflect systemic inflammation, endothelial dysfunction, capillary leakage, altered synthesis, and increased catabolism. Hypoalbuminemia has been recognized as

an important marker of poor prognosis in sepsis. [15] The combined marker LAR showed better clinical relevance by integrating tissue injury and inflammatory status. In our study, higher LAR was significantly associated with AKI, higher SOFA score, and mortality. These findings are consistent with Deng et al., who reported LAR as an independent predictor of AKI in patients with sepsis. [16] *Fang et al.* also demonstrated the prognostic role of LAR in septic patients. [10]

The ROC curve demonstrated good predictive performance of LAR with an AUC of 0.81. This suggests that LAR may be useful for early identification of patients at high risk of renal dysfunction before overt clinical deterioration. Unlike expensive biomarkers such as NGAL and KIM-1, LAR can be calculated from routinely available laboratory investigations. [17] [18] The association between elevated LAR and mortality may be explained by the relationship between severe inflammation, cellular injury, and multi-organ dysfunction. Similar inflammatory biomarker-based risk prediction strategies have been explored in sepsis and other critical illnesses. [6] [8]

CONCLUSION

The present study concludes that the Lactate Dehydrogenase to Albumin Ratio (LAR) is a valuable and effective predictor of acute kidney injury in patients with sepsis. Elevated LAR at admission is associated with increased risk of AKI, higher disease severity, and increased mortality. Given its simplicity and availability, LAR can be used as a practical tool for early risk stratification in sepsis patients.

STRENGTHS OF THE STUDY

Includes prospective study design, use of KDIGO criteria, evaluation of a practical biomarker, and assessment of clinically meaningful outcomes.

LIMITATIONS OF THE STUDY

Includes single-center design, moderate sample size, absence of serial LAR measurements, and possible residual confounding.

AUTHORS CONTRIBUTION

SBM and PKC contributed with intellectual content. PKD contributed with data collection and analysis of the data. MS contributed with preparation of the manuscript. All authors contributed equally to the editing and approving the final version of the manuscript.

FINANCIAL SUPPORT: Nil

CONFLICT OF INTEREST: There are no conflicts of interest.

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CITATION OF THIS ARTICLE

Pramod K C, Pawan Kumar D, Shyam B M, and Manoj S. Lactate Dehydrogenase-to-Albumin Ratio as a Predictor of Acute Kidney Injury in Patients with Sepsis: A Prospective Observational Study. Bull. Env. Pharmacol. Life Sci., Vol 15 [8] July 2026. 27-32