

Assessment of Prognostic Value of Lactate/Albumin Ratio in Sepsis

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How to citation this article: Vivek Bajaj, Manan Agarwal, Nikhil Gupta, Manjula Gupta, Simmi Dube, “Assessment of Prognostic Value of Lactate/Albumin Ratio in Sepsis”, IJMACR- March - 2025, Volume – 8, Issue - 2, P. No. 201 – 207.

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Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background: Sepsis is one of the leading causes of mortality and morbidity in intensive care units (ICUs) worldwide. Despite advances in medical care, the burden of sepsis remains significant, with high incidence and mortality rates reported globally and in India. Identification and prognostication of sepsis at an early stage is crucial for improving patient outcomes.

Objectives: This study aims to assess the prognostic value of the lactate-to-albumin ratio (LAR) in patients with sepsis.

Methodology: A prospective observational study was conducted over one year (2022-2023) involving 100 patients admitted with sepsis to the ICU of Gandhi Medical College and Hamidia Hospital, Bhopal. Serum lactate levels and serum albumin levels were recorded. The lactate-to-albumin ratio was calculated for each patient. Statistical analysis was performed using IBM

SPSS version 20. ROC curve analysis was used to evaluate the optimal cut-off value for the lactate-to-albumin ratio in predicting in-hospital mortality. A p-value of less than 0.05 was considered statistically significant.

Results: The results demonstrated a significant correlation between high lactate-to-albumin ratio and adverse sepsis outcomes. Patients with higher lactate-to-albumin ratio values had increased in-hospital mortality rates and longer ICU stays.

Conclusion: The findings suggest that the lactate-to-albumin ratio is a robust prognostic marker that can aid in early risk stratification of sepsis patients, potentially guiding therapeutic decisions and improving clinical outcomes ultimately reducing its associated morbidity and mortality.

Keywords: Sepsis, Lactate, Albumin, Lactate-to-albumin ratio

Introduction

According to the Sepsis-3 guidelines, sepsis is a dysregulated host response to infection is characterized by lethal organ dysfunction¹. Sepsis leads to high mortality rates and is an important cause of ICU admissions worldwide. Estimates from the WHO indicate the prevalence of sepsis to be 48.9 million cases in 2017, with 11 million fatalities. Sepsis is reported to be 56.4% common in ICUs in India, with fatality rates ranging from 20% to 50%^{3,4}. The epidemiology of sepsis in India is poorly understood, however, according to a large multicentric study conducted on 135 ICU, the prevalence of sepsis was 56.4% and according to the definition of sepsis 2 and sepsis 3, the prevalence of sepsis was 46.2% and 33.2% respectively, with a mortality rate of 27.6%⁵.

Sepsis outcomes are predicted using multiple prognostic indices such as Logistic Organ Dysfunction System (LODS), Acute Physiology and Chronic Health Evaluation II (APACHE II), Sequential Organ Failure Assessment (SOFA), and Multiple Organ Dysfunction Score (MODS)^{2,6,10}. However, these indices frequently offer forecasts that are too late, underscoring the importance of early and trustworthy biomarkers for prompt diagnosis and treatment. Sepsis is difficult to diagnose and treat early. Several indicators have been investigated for their ability to help with early diagnosis and prognosis, including blood glucose, total leukocyte count, serum albumin, platelet count, serum lactate, and procalcitonin^{11,12}. Serum albumin and lactate levels have demonstrated promise among them. While hypoalbuminemia shows the degree of underlying inflammation, elevated serum lactate implies tissue hypoperfusion and reduced oxygen supply¹³.

Historically, hyperlactatemia, tissue hypoperfusion, and systemic arterial hypotension have been linked to septic shock. The updated definition calls for the use of vasopressors to sustain a mean arterial pressure (MAP) of more than 65 mmHg and serum lactate levels greater than 2 mmol/L in cases of persistent hypotension. Reduced clearance of lactate in septic shock is a result of liver and renal disease. To direct resuscitation operations, lactate levels must be monitored; values greater than 2 mmol/L signify a serious state¹⁴.

One essential plasma protein, albumin, is involved in substance transport, pH regulation, and oncotic pressure maintenance. Serum albumin <35 g/L is known as hypoalbuminemia, and it is commonly observed in elderly hospital patients, malnourished individuals, and those with severe chronic illnesses¹⁵. Extended hospital stays, a higher rate of morbidity and death, and a higher rate of readmissions are all linked to low albumin levels. Reduced liver synthesis, greater loss, or redistribution can all lead to hypoalbuminemia. Increased vascular permeability in sepsis causes albumin to be lost into the interstitial space, which exacerbates hypoalbuminemia and worsens the prognosis¹⁶.

Lactate to albumin ratio has been identified as a potential combination biomarker for improved sepsis prognosis¹⁷. The lactate-to-albumin ratio provides comprehensive data on nutritional status and physiological changes, and these data can be very helpful in risk assessment and sepsis treatment. The lactate-to-albumin ratio is regarded as a reliable prognostic indicator of sepsis in several research studies. Multi-organ dysfunction and increased mortality are linked to elevated lactate-to-albumin ratio. The lactate-to-albumin ratio was discovered by Wang B et al. (2015) to be an independent predictor of mortality and multi-organ dysfunction syndrome (MODS)¹⁸. The

prognostic value of the lactate-to-albumin ratio in ICU patients was validated by Lichtenauer M et al. (2017), who proposed a threshold of 0.15 for unfavourable outcomes¹⁹. Shin J et al. (2018) emphasized that when it comes to 28-day mortality prediction, the lactate-to-albumin ratio is more reliable than lactate alone²⁰. According to Bou Chebl R et al. (2020) (2021), the Lactate-to-albumin ratio is a reliable indicator of mortality in sepsis and septic shock²¹. The lactate-to-albumin ratio is a useful measure for risk classification in critically ill patients and routinely performs superior than lactate alone in predicting in-hospital death.

The purpose of this study is to assess the significance of the lactate-to-albumin ratio in patients with sepsis admitted to a tertiary care hospital. The study aims to examine the usefulness of serum lactate and albumin levels and their ratios in risk classification and prediction of outcome in patients with sepsis.

Methodology

Our study is a prospective observational study and was carried out at Gandhi Medical College and Hamidia Hospital in Bhopal over a year. The objective was to assess the lactate/albumin (LA) ratio's predictive significance in sepsis patients. The study comprised a total of 100 sepsis patients as determined by the Systemic inflammatory response syndrome (SIRS) Criteria.

Inclusion Criteria

1. Patients with sepsis admitted to ICU.
2. Patients meeting SIRS criteria.

Exclusion Criteria

1. Patients requiring albumin supplementation (e.g., nephrotic syndrome, liver disease, burns).
2. Trauma patients.
3. Patients under 18 years old.

4. Pregnant females with sepsis.
5. Patients with malignancy.

Data Collection

Data collection involved patient history, sociodemographic variables, clinical presentation, comorbidities, physical examination, vitals, anthropometric measurements, and input/output charting. Specific investigations included complete blood count, random blood glucose, renal and liver function tests, serum lactate, serum albumin, arterial blood gas analysis, blood culture, and urine culture. The Systemic inflammatory response syndrome (SIRS) criteria were used to assess eligibility. The primary focus was the analysis of blood samples to calculate the lactate-to-albumin ratio. Patients were observed during their hospital stay to record the in-hospital mortality. Data analysis was performed using IBM SPSS software version 20. ROC curve analysis was used to determine the optimal lactate-to-albumin ratio cut-off, A p-value <0.05 was considered statistically significant.

Observations and Results

The mean age in our study was 47.31±17.33 years and the mean age of males and females was 46.39±16.29 and 48.82±19.04 years respectively. The most common diagnosis among patients with sepsis was pneumonia (43%), out of which 5 cases were associated with Diabetic Ketoacidosis (DKA), 4% were associated with Chronic obstructive pulmonary disease (COPD), 3% with acute liver failure, and 2% with aspiration pneumonia. This was followed by urinary tract infections (UTI) (17%) and among them, 10% of cases had simple UTI whereas 7% cases had complicated UTI. 12% of cases presented with DKA, which was associated with pneumonia, diabetic foot, acute pancreatitis, and UTI in 5%, 4%, 2%, and 1% cases

respectively. About 8% of cases had tuberculosis- either pulmonary (4%) or extrapulmonary (4%), 5% cases were known case of COPD, 5% cases presented with acute liver failure which was associated with Spontaneous Bacterial Peritonitis (SBP) in 2%. The spectrum of underlying conditions associated with sepsis is described in Figure 1. Out of 100 cases with sepsis enrolled in our study, we documented mortality in 56% of cases.

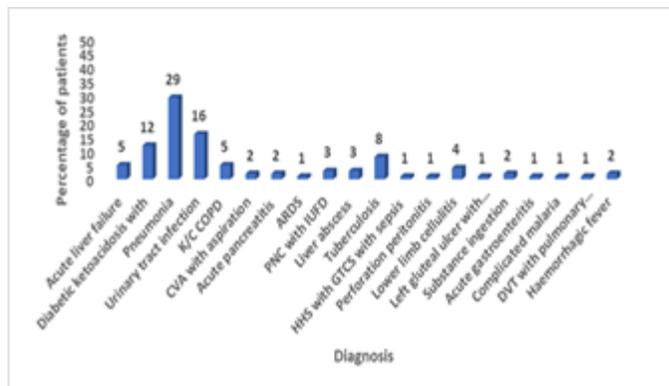


Figure 1: Distribution of cases according to diagnosis

Laboratory Findings and LAR

The mean serum lactate levels in patients with sepsis were 4.1 ± 2.2 mmol/L at day 0, which decreased to 2.97 ± 1.48 at day 1, 2.2 ± 1.1 at day 3, and 2.03 ± 1.61 at day 5. Overall, mean serum lactate levels at all the observations were documented to be significantly higher among patients with sepsis who died during illness as compared to those who survived and were discharged ($p < 0.05$).

Mean serum albumin levels were 2.87 ± 0.51 at day 0, 2.76 ± 0.45 at day 1, 2.7 ± 0.46 at day 3, and 2.89 ± 0.55 at day 5. Mean serum albumin levels were found to be significantly higher in cases with favourable outcomes who were discharged at day 0, day 3, and day 5 as compared to those who died ($p < 0.05$). The mean serum lactate to albumin ratio in cases with sepsis at day 0 was 1.49 ± 0.60 , which was higher among non-survivors (2.27 ± 1.79) as compared to survivors (0.52 ± 0.24).

Though throughout follow-up, the serum lactate to albumin ratio decreased as compared to baseline, but throughout the observation period, the mean lactate to albumin ratio remained significantly higher among non-survivors as compared to survivors ($p < 0.05$).

ROC Curve Analysis

The predictive accuracy of mean serum lactate to albumin levels was highest (0.985; 95% CI- 0.968 to 1) whereas that of serum lactate to albumin levels at day 0 was 0.943; 95% CI-0.899-0.987). At the cut-off of 0.650, the sensitivity of the mean of various observations of Serum lactate/ albumin ratio was 96.4% whereas specificity was 84.1% whereas that of lactate-to-albumin ratio at day 0 was 91.1% and 75% respectively. Similarly, the predictive ability of serum lactate level was also in excellent range (AUC-0.90-1) but serum albumin alone was not a good predictor of mortality (AUC-0.30- 0.40).

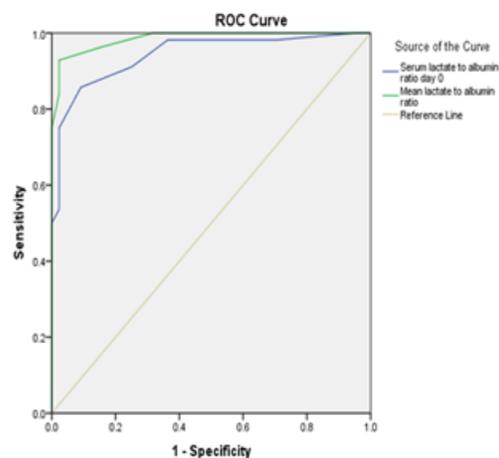


Figure 2: ROC curve analysis for Serum Lactate Albumin Ratio

Discussion

Patients with sepsis often have raised serum lactate levels which are suggestive of cellular dysfunction, enhanced aerobic glycolysis, tissue hypoperfusion, and lactic acidosis. These high values, particularly in situations of septic shock, imply decreased oxygen

delivery and hypoperfusion of the tissues. In our investigation, patients who did not survive had greater serum lactate levels on the day of admission, day 1, day 3, and day 5 than patients who were discharged ($p < 0.05$). In sepsis, serum albumin levels reflect the degree of underlying inflammation; lower levels are associated with more severe inflammation. Serum albumin levels among non-survivors were considerably less than those who survived on the day of admission, day 3, day 5, and on average ($p < 0.05$),

According to our study, the serum lactate to albumin ratio was significantly related to outcomes, with higher ratios observed in patients who did not survive ($p < 0.05$) at all observations except day 5. The shorter hospital stays for non-survivors resulted in higher ratios in these patients ($p < 0.05$). Our results were comparable with those of Chen X et al. (2021), who noticed that non-survivors had decreased serum albumin levels and higher mean lactate levels, which led to a greater lactate-to-albumin ratio²². In a similar vein, Shin J et al. (2018) and Purohit A et al. (2024) discovered noteworthy variations in these biomarkers between individuals who survived and those who did not, confirming the link between poor outcomes and increased lactate and decreased albumin²⁰.

In our study, the ROC curve analysis showed that serum lactate levels are a good indicator of mortality (AUC 0.90-1). Serum lactate had a 92.9% sensitivity and an 84.1% specificity at a cut-off of 1.950. Serum albumin (AUC 0.30-0.40) was a poor predictor of death on its own. However, the lactate-to-albumin ratio had a good predictive value (AUC 0.985), producing a sensitivity of 96.4% and specificity of 84.1% at a cut-off of 0.650. The Lactate-to-albumin ratio on the day of admission saw an AUC of 0.943 for this ratio, with 91.1% and 75%,

respectively, for sensitivity and specificity. Serum albumin levels were the least predictive, while serum lactate alone performed worse than the lactate-to-albumin ratio as a predictor of mortality.

Benge E et al. (2022) identified a strong correlation between greater lactate/albumin ratios and increased mortality in patients with sepsis, which corroborates our findings²³. In a similar vein, Chen X et al. (2021) found that the lactate-to-albumin ratio functioned as a risk factor with a strong relation to poorer prognosis²². Purohit A et al. (2024) also reported that the lactate-to-albumin ratio, with area under ROC curve of 0.99, has excellent predictive power for sepsis mortality²⁴. With an AUC of 0.976, Kabra R et al. (2023) discovered that the lactate-to-albumin ratio was a superior mortality predictor in sepsis cases than either lactate or albumin alone¹⁷.

The predictive power of these biomarkers was comparable, despite Shin J et al. (2018) reporting lower AUC values for the lactate-to-albumin ratio and lactate levels. Our results are further supported by Bou Chebl R et al. (2020), who discovered that the lactate-to-albumin ratio had an area under the curve of 0.67 for hospital mortality prediction.

Conclusion

Based on the results of our study, it could be concluded that though serum lactate level alone is a good predictor of mortality, the lactate-to-albumin ratio is better as a prognostic marker. In sepsis patients as it integrates two biomarkers - lactate and albumin. The use of the Lactate albumin ratio as a prognostic biomarker can aid physicians in early identification of high-risk sepsis patients. This allows for timely intervention and potentially improving outcomes. The simplicity and cost-effectiveness of measuring serum lactate and

albumin levels further support the clinical utility of lactate-to-albumin ratio.

Limitations

This study has several limitations. The small sample size of 100 patients from a single center limits the generalizability of the findings, highlighting the need for a larger, multicentric prospective study. Lactate clearance, a valuable dynamic marker, was not assessed, which may have limited the depth of prognostic evaluation. Additionally, early mortality within five days of ICU admission shortened the follow-up period, restricting the ability to track changes in the serum lactate to albumin ratio among non-survivors over time.

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