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Original Article

Internal Medicine Section

Clinical Utility of Serum Lactate and Albumin in Predicting Mortality in Patients with Sepsis Admitted to the Intensive Care Unit: A Prospective Cohort Study

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ABSTRACT

Introduction: Sepsis is a life-threatening condition characterised by systemic inflammation and multiorgan dysfunction in response to infection. Despite the specificity of prognostic scoring systems such as Sequential Organ Failure Assessment (SOFA) and Acute Physiology And Chronic Health Evaluation II (APACHE II), their limited sensitivity and reliance on multiple laboratory parameters highlight the need for simpler, effective biomarkers. Serum albumin, a negative acute-phase reactant and lactate, an organ hypoperfusion marker, are potential biomarkers for assessing the severity of sepsis.

Aim: To evaluate the prognostic significance of serial serum lactate and albumin levels, as well as their ratio, in predicting outcomes in Intensive Care Unit (ICU) patients with sepsis.

Materials and Methods: This prospective cohort study was conducted in the medical ICU of Yenepoya Medical College and Hospital, Mangaluru, Karnataka, India that included 95 adults admitted to the medical ICU with suspected sepsis, meeting the Sepsis-3 criteria. Serum lactate and albumin levels were measured on days 1, 3 and 5 post-diagnosis. Patient outcomes, including mortality and duration of hospital stay, were documented. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 27.0, which included Pearson's correlation to evaluate relationships between lactate and albumin levels, Student's t-test for group comparisons and Receiver Operating Characteristic (ROC) curve analysis to assess the predictive accuracy of the Lactate/Albumin Ratio (LAR).

Results: The study included 95 ICU patients with sepsis (mean age: 50.25±14.65 years; 63.16% male). Prolonged hospital stays (>15 days) were noted in 61.06% of patients, with 78.94% recovering. Survivors showed rising albumin levels (day 1: 2.82 g/dL; day 5: 3.43 g/dL) and declining lactate levels (day 1: 2.77 mmol/L; day 5: 1.27 mmol/L), while non survivors exhibited minimal increases in albumin (day 1: 2.87 g/dL; day 5: 3.05 g/dL) and persistently elevated lactate levels (day 1: 3.02 mmol/L; day 5: 3.35 mmol/L). On day 5, survivors had significantly higher albumin levels and lower lactate levels than non survivors. The LAR declined in survivors (day 1: 1.07; day 5: 0.54) and demonstrated marked predictive accuracy for mortality on day 5 (AUC=0.81, sensitivity=68%, specificity=95%), with diagnostic accuracy peaking at 89.21%.

Conclusion: The day 5 LAR is a strong predictor of mortality in ICU patients with sepsis. The inverse correlation between lactate and albumin levels underscores their utility for early risk stratification and management of sepsis.

Keywords: Biomarkers, Critical illness, Mortality, Organ dysfunction scores

INTRODUCTION

Sepsis is a life-threatening condition characterised by organ dysfunction resulting from a dysregulated host response to infection. Organ dysfunction can be identified as an acute change in the total SOFA score of two or more points [1,2]. Despite advances in critical care, sepsis remains a leading cause of morbidity and mortality globally, posing significant challenges to healthcare systems. Various predictive scoring systems, such as the SOFA and APACHE II scores, have been developed to assess prognosis. While these tools achieve high sensitivity and specificity in predicting mortality, they often fail to address the dynamic nature of sepsis progression [3], highlighting a growing interest in identifying novel biomarkers to enhance risk stratification and improve clinical outcomes.

In sepsis, low peripheral oxygenation triggers anaerobic glycolysis, leading to increased lactate production. While lactate was historically considered a byproduct of anaerobic metabolism [4], recent research suggests additional mechanisms, including beta-2 adrenergic receptor activation and reduced lactate clearance [5]. Elevated lactate levels are now recognised as indicators of tissue hypoxia and organ perfusion abnormalities, forming the basis for their inclusion in the surviving sepsis guidelines as a key marker for early goal-directed therapy [6]. However, the utility of serial lactate monitoring as a prognostic marker remains debated. Some studies support its predictive value [6,7], while others highlight outcome variability due to methodological differences and patient heterogeneity [8,9].

Serum albumin, another key biomarker, has been identified as a prognostic factor in sepsis [10]. During the early stages of sepsis, cytokine-induced endothelial changes result in capillary leak syndrome, causing albumin to shift from the intravascular to the interstitial space [11]. Declining albumin levels correlate with microvascular changes and may indicate an increased risk of tissue hypoxia [12]. These early alterations in albumin levels may address some of the limitations of traditional scoring systems, such as the SOFA score, in identifying vascular changes during the early course of sepsis [13]. Although lactate and albumin have been individually recognised as prognostic markers, their combined utility in the LAR remains underexplored. Previous studies have primarily focused on lactate clearance or albumin levels independently, with limited attention to their dynamic interplay and serial monitoring [7,8,10-12].

The prognostic value of the LAR has been highlighted in several studies; however, significant gaps remain in its clinical application. Kim S et al., demonstrated the utility of the Lactate/Albumin×Age (LAA) score for predicting mortality in emergency department settings,

but focused only on single-point measurements [14]. Similarly, Chen X et al., emphasised the value of the LAR as a predictor but relied on retrospective, single-centre data without evaluating temporal changes in lactate and albumin [15]. Lau KK et al., extended the use of the LAR to patients with necrotising fasciitis but limited their findings to single-point emergency department measurements and lacked validation across broader populations [16]. Abdou K et al., explored the LAR as a cost-effective prognostic marker in resource-limited settings, demonstrating its utility despite limitations in cohort size and short-term evaluations [17]. Similarly, Krishnamurthy HA and Kishor U, in a separate study, investigated the LAR's predictive accuracy for in-hospital mortality, focusing specifically on day 3 LAR [18]. While both studies highlighted the LAR's potential, they faced constraints related to limited cohort sizes and the absence of long-term trends or serial monitoring over an extended timeframe [17,18].

The aim of the present study was to evaluate the prognostic significance of serial serum lactate and albumin levels, as well as their ratio, in predicting outcomes in ICU patients with sepsis. By incorporating measurements taken on days 1, 3 and 5, the study captures temporal dynamics, providing a comprehensive understanding of the LAR's evolution as a prognostic marker. These findings aim to refine risk stratification, improve predictive accuracy for mortality and enhance clinical decision-making in sepsis management.

MATERIALS AND METHODS

The present prospective cohort study was conducted in the medical Intensive Care Unit (ICU) of Yenepoya Medical College and Hospital, Mangaluru, Karnataka, India, over a 12-month period, from January 2023 to December 2023, with patients presenting with suspected sepsis, as defined by the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) [2]. The Institutional Ethics Committee approved the study (IEC approval number: YEC-1/2022/184) and informed consent was obtained from all participants or their authorised representatives.

Sample size calculation: The sample size for the present study was calculated based on data from a previously conducted study, which indicated that 54.28% of sepsis patients had serum albumin levels below 3.5 g/dL [19]. Using this proportion as the expected prevalence (p=0.5428), with a 95% confidence level ($Z\alpha/2=1.96$) and an absolute margin of error of 10% (E=0.1), a sample size of 95 was determined using the following formula:

$$n=(Z^2\ \alpha/2)\ *p*\ (1-p)/E^2$$

Inclusion and Exclusion criteria: This study included adult patients aged 18 years or older who were admitted to the ICU with suspected or documented infection meeting the Sepsis-3 criteria. Eligible participants were required to have a Sequential Organ Failure Assessment (SOFA) score of two or more, indicating significant organ dysfunction. Specific clinical parameters defining eligibility included a PaO_2/FiO_2 ratio of less than 400 mmHg, a platelet count below 150,000/µL, a bilirubin level exceeding 1.2 mg/dL, a Mean Arterial Pressure (MAP) below 70 mmHg, a Glasgow Coma Scale (GCS) score of less than 13, or a serum creatinine level greater than 1.2 mg/dL. Patients with chronic liver disease, chronic kidney disease, malignancies, or a history of seizures were excluded from the study to minimise confounding factors that could independently influence serum lactate and albumin levels.

Study Procedure

A total of 95 patients who met the inclusion criteria were enrolled in the study. After diagnosing sepsis, serum albumin and arterial/venous lactate levels were measured on days 1, 3 and 5. The LAR was calculated at each time point. Patient outcomes, including mortality and duration of hospital stay, were recorded. Patients were classified as recovered if they were discharged home following clinical recovery, while those who succumbed to their illness during their hospital stay were classified as non recovered.

STATISTICAL ANALYSIS

Data were analysed using SPSS version 27.0. Qualitative variables were expressed as frequencies and percentages, while quantitative variables were presented as means±standard deviations. The student's t-test was used to compare the groups. Pearson's correlation was employed to evaluate relationships between lactate and albumin levels and ROC curve analysis determined the predictive accuracy of the LAR. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The study included 95 ICU patients with sepsis with a mean age of 50.25±14.65 years, males 60 (63.16%) and females 35 (36.84%). Prolonged hospital stays (greater than 15 days) were observed in 61.06% of patients and 78.94% recovered during their hospital stay. Pneumonia was the most common cause of admission (42.1%), followed by pyelonephritis (25.2%) and dengue (13.8%) [Table/Fig-1]. Serum albumin and lactate level trends were documented across all study participants on day 1, day 3 and day 5 [Table/Fig-2,3].

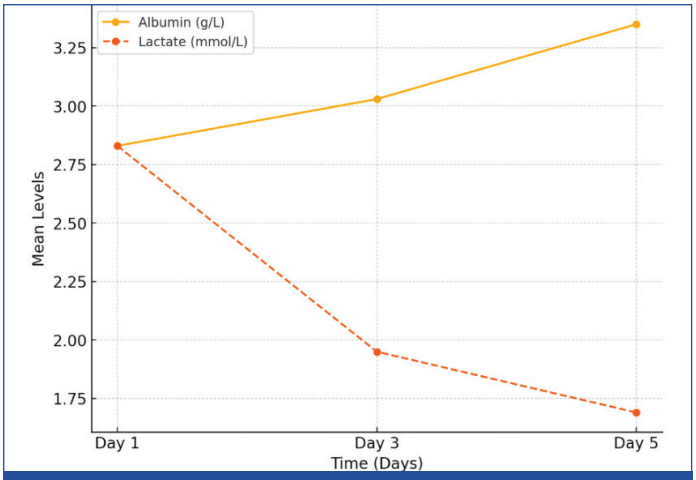
Characteristics	n (%)
Age (years)	
18-64	76 (80)
≥65	19 (20)
Gender	
Male	60 (63.16)
Female	35 (36.84)
Diagnosis	
Pneumonia	40 (42.1)
Pyelonephritis	24 (25.2)
Dengue	9 (13.8)
Leptospirosis	6 (6.3)
Tuberculosis	5 (5.2)
Undifferentiated febrile illness	4 (4.2)
Scrub typhus	2 (2.1)
Acute Gastroenteritis	2 (2.1)
Cellulitis	2 (2.1)
Pelvic inflammatory disease	1 (1)
Duration of hospital stay	
<15 days	37 (38.94)
>15 days	58 (61.06)
Final outcome	
Recovered	75 (78.94)
Death	20 (21.06)
Total	95

[Table/Fig-1]: Distribution of study participants based on demographic and clinical characteristics.

Day	Albumin (g/L) mean±SD	Lactate (mmol/L) mean±SD
Day 1	2.83±0.62	2.83±1.20
Day 3	3.03±0.56	1.95±1.06
Day 5	3.35±0.60	1.69±1.02

[Table/Fig-2]: Trend of serum albumin and lactate levels on days 1, 3 and 5.

Serum albumin levels steadily increased, while serum lactate levels decreased significantly over the study period. Survivors exhibited rising albumin levels (day 1: 2.82 g/dL; day 5: 3.43 g/dL) and



[Table/Fig-3]: Trends of serum albumin and lactate levels on days 1, 3 and 5.

declining lactate levels (day 1: 2.77 mmol/L; day 5: 1.27 mmol/L). In contrast, non survivors had minimal albumin increase (day 1: 2.87 g/dL; day 5: 3.05 g/dL) and persistently high lactate levels (day 1: 3.02 mmol/L; day 5: 3.35 mmol/L). On day 5, survivors exhibited significantly higher albumin levels (3.43±0.59 g/dL) than non survivors (3.05±0.55 g/dL, p=0.01). Conversely, on day 5, lactate levels were significantly lower in survivors (1.27±0.50 mmol/L) than in non survivors (3.35±1.70 mmol/L, p<0.001) [Table/Fig-4].

Variables	Outcome		t-statistic	p-value
	Recovered	Not recovered		
	Mean±SD	Mean±SD		
Albumin (g/L)				
Day 1	2.82±0.59	2.87±0.72	0.35	0.72
Day 3	3.05±0.51	2.96±0.70	0.66	0.51
Day 5	3.43±0.59	3.05±0.55	2.61	0.01
Lactate (mmol/L)				
Day 1	2.77±1.05	3.02±1.70	0.79	0.43
Day 3	1.68±0.51	3.05±1.79	6.02	<0.001
Day 5	1.27±0.50	3.35±1.70	9.50	<0.001

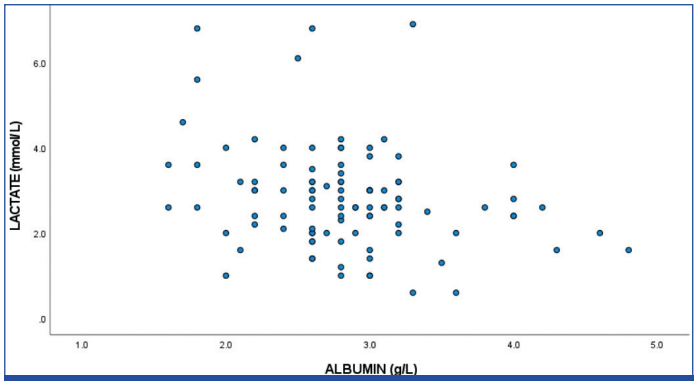
[Table/Fig-4]: Serum albumin and lactate levels by outcome on ICU days 1, 3 and 5.
Test used: student's t-test; p-value <0.05: Statistically significant

Pearson's correlation revealed a significant inverse relationship between serum lactate and albumin levels throughout the study period. On day 1, a weak negative correlation was observed (r=-0.27, p=0.007). The correlation strengthened significantly by day 3 (r=-0.34, p<0.001), indicating improved capillary integrity and perfusion. On day 5, the correlation slightly weakened (r=-0.19, p=0.04), suggesting additional clinical factors influencing outcomes [Table/Fig-5-8].

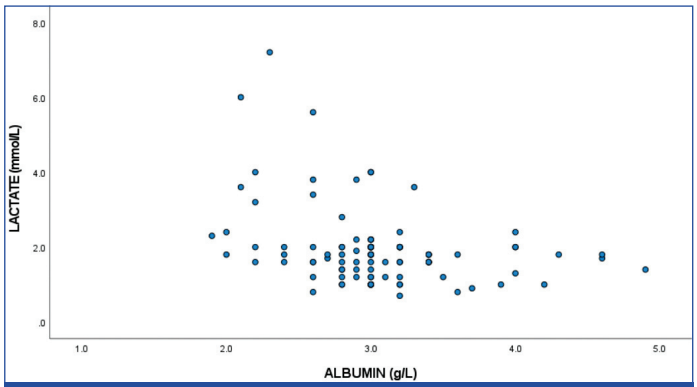
Day	Albumin (g/L)	Lactate (mmol/L)	r	p-value
	Mean±SD	Mean±SD		
1	2.83±0.62	2.83±1.21	-0.27	0.007
3	3.03±0.56	1.95±1.06	-0.34	<0.001
5	3.35±0.60	1.69±1.21	-0.19	0.04

[Table/Fig-5]: Correlation between serial albumin and lactate values among study participants (N=95).

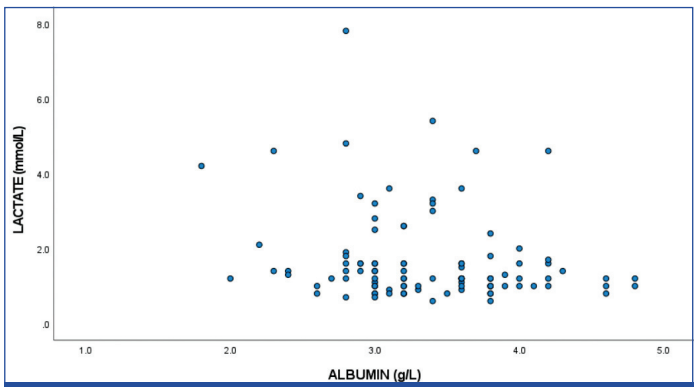
The LAR progressively declined over time, with the mean ratio decreasing from 1.07±0.61 on day 1 to 0.54±0.45 on day 5 among survivors [Table/Fig-9]. ROC curve analysis demonstrated that the day 5 LAR had the strongest predictive accuracy for mortality, with an AUC of 0.81 (p<0.001). At the optimal cut-off determined using Youden's Index, the ratio achieved a sensitivity of 68% and a specificity of 95%. The diagnostic accuracy of the LAR improved over the study period; on day 1, the diagnostic accuracy was



[Table/Fig-6]: Correlation between albumin and lactate values on day 1 among study participants (N=95).



[Table/Fig-7]: Correlation between albumin and lactate values on day 3 among study participants (N=95).



[Table/Fig-8]: Correlation between albumin and lactate values on day 5 among study participants (N=95).

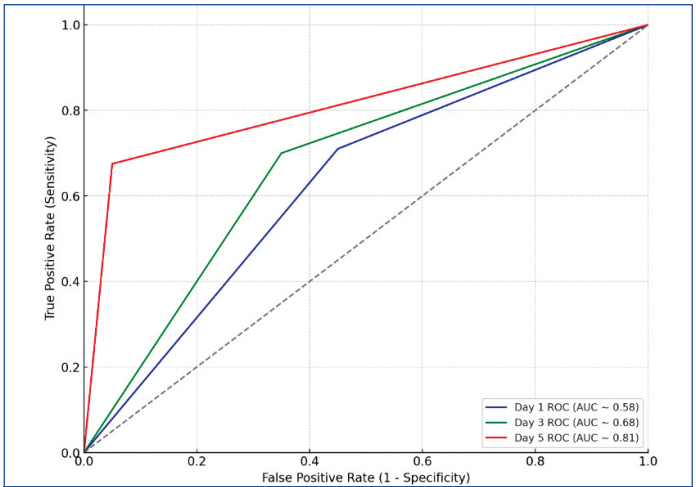
Days	Recovered	Not recovered	p-value
	LAR mean±SD	LAR mean±SD	
Day 1	1.07±0.61	1.40±0.71	0.06
Day 3	0.69±0.48	1.21±0.57	<0.01
Day 5	0.54±0.45	1.08±0.51	<0.01

[Table/Fig-9]: Trend of lactate albumin ratio among study participants.
LAR: Lactate/albumin ratio

50.54%, increasing to 66.05% on day 3 and peaking at 89.21% on day 5. This progression reflects the increasing reliability of the LAR as a prognostic marker for sepsis [Table/Fig-10,11].

DISCUSSION

The present prospective cohort study highlights significant trends in serum lactate and albumin levels among ICU patients with sepsis, demonstrating their prognostic value. Among the 95 patients in the present cohort, lactate levels among survivors progressively declined over time, with mean values decreasing from 2.77±1.05 mmol/L on day 1 to 1.27±0.50 mmol/L on day 5. In contrast, non survivors exhibited persistently elevated lactate levels, with values slightly increasing from 3.02±1.70 mmol/L on day 1 to 3.35±1.70 mmol/L on day 5. On day 5, lactate levels were significantly lower



[Table/Fig-10]: ROC curves with AUC for Lactate/Albumin Ratio (LAR) (Day 1, Day 3 and Day 5).

Variables	Lactate/Albumin Ratio (LAR)		
	Day 1	Day 3	Day 5
Sensitivity	71.3%	70.0%	67.5%
Specificity	45.0%	65.0%	95.0%
Positive predictive value	83.8%	88.9%	98.2%
Negative predictive value	28.1%	35.1%	42.2%
Diagnostic accuracy	50.5%	66.0%	89.2%

[Table/Fig-11]: Sensitivity, specificity, positive and negative predictive value and diagnostic accuracy of Lactate/Albumin Ratio (LAR) (N=95).

in survivors (1.27±0.50 mmol/L) than in non survivors (3.35±1.70 mmol/L, p<0.001). These findings reflect improved tissue perfusion, metabolic recovery and therapeutic efficacy among survivors, while ongoing hypoxia and metabolic derangements persisted among non survivors.

Serum albumin levels in the present cohort demonstrated a contrasting trend. Survivors showed a significant increase in serum albumin over time, from 2.82±0.59 g/dL on day 1 to 3.43±0.59 g/dL on day 5. This trend reflects improved vascular integrity and attenuation of systemic inflammation and capillary leakage, which are key factors in the pathophysiology of sepsis. Conversely, non survivors had persistently low albumin levels, with only marginal increases from 2.87±0.72 g/dL on day 1 to 3.05±0.55 g/dL on day 5. On day 5, albumin levels were significantly higher in survivors (3.43±0.59 g/dL) than in non survivors (3.05±0.55 g/dL, p=0.01).

The inverse correlation between serum lactate and albumin levels observed in the present study—weak on day 1 (r=-0.27, p=0.007), strengthening on day 3 (r=-0.34, p<0.001) and weakening again on day 5 (r=-0.19, p=0.04)—underscores the dynamic interplay between metabolic and vascular factors in sepsis. The LAR emerged as a prognostic marker in the present study. Survivors exhibited a significant decline in the ratio, from 1.07±0.61 on day 1 to 0.54±0.45 on day 5, reflecting combined improvement in perfusion and vascular function. In contrast, non survivors demonstrated consistently elevated ratios, decreasing slightly from 1.40±0.71 on day 1 to 1.08±0.51 on day 5. The difference between day 5 LAR values for survivors (0.54±0.45) and non survivors (1.08±0.51) was statistically significant (p<0.01).

The day 5 LAR showed the strongest predictive accuracy for mortality, with an Area Under the Curve (AUC) of 0.81 (p<0.001), sensitivity of 68% and specificity of 95%.

The findings of the present study on serum lactate levels align with those of Shadvar K et al., who evaluated the LAR in 151 ICU patients with septic shock. Their results demonstrated the prognostic utility of the LAR, achieving an AUC of 0.917 (95% CI: 0.861-0.956, p<0.001) at six hours post-ICU admission, outperforming lactate alone at 24 hours (AUC=0.904, 95% CI: 0.845-0.946, p<0.001) [20]. Similarly, Wang B et al., in a cohort of 54 ICU patients, identified elevated lactate levels and persistent hypoalbuminaemia in patients with Multiple Organ Dysfunction Syndrome (MODS). These findings, consistent with the present observations, highlight the role of lactate as a dynamic biomarker of tissue hypoxia and sepsis severity. Wang B et al., findings on lactate trends further validate the present results, showing that survivors exhibited significant lactate clearance compared to non survivors, reflecting improved metabolic recovery [21].

Serum albumin trends in the present study are consistent with those reported by Krishnamurthy HA and Kishor U, who observed declining albumin levels in septic patients due to systemic inflammation and capillary leakage. In their study of 122 ICU patients, albumin levels decreased from 3.14±0.14 g/dL on day 1 to 3.03±0.13 g/dL on day 3, particularly in non survivors. These trends were mirrored in the present findings, where survivors demonstrated significant increases in albumin over time, contrasting with marginal improvements in non survivors. They also reported a significant increase in the LAR during the same period, with non survivors exhibiting markedly higher values than survivors (day 3: 1.16±0.56 vs. 0.34±0.20, p<0.001). Receiver Operating Characteristic (ROC) analysis revealed excellent predictive performance for the LAR, with an AUC of 0.752 on day 1 and 0.944 on day 3, surpassing both lactate (AUC=0.938) and albumin (AUC=0.203) alone [18]. These findings align closely with our study, where elevated LAR consistently distinguished survivors from non survivors and demonstrated a strong correlation with disease severity and mortality.

Abdou K et al., in a cohort of 80 septic patients, compared the LAR with the C-reactive protein/Albumin Ratio (CAR) and found that the LAR was a superior prognostic marker for mortality prediction. The LAR achieved an AUC of 0.633 (p=0.044) compared to 0.484 (p=0.807) for the CAR, with elevated LAR values associated with poor outcomes, including greater requirements for cardiovascular support and mechanical ventilation among non survivors [17]. Similarly, Lau KK et al., in their study of 262 patients with necrotising fasciitis, demonstrated the LAR's superiority over lactate alone in predicting in-hospital mortality. They identified an optimal LAR cut-off of 1.61, achieving an Area Under the Receiver Operating Characteristic Curve (AUROC) of 0.76, consistent with our day 5 LAR findings. Notably, Lau KK et al., highlighted the synergistic impact of hypoalbuminaemia, with patients having an LAR >1.61 and low albumin levels (<3.0 g/dL) exhibiting significantly higher mortality rates. Their adjusted analysis revealed that the LAR's prognostic value remained significant (adjusted OR=1.48, 95% CI: 1.30-1.75, p<0.01) even after accounting for confounders such as shock, SOFA score and co-morbidities [16].

Chen X et al., in a large-scale study of 4,555 sepsis patients, evaluated the LAR and the composite Lactate/Albumin×Age (LAA) score. While the LAR alone achieved moderate predictive accuracy (AUC=0.61, p<0.0001), combining it with age significantly enhanced its performance (AUC=0.67, p<0.0001). An LAR ≥0.16 was identified as an independent predictor of mortality (p<0.001) in multivariate analysis, along with factors such as age ≥60 years, Body Mass Index (BMI) ≥24 kg/m², SOFA score ≥2 and Simplified Acute Physiology Score II (SAPS II) ≥40 [15]. Similarly, Kim S et al., in their cohort of 3,240 septic patients, introduced the LAA score, which achieved superior predictive accuracy (AUC=0.737) compared to SOFA and APACHE II. While Kim S et al., highlighted the value of incorporating age into prognostic models, our findings reaffirm the LAR's robust standalone performance (AUC=0.81 on day 5). These studies collectively illustrate the importance of integrating biomarkers with demographic and clinical parameters to optimise sepsis risk stratification and guide treatment strategies [14].

Limitation(s)

The influence of other baseline blood parameters and co-morbid conditions was not considered, which may have affected the study outcomes. Additionally, the lack of data on patients' nutritional status could have impacted the interpretation of serum albumin levels. Moreover, the study was conducted at a single centre, which may limit the generalisability of the results. Future multicentre studies with larger and more diverse cohorts are warranted to validate these findings.

CONCLUSION(S)

The present study establishes the LAR as a valuable prognostic tool for ICU patients with sepsis. The findings demonstrate that survivors consistently exhibited lower LARs over time, indicating improved metabolic recovery and reduced mortality risk. The progressive decline in the ratio among survivors, along with its association with mortality, underscores its utility in assessing sepsis progression and patient outcomes. By integrating the LAR into routine clinical practice, clinicians can enhance early risk stratification, prioritise interventions and improve decision-making for critically-ill patients. Future multicentre studies are necessary to validate these findings and standardise their application across diverse clinical settings.

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