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Lactate / albumin ratio as prognostic tool for risk stratification in septic patients admitted to ICU.

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ABSTRACT

INTRODUCTION: Sepsis stands as the primary cause behind intensive care unit (ICU) admissions. The most critical parameters in sepsis management have been shown to be early recognition. Management delays have been associated with increased mortality and morbidity The aim of this study is to study the lactate/albumin (L/A) ratio as prognostic tool for risk stratification in septic patients admitted to ICU.

MATERIALS AND METHODS: This prospective observational study was conducted with100 patients. Admitted in ICU with sepsis and septic shock were studied. Serum lactate/albumin ratio was calculated at the time of admission. Apache 2 and SOFA score was calculated at admission. All patients received initial treatment according standard protocol. All patients were followed up till discharge. An adverse outcome in terms of in hospital mortality, length of ICU stays and inotropic support was used in this study.

RESULTS: Lactate/albumin ratio >1.5(AUC 0.89) correctly predicted in-hospital mortality among 27% patients with sensitivity and specificity of 90% and 78.6% respectively (p value =0.001). Lactate/albumin ratio <1.50 (AUC 0.73) correctly predicted length of ICU stays <72 hours among 17% patients with sensitivity and specificity of 85% and 58.8% respectively (p value =0.001). Lactate/albumin ratio >1.50 (AUC 0.91) correctly predicted requiring inotropic support among 36% patients with sensitivity and specificity of 83.7% and 89.5% respectively (p value =0.001).

CONCLUSIONS: We concluded that lactate/albumin ratio was a stronger parameter than lactate, albumin, APACHE score and SOFA alone in predicting mortality, length of ICU stay and requiring noradrenaline inotropic support among sepsis patients in the ICU.

KEY WORDS: Albumin, lactate, mortality, sepsis.

INTRODUCTION

Sepsis is the primary cause behind intensive care unit (ICU), often coupled with concurrent multiple organ dysfunction syndrome, a leading factor in ICU patient mortality [1,2]. The extensive social and economic impact of sepsis places a substantial burden on healthcare resources [3]. Identifying people at a high risk of death early on is imperative. An alternative tool for risk stratification is the early warning score, which assists clinicians in tailoring timely treatment plans based on individual risk levels [4,5].

Despite the establishment of the Early Goal Directed Therapy (EGDT) guideline in 2001, global trends indicate a higher incidence of sepsis and septic shock, compared to the overall decrease in mortality rates [6]. The prognosis of critically ill patients plays a pivotal role in clinical routines, influencing subsequent therapy strategies, and emphasizing an elevated risk of posthospital discharge mortality. With a focus on long-term prognosis, research indicates an up to 20% increased risk of death in patients with sepsis, along with a greater susceptibility to future septic episodes [7]. Sepsis induces low peripheral oxygenation, triggering anaerobic glycolysis due to insufficient oxygen delivery, resulting in lactate production [8]. Elevated lactate levels correlate with tissue hypoxia. The timely recognition and administration of broad-spectrum antibiotics are critical in the treatment of sepsis, as delays have been linked to increased mortality and morbidity [9,10].

Identifying high-risk patients quickly remains a challenge, prompting ongoing efforts to pinpoint readily available and cost-effective biomarkers for prognostication and risk stratification. A substantial body of literature underscores the strong independent association between serum lactate, a surrogate for tissue perfusion, and mortality in critically ill patients [11,12]. However, relying solely on lactate levels for prognosis presents challenges. An emerging biomarker, the lactate to albumin ratio (L / A), addresses this limitation by incorporating albumin and considering nutritional status. Evidence suggests that serum albumin correlates with morbidity and mortality in critically ill patients, the L/A ratio a predictive tool for mortality and multiple organ failure in cases of sepsis [13]. In light of the limitations associated with lactate as a standalone marker and the imperative for an alternative indicator of disease severity, a growing body of literature has explored the prognostic value of the lactate-albumin ratio in predicting mortality and the onset of multiple organ failure in critically ill patients with sepsis [14].

The most recent definition of sepsis emphasises organ failure, specifically indicating two or more changes in the Sequential Organ Failure Assessment (SOFA) score. Commonly used and readily available predictive indicators include scoring systems such as the Acute Physiological and Chronic Health Evaluation II (APACHE II), the SOFA score, and biomarkers such as lactate (LAC) and procalcitonin (PCT). However, their retrospective establishment based on database analysis raises concerns about significant data loss that affects results. Their limited performance impedes their application to individual risk stratification [15]. In this backdrop, this study aims to investigate the lactate/albumin ratio as a prognostic tool for risk stratification in septic patients admitted to the ICU.

MATERIALS AND METHODS

It was a prospective observational study. It was carried out after approval from the institutional ethics committee (IEC / SHRC / OL / DNS / 23). Inclusion criteria were patients of any sex, age between 18 to 70 years, fever >38.0°C or hypothermia <36.0°C, hypotension <100/65, tachycardia >90 beats/minute, tachypnea >20 breaths/minute, PaO2 <32 mm Hg, leucocytosis >12 x 10^9/L or leucopoenia <4 x 10^9/L, SOFA score >2, lactate >2 mmol/L 18 to 60 years. Patients with chronic liver disease, chronic kidney disease, age less than 18 years and older than 70 years were excluded. The sample size was calculated using the study by Charan J. et al. [16]. The formula used was n = 4 pq / d2, where n is the required sample size, p = prevalence of cause, q = 1-p, d = precision. Taking 80% power, 5% significance level with 0.10 precision, the calculated sample size is 87. In this study, the sample size of 100 was taken for ease of calculation. The study method included patients presenting to the emergency department and admitted to the intensive care unit with sepsis and septic shock that met the inclusion and exclusion criteria. Serum lactate was measured at initial presentation to the emergency department, serum albumin level measured at the time of admission. The serum lactate/albumin ratio was calculated at the time of admission. The Apache 2 and SOFA score was calculated at admission. All patients received initial treatment according to the standard protocol. All patients were followed until discharge. In this study an adverse outcome was used in terms of hospital mortality (IHM), length of stay in ICU, and inotropic support was used in this study. The primary objectives of the study the were to study correlation of the level of the lactate / albumin ratio with organ failure and mortality in sepsis and septic shock. Secondary objectives of the study were to compare the prognostic significance of the serum lactate/albumin ratio with other prognostic indicators (APACHE 2, SOFA score) for adverse outcomes in terms of stay in the length of ICU and in hospital mortality.

In statistical analysis categorical variables were performed in the form of frequencies, percentages and mean ± SD. The unpaired t-test was used to compare continuous variables. The Pearson correlation coefficient was calculated. The analysis was performed by the receiving operating curve (ROC). The area under the curve (AUC) with its 95% confidence interval (CI) was calculated. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) with its 95% CI were calculated. The p value <0.05 was considered significant. All the analysis was carried out on SPSS 16.0 version.

RESULTS

A total of 100 patients were included in the study. More than a third of patients were <30 years of age (44%) followed by 41-50 (20%) and 30-40 & >50 (18%) years. The mean age of the patients was 35.49±14.62 years. About half of the patients were women (51%) and half were males (49%). The mean temperature (in 0C) and mean arterial pressure (mmHg) were 37.94±0.80 and 78.06±15.82 respectively. The mean heart rate and respiratory rate was 114.91±13.60 and 19.08±5.20 respectively. Noradrenaline-inotropic support was given to 43% of the patients.

The mean PaO2 and FiO2% was 72.29±8.74 and 22.33±4.87 respectively. The mean serum lactate and serum albumin was 4.52±1.11 and 3.04±0.18 respectively. In-hospital mortality was in 30% patients. The length of stay in the ICU stays <72 hours was in 20% of patients. The mean length of stay in the ICU was 107.28±53.01 hours (Table 1)

Table 1. Distribution of age (years), hemodynamic parameters, and laboratory parameters.

	Mean±SD
Age (Years)	35.49±14.62 (13-70)
Hemodynamic parameters	
Temperature	37.94±0.80
Mean arterial pressure	78.06±15.82
Heart rate	114.91±13.60
Respiratory rate	19.08±5.20
Laboratory parameters	
PaO2	72.29±8.74
FiO2%	22.33±4.87
Pa02:Fio2	332.59±57.70
Ph	7.30±0.09
HCO3	17.82±4.73
Na	132.40±9.47
K	3.43±0.85
Cr	1.92±1.96
HCT	37.92±8.31
TLC	10105.00±7161.43
Serum bilirubin	2.47±0.94
Platelet count	100.78±46.17
Serum lactate	4.52±1.11
Serum albumin	3.04±0.18

The lactate/albumin, the lactate/abundance, the lactate/volume ratio, theratio, theratio, the APACHE score, thescore, the SOFA score and serum lactateserum lactate were found to be significantly (p=0.001) higher among non-survivors than among survivors. Lactate/albumin ratio, APACHE score, SOFA score and serum lactate were found to be significantly (p<0.01) lower among patients who had a stay in the ICU <72 hours than ≥72 hours. Lactate/albumin ratio, APACHE score, SOFA score and serum lactate were significantly (p=0.001) higher among patients with inotropic support (Table 2).

Table 2. Comparison of parameters with in-hospital mortality, with length of stay in the ICU, with inotropic support.

Parameters with in-hospital mortality	Non survivors	Survivors	p-value[1]
Lactate/Albumin ratio	1.93±0.40	1.32±0.25	0.001*
APACHE score	13.53±6.38	8.79±5.90	0.001*
SOFA score	9.03±2.85	5.86±2.68	0.001*
Serum Lactate	5.70±1.01	4.02±0.71	0.001*
Parameters with length of ICU stay	<72 hours	≥72 hours	p-value[1]
Lactate/Albumin ratio	1.28±0.34	1.55±0.41	0.006*
APACHE score	5.50±5.42	11.39±6.10	0.001*
SOFA score	4.90±1.68	7.29±3.18	0.002*
Serum Lactate	3.94±1.00	4.67±1.11	0.008*
Parameters with Inotropic support	Noradrenaline	None	p-value1
Lactate/Albumin ratio	1.83±0.37	1.25±0.21	0.001*
APACHE score	14.02±.86	7.34±5.21	0.001*
SOFA score	9.77±1.96	4.58±1.46	0.001*
Serum Lactate	5.45±0.98	3.82±0.58	0.001*

[1]Unpaired t-test, *Significant

Lactate/albumin ratio >1.5 correctly predicted in-hospital mortality among 27% of patients with a sensitivity and specificity of 90% and 78.6% respectively. APACHE score >9 correctly predicted in-hospital mortality among 20% of patients with sensitivity and specificity of 66.7% and 67.1%, respectively. The SOFA score >6 correctly predicted in- hospital mortality among 23% of the patients with sensitivity and specificity of 76.7% and 68.6%, respectively. Serum lactate >5 correctly predicted in-hospital mortality among 25% of patients with sensitivity and specificity of 83.3% and 84.3%, respectively (Table 3, Figure 1).

The lactate/albumin ratio <1.30 correctly predicted the length of stay in the ICU stays <72 hours among 17% of 17% of patients with a sensitivity and specificity of 85% and 58.8%, respectively. APACHE score <8 correctly predicted length of ICU stays <72 hours among 15% patients with sensitivity and specificity of 75% and 71.3% respectively. The SOFA score <5 correctly predicted the length of ICU stays <72 hours among 10% of patients with sensitivity and specificity of 50% and 72.5%, respectively. Serum lactate <4 correctly predicted the length of ICU stays <72 hours among 17% patients with sensitivity and specificity of 85% and 60%, respectively (Table 4, Figure 2).

Table 3. Predictive values of parameters in predicting in-hospital mortality.

Parameters	Non survivors (%)	Survivors (%)	AUC 1	Sensitivity	Specificity	PPV	NPV
Lactate/ Albumin ratio							
>1.5	27.0	15.0	0.89	90.0	78.6	64.3	94.8
≤1.5	3.0	55.0					
APACHE score							
>9	20.0	23.0	0.71	66.7	67.1	46.5	82.5
≤9	10.0	47.0					
SOFA score							
>6	23.0	22.0	0.78	76.7	68.6	51.1	87.3
≤6	7.0	48.0					
Serum Lactate							
>5	25.0	11.0	0.90	83.3	84.3	69.4	92.2
≤5	5.0	59.0					

The % of ages are from the total number of cases, 1 p = 0.0001 (significant)

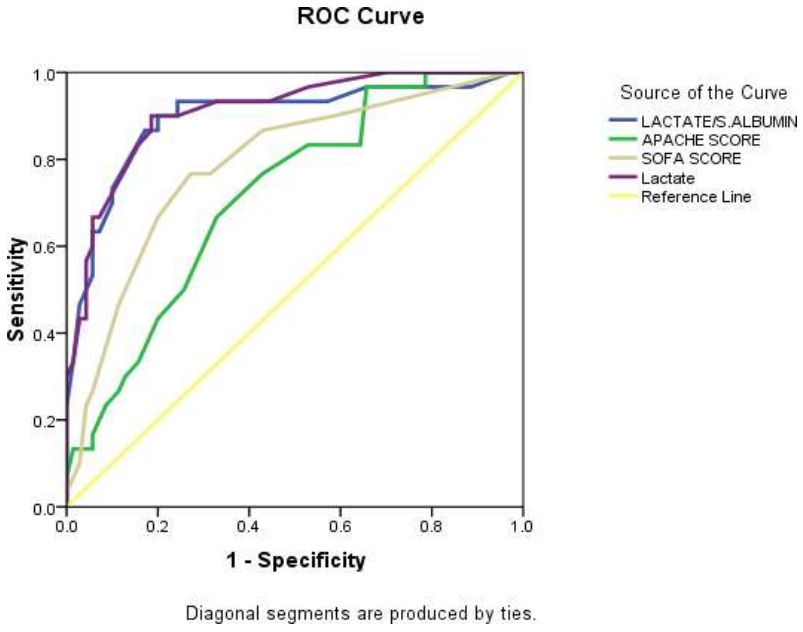

Figure 1. ROC curve showing the sensitivity and specificity of the parameters in predicting in-hospital mortality.

Table 4. Predictive values of parameters in predicting length of stay in the ICU.

Parameters	<72 hours (%)	>72 hours (%)	AUC	Sensitivity	Specificity	PPV	NPV
Lactate / albumin ratio							
<1.30	17.0	33.0	0.73	85.0	58.8	34.0	94.0
≥1.30	3.0	47.0					
APACHE score							
<8	15.0	23.0	0.79	75.0	71.3	39.5	91.9
≥8	5.0	57.0					
SOFA score							
<5	10.0	22.0	0.71	50.0	72.5	31.3	85.3
≥5	10.0	58.0					
Serum Lactate							
<4	17.0	32.0	0.72	85.0	60.0	34.7	94.1
≥4	3.0	48.0					

The % of ages are from the total number of cases, 1 p = 0.0001 (significant)

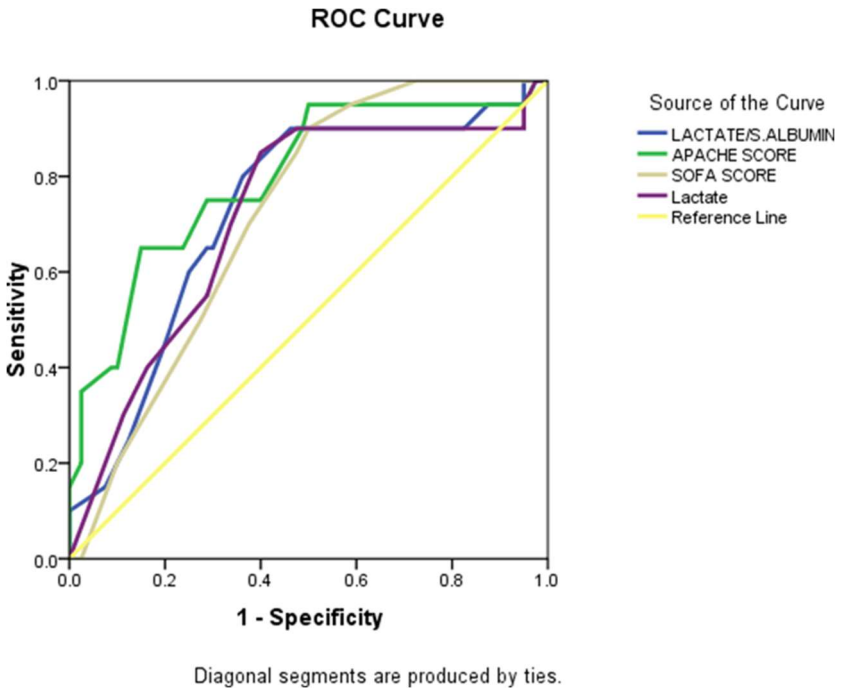

Figure 2. ROC curve showing the sensitivity and specificity of the parameters in predicting the length of stay in the ICU.

Lactate/albumin ratio >1.50 correctly predicted requiring inotropic support among 36% of patients with sensitivity and specificity of 83.7% and 89.5%, respectively. APACHE score >9 correctly predicted the need for inotropic support among 32% of the patients with sensitivity and specificity of 74.4% and 80.7%, respectively. The SOFA score >6 correctly predicted the need for inotropic support among 40% of patients with sensitivity and specificity of 93% and 91.2%, respectively. Serum lactate >4.5 correctly predicted that inotropic support among 38% patients with sensitivity and specificity of 88.4% and 91.2%, respectively. There was a significant (p=0.0001) positive correlation between the study parameters (Table 5, Figure 3).

Table 5. Predictive values of parameters in predicting inotropic support.

Parameters	Noradrenaline	None	AUC	Sensitivity	Specificity	PPV	NPV
Lactate/albumin ratio >1.50	36.0	6.0	0.91	83.7	89.5	85.7	87.9
Lactate/abundance ratio ≤1.50	7.0	51.0					
APACHE score >9	32.0	11.0	0.81	74.4	80.7	74.4	80.7
APACHE score ≤9	11.0	46.0					
SOFA score >6	40.0	5.0	0.97	93.0	91.2	88.9	94.5
SOFA score ≤6	3.0	52.0					
Serum Lactate >5	38.0	5.0	0.92	88.4	91.2	88.4	91.2
Serum Lactate ≤5	5.0	52.0					

The % of ages are from the total number of cases, 1p = 0.0001 (significant).

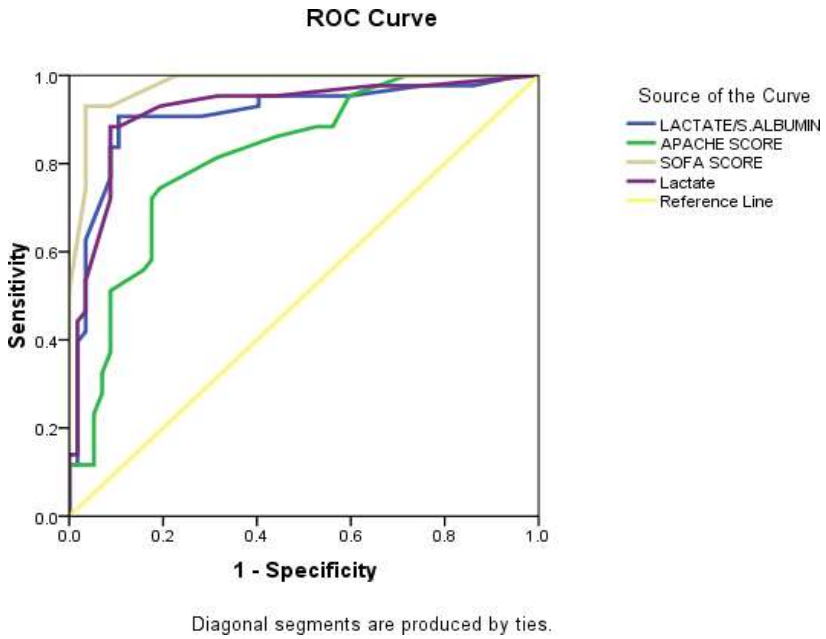

Figure 3. ROC curve showing the sensitivity and specificity of the parameters in predicting inotropic support.

DISCUSSION

Early treatment of sepsis improves the mortality and outcome [13,17]. Aublanc M. et al. stressed that the basic requirement for a sepsis diagnosis is organ dysfunction, which may delay the early identification and treatment of sepsis, thus affecting the prognosis of patients [18]. In-hospital mortality was in 30% patients in this study. Cakir E. et al. observed that the mortality rate was 42.7% (485/1136 patients with sepsis) [19]. In another study by Gharipour et al. the overall mortality of the ICU in the 6414 eligible ICU patients was 16.4% [20]. Li et al. found that the hospital mortality rate in the experimental group was 39.6% (248/626) [21]. Bou Chebl et al. found that overall in-hospital mortality was 58.4% with the mortalities of sepsis and septic shock being 45.8 and 67%, respectively [22].

This study observed that the lactate / omega ratio, APACHE score, SOFA score and serum lactate were found to be significantly (p=0.001) higher among non-survivors than among survivors. Lichtenauer et al. showed that nonsurvivors evidenced higher APACHE2 scores (27.8 vs. 24.5, $p < 0.001$) [14]. Non-survivors higher lactate levels ($p < 0.01$) and lower albumin levels ($p = 0.01$). In the study by Li et al. the median SOFA score was higher in the non-survival group than in the survival group ($p<0.001$) [21]. Bou Chebl et al. showed that the mean L/A ratio for all septic patients was 1.52 ± 1.37 [24]. The non-survivor group showed higher lactate levels (4.50 vs 3.19 mmol/L), lower albumin (2.56 vs. 2.95), and a higher L/A ratio (1.93 vs. 1.20) than the survival subgroup ($p < 0.001$).

This study revealed that Lactate/albumin ratio >1.5, APACHE score >9, SOFA score >6, serum lactate >5 correctly predicted in-hospital mortality 27%, 20% , 23% and 25% patients, respectively. Lichtenauer et al. reported that an optimal cut-off was calculated at 0.15 by means of Youden's index [14]. This cutoff was associated with significantly higher mortality (54% vs. 18%; $p < 0.001$). A lactate/albumin ratio >0.15 was associated with long-term adverse mortality (HR 2.50 95%CI 1.85–3.37; $p < 0.001$). They found that, in the short-term analysis, albumin alone is inferior ($p = 0.0001$) to the lactate/albumin ratio for the prediction of mortality. The lactate/albumin ratio may offer valuable prognostic information on long-term results by combining the dynamic parameter of lactate, reflecting the severity of acute disease, with albumin, a marker indicative of more enduring factors such as nutritional status.

Cakir et al. reported that in ROC analysis for mortality prediction, the area under the curve and the optimal cut-off values were 0.816 and >2.2 mmol/L for lactate, 0.812 and <26 g / L for albumin, and 0.869 and >0.71 for the L/A ratio [19]. The composite measure of the lactate/albumin ratio emerged as a more powerful predictor of mortality among sepsis patients in the ICU compared to the individual parameters of lactate or albumin alone. Gharipour et al. found that L/A showed a receiver operating characteristic area under the curve (ROC-AUC) value of 0.69 (95% CI 0.67, 0.70) to predict ICU mortality, higher than lactate 0.67 (95%CI: 0.65, 0.69) [20]. Patients with reduced lactate elimination demonstrated that the L/A ratio served as a more reliable prognostic marker for ICU mortality. The L/A ROC-AUC ratio was better in patients with sepsis (0.68 vs 0.66) and those who developed severe sepsis or septic shock (0.68 vs 0.66). Bou Chebl et al. observed that the area under the curve value for lactate was 0.61 (95% CI 0.57–0.65, $p < 0.001$) and for the L/A ratio

was 0.67 (95% CI 0.63–0.70, p < 0.001) [22]. The cutoff generated was 1.22 (sensitivity 59%, specificity 62%) for the L/A ratio in all septic patients and 1.47 (sensitivity 60%, specificity 67%) in patients with septic shock. The lactate / volume ratio emerged as a predictor of in-hospital mortality (p < 0.001).

Noer et al. determined the lactate / albumin ratio in sepsis patients, so that it can be used as a marker predictor of mortality in sepsis patients that is more accessible at a cheaper and more specific cost for sepsis that can be used in simple facilities without reducing accuracy [23]. They concluded that there is a significant positive relationship between the lactate/albumin ratio and SOFA score in patients with sepsis. They suggested that the serial lactate/albumin ratio associated with the SOFA score can be used as a marker for predictors of mortality in septic patients admitted to the ICU.

This study revealed that lactate/albumin ratio >1.5, APACHE score >9, SOFA score >6, serum lactate >4.5 correctly predicted the need for inotropic support in 36%, 32% , 40% and 38% of patients, respectively. There was a significant (p=0.0001) positive correlation among the study parameters in this study. Wang et al. showed that the higher the Acute Physiology and Chronic Health Evaluation II score, the greater the lactate/albumin ratio was discovered on day 1 (r = 0.5315, P < .0001) and day 2 (r = 0.5408, P < .0001), whereas the lower partial pressure of oxygen in arterial blood/fraction of the inspired oxygen ratio, the greater the lactate/albumin ratio was observed on day one (p < .0001) and day two (p < .0001) [13]. One of the limitations of this study was the small sample size and the short duration of study period. Studies with a larger sample size and long duration of the study period are required to produce more robust findings.

CONCLUSIONS

We concluded that the lactate/albumin ratio was a stronger parameter than lactate, albumin, APACHE score, and SOFA alone in predicting mortality, length of stay in the ICU and requiring noradrenaline inotropic support among sepsis patients in the ICU.

SUPPLEMENTARY INFORMATION

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Institutional Review Statement: *The study was conducted according to the guidelines of the Declaration of Helsinki.*
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Data Availability Statement: *The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.*
Conflicts of Interest: *The authors declare no conflicts of interest.*
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