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Research Article

ASSOCIATION OF LDL CHOLESTEROL AND ALKALINE PHOSPHATASE-TO-ALBUMIN RATIO WITH CLINICAL OUTCOMES IN SEPSIS PATIENTS ADMITTED TO INTENSIVE CARE UNIT: A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Background: Sepsis is a life-threatening condition characterized by a dysregulated host response to infection and is a major cause of mortality among critically ill patients in intensive care units (ICUs). Identifying reliable prognostic biomarkers is important for improving early risk stratification and clinical outcomes. Emerging evidence suggests that alterations in lipid metabolism and inflammatory markers, including low-density lipoprotein cholesterol (LDL-C) and the alkaline phosphatase-to-albumin ratio (APAR), may play a role in sepsis prognosis.

Methods: A prospective observational study was conducted among 51 adult patients diagnosed with sepsis or septic shock admitted to the ICU at JSS Hospital, Mysuru, India. Clinical, demographic, and laboratory data were collected within 24 hours of ICU admission. LDL-C levels were obtained from lipid profile analysis, and APAR was calculated using alkaline phosphatase and albumin levels. Statistical analysis was performed using JASP software (Version 0.95.4). Comparisons between survivors and non-survivors were conducted, and correlation as well as multivariate logistic regression analyses were performed to evaluate predictors of mortality.

Results: Among the 51 patients included in the study, 40 survived and 11 were non-survivors. LDL-C levels were lower in non-survivors compared to survivors (34.27 ± 26.89 vs 50.05 ± 28.18 mg/dL), while APAR values were higher among non-survivors (114.05 ± 204.49 vs 58.66 ± 45.59). However, these differences were not statistically significant. LDL-C demonstrated a significant negative correlation with procalcitonin levels ($r = -0.288$, $p = 0.045$). Multivariate logistic regression analysis showed that LDL-C, APAR, APACHE score, and albumin were not independent predictors of mortality.

Conclusion: Although lower LDL-C levels and higher APAR values were observed among non-survivors, these biomarkers were not independently associated with mortality in ICU patients with sepsis. Further large-scale multicenter studies are required to clarify the prognostic value of LDL-C and APAR in critically ill sepsis patients.

KEYWORDS: Sepsis, ICU Mortality, LDL Cholesterol, Alkaline Phosphatase-to-Albumin Ratio, APAR, Prognostic Biomarkers, Critical Care.

Introduction

Intensive Care Units (ICUs), also referred to as critical care units, manage patients experiencing severe physiological instability and organ dysfunction that exceed normal physiological limits. Due to the critical nature of these conditions, patients admitted to ICUs often exhibit higher mortality rates compared to those in other hospital departments[1]. Various prognostic scoring systems such as the Acute Physiology and Chronic Health Evaluation (APACHE) score and the Sequential Organ Failure Assessment (SOFA) score are commonly used in ICU settings to evaluate disease severity, predict clinical outcomes, and estimate mortality risk among critically ill patients[2].

Several factors influence the prognosis and length of ICU stay in critically ill patients. These include the patient's premorbid health status, the presence of comorbid conditions such as sepsis, acute respiratory distress syndrome (ARDS), chronic infections, and other systemic diseases, as well as the quality of care provided in the ICU[3]. Among these conditions, sepsis remains one of the most significant contributors to morbidity and mortality in critically ill patients. According to the World Health Organization (WHO), sepsis is defined as a life-threatening condition that arises when the body's immune response to infection causes widespread inflammation, leading to tissue damage, organ dysfunction, and potentially death. Due to its increasing global incidence and high mortality rate, sepsis has been recognized as a major global health concern.

Sepsis acquired in healthcare settings is considered one of the most serious complications during hospitalization, as it can significantly worsen patient prognosis and frequently necessitates admission to intensive care units[4]. The pathophysiology of sepsis involves a complex interplay of inflammatory, immune, and metabolic responses, frequently progressing to multiple organ dysfunction syndrome (MODS). Early identification and timely management are therefore crucial to improving survival outcomes. However, the absence of a single reliable and universally applicable biomarker continues to limit early risk stratification in sepsis patients[5].

Currently, biomarkers such as lactate, procalcitonin, and inflammatory cytokines are widely used in the clinical assessment of sepsis. Recent studies have also highlighted the potential role of lipid metabolism alterations during sepsis, particularly low-density lipoprotein cholesterol (LDL-C), as a prognostic marker associated with disease severity and mortality in critically ill patients[6].

In addition to traditional biomarkers, the alkaline phosphatase-to-albumin ratio (APAR) has recently emerged as a novel marker reflecting both inflammatory burden and nutritional status. Alkaline phosphatase contributes to endotoxin detoxification through dephosphorylation processes, whereas albumin serves as an indicator of systemic inflammation and physiological reserve. The combination of these parameters into APAR may provide a more integrated assessment of disease severity. Although APAR has demonstrated prognostic value in conditions such as cardiovascular disease, renal disorders, and malignancies, its role in sepsis remains relatively underexplored [7].

Therefore, the present study aims to evaluate the association of LDL-C and APAR with clinical outcomes and mortality among critically ill patients with sepsis. By examining both a traditionally studied biomarker (LDL-C) and a relatively novel parameter (APAR), this study seeks to provide additional insight into their potential utility in prognostic assessment within the ICU setting.

Materials and Methods

Study Population & Design

This was a prospective observational study conducted among 51 patients who met the inclusion criteria and were admitted to the ICU complex at JSS Hospital, Mysuru.

The sample size was determined based on the approximate patient turnover in the ICU monthly, allowing the researchers to collect adequate data within the available study duration.

Source of Material

The study was conducted at JSS Hospital, Agrahara, Mysuru, Karnataka, focusing on patients admitted to the Intensive Care Unit (ICU). Only patients whose clinical data met the predefined inclusion criteria were included in the study.

All participants or their legally authorised representatives were informed about the nature and purpose of the study before enrollment, and written informed consent was obtained. Ethical approval for conducting this prospective observational study was obtained from the Institutional Ethics Committee of JSS Medical College and Hospital before the initiation of data collection in the ICU complex of JSS Hospital, Mysuru.

Sample Selection Criteria

Inclusion Criteria

- Patients aged greater than 18 years and up to 80 years
- Patients diagnosed with sepsis or septic shock and admitted to the ICU

Exclusion Criteria

- Patients receiving statin therapy
- Patients with chronic liver disease
- Patients not willing to provide informed consent

Based on these criteria, eligible patient data were collected for analysis.

Data Collection

Primary data collection was initiated after obtaining approval

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from the Institutional Ethical Committee. Written informed consent was obtained from all patients who met the inclusion criteria. In cases where patients were unable to provide consent, consent was obtained from their legally authorized attendants or guardians. Data were collected from ICU records and patient charts to support the objectives of the study.

The information collected included demographic details such as age, gender, ethnicity, patient IP number, and date of admission. Clinical and vital parameters recorded included blood pressure, pulse rate, respiratory rate, and oxygen saturation (SpO_2). The APACHE score at the time of ICU admission was also recorded to assess the severity of illness. In addition, the presence of comorbidities, past medical history, and the requirement of intubation or ventilatory support were monitored and documented.

Laboratory investigations performed within 24 hours of ICU admission were also collected. These included hematological and biochemical parameters such as complete blood count (CBC) and liver function tests including aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), and albumin. Lipid profile parameters such as high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and total cholesterol were also recorded. Renal function tests including serum creatinine and blood urea nitrogen (BUN) were documented. Additionally, inflammatory and other relevant parameters such as procalcitonin, blood pH, and coagulation profile were recorded.

Information regarding the use of lipid-lowering medications, particularly statins, was also documented to ensure adherence to the exclusion criteria. Furthermore, the date of discharge or date of death of the patient was recorded to assess clinical outcomes. All collected data were systematically documented and analyzed to determine the outcomes of the study.

Statistical Analysis

All statistical analyses were performed using JASP statistical software (Version 0.95.4). Descriptive statistics were used to summarize the baseline demographic, clinical, and biochemical characteristics of the study population. Continuous variables were expressed as mean ± standard deviation (SD) along with minimum and maximum values where appropriate, while categorical variables were presented as frequencies and percentages.

Comparisons between survivors and non-survivors were performed to assess differences in clinical and laboratory variables. Continuous variables were analyzed using the independent sample t-test, whereas categorical variables were compared using the Chi-square test or Fisher's exact test, depending on the distribution of data.

To evaluate the relationship between biomarkers and disease severity parameters, Pearson correlation analysis was performed to determine the correlation between LDL-C, APAR, and clinical laboratory parameters such as procalcitonin, platelet count, creatinine, bilirubin, lactate levels, and APACHE score.

Furthermore, multivariate logistic regression analysis was conducted to identify independent predictors of mortality among ICU patients with sepsis. Variables including LDL-C, APAR, APACHE score, and albumin were included in the regression model to estimate adjusted odds ratios (OR) with 95% confidence intervals (CI).

A p-value < 0.05 was considered statistically significant for all analyses. All results were interpreted to assess the association of LDL-C and APAR with mortality and other clinical outcomes among critically ill patients with sepsis admitted to the ICU.

Results

Baseline Characteristics of the Study Population

A total of 51 patients were included in the study. The mean age of the participants was 59.3 ± 14.1 years, with 31 (60.8%) males. The mean pulse rate was 93.86 ± 22.00 beats/min, and the mean respiratory rate was 23.45 ± 9.51 breaths/min. The mean APACHE score was 17.41 ± 6.73, indicating moderate disease severity. The average hemoglobin level was 10.84 ± 2.43 g/dL, while the mean total leukocyte count was 17,737 ± 9,552 cells/mm^3. The mean platelet count was 2.46 ± 1.35 x10^3/µL, and the mean hematocrit was 33.89 ± 7.15%.

Regarding biochemical parameters, the mean sodium and potassium levels were 134.31 ± 7.86 mEq/L and 4.45 ± 1.02 mEq/L , respectively (Table 1). The mean alkaline phosphatase level was 191.02 ± 241.19 IU/L. Lipid parameters showed a mean LDL-C of 46.65 ± 28.40 mg/dL, HDL-C of 26.37 ± 12.24 mg/dL, and triglycerides of 176.69 ± 120.76 mg/dL. The mean APAR value was 70.61 ± 102.53. The mean length of hospital stay was 36.64 ± 56.56 days.

Table 1: Baseline Demographic, Clinical and Biochemical Characteristics of the Study Population

Variables	Total(N)	Mean	Std. Deviation	Minimum	Maximum
Pulse	51	93.863	22.000	48.00	141.0
Respiratory Rate	51	23.451	9.511	16.00	84.00
APACHE score	51	17.412	6.733	3.000	37.00
Hb	51	10.837	2.431	6.500	17.10
TC (total count)	51	17737.059	9552.721	3300	46290

Platelet count	51	2.455	1.346	0.100	6.320
PCV / HCT	51	33.892	7.152	21.80	52.70
Sodium	51	134.314	7.860	111.0	153.0
Potassium	51	4.447	1.023	2.700	7.200
Calcium	51	98.961	13.682	19.00	119.0
Alkaline phosphatase	51	191.020	241.193	39.00	1729
APAR	51	70.610	102.534	11.14	720.4
Total cholesterol	51	114.059	37.262	55.00	248.0
triglycerides	51	176.686	120.761	36.00	814.0
LDL-C	51	46.647	28.404	5.000	111.0
HDL-C	51	26.373	12.242	8.000	71.00
VLDL-C	51	36.729	14.563	15.00	76.00
LOS	51	36.640	56.561	0.000	216.0

Comparison of Clinical and Laboratory Variables Between Survivors and Non-Survivors

Among the study population, 40 patients survived and 11 patients were non-survivors. The mean age was slightly higher among non-survivors (63.3 ± 13.2 years) compared to survivors (58.2 ± 14.3 years), although this difference was not statistically significant (p = 0.462).

Although LDL-C levels were lower in non-survivors compared to survivors (38.0 ± 24.0 vs 48.8 ± 29.4 mg/dL) and APAR values were higher in non-survivors (116.3 ± 204.8 vs 59.6 ± 45.5), no statistically significant differences were identified, indicating limited discriminatory ability of these biomarkers (p = 0.107 and p = 0.393, respectively) (Table 2).

Other clinical variables, including APACHE score, albumin levels, and comorbid conditions such as septic shock, acute kidney injury, and liver injury, were more frequent among non-survivors; however, these differences did not reach statistical significance.

Clinical conditions such as septic shock, acute kidney injury, and liver injury were more frequent among non-survivors; however, these associations did not reach statistical significance.

Correlation Analysis

Correlation analysis revealed that LDL-C was significantly negatively correlated with procalcitonin levels (r = −0.288, p = 0.045), suggesting that lower LDL-C levels were associated with higher inflammatory activity (Table 3). However, LDL-C did not show significant correlations with other clinical parameters, including APACHE score, platelet count, creatinine, total bilirubin, and lactate levels.

Further analysis demonstrated that APAR had a borderline positive correlation with procalcitonin (r = 0.279, p = 0.052); however, this association did not reach statistical significance and should be interpreted with caution (Table 5). Neither LDL-C nor APAR showed significant correlations with other markers of disease severity.

Table 2: Comparison of Clinical and Laboratory Variables Between Survivors and Non-Survivors

Variable	Total (n=51)	Survivors (n=40)	Non-survivors (n=11)	p-value
Age (years)	59.3 ± 14.1	58.2 ± 14.3	63.3 ± 13.2	0.462
Male	31 (60.8%)	24 (60.0%)	7 (63.6%)	1.000
LDL-C	46.65 ± 28.40	48.8 ± 29.4	38.0 ± 24.0	0.107
Alkaline phosphatase	191.02 ± 241.19	173.6 ± 89.9	254.6 ± 468.4	0.412
Albumin	3.20 ± 1.25	3.11 ± 0.74	3.94 ± 2.37	0.387
APAR	70.61 ± 102.53	59.6 ± 45.5	116.3 ± 204.8	0.393
APACHE score	17.41 ± 6.73	17.8 ± 7.4	17.5 ± 4.1	0.565
Septic shock	30 (58.8%)	22 (55.0%)	8 (72.7%)	0.743
AKI	28 (54.9%)	24 (60.0%)	4 (36.4%)	0.097
Liver Injury	4 (7.8%)	2 (5.0%)	2 (18.2%)	0.199
ICU Stays (days)	24.33 ± 41.02	18.6 ± 13.9	15.7 ± 8.2	0.092

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Association of LDL-C and APAR With Clinical Outcomes

LDL-C levels were lower among non-survivors compared to survivors (34.27 ± 26.89 vs 50.05 ± 28.18 mg/dL), while APAR values were higher among non-survivors (114.05 ± 204.49 vs 58.66 ± 45.59). However, these differences were not statistically significant (p = 0.107 and p = 0.393, respectively) (Table 4).

Similarly, no statistically significant differences in LDL-C or APAR levels were observed in relation to acute kidney injury, septic shock, or liver injury.

3.5 Multivariate logistic regression analysis

Multivariate logistic regression analysis was performed to identify independent predictors of mortality. LDL-C (Adjusted OR = 1.021, 95% CI: 0.991–1.051, p = 0.174) and APAR (Adjusted OR = 0.993, 95% CI: 0.979–1.007, p = 0.306) were not independently associated with mortality (Table 6). Similarly, APACHE score and albumin levels were not significant predictors.

Overall, while trends were observed, the lack of statistical significance suggests limited standalone prognostic utility of LDL-C and APAR in this cohort.

Table 3: Correlation of LDL-C With Clinical and Laboratory Parameters.

Variable	LDL-C (r)	p-value
PROCALCITONIN	−0.288	0.045*
APACHE score	0.015	0.915
Platelet count	0.162	0.255
Creatinine	−0.002	0.987
Total Bilirubin	−0.114	0.426
BGA lactate	−0.242	0.090

Table 4: Association of LDL-C and APAR With Clinical Outcomes

Outcome	LDL-C (Mean ± SD)	p-value	APAR (Mean ± SD)	p-value
Mortality	50.05 ± 28.18 vs 34.27 ± 26.89	0.107	58.66 ± 45.59 vs 114.05 ± 204.49	0.393
AKI	49.05 ± 31.91 vs 44.83 ± 25.86	0.615	67.69 ± 59.18 vs 72.83 ± 127.02	0.849
Septic shock	45.07 ± 24.97 vs 47.31 ± 30.03	0.786	42.93 ± 22.52 vs 82.14 ± 119.79	0.067
Liver injury	47.47 ± 28.59 vs 37.00 ± 27.89	0.516	59.75 ± 44.50 vs 198.19 ± 348.30	0.485

Table 5: Correlation Analysis of LDL-C and APAR With Disease Severity Markers

Variable	LDL-C (r)	p-value	APAR (r)	p-value
APACHE score	0.015	0.915	0.195	0.171
Platelet count	0.162	0.255	−0.132	0.355
Creatinine	−0.002	0.987	0.079	0.582
Total Bilirubin	−0.114	0.426	0.142	0.322
BGA lactate	−0.242	0.090	−0.166	0.249
Procalcitonin	**−0.288**	**0.045***	0.279	0.052

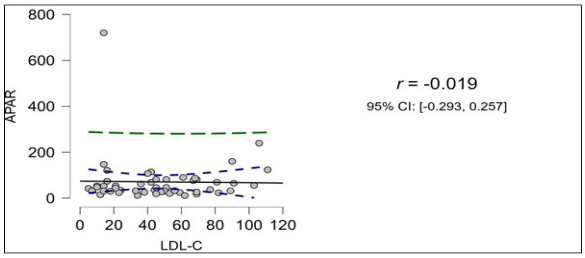

Figure 1A: Scatter plot showing the correlation between low-density lipoprotein cholesterol (LDL-C) and alkaline phosphatase-to-albumin ratio (APAR) among patients admitted to the ICU with sepsis. The analysis demonstrated no significant correlation between LDL-C and APAR (r = −0.019; 95% CI: −0.293 to 0.257).

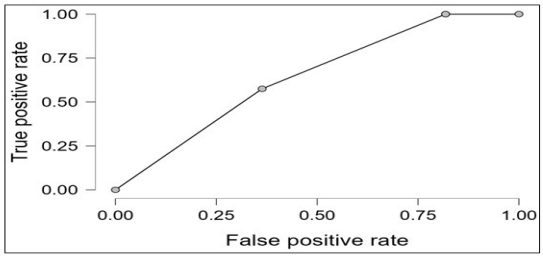

Figure 1B: Receiver Operating Characteristic (ROC) curve illustrating the predictive performance of the study model for clinical outcomes in sepsis patients admitted to the ICU.

Figure 1. Relationship Between LDL-C, APAR, and Predictive Performance for Clinical Outcomes in Sepsis Patients

Table 6: Multivariate Logistic Regression Analysis for Predictors of Mortality

Variable	Adjusted OR	95% CI	p-value
LDL-C	1.021	0.991 – 1.051	0.174
APAR	0.993	0.979 – 1.007	0.306
APACHE score	1.011	0.895 – 1.142	0.859
Albumin	0.600	0.263 – 1.371	0.226

Discussion

Sepsis continues to represent a significant contributor to morbidity and mortality among critically ill patients admitted to intensive care units worldwide[8]. Early identification of prognostic biomarkers is essential for improving risk stratification and clinical management in these patients[9]. In the present prospective observational study conducted among 51 ICU patients with sepsis, we evaluated the association of low-density lipoprotein cholesterol (LDL-C) and alkaline phosphatase-to-albumin ratio (APAR) with mortality and other clinical outcomes. Although LDL-C levels were lower and APAR values were higher among non-survivors, these differences were not statistically significant, indicating limited discriminatory ability of these biomarkers in predicting mortality. Furthermore, none of the evaluated variables, including LDL-C, APAR, APACHE score, and albumin, were identified as independent predictors of mortality.

The mean LDL-C level observed in our study population was relatively low compared to normal physiological levels, supporting existing evidence that lipid metabolism is significantly altered during sepsis. Inflammatory cytokines and endotoxins are known to reduce circulating lipoprotein levels through increased catabolism and decreased hepatic synthesis[10]. LDL-C plays a role in binding and neutralizing bacterial endotoxins, thereby contributing to host defense mechanisms [11]. Therefore, reduced LDL-C levels in sepsis may reflect heightened inflammatory activity and metabolic dysregulation rather than a direct causal relationship with clinical outcomes.

Although LDL-C levels were numerically lower among non-survivors, this difference did not reach statistical significance. Similar findings have been reported in previous studies, where reduced lipid levels were observed in critically ill patients but were not consistently associated with mortality. The lack of statistical significance in our study may be attributed to the relatively small sample size and heterogeneity in the study population, which could have limited the power to detect meaningful differences.

APAR, a relatively novel biomarker, has gained attention as a composite indicator reflecting both inflammatory burden and nutritional status. In our study, APAR values were higher among non-survivors, suggesting a possible association with disease severity. However, this difference was not statistically significant, and the markedly high standard deviation observed in APAR values (70.61 ± 102.53) indicates substantial variability within the study population. This variability may reflect differences in disease severity, comorbid conditions, and individual biochemical responses, which could have influenced the statistical outcomes and reduced the reliability of APAR as a standalone prognostic marker[12].

Alkaline phosphatase plays a role in detoxifying endotoxins through dephosphorylation mechanisms, whereas albumin reflects the nutritional and inflammatory status of the patient. Therefore, the APAR may represent a combined indicator of inflammatory burden and physiological stress in critically ill patients. However, similar to LDL-C, the difference in APAR values between survivors and non-survivors did not reach statistical significance in our analysis.

Correlation analysis demonstrated a significant negative association between LDL-C and procalcitonin levels, suggesting that lower LDL-C levels are associated with increased inflammatory activity. This finding aligns with the understanding that lipid metabolism is closely linked with immune responses during sepsis[13]. In contrast, APAR showed a borderline positive correlation with procalcitonin ($p = 0.052$); however, this did not reach statistical significance and should be interpreted with caution. Moreover, neither LDL-C nor APAR demonstrated significant correlations with other established markers of disease severity, such as APACHE score, platelet count, creatinine, bilirubin, or lactate levels.

Importantly, multivariate logistic regression analysis confirmed that LDL-C, APAR, APACHE score, and albumin were not independent predictors of mortality in this cohort. This highlights the complexity of sepsis pathophysiology, which involves multiple interacting mechanisms including immune dysregulation, endothelial dysfunction, metabolic alterations, and organ failure. As a result, reliance on a single biomarker may be insufficient to accurately predict clinical outcomes in sepsis patients

Overall, the findings of this study suggest that although LDL-C and APAR reflect underlying inflammatory and metabolic disturbances in sepsis, their independent prognostic value remains limited. These biomarkers may have a complementary role when used alongside established clinical scoring systems and other laboratory parameters, rather than serving as standalone predictors.

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Limitations

The findings of this study should be interpreted in light of certain limitations. First, the relatively small sample size may have limited the statistical power to detect significant associations. Second, the study was conducted at a single center, which may affect the generalizability of the results. Third, only baseline measurements obtained within 24 hours of ICU admission were analyzed, and dynamic changes in LDL-C and APAR during the course of illness were not evaluated, which may have provided greater prognostic insight. Additionally, the high variability observed in APAR values may have influenced the robustness of statistical analysis. Future studies with larger, multicenter cohorts and serial biomarker measurements are warranted to better define the prognostic utility of these parameters.

Conclusion

This prospective observational study evaluated the association of low-density lipoprotein cholesterol (LDL-C) and the alkaline phosphatase-to-albumin ratio (APAR) with clinical outcomes among sepsis patients admitted to the intensive care unit. The findings demonstrated that LDL-C levels were lower and APAR values were higher among non-survivors compared to survivors, suggesting a possible relationship between lipid metabolism, inflammatory response, and disease severity in sepsis.

However, these differences did not reach statistical significance, and neither LDL-C nor APAR were identified as independent predictors of mortality in multivariate logistic regression analysis. A significant negative correlation between LDL-C and procalcitonin was observed, indicating that lower LDL-C levels may be associated with increased inflammatory activity in sepsis.

Overall, the study suggests that although LDL-C and APAR may reflect underlying inflammatory and metabolic alterations in sepsis, their independent prognostic value remains uncertain. Further large-scale, multicenter studies with larger sample sizes and longitudinal biomarker assessment are required to better establish the clinical utility of these biomarkers in predicting outcomes among critically ill sepsis patients.

Conflict of Interest

The authors declare no conflict of interest.

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