JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Original Article

Predictive value of blood gas parameters and hematologic indices on survival in critically ill sepsis patients

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Abstract
Introduction: Sepsis is a life-threatening condition caused by an excessive immune response to infection, leading to severe tissue and organ damage. In resource-limited settings, early, low-cost, and readily available laboratory parameters may guide outcome prediction. This study aimed to evaluate the role of hematological indices and laboratory parameters in predicting mortality among intensive care unit (ICU) patients with sepsis.
Methodology: This retrospective study included adult sepsis patients admitted to the ICU between January 2018 and December 2023. Blood samples obtained within the first 6 hours of ICU admission were processed using standardized analyzers. Demographic data, laboratory results at admission, length of hospital stay, and mortality status were retrieved from the hospital database. Associations between hematological indices, laboratory parameters, and mortality were analyzed.
Results: A total of 180 patients were included; 40 died during hospitalization. No significant association was found between neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), or platelet-to-lymphocyte ratio (PLR) and mortality (NLR: $p = 0.834$, LMR: $p = 0.895$, PLR: $p = 0.192$). In contrast, pH levels showed a strong negative correlation with mortality ($p < 0.001$), while lactate levels were significantly positively correlated ($p = 0.006$). Carboxyhemoglobin and methemoglobin levels were not significantly related to mortality.
Conclusions**:** Low pH and high lactate levels were the strongest predictors of mortality in sepsis patients, highlighting the prognostic value of simple blood gas parameters, especially where advanced diagnostics are limited. Hematological indices showed no significant association with mortality. pH and lactate should be prioritized in clinical decision-making for sepsis patients.

Key words: Survival; intensive care units; sepsis; blood gas; hematologic index.

J Infect Dev Ctries 2025; 19(12):1809-1816. doi:10.3855/jidc.21586

(Received 10 March 2025 – Accepted 04 June 2025)

Introduction
Sepsis is a serious health issue that occurs when the body overreacts to infection, causing high morbidity and mortality worldwide [1]. This disease, which is associated with organ failure and a high risk of death, was designated a global health priority by the World Health Organization in 2017 [2]. Sepsis initially manifests itself with symptoms such as fever, chills, rapid breathing, and changes in blood pressure, while organ failure and septic shock may develop in later stages [3]. Factors such as the severity of the disease, the patient's health status, and the time it takes to access treatment affect mortality rates, which can reach up to 40–50% in intensive care unit (ICU) patients [2,5]. Antimicrobial therapy is one of the most critical elements in treating sepsis; however, it may be delayed due to nonspecific symptoms at the initial stage [6]. In many cases, the infectious agent cannot be determined due to the low sensitivity and long time required for culture results [7]. With a better understanding of the pathophysiology of sepsis, new biomarkers that can be used in the diagnosis and follow-up of the disease are being investigated. Regulation of the secretion of mediators is vital in preventing organ damage and multiple organ failure [8].

Currently, no early and accurate tests with high specificity and sensitivity exist that can predict mortality in sepsis other than scoring systems used in ICU patients [9]. Reliable, easily applicable, widely accessible, and low-cost laboratory tests such as hematological indices and biochemical parameters are of particular interest for predicting mortality in sepsis patients [10]. Among these, arterial blood gas analysis plays a critical role in assessing metabolic disturbances and organ dysfunction. In sepsis, abnormalities in arterial blood gas parameters such as pH and lactate can reflect tissue hypoperfusion and cellular distress, both of which are associated with increased mortality. Despite their frequent use in ICU practice, the predictive utility of arterial blood gas parameters such as pH, lactate, carboxyhemoglobin (COHb), and methemoglobin (MetHb) for mortality in sepsis remains understudied.

In this study, we aimed to evaluate the predictive value of commonly used and easily accessible hematological indices, including the neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), and platelet-to-lymphocyte ratio (PLR), and also assessed arterial blood gas parameters, including pH, lactate, carboxyhemoglobin (CoHb), and methemoglobin (MetHb) in relation to mortality among adult ICU patients with sepsis.

Methodology

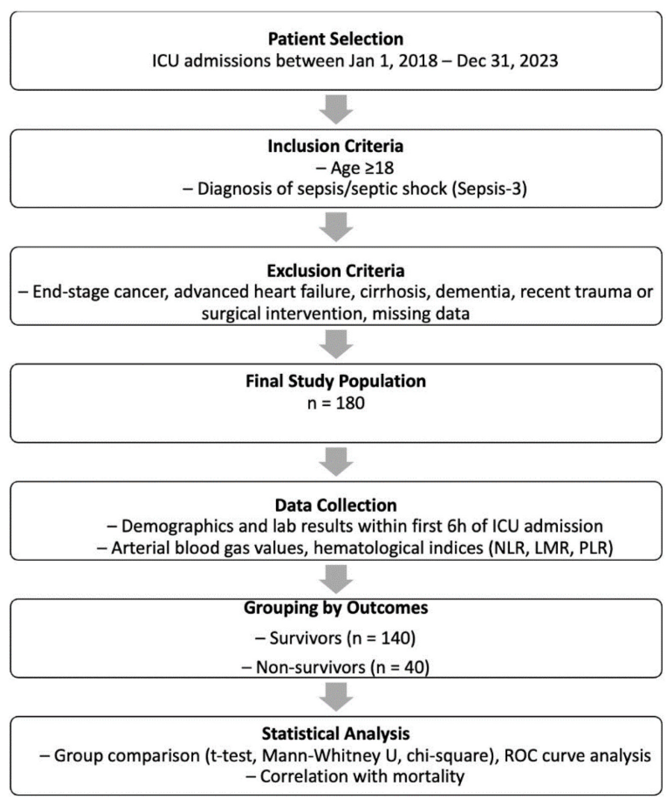
Setting and Participants

This single-center retrospective study included patients between January 1, 2018 and December 31, 2023 who were admitted to the ICU of Diyarbakır SBÜ Gazi Yaşargil Training and Research Hospital with a diagnosis of sepsis/septic shock according to the clinical diagnosis criteria of "3rd Sepsis Consensus (Sepsis-3) Report" [3] jointly published by the Society of Critical Care Medicine (SSSM) and the European Society of Intensive Care Medicine (ESICM) and adopted in the "International Sepsis and Septic Shock Management Guide" [11]. Patients under 18 years of age, with missing data in their files, end-stage cancer, advanced heart failure, dementia, cirrhosis, a history of recent trauma, and those who had undergone recent surgical intervention were excluded. Our study was approved by the 'SBÜ Gazi Yaşargil Training and Research Hospital Clinical Research Ethics Committee' with the decision numbered 17 on 19.04.2024. Because the study was retrospective, participants were not asked to provide written informed consent when enrolled, and The Clinical Research Ethics Committee waived the need for consent to participate. All procedures followed the Turkish Medicine and Medical Devices Agency Good Clinical Practices Guidelines and the Declaration of Helsinki.

Patient Characteristics and Procedures

Patients' electronic health records from the hospital's database were scanned for each participant. Patients' age, gender, number of days of admission, and discharge method, either exitus or survival, were recorded. All blood samples were collected within the first 6 hours of ICU admission. Laboratory analyses were performed using the same automated analyzers throughout the study period to ensure consistency. Baseline laboratory findings including white blood cell count, neutrophile, lymphocyte, monocyte, hemoglobin, platelets, urea, creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), albumin, uric acid, sodium, potassium, calcium, magnesium, C-reactive protein and arterial blood gas parameters including lactate, COHb, and MetHb were recorded. The hematological indices of NLR, LMR, and PLR were calculated using ICU admission data. The study's primary outcome was in-hospital mortality within 28 days from any cause. We divided patients into "survivors" and "non-survivors" groups according to death records. A visual representation of the study design and patient selection process is provided in Figure 1.

Figure 1. Study flowchart illustrating patient selection, exclusion criteria, data collection, and outcome grouping.



ICU: Intensive care unit; n: absolute number; NLR: neutrophile-to-lymphocyte ratio; LMR: lymphocyte-to-monocyte ratio; PLR: platelet-to-lymphocyte ratio; ROC: Receiver Operator Characteristic.

Statistical Analysis

The distribution of the data was evaluated using the Shapiro-Wilk test. For parametric variables, data are given as mean (standard deviation), and the Student's T test was applied with appropriate data. Non-parametric variables are presented as median (interquartile range-IQR), and the Mann-Whitney U test was applied with proper data. The categorical variables were expressed as the total percentage and compared using the chi-square test. To evaluate the predictive power of laboratory parameters for 28-day mortality**,** ROC curve analysis and Area Under the Curve (AUC) values were calculated, along with cut-off values, sensitivity, and specificity. Point biserial correlation was calculated to assess the potential correlation of hematologic indices and arterial blood gas parameters with mortality. Multivariate logistic regression was performed for age and all study parameters. Statistical Package for Social Sciences (SPSS) Ver. 26.0 commercial software was used for the described statistical analyses. Statistical significance was accepted at the level of $p < 0.05$.

Results

This retrospective study included 180 adult sepsis patients with a median age of 77.5 (18) years, and 51.1% (n = 92) were female. The age, gender, and baseline laboratory findings are given in Table 1. Among baseline laboratory findings, while urea, creatinine, AST, LDH, and CRP were significantly higher in the non-survivor group, calcium and magnesium levels were higher in the survivor group ($p < 0.05$ for all). Besides, other laboratory findings, including white blood cell count, hemoglobin, platelet count, ALT, potassium, sodium, albumin, and uric acid, were similar between survivors and non-survivors ($p > 0.05$ for all).

The overall in-hospital mortality rate of participants was 22.2% (n = 40). As reported in Table 2, while hematologic indices of NLR, LMR, PLR, and arterial blood gas parameters of COHb and MetHb were similar between survivors and non-survivors ($p > 0.05$ for all), lactate levels were significantly higher, and pH was significantly lower in the non-survivor group ($p < 0.05$ for both).

The ROC analysis showed that only pH (AUC = 0.791, $p < 0.001$) and lactate (AUC = 0.643, $p = 0.006$) had significant discriminatory ability for predicting mortality. NLR (AUC = 0.511), LMR (AUC = 0.507), PLR (AUC = 0.432), COHb (AUC = 0.415), and MetHb (AUC = 0.571) did not show significant predictive value ($p > 0.05$ for all). Cut-off values for each index and arterial blood gas parameter, and

Table 1. General characteristics and baseline laboratory findings of the patients.

	Total (n=180)	Survivors (n = 140)	Non-Survivors (n = 40)	*p*
Age, median (IQR)	77.5 (18)	79 (18)	76 (17)	0.979
Female gender, % (n)	51.1 (92)	39.4 (71)	11.7 (21)	0.842
WBC (10^3 u/L), median (IQR)	12.05 (10)	12 (10)	13.5 (10.8)	0.461
Hemoglobin (g/dL), median (IQR)	11.6 (3)	11.6 (3)	12 (4.8)	0.949
Platelets (cells × 10^3/uL), mean (SD)	238 (116)	246 (114)	207 (118)	0.670
Urea (mg/dL), median (IQR)	74.5 (94)	64 (83)	128 (117)	< 0.001
Creatinine (mg/dL), median (IQR)	1.35 (1.8)	1.2 (1.5)	2.5 (3)	0.001
AST (U/L), median (IQR)	28.5 (56)	26 (37)	49 (137)	0.017
ALT (U/L), median (IQR)	21 (35)	19 (27)	31 (115)	0.400
Potassium (mmol/L), median (IQR)	4.15 (1.3)	4.1 (1.28)	4.6 (1.73)	0.051
Sodium (mmol/L), median (IQR)	138 (7)	138 (7)	136 (8)	0.192
CRP (mg/L), median (IQR)	100 (127)	82 (104)	166 (161)	< 0.001
Albumin (g/L), mean (SD)	26.26 (7.1)	26.8 (7.2)	24 (6.5)	0.400
LDH (U/L), median (IQR)	321 (256)	298 (236)	432 (435)	0.002
Calcium (mg/dL), median (IQR)	8.5 (1.1)	8.6 (1)	7.9 (1.5)	< 0.001
Uric acid (mg/dL), median (IQR)	4 (2)	4 (2)	4.1 (2.2)	0.523
Magnesium (mg/dL), median (IQR)	1.9 (0.3)	1.9 (0.4)	1.75 (0.6)	0.006

n: Absolute number; IQR: Inter quantile range; SD: Standard deviation WBC: White blood cell; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; CRP: C-reactive protein; LDH: Lactate dehydrogenase, p < 0.05 were significant.

Table 2. Comparison of laboratory values between groups.

	Total (n=180)	Survivors (n = 140)	Non-Survivors (n = 40)	*p*
NLR, median (IQR)	10.0 (13n2)	10 (13.6)	10 (9.6)	0.834
LMR, median (IQR)	1.9 (2.7)	1.8 (2.6)	2 (3.5)	0.895
PLR, median (IQR)	196 (231)	204 (218)	174 (299)	0.192
PH, median (IQR)	7.30 (0.20)	7.40 (0.1)	7.2 (0.5)	< 0.001
Lactate (mmol/L), median (IQR)	2.4 (2.5)	2.3 (2)	3.9 (6.1)	0.006
COHb (%), median (IQR)	0.7 (0.8)	0.7 (0.8)	0.8 (1)	0.413
MetHb (%), median (IQR)	0.7 (1.5)	0.6 (1.5)	0.9 (1.5)	0.170

n: Absolute number; IQR: Inter quantile range; NLR: neutrophile-to-lymphocyte ratio; LMR: lymphocyte-to-monocyte ratio; PLR: platelet-to-lymphocyte ratio; COHb: carboxyhemoglobin; MetHb: methemoglobin; $p < 0.05$ were significant.

Table 3. Point Biserial Correlation and ROC analyses of patient survival across NLR, LMR, PLR, and blood gas parameters.

	Point Biserial Correlation		ROC				
	r	***p***	**Cut-off**	**Sensitivity (%)**	**Specificity (%)**	**AUC, CI**	***p***
NLR	0.016	0.830	10.05	50.0	49.3	0.511, 0.410 – 0.612	0.830
LMR	0.010	0.895	1.95	52.5	52.1	0.507, 0.399 – 0.615	0.895
PLR	-0.098	0.192	172.3	52.5	39.3	0.432, 0.323 – 0.541	0.192
pH	-0.433	< 0.001	7.35	82.5	56.4	0.791, 0.712 – 0.871	< 0.001
Lactate	0.206	0.006	2.85	62.5	60.7	0.643, 0.534 – 0.752	0.006
COHb	0.610	0.414	0.75	52.5	53.6	0.415, 0.437 – 0.647	0.415
MetHb	0.103	0.170	0.75	57.5	57.1	0.571, 0.474 – 0.668	0.171

ROC: Receiver Operator Characteristics; AUC: Area under curve; CI: Confidence Interval; NLR: neutrophile-to-lymphocyte ratio; LMR: lymphocyte-to-monocyte ratio; PLR: platelet-to-lymphocyte ratio; COHb: carboxyhemoglobin; MetHb: methemoglobin; $p < 0.05$ were significant.

correlation with mortality, were given in Table 3. Also, ROC curve diagrams are displayed in Figure 2.

A multivariate logistic regression analysis was performed, and the results of age, NLR, LMR, PLR, and blood gas parameters are given in Table 4.

Discussion

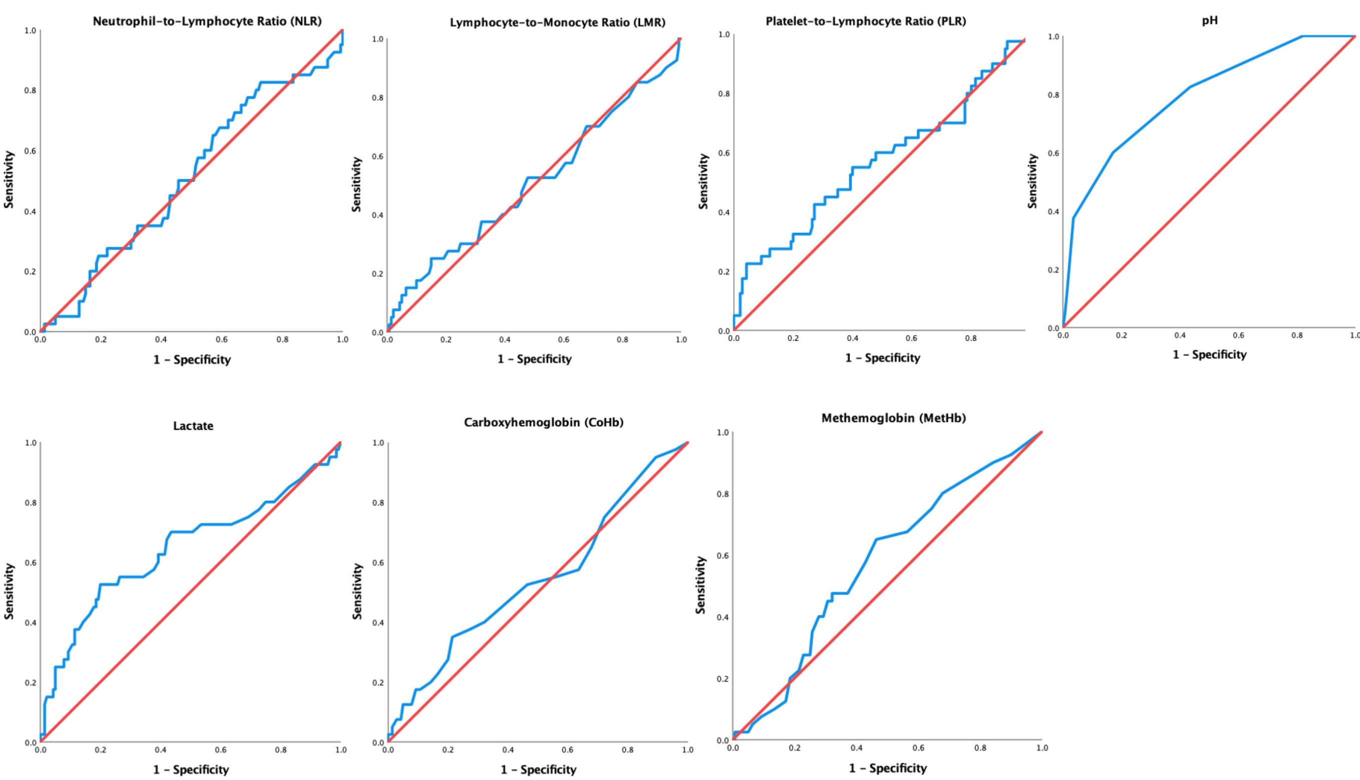
Sepsis is a life-threatening condition that results from an uncontrolled immune response to infection and leads to organ dysfunction [11]. There are often delays in the diagnosis of sepsis, and this condition is associated with high mortality rates [3]. The definition

Table 4. Multivariate logistic regression analysis of age, NLR, LMR, PLR, and blood gas parameters.

	B	**EXP (B)**	**95 % Confidence Interval**		***p***
			Lower	**Upper**	
NLR	0.006	1.006	0.981	1.032	0.633
LMR	0.027	1.028	0.906	1.166	0.672
PLR	0.000	1.000	0.998	1.002	0.860
pH	-8.851	0.000	0.000	0.006	**< 0.001**
Lactate	0.174	1.190	1.026	1.381	**0.021**
COHb	0.591	1.807	0.851	3.837	0.124
MetHb	0.303	1.355	0.846	2.168	0.206
Age	0.019	1.019	0.993	1.046	0.145

NLR: neutrophile-to-lymphocyte ratio; LMR: lymphocyte-to-monocyte ratio; PLR: platelet-to-lymphocyte ratio; COHb: carboxyhemoglobin; MetHb: methemoglobin; $p < 0.05$ were significant.

Figure 2. ROC-AUC graphs of hematologic indices and blood gas parameters in prediction of in-hospital mortality among critically ill sepsis patients. (ROC: Receiver Operator Characteristic).



has been updated over time, and a new conceptual and practical framework has been presented to explain the systemic inflammatory response to infection [12]. Although it is difficult to determine the exact incidence and mortality rates of sepsis in our country, sepsis continues to be a significant infectious problem, particularly in intensive care units [13]. As the frequency and mortality of sepsis increase, early diagnosis and treatment have become more critical. Particularly in resource-limited settings, the use of rapid, accessible, and low-cost laboratory parameters for early prognosis can be invaluable in guiding initial clinical decisions. Many studies have been conducted on this topic. Our study evaluated the role of NLR, LMR, PLR, pH, lactate, COHb, and MetHb parameters in the initial blood samples of patients diagnosed with sepsis and hospitalized in ICUs to predict prognosis.

This study evaluated the relationship between the NLR and mortality in sepsis patients. In the study by Tavşanoğlu *et al.,* no significant difference was found between NLR levels at the first presentation and mortality. However, NLR was reported to be significantly higher in severe sepsis patients requiring vasopressor support [14]. Similarly, this study found no significant relationship between NLR and mortality ($r = 0.016$, $p = 0.830$). Hwang *et al.* divided NLR levels into five groups in critically ill sepsis patients, examined changes over time, and showed that high NLR levels were associated with mortality. However, they determined that mortality was highest in the group with the lowest NLR level and suggested that this could be due to bacterial infections related to neutropenia [15]. In this study, NLR was lower in the group that died, but this difference was not statistically significant. These differences between studies may be related to methodological variations, population heterogeneity, and whether dynamic or static values were assessed. Zahorec *et al.* determined that NLR showed a significant relationship with mortality in sepsis patients treated in the intensive care unit [16]. However, only oncology patients were examined in this study, and the analysis was performed using dynamic NLR values. In conclusion, while some studies have shown that NLR is associated with mortality, no such relationship was found in this study ($p = 0.834$).

This study investigated the relationship between PLR and LMR and mortality in sepsis and septic shock patients. The findings revealed that PLR was negatively associated with mortality, but this relationship was not statistically significant ($r = -0.098$, $p = 0.192$). According to ROC analysis, at a threshold value of 172.3, the sensitivity of PLR was 52.5%, the specificity was 39.3%, and the AUC value was calculated as 0.432 (CI: 0.323–0.541). These results suggest that PLR is an inadequate parameter in predicting mortality. In comparison to previous studies, Zencir *et al.* reported that PLR was significantly higher in the mortality group in infective endocarditis patients ($p = 0.008$) [17]. However, in the study by Duman *et al.,* no significant difference was found in terms of PLR in patients with sepsis and septic shock ($p = 0.737$), and no significant difference was found between the groups with and without mortality ($p = 0.336$) [18]. In the meta-analysis by Wang *et al.,* it was reported that PLR levels were higher in patients who did not survive sepsis. Still, it was emphasized that the number of patients, population, and racial differences could affect these results [19].

Blood gas analysis is an essential diagnostic and monitoring tool frequently used in emergency departments and ICUs. In our study, lactate levels were found to have a significant positive relationship with mortality ($r = 0.206$, $p = 0.006$). According to ROC analysis, lactate's threshold value was 2.85 mmol/L. This threshold value determined sensitivity as 62.5% and specificity as 60.7%. The AUC value was 0.643 (CI: 0.534–0.752), indicating that lactate levels are a significant parameter in predicting mortality. These findings are in line with prior research suggesting that elevated lactate reflects impaired tissue perfusion and is an early indicator of sepsis severity. A meta-analysis by Gu *et al.* demonstrated that early lactate clearance-guided therapy significantly reduces mortality in septic patients, supporting its use as a target for resuscitation strategies in the ICU setting [20]. Similarly, a prospective study conducted in East Africa reported that lactate clearance within the first 8 hours was independently associated with reduced 72-hour mortality in critically ill febrile children, emphasizing its prognostic utility even in low-resource settings [21]. Liu *et al.* determined pH and base deficit to be essential variables in predicting mortality in patients with sepsis [22]. In a meta-analysis, the mean pH value of patients who did not survive was calculated as 7.21 and that of survivors as 7.31 [23]. In the study by Wernly *et al*., it was found that the combination of acidosis and high lactate increased the risk of mortality, and this model (AUC 0.63) was a stronger predictor than acidosis alone (AUC 0.59) [24]. Schork *et al.* further emphasized that minimum pH and peak lactate within the first 24 hours were strong predictors of ICU mortality, reinforcing their combined prognostic utility [25]. Our results, which demonstrated a strong association between low pH values and mortality ($p < 0.001$), support this combined prognostic utility. In the survey conducted by Kliegel *et al.* in post-resuscitation patients, lactate level > 2.0 mmol/L at 48 hours predicted mortality with 86% specificity [26]. These studies generally concluded that high lactate levels predicted mortality, but the exact threshold values may vary. The findings obtained in this study are broadly consistent with the literature and support the idea that pH and lactate levels are essential biomarkers for predicting mortality in patients with sepsis. Given their availability, speed, and low cost, pH and lactate levels may be especially useful in early risk stratification, particularly in resource-constrained ICU settings.

MetHb is a form of hemoglobin with no oxygen-carrying capacity and is generally kept below 1%. Schuerholz *et al.,* in a retrospective study, examined MetHb levels in 655 intensive care patients and found that MetHb levels were higher in 211 patients diagnosed with sepsis. A significant correlation was found between SOFA scores and MetHb levels [27]. Ohashi *et al.,* in their study comparing 14 patients with sepsis and septic shock with 31 nonseptic patients, reported that MetHb levels were significantly higher in patients with sepsis [28]. However, our study found no statistically significant relationship between MetHb and mortality (r = 0.103, p = 0.170). According to ROC analysis, the threshold value for MetHb was determined as 0.75, and sensitivity was calculated as 57.5% and specificity as 57.1% at this value. The AUC value was 0.571 (CI: 0.474–0.668), and it was stated that this value has limited prognostic value regarding mortality prediction.

Although the exact values of COHb levels in healthy individuals are not clearly established, several studies have reported elevated COHb levels in patients with sepsis. In a prospective study by Moncure *et al*., 76 blood gas samples from 46 trauma patients with sepsis showed significantly higher COHb levels in sepsis and severe sepsis, particularly in patients with hypotension [29]. Similarly, Hunter *et al.* found increased COHb levels in blood samples from 32 surgical ICU patients [30]. However, this study defined "critically ill" based on ICU scoring rather than SIRS criteria [30]. In our study, COHb levels were considered indicators of both carbon monoxide exposure and impaired oxygen transport. Despite this, we found no significant association between COHb and mortality (r = 0.610, p = 0.414). ROC analysis showed a threshold value of 0.75, with 52.5% sensitivity and 53.6% specificity. The AUC was 0.415 (CI: 0.437–0.647), suggesting limited prognostic utility. Our findings indicate that COHb and MetHb may have limited value as standalone mortality predictors in sepsis and should not be prioritized over more practical markers such as pH and lactate.

Our study has several limitations. The main limitations include its retrospective and single-center design, as well as the small sample size. Additionally, more relevant or comprehensive predictors, including comorbid conditions, prognostic scores such as the Charlson Comorbidity Index, APACHE-II, and SOFA, or laboratory tests such as procalcitonin and CRP, could have improved the results of our study. Unfortunately, we could not access more detailed data of participants through the hospital record system due to the lack of data in the hospital's electronic health record database. Similarly, sequential values of hematologic indices following admission could not be analyzed for the same reason. Another limitation is the relatively high median age of the study population, which may have confounding effects on mortality risk due to age-related factors such as cardiovascular vulnerability. However, due to the retrospective design and limited number of events, adjustment for age in multivariate models could not be reliably performed. This limitation should be addressed in future prospective studies.

Conclusions

This study examined the predictive value of baseline blood gas parameters and hematologic indices, including NLR, PLR, and LMR, on mortality among sepsis patients admitted to ICUs. The results revealed that while higher lactate levels and lower pH were significantly associated with higher mortality rates, the hematologic indices of NLR, LMR, PLR, and arterial blood gas parameters of COHb and MetHb had no predictive value on in-hospital mortality. Given their clinical accessibility and cost-effectiveness, pH and lactate measurements may be essential tools for risk stratification, particularly in environments with limited diagnostic capacity. Considering the limitations of the study, prospective and multicenter studies including larger patient populations are needed to obtain more precise outcomes.

Acknowledgements
This study was conducted at the University of Health Sciences, Gazi Yasargil Training and Research Hospital.

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Conflict of interest
No conflict of interest is declared.

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