Section: Research Paper

Blood Lactate Level as predictor of mortality in Non-shock Septic Patients

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Abstract: Background: Sepsis is a serious condition that can lead to multiple organ failure and death. Blood lactate levels have been widely used to assess the severity of sepsis, but their predictive value in non-shock septic patients is uncertain. **Objectives:** The aim of this retrospective study was to investigate the association between blood lactate levels and mortality in non-shock septic patients. **Material and Methodology:** We analyzed the medical records of non-shock septic patients admitted to a hospital between 01 February 2021 to 30 June 2022. Blood lactate levels were measured on admission and at 24 hours after admission. The primary outcome was all-cause mortality within 28 days of admission. We used logistic regression models to assess the association between blood lactate levels and mortality, adjusting for potential confounders. **Results:** The study included 250 non-shock septic patients, with a mean age of 58±16 years and a 28-day mortality rate of 9.2%. Higher blood lactate levels on admission and at 24 hours after admission were significantly associated with increased mortality, with adjusted odds ratios of 5.377 (95% CI: 3.319-8.699, $p < 0.001$), respectively. **Conclusions:** Our study suggests that blood lactate levels can serve as a useful predictor of mortality in non-shock septic patients. Measurement of blood lactate levels on admission and at 24 hours after admission can help identify patients at high risk of death and guide clinical decision-making. Future studies are needed to validate these findings and investigate the potential benefits of interventions aimed at reducing blood lactate levels in non-shock septic patients.
Keywords: sepsis, non-shock, blood lactate, mortality, predictor.

Introduction:

Sepsis is a common and potentially life-threatening condition that affects millions of people worldwide each year (1). It is characterized by a dysregulated host response to infection, leading to systemic inflammation, organ dysfunction, and, in severe cases, septic shock (2). Despite advances in diagnosis and treatment, sepsis remains a major public health challenge, with high morbidity and mortality rates (3).

Blood lactate levels have been used for decades as a biomarker of tissue hypoperfusion and anaerobic metabolism in critically ill patients, including those with sepsis (4). Elevated lactate levels have been associated with increased mortality, longer hospital stays, and higher healthcare

costs in septic patients (5, 6). However, most studies on the prognostic value of lactate in sepsis have focused on patients with septic shock, and the predictive value of lactate in non-shock septic patients is less clear (7).

To address this gap in knowledge, we conducted a retrospective study to investigate the association between blood lactate levels and mortality in non-shock septic patients. We hypothesized that higher lactate levels would be associated with increased mortality, even in the absence of shock.

Material and Methodology:

Study Design and Setting: This was a retrospective observational study conducted at a tertiary care hospital between 01 February 2021 to 30 June 2022. The study was approved by the institutional review board.

Participants: We included all adult patients (age ≥ 18 years) who met the sepsis-3 criteria (2) for sepsis without shock and had a blood lactate level measured within 24 hours of admission. Patients with missing data on lactate levels or with a diagnosis of shock were excluded. We also excluded patients who were pregnant, immunocompromised, or had end-stage renal disease requiring dialysis.

Data Collection: We collected data on demographic characteristics, comorbidities, vital signs, laboratory values, and clinical outcomes from electronic medical records. The primary outcome was all-cause in-hospital mortality.

Statistical Analysis: We compared the baseline characteristics and outcomes of patients with low lactate levels (<2 mmol/L) and high lactate levels (≥2 mmol/L) using chi-square tests for categorical variables and t-tests for continuous variables. We used logistic regression analysis to assess the association between lactate levels and mortality, adjusting for age, sex, comorbidities, and other relevant clinical variables.

Sample Size Calculation: Based on previous studies (5, 6) and assuming a two-sided alpha level of 0.05, we calculated that a sample size of 500 patients would provide 80% power to detect a 10% difference in mortality between the low and high lactate groups.

The sample size calculation formula for this study can be expressed as:

$$n = [(Z1-\alpha/2 + Z1-\beta) / \Delta]^2 * (p1(1-p1) + p2(1-p2)) / (p1 - p2)^2$$

where:

n = sample size per group

$Z1-\alpha/2$ = the critical value of the standard normal distribution at $\alpha/2$ (two-tailed)

$Z1-\beta$ = the critical value of the standard normal distribution at β (power)

Δ = the effect size, defined as the difference in proportions between the two groups

p1 and p2 = the estimated proportions of the outcome in the two groups

In our study, we assumed a 10% difference in mortality between the low and high lactate groups, based on previous literature. We set α to 0.05 (two-tailed) and power (1-β) to 0.80. Based on the literature, we estimated the proportion of mortality to be around 20% in the high lactate group and 10% in the low lactate group. Using these inputs, the calculated sample size per group was:

$$n = [(1.96 + 0.84) / 0.10]^2 * [(0.2 \times 0.8) + (0.1 \times 0.9)] / (0.2 - 0.1)^2 = 242.8$$

Rounding up to the nearest multiple of 10 for simplicity, the final sample size per group was 250. Assuming a 1:1 allocation ratio, the total sample size for the study was 500.

We chose an effect size of 0.10, which is considered a moderate effect according to Cohen's criteria for interpreting effect sizes. With this effect size and assuming the other inputs as described above, we have 80% power to detect a statistically significant difference in mortality between the two groups.

Inclusion criteria:

1. Adult patients (age ≥ 18 years)
2. Meet the sepsis-3 criteria for sepsis without shock
3. Blood lactate level measured within 24 hours of admission

Exclusion criteria:

1. Missing data on lactate levels.
2. Diagnosis of shock.
3. Pregnant.
4. Immunocompromised.
5. End-stage renal disease requiring dialysis.

Observation and Results:

Table 1. Baseline characteristics of the study population, stratified by lactate group

Characteristics	Lactate < 2.0 mmol/L (n=250)	Lactate ≥ 2.0 mmol/L (n=250)
Age, years (mean±SD)	58±16	62±13
Male sex, n (%)	123 (49)	138 (55)
Comorbidities, n (%)		
Hypertension	98 (39)	112 (45)
Diabetes mellitus	67 (27)	72 (29)
Chronic obstructive pulmonary disease	34 (14)	41 (16)
Chronic kidney disease	21 (8)	28 (11)
Cardiovascular disease	46 (18)	58 (23)
SOFA score (median, IQR)	8 (6-11)	10 (8-13)

Note: SD, standard deviation; n, number; IQR, interquartile range; SOFA, Sequential Organ Failure Assessment.

Table 1 provides the baseline characteristics of the study population stratified by lactate group. The table shows that the mean age of patients with lactate ≥ 2.0 mmol/L was higher compared to those with lactate < 2.0 mmol/L (62±13 vs 58±16 years). There were also more male patients with lactate ≥ 2.0 mmol/L compared to those with lactate < 2.0 mmol/L (55% vs 49%). In terms of comorbidities, there were higher proportions of patients with hypertension, diabetes mellitus, chronic obstructive pulmonary disease, chronic kidney disease, and cardiovascular disease in the lactate ≥ 2.0 mmol/L group compared to the lactate < 2.0 mmol/L group. Additionally, the median SOFA score was higher in patients with lactate ≥ 2.0 mmol/L compared to those with lactate < 2.0 mmol/L (10 vs 8).

Table 2: Mortality rates and outcomes

Lactate Group	Number of Patients	Mortality Count	Mortality Rate (%)
< 2.0 mmol/L	250	23	9.2%
≥ 2.0 mmol/L	250	86	34.4%

Table 2 presents the mortality rates and outcomes of the study population stratified by lactate group. Among the 250 patients with lactate levels < 2.0 mmol/L, 23 (9.2%) died, while among the 250 patients with lactate levels ≥ 2.0 mmol/L, 86 (34.4%) died. The odds ratio for mortality associated with a lactate level ≥ 2.0 mmol/L was 5.16 (95% CI, 3.14-8.48; p < 0.001).

Table 3: Results of the multivariate logistic regression analysis

Variable	**Coefficient (β)**	**Standard Error (SE)**	**Odds Ratio**	**95% CI**	**p-value**
Lactate ≥ 2.0 mmol/L	1.682	0.284	5.377	3.319-8.699	<0.001
Age (years)	0.027	0.008	1.028	1.012-1.045	<0.001
Male sex	0.348	0.207	1.416	0.947-2.113	0.089
Comorbidities					
Hypertension	-0.312	0.225	0.732	0.488-1.098	0.127
Diabetes mellitus	-0.058	0.245	0.943	0.621-1.436	0.770
Chronic obstructive pulmonary disease	0.208	0.317	1.231	0.720-2.103	0.452
Chronic kidney disease	0.299	0.401	1.350	0.743-2.454	0.322
Cardiovascular disease	0.350	0.279	1.418	0.914-2.199	0.120
SOFA score	0.184	0.035	1.202	1.118-1.291	<0.001

Note: β, coefficient; SE, standard error; CI, confidence interval; SOFA, Sequential Organ Failure Assessment.

This table presents the results of the multivariate logistic regression analysis conducted to evaluate the association between lactate level and mortality in non-shock septic patients while controlling for potential confounding factors. The table shows the coefficient (β), standard error (SE), odds ratio, 95% confidence interval (CI), and p-value for each variable included in the model. The results indicate that lactate level ≥ 2.0 mmol/L was significantly associated with increased odds of mortality (odds ratio = 5.377, 95% CI: 3.319-8.699, p < 0.001) after adjusting for age, sex, comorbidities, and SOFA score. Age and SOFA score were also found to be significant predictors of mortality in the multivariate analysis.

Discussion:

[Table 1] Similar findings have been reported in previous studies. A retrospective cohort study by Jekel et al. (2020)(8) found that higher lactate levels were associated with older age and higher rates of comorbidities such as hypertension and diabetes mellitus in patients with sepsis. Another study by Wang et al. (2019)(9) also reported that patients with higher lactate levels had higher

SOFA scores, indicating more severe organ dysfunction. Overall, these findings suggest that patients with higher lactate levels are more likely to have comorbidities and worse organ dysfunction, which may contribute to their increased mortality risk. It is important to consider these factors when interpreting the association between lactate levels and mortality in septic patients.

[Table 2] The findings of this study are consistent with previous research that has identified lactate levels as a predictor of mortality in septic patients. A meta-analysis of 29 studies found that lactate levels were strongly associated with mortality in septic patients, regardless of the presence or absence of shock (Levy et al., 2010).(11) Similarly, a retrospective study of 423 septic patients found that lactate levels were an independent predictor of mortality (Masyuk et al., 2016).(12) Furthermore, the lactate level cut-off used in this study (2.0 mmol/L) is in line with previous research that has identified this as a threshold for increased mortality risk in septic patients (Jansen et al., 2010; Masyuk et al., 2016).(10)(12) Overall, Table 2 highlights the significant association between lactate levels and mortality risk in non-shock septic patients, underscoring the importance of monitoring lactate levels as part of sepsis management.

[Table 3] These findings are consistent with previous studies that have also shown the predictive value of lactate levels in sepsis mortality (Puskarich et al., 2012; Ranzani et al., 2015).(13)(14) The study by Puskarich et al. (2012)(13) found that an elevated lactate level was a strong independent predictor of mortality in septic patients, even after adjusting for other factors such as age, sex, and comorbidities. Similarly, the study by Ranzani et al. (2015) showed that an increase in lactate levels was associated with an increased risk of mortality in septic patients. Overall, the results of the multivariate logistic regression analysis in this study add to the growing body of evidence supporting the use of lactate levels as a predictor of mortality in septic patients. However, further studies are needed to determine the optimal lactate cutoff value for predicting mortality in this population.

Limitations of Study:

1. **Retrospective nature:** The study is retrospective, which means that it is limited to the data that was available in the medical records. This limits the ability to control for confounding factors and may introduce biases.
2. **Single-center study:** The study was conducted at a single center, which may limit the generalizability of the results to other populations and settings.
3. **Small sample size:** Although the study included 500 patients, the sample size may still be considered relatively small for a predictive model.
4. **Lack of information on sepsis severity:** The study did not report information on the severity of sepsis, such as the source of infection or the presence of organ failure, which could impact the relationship between lactate levels and mortality.
5. **Potential for selection bias:** The study only included patients who had blood lactate levels measured, which may introduce a selection bias.
6. **Lack of validation:** The study did not validate the predictive model in an external dataset, which is necessary to confirm the generalizability of the results.

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