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Evaluation of serum lactate as a predictor for morbidity in sepsis and trauma cases in a tertiary care hospital

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ABSTRACT

Background. The management of sepsis relies heavily on the early detection of sepsis and initial fluid resuscitation, followed by lung-protective ventilation. The therapies used to treat sepsis and septic shock include vasopressor therapy, inotropic therapy, antimicrobial therapy, hemodynamic support, immunomodulation, source control, blood product administration, glucose control, renal replacement therapy, and nutrition.

Materials and methods. Patients were initially examined to find signs of severe sepsis. Exclusion criteria were applied if fewer than two systemic inflammatory response syndrome criteria were present, or if infection was not suspected. Seventy-six patients were selected, and serum lactate, along with other necessary blood investigations, was measured.

Results. In this study, approximately 74% of patients were aged between 25 and 50 years. About 23% were older than 50 years, and only 2% were younger than 25 years. The average age was 48.87 years with a standard deviation of 3.21. There was a statistically significant association between serum lactate levels and outcomes ($P<0.05$).

Conclusion. The primary goals in sepsis management are early detection and initial fluid resuscitation. A recent comparison of septic shock patients with and without elevated lactate levels suggests that factors other than sepsis itself may contribute to lactate production. Our study supports these findings.

Keywords: septic shock, sepsis, morbidity, trauma, serum lactate

INTRODUCTION

When the body's response to infection becomes disordered, a condition known as sepsis can develop. Sepsis leads to a rapid decline in health, often resulting in the sudden failure of multiple organs and has a high mortality rate[1]. Approximately 50% of individuals who experience septic shock will die from it. The mortality rates associated with sepsis are directly related to the severity of the condition and the number of organs affected.

Sepsis is characterized by a complex pathophysiology that includes both pro-inflammatory and anti-inflammatory cellular and molecular changes in response to infections, which ultimately cause systemic inflammation and organ failure [2,3]. This condition results from several factors, including endothelial injury, increased permeability of blood vessels, dysfunction of small blood vessels, activation of the coagulation system, and decreased tissue oxygenation.

The development of sepsis syndrome (SIRS) is driven by the pro-inflammatory response, the failure of the compensatory anti-inflammatory response (CARS), and immunoparalysis. Sepsis progresses through three phases: the initial phase, which involves the release of bacterial toxins; the middle phase, which involves the production of inflammatory mediators; and the final phase, which involves the effects of certain mediators.

Before starting antimicrobial treatment, physicians conduct a series of tests to determine the extent of the infection and whether any organs are failing[4,5]. These tests include a complete blood count, coagulation profile, all electrolytes, serum creatinine, glucose levels, and two sets of blood cultures. Diagnosing sepsis requires the symptoms and

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signs of systemic inflammation, organ failure, and tissue perfusion abnormalities.

In this manner, patients at high risk for complications can access biomarkers, and the progression of the disease can be monitored. Biomarkers provide crucial information about disease activity, the presence or absence of sepsis, and its severity, which aids in effective treatment and improved outcomes [6]. Diagnosing sepsis typically involves measuring procalcitonin, C-reactive protein (CRP), complement proteins, organ failure indicators, and markers of the immunosuppressive phase.

Lactic acid was discovered in sour milk in 1780 by Karl Wilhelm Scheele. It wasn't until 1843 and 1851 that Johann Joseph Scherer demonstrated the presence of lactic acid in human blood, and even then only under diseased conditions. Lactic acid is one of the most significant organic acids, used extensively in both biotechnology and industry.

Septic shock occurs when the inflammatory response to an infection leads to decreased tissue oxygenation, fluid loss, blood vessel dilation, and heart failure [7]. The primary causes of death in this condition are low blood pressure and multiple organ failures that do not respond to treatment. Effective therapy for sepsis and septic shock relies on prompt diagnosis, rapid fluid resuscitation, and lung-protective ventilation. The treatment regimen includes a variety of approaches, such as vasopressor therapy, inotropic therapy, antimicrobial therapy, hemodynamic support, immunomodulation, source control, blood product administration, glycemic management, renal replacement therapy, and nutritional support.

MATERIALS AND METHODS

Patients were initially examined for signs of severe sepsis. Exclusion criteria included cases where two or more systemic inflammatory response syndrome criteria were not present or infection was not suspected. Selected patients had serum lactate and other relevant samples taken.

Inclusion criteria

All trauma cases in the emergency department within 12 hours of injury; patients suspected to have or with symptoms and signs of sepsis; and age groups between 18 to 60 years, inclusive of both genders.

Exclusion criteria

Conditions that may alter serum lactate and confound the results such as myocardial infarction, active liver diseases, anemia, malignancies, chronic smoking, and alcohol abuse, as well as patients reporting with poisoning.

Study period

The study was conducted over a period of 18 months.

Sampling method

The sampling method used was purposive sampling. The minimum required sample size was calculated to be 76 patients.

Data collection tools

Blood sample collection for serum lactate, serum creatinine, serum bilirubin, coagulation profile, complete blood count, blood and urine culture, CRP, and procalcitonin. Spirometry was used for pulmonary function tests.

Data analysis method

Qualitative variables were expressed in percentages. The chi-square test was used to assess the association of different variables. The difference in parametric distribution between the variables was assessed by the T-test.

In the study “Evaluation of serum lactate as a predictor for morbidity in sepsis and trauma cases in a tertiary care hospital”, utilizing multivariate regression analysis could significantly refine the assessment of serum lactate's predictive value by adjusting for various confounders like comorbidities and differences in treatment protocols. This approach would isolate the direct effects of serum lactate on patient outcomes, offering clearer insights into its role as an independent predictor.

However, the implementing multivariate regression was not feasible within the current study design, due to several factors:

1. **Study scope and resources:** The original design and resource allocation could not have supported the complexity of multivariate analysis due to limitations in software, statistical expertise, and funding.
2. **Data availability:** The necessary data to perform a robust multivariate analysis, such as detailed records on all potential confounders, have not been collected because the focus was narrow, and our study is a preliminary investigation into a potential hypothesis.
3. **Study design and objectives:** Our study hasbeen primarily exploratory, aiming to establish a correlation rather than to explore causation in depth.
4. **Complexity and interpretability:** A simpler model was chosen to keep the analysis interpretable and to ensure that the findings are accessible and actionable for clinical practitioners who need straightforward answers about risk factors and outcomes.

5. **Sample size:** The sample size of 76 patients might limit the power of a multivariate analysis. Multivariate techniques require larger datasets to effectively estimate the effects of multiple predictors while adjusting for confounders. The risk of overfitting the model with too many variables relative to the number of events (patient deaths or severe outcomes) was a critical consideration.

RESULTS

In this study, a total of 76 participants were analyzed, according to age, gender, and clinical outcomes. The majority of participants, 56 individuals (74%), were aged between 25 and 50 years, while 18 participants (23%) were over 50 years old, and a small portion, 2 participants (2%), were under 25 years (Figure 1). The average age of participants was 48.87 years with a standard deviation of 3.21. Regarding gender distribution, approximately 63% of the participants were male, while 37% were female (Figure 2).

A notable aspect of the study was the necessity for ventilation among the participants. About 16% of the patients required mechanical ventilation, indicating a subset of patients with more severe clinical presentations. This aspect of the study highlights the critical care needs of a significant portion of the patient population (Table 1).

The survival outcomes were closely monitored throughout the study. Of the 76 participants, 55 patients (72%) survived, whereas 21 patients (28%) did not survive, providing a clear overall survival rate within the study cohort (Table 2, Figure 3). This survival data underscores the importance of continuous monitoring and intervention as necessary for the management of critically ill patients.

TABLE 1. Requirement of ventilation among study participants

Ventilation	Frequency	Percentage	n(%)
Yes	12	16	12 (16%)
No	64	84	64 (84%)
Total	76	100	76 (100%)

TABLE 2. Serum lactate levels at 0-3 hours, 24 hours and 48 hours and outcome

Serum lactate levels (mg/dl)	Survivors n(%)	Non-survivors n(%)	Total n(%)
0-3 hours			
>4.0	6 (24%)	19 (76%)	25 (100%)
≤4.0	49 (96%)	2 (4%)	51 (100%)
Total	55 (72%)	21 (28%)	76 (100%)
24 hours			
>4.0	1 (9%)	10 (91%)	11 (100%)
≤4.0	54 (83%)	11 (17%)	65 (100%)
Total	55 (72%)	21 (28%)	76 (100%)
48 hours			
>4.0	1 (14%)	6 (86%)	7 (100%)
≤4.0	54 (78%)	15 (22%)	69 (100%)
Total	55 (72%)	21 (28%)	76 (100%)

Blood lactate values were observed at different intervals—0-3 hours, 24 hours, and 48 hours—and were correlated with patient outcomes (Table 2, Figure 4)). At the 0-3 hour mark, 25 patients had serum lactate levels greater than 4.0 mg/dl, among whom 6 patients (24%) survived while 19 patients (76%) did not survive. Conversely, 51 patients had blood lactate values of 4.0 mg/dl or less, with a significantly higher survival rate among 49 patients (96%), and only 2 patients (4%) did not survive.

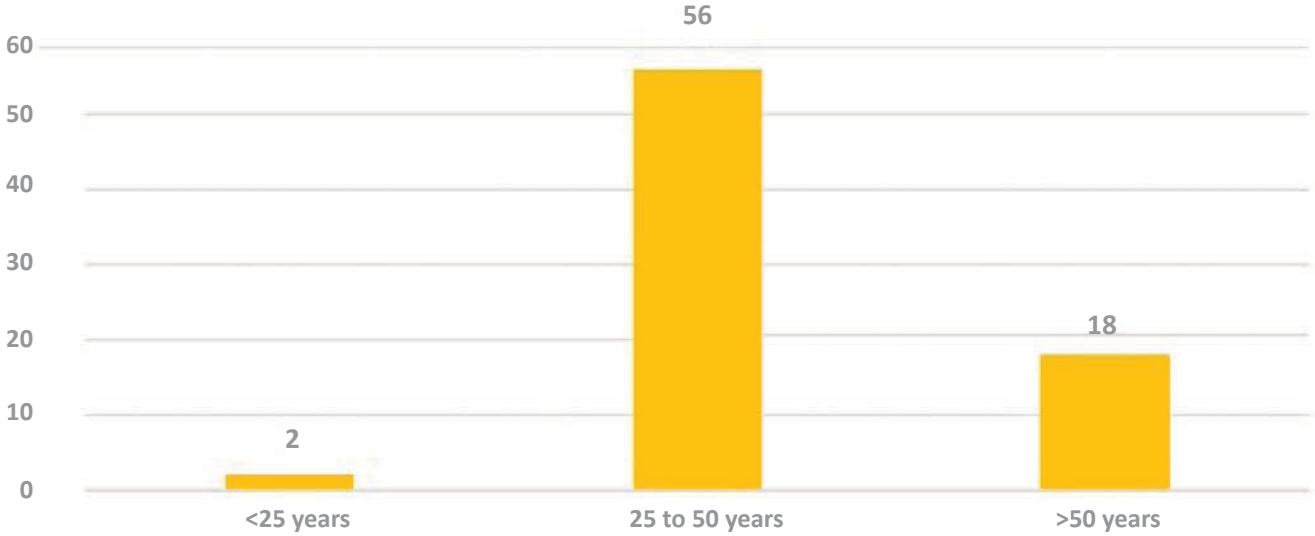

FIGURE 1. Age wise distribution of study participants

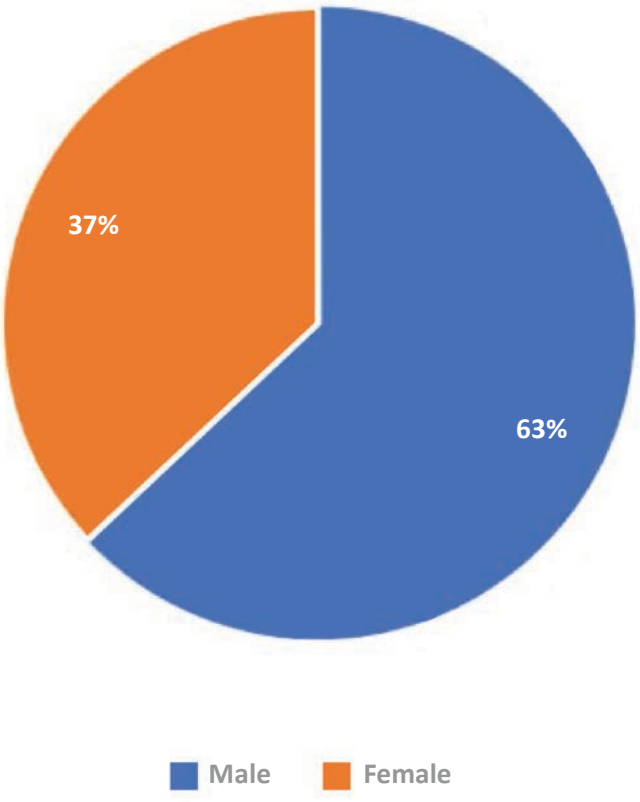

FIGURE 2. Gender wise distribution of study participants

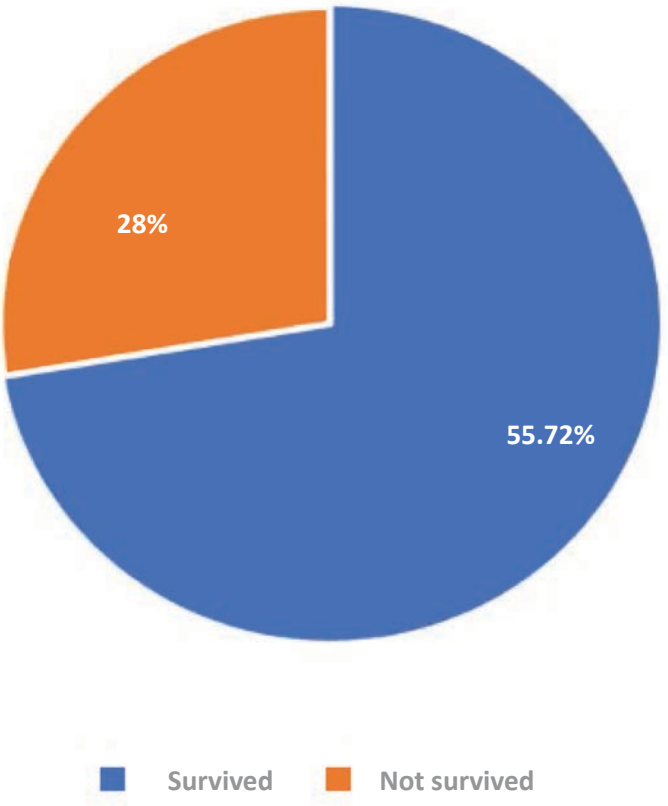

FIGURE 3. Outcome of study participants

At the 24-hour interval, the data showed that 11 patients had serum lactate levels greater than 4.0 mg/dl, with just 1 patient (9%) surviving and 10 patients (91%) not surviving. In contrast, 65 patients had blood lactate values of 4.0 mg/dl or less, with 54 patients (83%) surviving and 11 patients (17%) not surviving. This trend continued to highlight the prognostic value of blood lactate levels in patient outcomes.

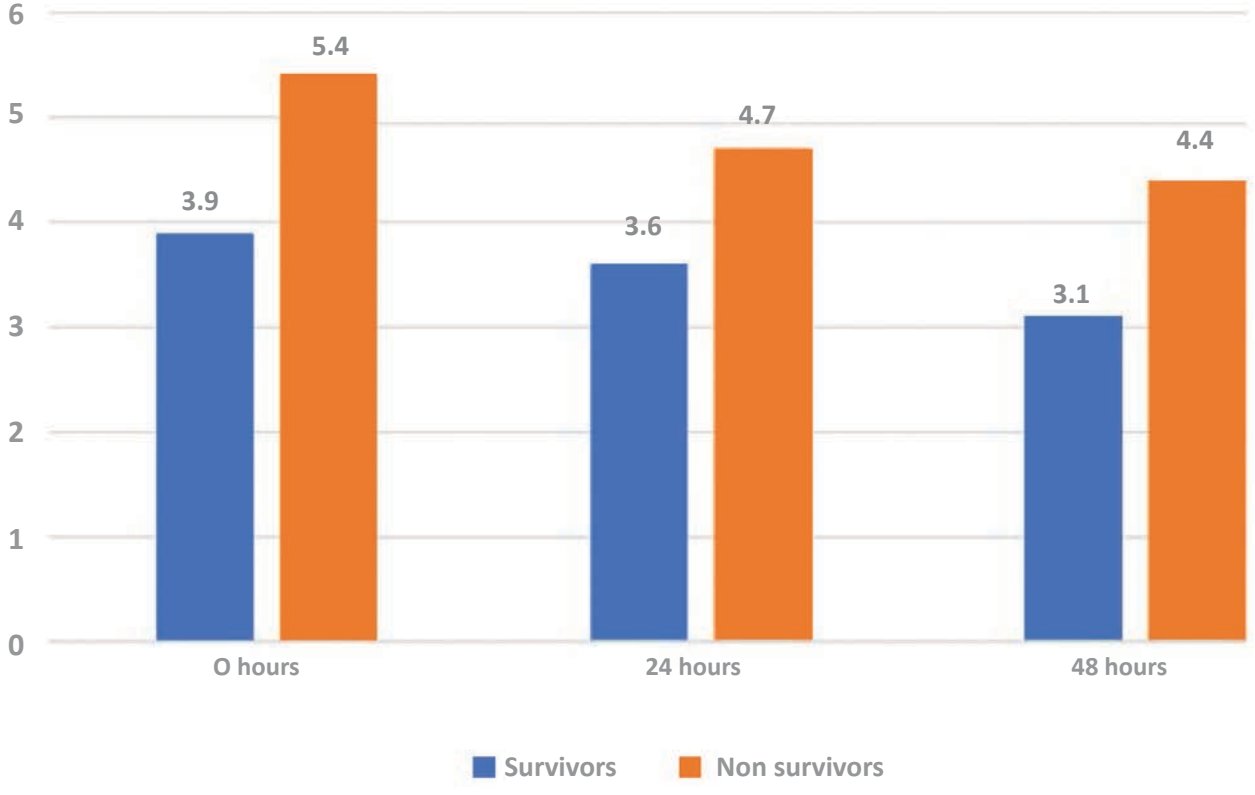

FIGURE 4. Association between serum lactate levels and outcome

By the 48-hour mark, 7 patients had serum lactate levels of more than 4.0 mg/dl, with 1 survivor (14%) and 6 non-survivors (86%). Meanwhile, 69 patients had blood lactate values of 4.0 mg/dl or less, with 54 survivors (78%) and 15 non-survivors (22%). These findings consistently show a statistically significant relationship between serum lactate levels and patient outcomes ($P<0.05$), reinforcing the importance of monitoring serum lactate as a prognostic marker in critical care settings.

DISCUSSION

Sepsis involves both inflammatory and coagulation pathways that occur in response to microbial insults. This process, characterized by pro-inflammatory cytokines, procoagulants, and adhesion molecules released from immune cells, results in systemic inflammatory response syndrome (SIRS) or sepsis symptoms.

For patients presenting with trauma and signs and symptoms of sepsis, serum lactate levels are recognized as predictors of survival or mortality. Studies indicate that vigorous treatment within 24 hours of injury, which normalizes serum lactate, leads to positive outcomes. Critical components of aggressive treatment include timely resuscitation, antibiotics, surgical intervention, and vasopressor use, all aiming to improve patient survival. However, outcomes vary among patients due to individual pre-existing conditions that affect their response to injury.

Combining these markers with lactate levels provides a multi-dimensional view of a patient's condition, facilitating a more tailored and effective management strategy. This approach not only aids in the early detection of potential complications but also enhances ongoing monitoring and adjustment of treatment plans. Future studies should investigate the potential of a multi-marker approach in predicting outcomes for sepsis and trauma patients. This could involve longitudinal studies that track the evolution of these biomarkers in relation to patient outcomes, enabling clinicians to better understand their combined prognostic value while potentially leading to the development of integrated scoring systems to more accurately predict patient trajectories and optimize care.

Severe sepsis has a fatality rate of between 20% and 50%, with its prevalence rising by 1.5% each year. It is one of the leading causes of death among critically ill patients and the second most common cause of death overall in the United States. This rise is attributed to demographic changes, the use of stronger antibiotics, immunosuppressive therapies, and invasive technologies in treating infections and neoplastic diseases, along with the disease's increasing prevalence and emergence in new patient populations.

Approximately half of the critically ill patients undergoing treatment for sepsis have normal serum lactate levels, a phenomenon whose pathophysiology remains unclear. Despite this, serum lactate remains a reliable predictor of mortality even among the sickest patients. Initial serum lactate levels are independently linked to mortality when patients present with septic shock in emergency departments, making it a potentially reliable prognostic indicator.

Chronic kidney disease (CKD) can also elevate blood lactate levels due to decreased clearance. However, there were insufficient CKD or liver failure patients in this analysis to obscure the relationship between elevated blood lactate and mortality. Common sepsis foci included the pulmonary and urogenital tracts.

Acute renal failure (41.7%) and respiratory failure (39.3%) were the most common complications during hospitalization. According to Mikkelson ME et al., the most frequent complications were renal (43.4%) and neurological (34.2%). There is a negative correlation between increased lactate levels and outcomes, with some studies identifying a substantial correlation between mortality and a lactate cutoff of 4 mmol/L to distinguish sepsis from severe sepsis.

Arnold RC et al. identified an independent predictor as lactate non-clearance. Their multicenter prospective study found that an inability to clear lactate during resuscitation significantly heightened the risk of death.

Previous studies have consistently shown that elevated serum lactate levels are linked to increased mortality rates in both the hospital and ICU. These findings have influenced management strategies that prioritize early assessment and interventions targeting blood lactate levels.

Filho RR et al. conducted a retrospective cohort study to identify the initial blood lactate level most strongly associated with 28-day mortality in resuscitated septic shock patients. Using ROC curve analysis, they found that baseline lactate levels above 2.5 mmol/L had the highest area under the curve for predicting 28-day mortality. Mortality was 16.9% in patients with lactate levels above 2.5 mmol/L, compared to 5.8% in those with levels below this threshold. Adjusted Cox regression analysis confirmed that initial lactate levels exceeding 2.5 mmol/L, along with SOFA scores at ICU admission, were independently linked to higher 28-day mortality. This study suggests that a lactate level above 2.5 mmol/L is a strong predictor of 28-day mortality in severe sepsis and septic shock, supporting the need for further prospective studies to explore its potential as a resuscitation trigger.

The current findings emphasize the prognostic importance of serum lactate levels for predicting immediate survival in sepsis and trauma, with elevated levels indicating acute risk and correlating with higher mortality in critical care. Beyond identifying immediate threats, lactate monitoring may predict long-term outcomes, an area our study has not yet addressed. Future research could greatly benefit from examining long-term recovery trajectories of patients with initially high lactate levels, including monitoring post-discharge recovery and identifying persistent complications like organ dysfunction or cognitive impairments. Furthermore, interventional studies focusing on aggressive management of lactate levels could assess their impacts on long-term morbidity and mortality, while exploring biological mechanisms behind prolonged elevations.

Monitoring lactate clearance allows for a more nuanced assessment of patient status beyond initial presentation, helping to distinguish between patients who are improving and those who remain at high risk. This approach adds a valuable dimension to the prognosis of sepsis and trauma patients, as rapid changes in lactate levels can indicate the success or failure of therapeutic interventions and help guide further clinical decisions.

Limitations

- **Age range limitation:** Includes only patients aged 18 to 60, excluding pediatric and elderly populations who are highly vulnerable to sepsis and trauma.
- **Exclusion of specific medical conditions:** Omits patients with myocardial infarction, liver diseases, anemia, and malignancies, limiting insights into lactate dynamics under these conditions.
- **Time window restriction for trauma cases:** Limited to trauma presentations within 12 hours, missing potential late-presenting cases with significant outcomes.
- **Lifestyle factors:** Excludes chronic smokers and alcoholics, which may affect the study's generalizability due to different baseline lactate levels.
- **Focus on already suspected sepsis cases:** May overlook the potential of serum lactate in detecting early or subtle cases of sepsis.
- **Sampling bias:** Utilizes purposive sampling, potentially introducing bias and limiting the representativeness of the study results.

CONCLUSION

The main objectives in managing sepsis and septic shock are early identification and prompt fluid resuscitation. Recent studies comparing septic shock patients, irrespective of elevated lactate levels, suggest that factors beyond lactate may contribute to the condition. Our study aligns with these findings, indicating that while serum lactate is an important biomarker, other underlying mechanisms also contribute to the progression and outcomes of sepsis. Thus, a comprehensive approach considering multiple factors is essential for effective management and improved patient outcomes in sepsis and septic shock.

Recommendations for future research:

- Expand age criteria to include all age groups.
- Include a wider range of medical and lifestyle conditions to enhance understanding.
- Extend the trauma time window to capture data on late presentations.
- Investigate the role of other biomarkers in conjunction with serum lactate.
- Diversify study settings to include community hospitals and tertiary care centers for broader applicability.
- Provide a detailed rationale for any exclusions to clearly understand their impact and mitigate confounding factors.

Conflict of interest:
There are no conflicts of interest.

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