



SERUM LACTATE LEVEL AS PREDICTOR OF OUTCOME IN SEPSIS PATIENTS IN INTENSIVE CARE UNIT

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ABSTRACT **Background-** Sepsis is a common critical condition caused by the body's overwhelming response to certain infective agents. Many biomarkers, including the serum lactate level, have been used for sepsis diagnosis and guiding treatment. Recently, the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) recommended the Sequential Organ Failure Assessment (SOFA) and the quick SOFA (qSOFA) rather than lactate for screening sepsis and assess prognosis. This study explores correlation between blood lactate levels in patients with sepsis admitted into the intensive care unit and their hospital outcomes. **Materials and Methods-** This was an observational study conducted in the Department of Medicine, in a tertiary care hospital of India conducted for a period of 2 years. Sepsis Patients admitted into Intensive Care Unit (ICU) above 18 years of age were included in the study. Information was collected through a pre-tested and structured proforma for each patient. Serum Lactate levels at admission, 6 hours after admission and 24 hourly for the next 3 days was recorded to observe for lactate clearance from the body. The role of lactate monitoring helped in determining prognostic potential and focus on early stage of sepsis management. Lactate clearance and organ dysfunction was assessed and outcome was quantified using SOFA scoring. **Results-** Being a quantitative data, normality of data was tested using Shapiro-wilk test. Mann-Whitney U test was used to compare between patients with different outcome. Serum lactate levels (at 6 hours) was higher in patients who couldn't survive (10.33) as compared to group of patients who survived (4.82) and the difference between the two was statistically significant ($p = 0.001$). **Conclusion-** The predictive usefulness of serial serum lactate monitoring for morbidity and mortality is confirmed by this study. However, it would be prudent to note that recovering from such an insult takes a lot of time. Even if a critical patient has survived the current crisis, lactate readings should likely be monitored for longer periods of time.

KEYWORDS : Lactate, SOFA, Sepsis, Serum serial lactate, qSOFA

INTRODUCTION

Sepsis is a potentially fatal organ failure brought on by an improperly controlled host response to an infection. In a subgroup of sepsis called shock, particularly severe metabolic, cellular, and circulatory abnormalities are linked to a higher risk of death than sepsis alone. [1,2] Adenosine triphosphate is produced in shock situations by the anaerobic metabolism of glucose. Lactate is produced as a result of this procedure. Serum lactate levels are traditionally low in normal individuals. The reference range is around 1 ± 0.5 mmol/L. Blood lactate concentrations should not exceed 2 mmol/L. [3] In patients with sepsis, lactate buildup is a sign of tissue hypoperfusion and has been linked to higher rates of morbidity and mortality in a variety of conditions, including trauma, sepsis, multiple organ failure, and geriatric individuals. [4,5]

Patients who are critically ill frequently have hyperlactatemia, or elevated blood lactate levels. Lactate levels can rise as a result of mechanisms unrelated to tissue oxygenation, while being routinely used to diagnose deficient tissue oxygenation. Increased glycolysis could play a significant role in the development of hyperlactatemia, particularly in critically ill individuals. However, the presence of elevated lactate levels has significant effects on the morbidity and mortality of patients who are hyper-lactatemic. Structured lactate measurements should be included in resuscitation protocol, since lactate levels can be quickly determined at the bedside from a variety of sources. [3,6]

Severity of sepsis and MODS has been predicted and indicated by serum lactate. It might be conceivable to use serum lactate as a standalone predictive measure of sepsis if there is a significant association between serum lactate levels and patient outcomes. This study intends to investigate this potential with the aim to study correlation between blood lactate levels in patients with sepsis admitted into the intensive care unit and their hospital outcomes.

MATERIALS AND METHODS

This was an observational study conducted from March 2020 to September 2022 in the Department of Medicine, at a tertiary care hospital of Maharashtra in central India. Sepsis patients admitted into Intensive Care Unit (ICU) above 18 years of age who gave written

informed consent were included in the study.

Inclusion Criteria- Age group > 18 years. Patients with more than one manifestation which includes: 1. Body temperature greater than 38°C or less than 36°C . 2. Heart rate greater than 90 beats per min. 3. Hyperventilation as indicated by respiratory rate > 20/min or PaCO_2 less than 32 mmHg. 4. An alteration in the WBC count such count greater than 12000/cmm, a count less than 4000/cmm. 5. Evidence of infection. 6. Tissue hypoperfusion, such as arterial hypotension, oliguria, sensory abnormalities, delayed capillary filling time, were included.

Exclusion Criteria- Cases with following factors were excluded from the study: 1) Receiving Biguanides- as it alters the Lactate metabolism. 2) Patients who did not present serum lactate level determinations in the first six hours after admission

Approval from institutional ethical committee was obtained before start of study. Information was collected through a pre-tested and structured proforma for each patient. Patients underwent detailed history, clinical examination and laboratory investigations. Patient's clinical history and examination findings were recorded prospectively. Serum Lactate levels at admission, 6 hours after admission and 24 hourly for the next 3 days was recorded to observe for lactate clearance from the body. The role of lactate monitoring helped in determining prognostic potential and focus on early stage of sepsis management. Lactate clearance and organ dysfunction was assessed and outcome was quantified using SOFA scoring. The expected outcome was the determination of prognostic potential of Lactate for focus on early stage of sepsis management.

RESULTS

The data was entered and cleaned using MS-Excel and analyzed statistically using SPSS-25. Quantitative variables were expressed as mean value + standard deviation or median. Qualitative data was expressed as percentages (%) and proportion. Normality of data was tested using Shapiro-wilk test. Mann-Whitney U test was used to compare between patients with different outcome. There were a total of 100 patients who fulfilled the inclusion criteria and the results were as follows.

Table 1- Descriptive statistics for different variable

Variables	Mean $\pm$ Std. Deviation
Age (years)	46.48 $\pm$ 18.53
Systolic blood pressure (mm Hg)	122.40 $\pm$ 33.99
Diastolic blood pressure (mm Hg)	77.56 $\pm$ 16.85
Heart rate (beats/minute)	109.7 $\pm$ 21.67
Respiratory rate (breaths per minute)	25.94 $\pm$ 5.31
Oxygen Saturation (%)	94.43 $\pm$ 7.26
Haemoglobin (gm%)	11.83 $\pm$ 3.42
Total leukocyte count (per mm ³)	15,664.06 $\pm$ 7006.05
Platelets count (lacs per mm ³)	2.03 $\pm$ 1.20
Total Bilirubin (mg/dL)	2.55 $\pm$ 4.55
Direct Bilirubin (mg/dL)	1.11 $\pm$ 2.32
SGOT (U/L)	121.3 $\pm$ 630.96
SGPT (U/L)	67.16 $\pm$ 277.76
Serum Sodium	134.96 $\pm$ 8.11
Serum Potassium	4.42 $\pm$ 0.78
Serum Creatinine	1.81 $\pm$ 2.03
Serum Urea	48.97 $\pm$ 33.49
ESR	25.60 $\pm$ 14.67
Serum C-reactive protein (CRP)	59.55 $\pm$ 63.86
Glasgow Coma Score (GCS)	11.01 $\pm$ 3.01
SOFA Score	4.61 $\pm$ 2.97
Serum lactate (at admission)	5.61 $\pm$ 3.09
Serum lactate (at 6 hours)	5.26 $\pm$ 3.29
Serum lactate (at 24 hours)	4.16 $\pm$ 3.13
Serum lactate (at 48 hours)	3.26 $\pm$ 2.46
Serum lactate (at 72 hours)	2.71 $\pm$ 3.25

Table 1 shows the descriptive statistics for different variables in our study. Mean age for patients in our study was 46.48 years. Mean systolic blood pressure (SBP) and mean diastolic blood pressure (DBP) were 122.40 and 77.56 mm Hg respectively. Mean hemoglobin concentration for our study population was found to be 11.83 gm% while mean total leukocytes count was 15,664.06 per mm³. Mean serum lactate levels was found to be 5.61, 5.26, 4.16, 3.26 and 2.71 at admission, 6 hours, 24 hours, 48 hours and 72 hours respectively. SOFA score average for our study population was found to be 4.61 while Glasgow coma score (GCS) was 11.01 respectively.

Table 2-Comparison between S. lactate levels and Outcome

Duration	S. lactate	Outcome		p value*
		Survived	Death	
At admission	Normal (≤ 1.5)	04 (4.3)	00 (0)	1.00*
	Raised (> 1.5)	88 (95.7)	08 (100)	
	Total	92 (100)	08 (100)	
At 6 hours	Normal (≤ 1.5)	04 (4.3)	00 (0)	1.00*
	Raised (> 1.5)	88 (95.7)	08 (100)	
	Total	92 (100)	08 (100)	
At 24 hours	Normal (≤ 1.5)	17 (18.5)	00 (0)	0.60*
	Raised (> 1.5)	75 (81.5)	07 (100)	
	Total	92 (100)	07 (100)	
At 48 hours	Normal (≤ 1.5)	23 (25)	00 (0)	0.56*
	Raised (> 1.5)	69 (75)	04 (100)	
	Total	92 (100)	04 (100)	
At 72 hours	Normal (≤ 1.5)	33 (35.9)	00 (0)	1.00*
	Raised (> 1.5)	59 (64.1)	01 (100)	
	Total	92 (100)	01 (100)	

*Fischer Exact test

Table 2 shows the comparison between serial serum lactate levels (at admission, 6 hours, 24 hours, 48 hours and 72 hours) and outcome observed in our study. Out of the total 100 patients, 92 were discharged while 8 were deceased. The association between serial serum lactate levels and outcome was not found to be statistically significant.

Table 3- Comparison of S. lactate (at 6 hours) with Outcome

Outcome	Mean	Standard Deviation	U, p value*
Survived	4.82	2.97	65, 0.001
Died	10.33	2.59	

* p value < 0.05 statistically significant; Mann Whitney U test used

Table 3 shows the comparison of serum lactate levels (at 6 hours) with outcome observed in present study. Serum lactate levels (at 6 hours)

was higher in patients who couldn't survive (10.33) as compared to group of patients who survived (4.82) and the difference between the two was statistically significant ($p = 0.001$).

DISCUSSION

In the present study the distribution of patients according to outcome observed in them was that majority of patients (92%) survived and got discharged. Out of total patients, 8% of patients died. Mean age for patients was 46.48 years. Mean systolic blood pressure (SBP) and mean diastolic blood pressure (DBP) were 122.40 and 77.56 mm Hg respectively. Mean hemoglobin concentration was found to be 11.83 gm% while mean total leukocytes count was 15,664.06 per mm³. Mean serum lactate levels was found to be 5.61, 5.26, 4.16, 3.26 and 2.71 at admission, 6 hours, 24 hours, 48 hours and 72 hours respectively. 91 patients who had survived and eight patients (8) who had death as their outcome while only one (1) patient had normal serum lactate level (≤ 1.5) who had survival as the outcome. The association between serum lactate levels (at admission) and outcome was not found to be statistically significant ($p = 1$). Raised serum lactate levels (> 1.5) was seen in 88 patients who had survived and eight patients (8) who had death as their outcome while only four (04) patients had normal serum lactate level (≤ 1.5) who had survival as their outcome. The association between serum lactate levels (at 6 hours) and outcome was found to be statistically significant ($p = 0.001$). Raised serum lactate levels (> 1.5) was seen in 75 patients who had survived and seven patients (8) who had death as their outcome while 17 patients had normal serum lactate level (≤ 1.5) who had survival as their outcome. The association between serum lactate levels (at 24 hours) and outcome was not found to be statistically significant ($p = 0.60$). Serum lactate levels (> 1.5) was seen in 69 patients who had survived and four patients (04) who had death as their outcome while 23 patients had normal serum lactate level (≤ 1.5) who had survival as their outcome. The association between serum lactate levels (at 48 hours) and outcome was not found to be statistically significant ($p = 0.56$).

Similar studies such as **Innocenti, F et al** it was found in the period November 2011–December 2016, we enrolled 268 patients, admitted in High-Dependency Unit with a diagnosis of sepsis. Lactate dosage was performed at admission (T0), after 2 h (T2), 6 h (T6) and 24 h (T24); At every evaluation, the lactate level was higher in patients with shock than in those without (T0 3.8 $\pm$ 3.8 vs 2.4 $\pm$ 2.1; T6 2.9 $\pm$ 3.2 vs 1.6 $\pm$ 1.1; T24 3.0 $\pm$ 4.4 vs 1.4 $\pm$ 0.9 meq/L, all $p < 0.001$). Among patients with shock, an analysis for repeated measures confirmed a more marked lactate level reduction in survivors compared with non-survivors, both by day-7 and in-hospital mortality ($p = 0.057$ and $p = 0.006$). Higher lactate levels and decreased clearance were associated with an increased short-term and intermediate-term mortality regardless of the presence of shock.[7]

In a study by **Oliveros-Rodríguez H et al**, 233 patients participated. The average age was 38 years. 78% of the patients were male, with 21% of the mortality at seven days in the ICU. The average of length of stay for survive patients was nine days in contrast to five days of mortality patient. The lactic acid average was associated with mortality at seven days in the three time measurements.[8]

Dubey et al conducted a study among 160 sepsis patients having scores greater than two on the sequential organ failure assessment (SOFA). Ninety percent of the patients had blood lactate levels ≥ 4 mmol/L, with a mean of 5.1 $\pm$ 1.2 mmol/L. 75.6% of patients had a mean AG of ≥ 12 , with a mean of 14.0 $\pm$ 3.9. Likewise, patients with AG ≥ 12 had a larger percentage of patients with lactate levels ≥ 4 mmol/L than patients with AG < 12 (95.9% vs. 71.8%, $p < 0.0001$). For both serum lactate (AUC 0.797, $p < 0.0001$) and AG (AUC 0.835, $p < 0.0001$), the AUC of ROC in predicting mortality was significant.[9] Other recent significant works by **Park H et al**, **Noparatkailas N et al**, **Zhang b et al** and **Alshiakh SM et al** have serum lactate level as predictor of outcome in sepsis patients in intensive care unit.[10-13]

CONCLUSION

The predictive usefulness of serial serum lactate monitoring for morbidity and mortality is confirmed by this study. In individuals who have suffered trauma or sepsis, serial lactate levels can be utilized to predict a grave prognosis. However, it would be prudent to note that recovering from such an insult takes a lot of time. Even if a critical patient has survived the current crisis, lactate readings should likely be monitored for longer periods of time. Regular lactate analysis would be useful in these individuals, but it would also rely on availability and

test costs. The aforementioned concept is not supported by any published studies. Serial blood lactate analysis will remain helpful in predicting shock in the context of normal physiological parameters, predicting the emergence of multiorgan dysfunction as a shock consequence, and assessing the response to early resuscitation.

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