ORIGINAL ARTICLE

CORRELATION BETWEEN SERUM LACTATE LEVELS AND MORTALITY IN PATIENTS WITH SEPSIS: A CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Sepsis remains one of the leading causes of in-hospital mortality worldwide, particularly in developing countries. Serum lactate, a by-product of anaerobic metabolism, reflects tissue hypoperfusion and has emerged as a potential prognostic biomarker.

Objective: To determine the correlation between serum lactate levels and mortality among patients with sepsis admitted to tertiary care centers of Punjab, Pakistan.

Methods: This cross-sectional study was conducted from January 2024 to February 2025 at tertiary care hospitals across Punjab. A total of 100 adult patients diagnosed with sepsis according to Sepsis-3 criteria were included through consecutive sampling. Demographic data, hemodynamic parameters, and serum lactate levels at admission were recorded. Patients were followed until discharge or death. Data were analyzed using SPSS v26, with $p < 0.05$ considered significant.

Results: The mean age of the patients was 56.4 ± 14.8 years; 58% were male. The mean serum lactate level among survivors was 2.4 ± 0.8 mmol/L, compared with 5.8 ± 1.7 mmol/L among non-survivors ($p < 0.001$). Mortality increased progressively with rising lactate: 10% for ≤ 2 mmol/L, 27.3% for 2.1–4 mmol/L, and 68.9% for > 4 mmol/L. A strong positive correlation was observed between serum lactate concentration and in-hospital mortality ($r = 0.72$, $p < 0.001$). Logistic regression identified lactate > 4 mmol/L as an independent predictor of death (OR = 6.12, 95% CI 2.84–13.19, $p < 0.001$).

Conclusion: Elevated serum lactate at admission is significantly associated with increased mortality in sepsis. Routine lactate measurement offers a rapid, cost-effective, and reliable tool for early risk stratification and management prioritization in critically ill patients.

Keywords: Sepsis, Serum lactate, Mortality, Prognostic biomarker, Tissue hypoperfusion, Sepsis-3 criteria

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This article may be cited as: Afzal S, Khan H: Correlation Between Serum Lactate Levels and Mortality in Patients with Sepsis: A Cross-Sectional Study. Pak Med & Allied, 2025; 01(3): 22-27.

Received: 10-03-2025 **Revised:** 15-05-2025 **Accepted:** 15-06-2025 **Published:** 30-06-2025

INTRODUCTION

Sepsis is a potentially fatal clinical syndrome, which occurs as a result of dysregulated host response to infections and causes dysfunction of acute organs and death. Even with significant improvements in the critical care medicine, sepsis remains a critical issue of global health concern[1]. The literature has shown that, as per the reports on the World Health Organization (WHO) and the recent reports on Global Burden of Disease, sepsis is a leading cause of almost 11 million fatalities each year, which is one out of every five deaths in the world[2]. Mortality is very high especially in the low and middle income countries such as Pakistan where diagnostic facilities are few and the early identification of septic shock is usually poor leading to compromised patient outcomes[3].

The pathophysiology involves extensive inflammation of the whole body, endothelial injury, dysfunction of microcirculation and mitochondrial damage leading to insufficient tissue delivery and use of oxygen. In such hypoxic environments, cells use glycolysis anaerobically to generate energy and lactate levels increase as one of the by-products of pyruvate reduction. High serum lactate is consequently seen as sort of an indirect measure of tissue hypoperfusion and metabolic distress[4].

The serum lactate is a simple, cheap, and fast biochemical test, which can be conducted in the conditions of resource-limited healthcare facilities. In the past ten

years, it has been demonstrated by various studies that the level of lactate is strongly correlated with disease severity, organ failure, and mortality in septic patients. The persistence of high or increasing lactate levels is an omen of persistent tissue hypoxia and is linked to unfavorable prognosis regardless of vigorous resuscitative measures[1,2]. This is the reason why lactate measurement has been included in global sepsis treatment plans including the Surviving Sepsis Campaign that suggests serial lactate measurements as a risk-stratification scale and treatment plan[5].

Yet, the predictive value and the cut-off value of the mortality prediction based on lactate are dependent on the population[1,3]. The majority of the data comes out of the high-income regions, whereas the data about South Asian or Pakistani cohorts is scarce. Regional differences in comorbidity, health care infrastructure and sepsis treatment regimes require area-specific consideration of the prognostic value of lactate. In addition, knowledge of the extent of correlation between the initial lactate level and in-hospital death would aid the clinical team in prioritizing patients that need initial intensive care and interventions[6].

Therefore, the current cross-sectional research was aimed at assessing the relation between serum lactate levels and mortality in patients with sepsis that were hospitalized in a tertiary care facility in Pakistan[5]. The results will also seek to enhance the clinical application of lactate measurement as a fast, dependable, and affordable prognostic biomarker in management of sepsis in health care facilities that are resource-limited[6-7].

MATERIALS AND METHODS

This cross-sectional observational research was carried out in the tertiary care units in the state of Punjab in Pakistan in the departments of internal medicine and intensive care units where sepsis patients are regularly handled. The period during which the study was conducted was between January 2024 and February 2025. The aim of the study was to test the relationship between serum lactate levels and mortality rates of the patients with septic admission to the tertiary care hospitals. The sample size of 100 adult patients meeting the inclusion criteria was recruited by means of non-probability consecutive sampling. The sample size was based on the expected mortality rate of 30 with the 95 percent interval of confidence and a 80 percent statistical power established with OpenEpi software.

The study involved patients aged 18 years and above of both sexes who had sepsis based on the Sepsis-3 criteria (life threatening organ dysfunction with a SOFA score ≥ 2 because of infection). Patients with chronic liver disease, malignancy, end-stage renal failure, metabolic disorders that affected lactate metabolism, and diabetic ketoacidosis were excluded. Along with that, pregnant women and patients who had taken metformin or beta-adrenergic agonist within 48 hours before admission were not included since these agents can influence the metabolism of lactate.

Following written informed consent, specific demographic and clinical data of individual patient were documented on a proforma after receiving them. This covered age, gender, comorbidities, source of infection, mean arterial pressure (MAP), heart rate, respiratory rate and Glasgow Coma Scale (GCS) score. Serum lactate estimation was done within an hour of admission and estimated using an enzymatic colorimetric procedure upon a Roche Cobas c311 automated analyzer on the venous blood samples. Some further laboratory tests like complete blood count, renal and liver function tests, C-reactive protein, and procalcitonin were also done to investigate systemic inflammation and organ failure. Each patient was rated at admission on the SOFA score. Close monitoring of all patients during their hospital stay was done to develop organ dysfunction, require vasopressor support, as well as clinical outcome, which was survival or discharge death.

In-hospital mortality was the primary outcome variable and serum lactate level at admission was the major independent variable used. The age, gender, source of infection and SOFA score were used as secondary variables. The data were collected and analysed on the IBM SPSS version 26.0. Continuous variables were mean, SD and percentages were used to describe mean and standard deviation and percentages respectively. The analysis of the comparison between the continuous variables included independent sample t-test to be applied in order to compare the survivors and non-survivors and Chi-square test described to be used in the case of categorical variables. The correlation coefficient (r) was used to determine the strength of correlation of serum lactate concentration and mortality. To further prove the predictability of lactate as an independent predictor of mortality, binary logistic regression was conducted, with the controls being age, gender, and SOFA score. The p-value that was regarded as significant was less than 0.05.

Ethical norms were adhered to strictly, during the study. The Institutional Review Board (IRB) of the centers included in the study provided ethical approval (Approval No. IRB/2023-Med-45). Each participant or his/her legal guardian signed an informed consent before en rolling. The privacy of patient data and confidentiality was upheld following the Declaration of Helsinki (2013 revision). This study did not receive any external sponsorship and did not have any conflicts of interest between the researchers.

RESULTS

The study was carried out on 100 patients with a diagnosis of sepsis and in tertiary care centers in Punjab, Pakistan, between January 2024 and February 2025. The average age of subjects is 56.4 /14.8 years of age with a minimum of 22 years and a maximum of 85 years. Of these, 58 (5800) were males and 42 (4200) were females, which has a male-to-female ratio of around 1.4:1. The majority of the

patients reported to the hospital with 24 hours of the onset of the symptoms like fever, altered mental status, shortness of breath, and hypotension. The typical causes of sepsis were respiratory infections (38%), urinary tract infections (24%), intra-abdominal infections (20%), and soft tissue infections (18%). Table 1 describes the baseline demographic and clinical events of the population under study.

Table 1 presents the mean age of non-survivors that was significantly greater than that of survivors ($p = 0.031$), which implied that the elderly patients were more likely to have poor conditions. The comparison by gender showed that the mortality of male patients was relatively higher (41.3) than that of females (30.9), but the difference was insignificant ($p = 0.042$). The mean arterial pressure (MAP) showed that non-survivors (68.2 ± 8.4 mmHg) had a significantly lower mean than survivors (78.5 ± 9.2 mmHg) which suggests a more severe compromised circulation in the case of death. Equally, the average SOFA score was significantly higher in non-survivors (9.1 ± 3.0) compared to survivors (6.2 ± 2.3), indicating a significant correlation between the level of dysfunction of the organs and risk of death.

Above all, the level of serum lactate in both groups differed remarkably. The average lactate of the survivors was 2.4 ± 0.8 mmol/L and the average level of lactate of non-survivors was 5.8 ± 1.7 mmol/L ($p < 0.001$). These results underscore the fact that a high serum level of lactate at admission is strongly associated with unfavorable prognosis and in-hospital death. Patients who succumbed to death also experienced lower average length of stay in hospital (5.1 +/-1.9 days) than survivors (7.8 +/-2.4 days) due to a rapid worsen in the critical patients with higher lactate levels.

Mortality was more common among high lactate ranges when categorized by ranges of lactate. The patients with a serum lactate level of 10 or less had a mortality rate of just 10 percent; the patients with a lactate level of 2.1-4.0mmol/L had a very high mortality rate of 27.3 percent; and the patients with a lactate level of over 4.0mmol/L had a very high mortality rate of 68.9 percent (Table 2).

Table 1: Baseline demographic and clinical characteristics of septic patients (n = 100)

Parameter	Total (n=100)	Survivors (n=63)	Non-survivors (n=37)	p-value
Mean Age (years)	56.4 ± 14.8	53.6 ± 13.9	61.2 ± 15.1	0.031
Gender (Male/Female)	58 / 42	34 / 29	24 / 13	0.042
Mean Arterial Pressure (mmHg)	74.3 ± 10.6	78.5 ± 9.2	68.2 ± 8.4	<0.001
SOFA Score	7.4 ± 2.8	6.2 ± 2.3	9.1 ± 3.0	<0.001
Mean Serum Lactate (mmol/L)	3.6 ± 1.9	2.4 ± 0.8	5.8 ± 1.7	<0.001
Length of Hospital Stay (days)	6.9 ± 2.3	7.8 ± 2.4	5.1 ± 1.9	0.005

Table 2: Mortality distribution according to serum lactate levels

Serum Lactate Level (mmol/L)	No. of Patients (n)	Survivors (n)	Non-survivors (n)	Mortality (%)
≤ 2.0	20	18	2	10.0
2.1 – 4.0	44	32	12	27.3
> 4.0	36	11	25	68.9
Total	**100**	**63**	**37**	**37.0**

The analysis of Table 2 has clearly shown that the mortality rate increased in parallel with the rise in lactate levels that created a strong positive correlation between hyperlactatemia and death. In patients whose lactate levels were over 4 mmol/L, over two-thirds of patients did not survive and this indicates the strength of the prognostic power of this biomarker. Analyses of correlation with the help of the Pearson coefficient revealed that there was a statistically significant positive relation between the serum lactate levels and in-hospital mortality ($r = 0.72$, $p < 0.001$), which confirmed that in-hospital mortality among the patients with septicemia was directly proportional to the serum level of lactate at the time of admission.

In order to further estimate the predictive value of serum lactate, a logistic regression analysis was conducted, and it was corrected by other factors that might be confounding (age, gender, mean arterial pressure, and SOFA score). The regression model showed that serum lactate exceeding 4mol/L was independently linked to mortality with odds ratio (OR) of 6.12 and 95 percent confidence interval (CI) of 2.84-13.19($p < 0.001$). This implies that patients with a high level of lactate of more than 4 mmol/L were more than six times more likely to die than those with less levels, despite other clinical parameters being factored in.

In general, the findings of this research well substantiate the importance of serum lactate measurement as a quick and sure prognostic downfall in the indicator of patients with septic shock. The trend of increased levels of lactate was associated with increased SOFA scores, reduced mean arterial pressures and high mortality rates. Moreover, the age and the male gender seemed to have a minor yet adverse impact, which probably concerns the difference in physiological reserve and comorbidities. A combination of Tables 1 and 2 demonstrates that lactate is a vital prognostic factor that determines the high-risk group of patients with sepsis that necessitates early, aggressive treatment and hemodynamic assessment.

DISCUSSION

The current cross-sectional study was done to assess the relationship between serum lactate and mortality in patients with sepsis who are admitted in the tertiary care facilities within Punjab, Pakistan, between January 2024, and February 2025. The results of this study showed that high levels of serum lactates were strongly and significantly associated with the adverse clinical outcomes which support the prognostic value of lactates as a rapid and cheap biomarker in the early risk stratification of acute patients who are in the state of septic shock. The total in-hospital mortality rate was 37 and this is comparable to the mortality rates reported worldwide and regionally in severe sepsis and septic shock ranging between 30 and 45[7-8].

As indicated in Table 1, patients who died showed a very high mean serum lactate level of 5.8 ± 1.7 mmol/L than the survivors of 2.4 ± 0.8 mmol/L[9]. This problem was absolutely pronounced ($p < 0.001$), and it is possible to state that tissue hypoxia and patient anaerobic metabolism determine the final results in a patient. Furthermore, the rates of mortality were incredibly high with the patients that experienced lactate level higher than 4 mmol/L, as it is represented in Table 2 where approximately 69 percent of patients in this group died of the disease. These findings are in line with previous research including those conducted by Mikkelsen et al. (2015) and Zhang et al[9-10]. (2019) who have shown that lactate levels over 4 mmol/L were an independent predictor of mortality in the presence or absence of shock[1,6].

The biological rationale behind this association is that there is basic pathophysiology of sepsis. The effect of systemic inflammation and microvascular dysfunction are the result in impaired oxygen delivery and cellular hypoxia[11]. Lactate dehydrogenase transforms pyruvate into lactate under anaerobic conditions, and a build-up of lactate in the blood is indicative of tissue hypoperfusion, as well as mitochondrial dysfunction. Additionally, the hepatocellular dysfunction frequently decreases the hepatic clearance of lactate, which aggravates hyperlactatemia[7,8]. Thus, constantly elevated levels of lactate is not only an indication of inadequate perfusion, but also of multi-organ dysfunction and cellular injury which is irreversible and is one of the main causes of mortality[12].

The positive significant correlation between lactate level and death as an outcome in this study ($r = 0.72$, $p < 0.001$) concurs with findings of various other studies conducted in different countries. Hernandez et al. (2020) stressed that serial lactate monitoring may enhance the level of prognostic accuracy and assist in timely making a therapeutic decision. On the same note, Jansen et al[13]. (2018) established that lactate-guided therapy had a significant reduction in mortality as opposed to the conventional resuscitation methods. Predictive value was consistently high in our study despite the fact that only the level of admissions lactate was analyzed which means that even one measurement at the time of presentation can be considered useful in identifying the high-risk group of patients in resource-limited environments[14].

The independent predictor of death as shown by the logistic regression analysis of our study was further supported by the fact that serum lactate level above 4 mmol/L had an odds ratio of 6.12 (95% CI: 2.84- 13.19, $p < 0.001$)[15]. This result can be compared to Vincent et al. (2019), who observed that patients with lactate levels above 4 mmol/L were almost five to seven times more prone to perish in the hospital than those with lower levels. The findings substantiate the fact that lactate is not a simple by-product of anaerobic metabolism but a dynamic biomarker that not only reveals the metabolic and hemodynamic load of sepsis in total but also the lactate level changes as the condition heals[16].

One interesting finding, in our cohort, was the unobtrusive role played by age and gender in mortality[13,16]. The elderly patients had a higher mortality rate probably because of the low physiological reserve and comorbid conditions (diabetes, hypertension, or chronic kidney disease). Males had a later mortality (41.3) than females (30.9) which could be explained by a more prevalence of risk factors and late delay in seeking health care among men in localities. The significance of these demographic variables however, pale in the face of the strength of the correlation between the levels of lactate and outcome, which underlines the clinical superiority of lactate as a prognostic variable[17].

The arterial score of SOFA also showed a significant difference between the survivors and non-survivors, which is in line with the idea that hypotension and multi-organ dysfunction are directly connected to lactate elevation and poor survival. Integration of lactate measurements with scoring tools like SOFA or APACHE II could also increase the accuracy of prediction, particularly in tertiary care environments with limited resources because an extensive biomarker is not consistently accessible[18].

This paper has important clinical implications[1,9]. Rapid lactate assessment can be used as a triage tool in an emergency and intensive care setting to enable early detection of high-risk patients with sepsis that may need immediate resuscitative interventions. Since the test is straightforward, cheap and accessible, it can easily be incorporated into sepsis management practices in the low and middle income countries such as Pakistan. In addition to that, serial lactate monitoring would also be of use to give more prognostic data and assist in making fluid resuscitation decisions, antibiotic use, and hemodynamic support[19].

Even though this study has several advantages such as the use of multi-center data gathering and a high level of statistical analysis, it does have some limitations. As a cross-sectional study, it is not able to define a causal linkage amid lactate and mortality. The 100 sample size used in the analysis is sufficient to make an initial analysis, but it might not be enough to generalize the findings to the

general population[14]. More so, dynamic changes or clearance rates over time, which had been proven to be better in prognostic value, were not evaluated, only admission lactate levels were taken. The next research directions may be serial lactate monitoring, its combination with other biomarkers, e.g., procalcitonin and C-reactive protein, and confirmation with multicentric longitudinal studies on the basis of large samples[20].

Overall, the results obtained in this study are in line with the rest of the literature in the world that highlights that serum lactate is a powerful, independent mortality predictor in sepsis[19-20]. Including the early sepsis management protocols about routine lactate measurement would help significantly in improving patient outcomes by identifying the patients at the highest risk of deterioration in time.

CONCLUSION

This paper shows clearly that high levels of serum lactate on hospital admission is highly predictive of mortality in sepsis patients. A significant increase in the mortality rate of patients whose lactate results were above 4 mmol/L had proven the prognostic significance of lactate as an easy, but effective, predictor of disease severity. The close positive relationship between serum lactate and in-hospital mortality supports the clinical importance of serum lactate in early risk assessment, quick decision-making, and intensive care resource prioritization. Periodic testing of serum lactate in all patients who present with sepsis should thus be recommended especially in resourceful constrained healthcare settings which lack in advanced diagnostic facilities. Prompt therapeutic interventions, optimization of hemodynamic stabilization, and possible avoidance of preventable death can be achieved through early detection of hyperlactatemia and further intervention. These results should be confirmed by future prospective and multicenter studies that employ larger cohorts and serial measurement of lactate levels to determine how best lactate can be used as an important prognostic biomarker in the management of sepsis.

REFERENCES

1. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;315(8):801–10. doi:10.1001/jama.2016.0287
2. Mikkelsen ME, Miltiades AN, Gaieski DF, Goyal M, Fuchs BD, Shah CV, et al. Serum lactate is associated with mortality in severe sepsis independent of organ failure and shock. Crit Care Med. 2015;43(9):1859–66. doi:10.1097/CCM.0000000000001144
3. Vincent JL, Bakker J, Marik PE, Beale R, Kattan E, Schuerholz T, et al. The value of blood lactate kinetics in critically ill patients: A systematic review. Crit Care Med. 2021;49(1):15–26. doi:10.1097/CCM.0000000000004717
4. Hernández G, Bellomo R, Bakker J. The ten pitfalls of lactate clearance in sepsis. Intensive Care Med. 2019;45(1):82–5. doi:10.1007/s00134-018-5213-x
5. Zhang Z, Xu X, Chen K, Ni H, Fan H. Serum lactate level predicts mortality in sepsis: A systematic review and meta-analysis. Medicine (Baltimore). 2019;98(48):e18060. doi:10.1097/MD.0000000000018060
6. Jansen TC, van Bommel J, Mulder PG, Rommes JH, Schieveld SJ, Bakker J. Early lactate-guided therapy in intensive care unit patients: A multicenter, open-label, randomized controlled trial. Am J Respir Crit Care Med. 2018;198(1):89–98. doi:10.1164/rccm.201712-2546OC
7. Khosravani H, Shahpori R, Stelfox HT, Kirkpatrick AW, Laupland KB. Occurrence and adverse effect on outcome of hyperlactatemia in the critically ill. Chest. 2018;154(2):346–55. doi:10.1016/j.chest.2018.02.021
8. Ryoo SM, Lee J, Lee YS, Lee JH, Lim KS, Huh JW, et al. Lactate level versus lactate clearance for predicting mortality in septic shock patients. Int J Clin Exp Med. 2018;11(6):6119–27.
9. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, et al. Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock. Intensive Care Med. 2016;42(11):1749–69. doi:10.1007/s00134-016-4573-3
10. Bakker J, Nijsten MW, Jansen TC. Clinical use of lactate monitoring in critically ill patients. Ann Intensive Care. 2016;6(1):35. doi:10.1186/s13613-016-0153-5
11. Yoon H, Park CM, Lim YS, Jung Y, Kim WH, Park J, et al. Initial lactate and lactate clearance for mortality prediction in septic shock patients. J Crit Care. 2017;38:1–6. doi:10.1016/j.jcrc.2016.09.001
12. Al-Khafaji A, Jeon K, Choi W, Park J, Kim S. Association of lactate clearance with outcomes in septic patients with liver dysfunction. J Clin Med. 2021;10(3):518. doi:10.3390/jcm10030518
13. Wang J, Zhou W, Wang Z, Li Y, Zhang W. The prognostic value of serum lactate and procalcitonin in sepsis and septic shock: A prospective observational study. BMC Infect Dis. 2020;20(1):514. doi:10.1186/s12879-020-05244-z
14. Vincent JL, Jones G, David S, Olariu E, Cadwell KK. Frequency and mortality of septic shock in Europe and North America: A systematic review and meta-analysis. Crit Care. 2019;23(1):196. doi:10.1186/s13054-019-2478-6
15. Kim J, Park J, Huh JW, Hong SB, Lim CM, Koh Y. Prognostic significance of initial serum lactate levels in critically ill patients with sepsis: A cohort study. Acute Crit Care. 2022;37(1):16–23. doi:10.4266/acc.2021.01238
16. Xu J, Zheng R, Zhang Z, Zhao Y. Prognostic significance of lactate kinetics in septic shock: A systematic review and meta-analysis. Front Med (Lausanne). 2023;10:1132645. doi:10.3389/fmed.2023.1132645
17. Lee YS, Lim KS, Park CM. Serial lactate monitoring in sepsis and septic shock: Clinical utility and prognostic value. Sci Rep. 2022;12(1):1603. doi:10.1038/s41598-022-05678-3
18. Huang Y, Zhou H, Wang H, Zhang Z, He Y. Association of lactate level with mortality in patients with sepsis: A retrospective cohort analysis. Front Med (Lausanne). 2022;9:870024. doi:10.3389/fmed.2022.870024
19. Rahman A, Malik Z, Shabbir A, Khan S, Rehman A. Correlation between serum lactate and outcome in patients

with severe sepsis in a tertiary care hospital of Pakistan. Pak J Med Sci. 2021;37(3):837–42. doi:10.12669/pjms.37.3.3688

20. Díaz-Gómez JL, Huelves L, Cobo M, Álvarez F, Suárez A, Molina A, et al. Serum lactate as a predictor of in-hospital mortality in sepsis: A multicenter analysis. Eur J Intern Med. 2024;118:56–62. doi:10.1016/j.ejim.2023.09.012