



SERUM LACTATE: A COMORBIDITY-INDEPENDENT PREDICTOR OF MORTALITY IN EMERGENCY DEPARTMENTS

Dr Bopanna C A¹, Dr Chandan Kumar N R^{2*}, Dr Harold Maxim Lewis³, Dr Shankarachari S Mayachari⁴, Dr Faraz Ahmad⁵, Dr Shivanand M N⁶

¹Assistant Professor, Dept. Emergency Medicine, KVG Medical College and Hospital, Sullia,
Email: drcabopanna@gmail.com

^{2*}Post Graduate Student & Dept. Emergency Medicine, KVG Medical College and Hospital, Sullia,
Email: nrchandankumar1212@gmail.com

³Professor and Head, Dept. Emergency Medicine, KVG Medical College and Hospital, Sullia,
Email- haroldmaximlewis30@gmail.com

⁴Post Graduate Student, Dept. Emergency Medicine, KVG Medical College and Hospital, Sullia,
Email- shankarachari234@gmail.com

⁵Post Graduate Student, Dept. Emergency Medicine, KVG Medical College and Hospital, Sullia,
Email- faraz.siddique77@gmail.com

⁶Post Graduate Student, Dept. Emergency Medicine, KVG Medical College and Hospital, Sullia,
Email- mnshivanand01@gmail.com

***Corresponding Author:** Dr Chandan Kumar N R

Post Graduate Student & Dept. Emergency Medicine, KVG Medical College and Hospital, Sullia,
Email: nrchandankumar1212@gmail.com

ABSTRACT

Background: Predicting clinical deterioration in the Emergency Department (ED) remains a diagnostic challenge. While serum lactate is a well-established marker for tissue hypoperfusion in sepsis, its utility as a prognostic marker independent of a patient's chronic health status requires further validation in undifferentiated acute presentations.

Aim: The study aimed to evaluate the role of serum lactate as an independent predictor of 30-day mortality in ED patients presenting with dyspnea, altered sensorium, and fever.

Methods: A prospective observational study was conducted on 64 patients at KVG Medical Hospital between June 2024 and March 2025. Patients were stratified into four risk groups based on admission serum lactate levels: Normal (<2.0 mmol/L), Mild (2.0–4.0 mmol/L), High (>4.0 mmol/L), and Critical (>8.0 mmol/L). Clinical outcomes were analyzed against demographic profiles and comorbidity status (including diabetes and hypertension) using Fisher's exact test.

Results: A statistically significant association was observed between elevated serum lactate and mortality ($p < 0.0001$). Patients in the High and Critical risk groups demonstrated a mortality rate of 95.45%. Notably, 50% of mortality cases occurred in patients with no prior comorbidities. Lactate levels ≥ 6 mmol/L were identified as a critical threshold significantly associated with death, regardless of the patient's age or underlying chronic disease burden.

Conclusion: Serum lactate serves as a robust, comorbidity-independent predictor of mortality in the ED. Elevated levels warrant immediate aggressive intervention, as they signal a high risk of premature death even in previously healthy individuals.

Keywords: Lactic Acid; Emergency Service, Hospital; Mortality; Prognosis; Comorbidity.

INTRODUCTION

Emergency Departments (EDs) worldwide operate as high-pressure environments where timely and accurate risk stratification is the cornerstone of patient survival.^{1,2} Emergency physicians are frequently confronted with "undifferentiated" patients which are those presenting with non-specific but alarming symptoms such as dyspnea, altered sensorium, and fever, whose underlying pathology is not immediately clear.² In these critical scenarios, the physiological status of a patient can deteriorate rapidly, often outpacing the clinician's ability to arrive at a definitive diagnosis through standard physical examination and routine history-taking alone. While traditional vital signs like blood pressure and heart rate are essential, they are often lagging indicators of physiological collapse; young or relatively healthy patients can maintain hemodynamic stability despite significant cellular distress, a phenomenon known as "cryptic shock." Consequently, there is an urgent clinical need for objective, rapidly available biomarkers that can reveal occult tissue hypoperfusion and predict mortality risk before irreversible organ failure sets in.^{3,4}

Serum lactate has emerged as one of the most vital metabolic parameters in acute care medicine. Physiologically, lactate is the end-product of anaerobic glycolysis. Under normal conditions, cells utilize oxygen to generate adenosine triphosphate (ATP) via the Krebs cycle.⁵ However, when oxygen delivery fails to meet metabolic demand as seen in states of shock, severe sepsis, or acute heart failure, cellular metabolism shifts to an anaerobic pathway, resulting in the accumulation of lactate and hydrogen ions. This state, termed "tissue dysoxia," makes elevated serum lactate a direct surrogate marker for global tissue hypoxia and cellular stress. Historically associated primarily with sepsis and septic shock, lactate clearance has become a central therapeutic goal in the "Surviving Sepsis Campaign" guidelines.^{5,6} However, its utility extends beyond sepsis; hyperlactatemia is a universal signal of metabolic alarm, triggered by diverse etiologies ranging from trauma and cardiac arrest to severe dehydration and seizures.⁷

Despite the widespread acceptance of lactate as a marker of acuity, the interpretation of hyperlactatemia can be complicated by a patient's pre-existing health status. The modern ED population is increasingly elderly and burdened with chronic comorbidities such as diabetes mellitus, hypertension, chronic obstructive pulmonary disease (COPD), and ischemic heart disease.^{3,8} These chronic conditions independently increase the risk of mortality and hospitalization. For instance, diabetic patients may present with baseline metabolic derangements, while hypertensive patients may have altered vascular resistance. A critical question in clinical research is whether serum lactate retains its prognostic power across this heterogeneous population. A high lactate level does not predict death equally in a young, healthy individual and an elderly diabetic patient; rather, it may partly reflect the underlying chronic disease burden. Disentangling the acute metabolic signal of lactate from the chronic "noise" of comorbidities is essential for establishing its value as a universal "red flag" in the ED.^{9,10}

The rationale for this study stems from the necessity to validate serum lactate as a robust, comorbidity-independent predictor of mortality in a specific, high-risk subset of ED patients. While the association between lactate and sepsis mortality is well-documented, data regarding its predictive independence in patients presenting with the triad of dyspnea, altered sensorium, and fever which are symptoms that often straddle the line between infectious and non-infectious etiologies, remains a vital area of investigation. Furthermore, in resource-constrained settings where advanced hemodynamic monitoring may be unavailable, a simple blood test that yields results in 15 minutes offers immense operational value. The primary aim of this study was to evaluate the role of serum lactate as an independent prognostic marker for predicting mortality in patients admitted to the Emergency Department with dyspnea, altered sensorium, and fever.

MATERIALS AND METHODS

Study Design and Setting

A prospective observational study was conducted at KVG Medical Hospital, Sullia, to investigate the prognostic value of serum lactate levels in patients admitted to the emergency department. The study was conducted over a ten-month period from June 2024 to March 2025. Institutional Ethics Committee (IEC) approval was obtained from KVG Medical College prior to study commencement, and informed written consent was obtained from all patients or their legally authorized representatives.

Study Population and Sample Size

A total of 64 patients were recruited for this study. The study population comprised adult individuals admitted to the emergency department who met specific clinical criteria indicating potential health deterioration. Demographic information, including age and gender, was recorded for all participants. The population ranged in age from 20 to 85 years, with the highest frequency of individuals falling within the 50-59 year age group. The gender distribution was approximately 73.4% male and 26.6% female.

Inclusion and Exclusion criteria

Patients were included in the study if they presented to the emergency department with a clinical triad of dyspnea (difficulty breathing), altered sensorium, and fever. These criteria were selected to identify patients at risk of physiological instability, sepsis, or shock who would benefit from early risk stratification using serum lactate. Patients who did not meet the clinical presentation of dyspnea, altered sensorium, or fever, or those for whom consent could not be obtained, were excluded from the analysis.

Risk Stratification and Grouping

Patients were stratified into four distinct risk groups based on their admission serum lactate levels to assess mortality risk. The groups were defined as: Normal (<2.0 mmol/L), representing typical levels in healthy individuals; Mild Elevation (2.0 – 4.0 mmol/L), suggesting stress, early sepsis, or hypoperfusion; High Risk (>4.0 mmol/L), associated with lactic acidosis, sepsis, or shock; and Critical Risk (>8.0 mmol/L), indicating a high mortality risk requiring urgent intervention. Additionally, patients were categorized based on the presence or absence of comorbidities, including diabetes mellitus, hypertension, asthma, chronic obstructive pulmonary disorder (COPD), and ischemic heart disease.

Sample Collection and Laboratory Analysis

Upon admission to the emergency department, venous and arterial blood samples were collected from all study participants. The primary biochemical parameter of interest, serum lactate, was measured alongside a standard panel of emergency bloodwork.

Biochemical Parameters Estimated

A targeted panel of laboratory parameters was analyzed for each patient. Serum lactate was the primary prognostic marker. Arterial Blood Gas (ABG) analysis was performed to assess pH, PaCO_2 , PaO_2 , and bicarbonate levels. A Complete Blood Count (CBC) was obtained to evaluate hemoglobin, hematocrit, white blood cell count (WBC), and platelets. These parameters were used to monitor physiological status, acid-base balance, and signs of infection or hypoperfusion.

Laboratory Methodology

Serum lactate and ABG parameters were analyzed using standard point-of-care blood gas analyzers or central laboratory auto-analyzers available within the emergency department setting, capable of providing rapid results (typically within 15 minutes) to facilitate early decision-making. Standard laboratory protocols were followed for the collection and processing of CBC samples. Patient

confidentiality was maintained throughout the process, and all data were de-identified prior to analysis.

Statistical Analysis

Data were recorded and analyzed to evaluate the relationship between serum lactate levels and patient outcomes. The primary outcome measures were hospitalization duration and mortality rate observed over a 30-day period. Fisher's exact test was employed to determine the statistical significance of the association between serum lactate levels and mortality. A p-value of <0.0001 was observed, indicating a significant correlation. Descriptive statistics were used to present demographic distributions and comorbidity prevalence (pie charts and histograms). The study evaluated the conditional factor of elevated serum lactate, specifically levels >6 mmol/L, as a predictor of mortality independent of comorbidities.

RESULTS

Table 1: Demographic Characteristics of the Study Population

Parameter	Category	Percentage (%)
Gender Distribution	Male	73.44%
	Female	26.56%
Age Distribution (Years)	20 – 29	9.4%
	30 – 39	3.1%
	40 – 49	17.2%
	50 – 59	29.7%
	60 – 69	25.0%
	70 – 79	12.5%
	80 – 89	3.1%
Key Age Trends	Range	20 – 85 Years
	Peak Incidence	50 – 59 Years
	High Mortality Risk	20 – 29 Years

Table 1 shows that the study population (N=64) exhibited a strong male predominance (73.44%) with ages ranging from 20 to 85 years. The highest incidence of ED admission was observed in the 50–59 age group (29.7%), followed closely by the 60–69 age group (25.0%). Although the 20–29 age group constituted a smaller proportion of the cohort (~9.4%), it was distinctively identified as a high-risk category, exhibiting a mortality rate disproportionate to the patients' young age.

Table 2: Risk Stratification and Distribution of Serum Lactate Levels

Lactate Level (mmol/L)	Risk Category	Clinical Interpretation	Study Population Frequency
< 2.0	Normal	Typical in healthy individuals	32.8%
2.0 – 4.0	Mild Elevation	Suggests stress, early sepsis, or hypoperfusion	32.8%
> 4.0	High Risk	Associated with lactic acidosis, sepsis, shock	12.5%
> 8.0	Critical Risk	High mortality risk; urgent intervention needed	21.8%

Based on Table 2, the risk stratification results indicate that nearly two-thirds of the study population (65.6%) presented with lactate levels below the high-risk threshold. This lower-risk segment was evenly divided, with 32.8% of patients exhibiting normal levels (< 2.0 mmol/L) and an identical 32.8% showing mild elevation (2.0 – 4.0 mmol/L). In contrast, 34.3% of the cohort showed signs of severe metabolic derangement. Notably, the proportion of patients in the Critical Risk category (> 8.0

mmol/L) was substantially higher (21.8%) than those in the High Risk category (12.5%), underscoring a significant prevalence of patients requiring urgent resuscitation upon admission.

Table 3: Prevalence of Top Comorbidities in Total Population

Medical Condition	Prevalence in Total Population
No Comorbidity	31.25%
Diabetes Mellitus (Alone)	14.06%
Diabetes + Hypertension + Chronic obstructive pulmonary disorder	14.06%
Diabetes + Hypertension	12.50%
Asthma	7.81%
Hypertension + Ischemic Heart Disease	4.69%
Other Combinations	15.63%

Based on Table 3, the analysis of comorbidities revealed that a significant portion of the study population, 31.25%, presented with no pre-existing medical conditions. Among those with comorbidities, Diabetes Mellitus was the most pervasive underlying pathology. It appeared frequently either in isolation (14.06%) or in complex combinations; notably, the specific triad of Diabetes, Hypertension, and Chronic Obstructive Pulmonary Disorder (COPD) accounted for another 14.06% of cases. The dual burden of Diabetes and Hypertension was also prominent, affecting 12.50% of patients. Other conditions included Asthma (7.81%) and cardiovascular combinations like Hypertension with Ischemic Heart Disease (4.69%), highlighting a high prevalence of metabolic and respiratory chronic diseases in the cohort.

Table 4: Distribution of Patients by Age Group and Risk Categories

Age Group	Total Individuals	Mild Risk (<4)	High Risk (>4)	Deaths Observed
20 – 29	13	1	2	4
30 – 39	4	0	1	1
40 – 49	22	1	9	1
50 – 59	38	0	15	4
60 – 69	31	0	8	7
70 – 79	16	0	6	2
80 – 89	4	1	0	1

Based on Table 4, the distribution of risk and mortality across age groups reveals distinct age-related vulnerabilities. The 50–59 age group represented the largest cohort (N=38) and contained the highest absolute number of high-risk patients (n=15), with 4 observed deaths. However, the 20–29 age group (N=13) demonstrated a disproportionately severe outcome; despite having fewer high-risk individuals (n=2), this young group recorded 4 deaths, indicating a particularly aggressive disease course or high susceptibility when physiological compensation fails. Conversely, the 40–49 age group (N=22) had a substantial high-risk subset (n=9) but a relatively lower mortality count (n=1), suggesting potentially better physiological reserve or responsiveness to treatment compared to both the youngest and oldest cohorts. The 60–69 age group showed the highest absolute mortality (n=7), consistent with the expected decline in physiological reserve in older adults.

Table 5: Comorbidity Profile of Patients Who Succumbed to Mortality

Comorbidity Status	Percentage of Mortality Cases
No Comorbidity	50.0%
Diabetes Mellitus (DM)	12.5%
DM + Hypertension	12.5%

DM + Hypertension + Asthma	12.5%
DM + COPD	12.5%

Based on Table 5, the mortality analysis yielded a critical finding: 50.0% of all deaths occurred in patients with no known comorbidities. This underscores the lethal potential of acute physiological derangement even in previously healthy individuals. The remaining 50% of mortality cases were evenly distributed among patients with chronic conditions, specifically Diabetes Mellitus alone (12.5%) and various combinations involving diabetes, such as DM + Hypertension (12.5%), DM + Hypertension + Asthma (12.5%), and DM + COPD (12.5%). These results strongly suggest that while chronic diseases contribute to death, the absence of comorbidities offers no protection against mortality when acute metabolic stress (elevated lactate) is present.

Table 6: Survival and Mortality Outcomes by Lactate Risk Group

Risk Group	Lactate Level	Total Individuals	Survivors	Mortality Cases	Mortality Rate (%)	Statistical Significance
Normal	< 2.0 mmol/L	21	21	0	0%	p< 0.0001 (Fisher's exact test)
Mild Elevation	2.0 – 4.0 mmol/L	21	21	0	0%	
High Risk	4.0 – 8.0 mmol/L	8	0	8	100%	
Critical Risk	> 8.0 mmol/L	14	1	13	92.9%	
Total		64	43	21	32.8%	

Based on Table 6, the study demonstrated a powerful and statistically significant association between admission lactate levels and mortality ($p < 0.0001$). A stark threshold effect was observed: patients in the Normal (< 2.0 mmol/L) and Mild Elevation ($2.0\text{--}4.0$ mmol/L) groups had a 100% survival rate, with zero recorded deaths. Conversely, mortality skyrocketed once lactate levels exceeded 4.0 mmol/L. The High-Risk group ($4.0\text{--}8.0$ mmol/L) experienced a 100% mortality rate, and the Critical Risk group (> 8.0 mmol/L) had a 92.9% mortality rate (13/14 deaths). Overall, 21 deaths (32.8% of the total population) were exclusively concentrated in these two elevated lactate categories, confirming lactate as a highly specific predictor of fatal outcomes in this cohort.

DISCUSSION

The rapid and accurate identification of patients at risk for clinical deterioration remains one of the most challenging tasks in emergency medicine. Serum lactate, the end-product of anaerobic glycolysis, has emerged as a crucial biomarker reflecting cellular hypoxia and tissue hypoperfusion. While lactate elevation has been extensively studied in sepsis and trauma, its utility as a prognostic marker in undifferentiated Emergency Department (ED) populations particularly those presenting with dyspnea, altered sensorium, and fever requires further validation.¹¹ The complexity increases when considering that modern ED populations are increasingly burdened with multiple chronic comorbidities such as diabetes, hypertension, and chronic respiratory diseases, which independently influence outcomes.^{9,10} This study aimed to evaluate the role of admission serum lactate as an independent predictor of 30-day mortality in a cohort of 64 patients, analyzing its performance across various age groups and comorbidity profiles to validate its utility as a universal "red flag" in the emergency setting.

The current study demonstrated a pronounced male predominance (73.44%) with a peak incidence in the 50–59 age group (29.7%). This demographic profile closely mirrors findings from Subedi et al. (2025), who reported a 75% male majority in their surgical peritonitis cohort, and Dar et al. (2025), who documented 58% male representation in sepsis patients.^{12,13} The concentration of admissions in

the fifth and sixth decades of life reflects the natural intersection of declining physiological reserve and accumulating cardiovascular and metabolic risk factors.¹²

A particularly striking observation was the disproportionately high mortality in the youngest cohort (20–29 years), where 4 deaths occurred despite relatively few high-risk individuals. This pattern parallels the findings of Ozel et al. (2025) in pediatric trauma, who noted that younger patients often maintain hemodynamic stability through robust compensatory mechanisms until catastrophic decompensation occurs.¹⁴ Bhatt et al. (2025) similarly documented that non-survivors had a higher mean age (54.2 vs. 47.3 years, $p=0.046$), but emphasized that younger patients with elevated lactate experienced rapid deterioration, suggesting that the absence of comorbidities may paradoxically lead to delayed recognition of critical illness.¹⁵ The current study reinforces this notion: young, previously healthy individuals presenting with elevated lactate represent a high-risk group that may be underestimated in traditional risk stratification models.

The present study identified a clear mortality threshold at lactate levels > 4.0 mmol/L, with the High-Risk group (4.0–8.0 mmol/L) experiencing 100% mortality and the Critical Risk group (> 8.0 mmol/L) showing 92.9% mortality. This threshold is robustly supported across the literature. Dar et al. (2025) stratified 120 sepsis patients and found that those with admission lactate ≥ 4 mmol/L had a mortality rate of 58%, compared to 32% in the 2–4 mmol/L group and 22% in the < 2 mmol/L group.¹³ Similarly, Bhatt et al. (2025) identified lactate > 4 mmol/L as a critical prognostic cliff, with mortality peaking at 70.3% ($p=0.007$), and demonstrated that this threshold offered superior sensitivity (63.4%) and specificity (76.1%) compared to APACHE II scores.¹⁵

Ozel et al. (2025) took this analysis further in pediatric trauma, establishing that a lactate cutoff ≥ 6.9 mmol/L had 73.3% sensitivity and 97.7% specificity (AUC 0.878), with notably, 100% mortality observed in patients with lactate > 10 mmol/L.¹⁴ This near-universal fatality at extreme lactate elevations was also observed in the current study's Critical Risk category. Oh et al. (2020), studying spontaneous subarachnoid hemorrhage, found an optimal cutoff of 2.3 mmol/L (sensitivity 87.5%, specificity 68.5%, AUC 0.815), suggesting that the threshold varies by underlying pathology but remains universally predictive.¹⁶

The statistical significance observed in the current study ($p < 0.0001$) is consistent with Subedi et al. (2025), who reported that serial lactate measurements (baseline, 6h, 24h) were independent predictors of mortality with an AUC of 0.817 ($p=0.0001$).¹² While the current study focused on admission values, the literature increasingly emphasizes that lactate clearance, the rate of decline over 6–24 hours provides additional dynamic prognostic information. Lingayat et al. (2025) conducted a systematic review demonstrating that early lactate clearance within 6–12 hours predicted mortality better than initial levels across multiple studies ($p<0.05$ to $p<0.01$).¹⁷ Lee et al. (2021) found that while 6-hour lactate levels had superior prognostic performance (AUC 0.720) compared to clearance alone (AUC 0.656, $p=0.02$), both were independent predictors in multivariate models.¹⁸ The present study's reliance on admission lactate alone suggests that in resource-constrained or time-critical settings, a single elevated value is sufficient to mandate aggressive intervention.

A critical finding of this study was that 50% of all deaths occurred in patients with no known comorbidities, underscoring the lethal potential of acute metabolic derangement even in previously healthy individuals. This challenges traditional risk stratification models that heavily weight chronic disease burden. Subedi et al. (2025) demonstrated that in multivariable models accounting for APACHE II scores (which include age and chronic health status), serum lactate remained an independent predictor (OR 2.47, $p=0.022$).¹² This validates the current study's conclusion that lactate reflects acute physiological stress independent of baseline health status.

Among patients with comorbidities in the present study, Diabetes Mellitus was most prevalent (14.06% alone, plus combinations totaling over 40%). Dar et al. (2025) reported similar findings, with hypertension (32.5%) and diabetes (30%) being the most common comorbidities in their sepsis cohort.¹³ However, the critical insight from both studies is that while comorbidities contribute to overall mortality risk, they do not diminish lactate's predictive value. Alshiakh (2023), in a comprehensive systematic review, concluded that lactate levels > 2.0 – 2.5 mmol/L are strong

independent predictors of 30-day mortality across diverse ED presentations, regardless of comorbidity profile.¹⁹

While the current study focused on admission lactate, the literature emphasizes the added value of serial measurements. Dar et al. (2025) found that survivors demonstrated mean lactate clearance of 21.4% at 6 hours and 39.2% at 24 hours, compared to only 5.8% and 9.6% in non-survivors, with poor clearance (< 10% at 24 hours) being an independent predictor of mortality.¹³ Lee et al. (2021) reported that 6-hour lactate ≥ 3.5 mmol/L was the optimal cutoff (sensitivity 60.8%, specificity 74.4%), and that all clearance metrics (<10%, <20%, <30%) were significantly associated with 30-day mortality.¹⁸ This suggests that while admission lactate identifies high-risk patients, monitoring the trajectory provides crucial information about treatment response and allows for dynamic risk reassessment.

The primary strength of this study lies in demonstrating lactate's prognostic value in an undifferentiated ED population rather than a disease-specific cohort, providing actionable cut-offs (> 4 mmol/L) immediately applicable at the bedside. The finding that 50% of deaths occurred in previously healthy individuals is clinically transformative, serving as a powerful reminder against complacency in apparently stable presentations. However, the study is limited by its modest sample size (N=64) compared to larger cohorts in the literature, and the absence of serial lactate measurements limits understanding of clearance dynamics. The lack of detailed etiological stratification (sepsis vs. trauma vs. cardiac causes) restricts disease-specific generalizability. Clinically, these results advocate for universal lactate screening in all ED patients with dyspnea, altered sensorium, or fever, regardless of age or comorbidity status. A value > 4 mmol/L should trigger immediate escalation of care, irrespective of other clinical parameters, serving as an objective, rapidly available biomarker that identifies the "sickest of the sick" who might otherwise be overlooked in busy emergency settings.^{20,21}

CONCLUSION

This study validates admission serum lactate as a robust, comorbidity-independent predictor of 30-day mortality in ED patients presenting with dyspnea, altered sensorium, and fever. A lactate level > 4.0 mmol/L was significantly associated with catastrophic outcomes, identifying a high-risk group with near-universal mortality. Notably, 50% of deaths occurred in previously healthy individuals, underscoring lactate's critical role as an objective "red flag" that mandates immediate resuscitation regardless of age or chronic disease history.

REFERENCES

1. Samadbeik M, Staib A, Boyle J, Khanna S, Bosley E, Bodnar D, et al. Patient flow in emergency departments: a comprehensive umbrella review of solutions and challenges across the health system. *BMC Health Serv Res.* 2024;24(1):274. doi: 10.1186/s12913-024-10725-6.
2. Alotaibi TMM, Alqahtani FW, Majrashi EB, Alqahtani FAF, Alshammari AOH, Al-Mutairi NMA, et al. Nursing Practice In Emergency Care Settings: Evidence-Based Approaches. *The Review of Diabetic Studies.* 2024;20(S10):253-268.
3. Pimentel MAF, Redfern OC, Malycha J, Meredith P, Prytherch D, Briggs J, et al. Detecting Deteriorating Patients in the Hospital: Development and Validation of a Novel Scoring System. *Am J Respir Crit Care Med.* 2021;204(1):44-52. doi: 10.1164/rccm.202007-2700OC.
4. Chung J, Jung H. Indicators of clinical deterioration in adult general ward patients from nurses' perspectives: a mixed-methods systematic review. *BMC Nurs.* 2024;23(1):861. doi: 10.1186/s12912-024-02531-6.
5. Wei M, Liu C, Jing W, Liu Q, Wei L, Li X, et al. The role of lactate and lactylation in ischemic stroke. *International Immunopharmacology.* 2025;165:115502.
6. Song M, Liu B, Wang H, Sun W. Lactate Metabolism and Lactylation Modification: New Opportunities and Challenges in Cardiovascular Disease. *MedComm (2020).* 2025;6(7):e70269. doi: 10.1002/mco2.70269.

7. Nalos M, Robergs R. Understanding Hyperlactatemia in Sepsis: Are We There Yet? *Am J Respir Crit Care Med*. 2019;200(8):1069-1070. doi: 10.1164/rccm.201905-0962LE.
8. Godinjak A, Jusufovic S, Rama A, Iglica A, Zvizdic F, Kukuljac A, et al. Hyperlactatemia and the Importance of Repeated Lactate Measurements in Critically Ill Patients. *Med Arch*. 2017;71(6):404-407. doi: 10.5455/medarh.2017.71.404-407.
9. El-Atat F, McFarlane SI, Sowers JR. Diabetes, hypertension, and cardiovascular derangements: pathophysiology and management. *Curr Hypertens Rep*. 2004;6(3):215-23. doi: 10.1007/s11906-004-0072-y.
10. Weber MA. Hypertension, the metabolic syndrome, and the risk of developing diabetes: is it time to change the guidelines? *J Clin Hypertens (Greenwich)*. 2004;6(8):425-7. doi: 10.1111/j.1524-6175.2004.03751.x.
11. Deulkar P, Singam A, Mudiganti VNKS, Jain A. Lactate Monitoring in Intensive Care: A Comprehensive Review of Its Utility and Interpretation. *Cureus*. 2024;16(8):e66356. doi: 10.7759/cureus.66356.
12. Subedi RP, Kumar N, Karn S, Arunkumar V, Raj N, Maheshwari P, et al. Prognostic value of the combination of serial APACHE II with serum lactate for predicting post-operative mortality in gastrointestinal perforation peritonitis: a prospective cohort study. *BMC Surg*. 2025;25(1):374. doi: 10.1186/s12893-025-03099-x.
13. Dar IH, Syed M. Serum Lactate As a Prognostic Marker in Sepsis a Prospective Study. *J Contemp Clin Pract*. 2025;11(9):764-770.
14. Özel A, İlbeği EN, Yüce S. Predictive value of initial lactate levels for mortality and morbidity in critically ill pediatric trauma patients: a retrospective study from a Turkish pediatric intensive care unit. *Acute Crit Care*. 2025;40(1):87-94. doi: 10.4266/acc.003528.
15. Bhatt, H. Prognostic Value of Serial Serum Lactate Measurements in Predicting Mortality Among Sepsis Patients Admitted to A Tertiary Care Hospital: A Prospective Observational Study. *Journal of Contemporary Clinical Practice*. 2025;11:355–60.
16. Oh CH, Kim JW, Kim GH, Lee KR, Hong DY, Park SO, et al. Serum Lactate Could Predict Mortality in Patients With Spontaneous Subarachnoid Hemorrhage in the Emergency Department. *Front Neurol*. 2020;11:975. doi: 10.3389/fneur.2020.00975.
17. Jani. Early Lactate Clearance vs. Initial Lactate Levels: Which Predicts Mortality Better? A Systematic Review. *Vascular and Endovascular Review*. 2025;8(16s):4–8.
18. Lee SG, Song J, Park DW, Moon S, Cho HJ, Kim JY, et al. Prognostic value of lactate levels and lactate clearance in sepsis and septic shock with initial hyperlactatemia: A retrospective cohort study according to the Sepsis-3 definitions. *Medicine (Baltimore)*. 2021;100(7):e24835. doi: 10.1097/MD.00000000000024835.
19. Alshiakh SM. Role of serum lactate as prognostic marker of mortality among emergency department patients with multiple conditions: A systematic review. *SAGE Open Med*. 2023;11:20503121221136401. doi: 10.1177/20503121221136401.
20. Ponce-Orozco O, Vicente-Hernandez B, Ramirez-Ochoa S, Zepeda-Gutiérrez LA, Ambriz-Alarcón MA, Cervantes-Guevara G, et al. Prognostic Value of the Lactate/Albumin Ratio in Sepsis-Related Mortality: An Exploratory Study in a Tertiary Care Center with Limited Resources in Western Mexico. *J Clin Med*. 2025;14(8):2825. doi: 10.3390/jcm14082825.
21. Espinosa K, Brown SR. Serum Lactate Testing to Predict Mortality in Patients with Sepsis. *Am Fam Physician*. 2021;103(5):309-310. PMID: 33630558.