

Research Article**Correlation of NEWS2 Score with Vitamin D, Thiamine, and Serum Lactate Levels in Patients with Sepsis****Dr Fouzia Almas¹, Dr Mohammed Manzoor Patel², Ahemer Siddiqui³**¹Senior Resident, Department of General Medicine, Gulbarga Institute of Medical Sciences, Gulbarga, India.²Senior Resident, Department of Anaesthesiology, Gulbarga Institute of Medical Sciences, Gulbarga, India.³Senior Resident, Department of General Medicine, Yadgir Institute of Medical Sciences, Mudnal, Yadgir, India.**Received Date: 28/01/2026 Accepted: 11/02/2026 Published Date: 13/03/2026****Corresponding Author:** Dr. Mohammed Manzoor Patel, Senior Resident, Department of Anaesthesiology, Gulbarga Institute of Medical Sciences, Gulbarga, India.**Email:** mmpatel3166@gmail.com**ABSTRACT**

Background: Sepsis remains a major cause of morbidity and mortality worldwide despite advances in critical care. Early identification of disease severity is essential for timely intervention. The National Early Warning Score 2 (NEWS2) is a validated bedside scoring system used for early detection of clinical deterioration. Vitamin D deficiency, thiamine deficiency, and elevated serum lactate have individually been associated with adverse outcomes in sepsis; however, their relationship with NEWS2 score has not been extensively investigated. **Objectives:** To determine the correlation of NEWS2 score with serum vitamin D, thiamine, and serum lactate levels in patients with sepsis. **Materials and Methods:** A hospital-based prospective observational study was conducted among 100 adult patients with sepsis admitted to the Department of General Medicine and Medical Intensive Care Unit of a tertiary care hospital. NEWS2 score was calculated at admission, and serum vitamin D, thiamine, and serum lactate levels were

measured. Patients were categorized according to sepsis severity based on NEWS2 score. Statistical analysis included descriptive statistics, Student's *t*-test, Chi-square test, Fisher's exact test, and Pearson's correlation coefficient. A *p*-value <0.05 was considered statistically significant. **Results:** The mean age of the study participants was 56.8±15.2 years, and 61% were males. Respiratory tract infection was the commonest source of sepsis (38%). The mean NEWS2 score was 8.3±2.4. The mean serum vitamin D, thiamine, and serum lactate levels were 17.6±6.8 ng/mL, 58.4±18.3 nmol/L, and 3.84±1.41 mmol/L, respectively. Vitamin D deficiency was present in 68%, thiamine deficiency in 42%, and elevated serum lactate (>2 mmol/L) in 77% of patients. NEWS2 score showed a significant negative correlation with serum vitamin D (*r*=-0.63, *p*<0.001) and thiamine (*r*=-0.49, *p*<0.001), while a strong positive correlation was observed with serum lactate (*r*=0.72, *p*<0.001). Patients with severe NEWS2 scores had significantly lower vitamin D and

thiamine levels and significantly higher serum lactate levels compared with patients having moderate NEWS2 scores (all $p < 0.001$). **Conclusion:** NEWS2 score demonstrated significant correlations with serum vitamin D, thiamine, and serum lactate levels in patients with sepsis. Higher NEWS2 scores were associated with lower vitamin D and thiamine concentrations and higher serum lactate levels, suggesting that integration of physiological scoring with selected biochemical markers may improve early risk stratification and identification of patients with severe sepsis.

KEYWORDS: Sepsis. NEWS2 Score. Serum Lactate.

INTRODUCTION

Sepsis is a life-threatening syndrome characterized by a dysregulated host response to infection, resulting in acute organ dysfunction and high morbidity and mortality. Despite remarkable advances in antimicrobial therapy, intensive care management, and organ support, sepsis remains one of the leading causes of death among critically ill patients worldwide. According to the Third International Consensus Definitions (Sepsis-3), sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. Early recognition of disease severity is essential because delayed diagnosis and treatment significantly increase the risk of multiorgan failure, prolonged hospitalization, and mortality. Clinical scoring systems such as the National Early Warning Score 2 (NEWS2) have emerged as reliable bedside tools for identifying patients at risk of clinical deterioration by incorporating physiological parameters including respiratory rate, oxygen saturation, systolic blood pressure, pulse rate, temperature, and level of consciousness. Compared with earlier scoring systems, NEWS2 offers greater sensitivity in detecting

early clinical deterioration and predicting adverse outcomes in patients with sepsis.^[1]

In addition to clinical scoring systems, several biochemical markers have been investigated to improve risk stratification in sepsis. Vitamin D has gained considerable attention because of its immunomodulatory, anti-inflammatory, and antimicrobial properties. Vitamin D receptors are expressed on various immune cells, including macrophages, dendritic cells, T lymphocytes, and B lymphocytes, suggesting an important role in innate and adaptive immunity. Deficiency of vitamin D is highly prevalent among critically ill patients and has been associated with increased susceptibility to infections, exaggerated inflammatory responses, prolonged intensive care unit stay, and increased mortality. Low serum vitamin D concentrations may impair production of antimicrobial peptides such as cathelicidin and defensins, thereby compromising host defense mechanisms against bacterial infections.^[2]

Thiamine (vitamin B1) is another essential micronutrient involved in cellular energy metabolism. As a cofactor for pyruvate dehydrogenase and transketolase enzymes, thiamine facilitates aerobic glucose metabolism and ATP generation. During sepsis, increased metabolic demands, poor nutritional status, and enhanced urinary losses frequently lead to thiamine deficiency. Deficiency impairs oxidative metabolism, resulting in accumulation of pyruvate and conversion to lactate, thereby contributing to lactic acidosis and cellular dysfunction. Previous studies have suggested that thiamine supplementation may improve lactate clearance and organ function in selected patients with septic shock, although evidence remains inconsistent.^[3]

Serum lactate is one of the most widely accepted biochemical markers of tissue hypoperfusion and disease severity in sepsis. Elevated lactate levels reflect impaired tissue

oxygen utilization, mitochondrial dysfunction, and increased anaerobic metabolism. Persistent hyperlactatemia is strongly associated with multiorgan dysfunction, septic shock, and increased mortality. Consequently, serum lactate measurement has become an integral component of sepsis management guidelines and is widely used to assess treatment response and prognosis.^[4]

Although vitamin D deficiency, thiamine deficiency, and elevated serum lactate have individually been associated with poor outcomes in sepsis, limited studies have evaluated their correlation with NEWS2 score in a single clinical setting. Understanding these relationships may provide valuable insights into disease severity, facilitate early risk stratification, and identify patients who may benefit from targeted metabolic interventions. Therefore, the present study was undertaken to evaluate the correlation of NEWS2 score with serum vitamin D, thiamine, and serum lactate levels among patients with sepsis attending a tertiary care hospital.^[5]

AIM

To determine the correlation of NEWS2 score with serum vitamin D, thiamine, and serum lactate levels in patients with sepsis.

OBJECTIVES

1. To estimate serum vitamin D, thiamine, and serum lactate levels in patients with sepsis.
2. To determine the correlation between NEWS2 score and serum vitamin D, thiamine, and serum lactate levels.
3. To evaluate the association of these biochemical markers with the severity of sepsis as assessed by NEWS2 score.

MATERIALS AND METHODOLOGY

Source of Data

The data were collected from patients diagnosed with sepsis who were admitted to the Department of General Medicine and Medical Intensive Care Unit (MICU) of the tertiary care teaching hospital during the study period. Clinical information, laboratory investigations, and NEWS2 scores were recorded using a predesigned case record form.

Study Design

A hospital-based prospective observational cross-sectional study was conducted.

Study Location

The study was conducted in the Department of General Medicine and Medical Intensive Care Unit (MICU) of a tertiary care teaching hospital.

Study Duration

The study was carried out over a period of 18 months, including patient recruitment, laboratory investigations, data collection, statistical analysis, and preparation of the final report.

Sample Size

A total of 100 consecutive eligible patients diagnosed with sepsis were enrolled in the study.

Inclusion Criteria

- Patients aged 18 years or above.
- Patients fulfilling Sepsis-3 diagnostic criteria.
- Patients admitted with suspected or confirmed bacterial infection.
- Patients who provided written informed consent or consent from legally authorized representatives.

Exclusion Criteria

- Patients younger than 18 years.
- Pregnant or lactating women.
- Patients already receiving vitamin D or thiamine supplementation during the preceding four weeks.
- Patients with chronic liver failure.
- Patients with end-stage renal disease on dialysis.

- Patients with known malabsorption syndromes.
- Patients with active malignancy receiving chemotherapy.
- Patients with autoimmune disorders on immunosuppressive therapy.
- Patients who refused consent.

Procedure and Methodology

After obtaining approval from the Institutional Ethics Committee, eligible patients admitted with suspected or confirmed sepsis were screened according to the inclusion and exclusion criteria. Written informed consent was obtained before enrolment.

A detailed history regarding presenting complaints, duration of illness, associated comorbidities, medication history, and previous hospital admissions was recorded. General physical examination and systemic examination were performed.

At admission, physiological parameters required for calculation of the NEWS2 score were recorded, including:

- Respiratory rate
- Oxygen saturation
- Requirement of supplemental oxygen
- Pulse rate
- Systolic blood pressure
- Body temperature
- Level of consciousness (AVPU)

The NEWS2 score was calculated immediately after admission using the standard scoring system.

Routine laboratory investigations including complete blood count, renal function tests, liver function tests, blood glucose, C-reactive protein, blood cultures (where indicated), arterial blood gas analysis, and serum lactate were performed according to hospital protocol.

Approximately 8–10 mL of venous blood was collected under aseptic precautions before initiation of definitive treatment whenever feasible. Blood samples were used

for estimation of serum vitamin D, serum thiamine, and serum lactate.

Patients received standard treatment according to institutional sepsis management protocols. No intervention related to vitamin supplementation was administered as part of the study. Clinical outcomes were recorded until discharge or death.

Sample Processing

Venous blood samples were collected under aseptic precautions.

- Serum Vitamin D: Blood was centrifuged, and serum was separated. Serum 25-hydroxyvitamin D [25(OH)D] levels were estimated using a Chemiluminescent Immunoassay (CLIA).
- Serum Thiamine: Whole blood samples were processed according to laboratory protocol, and thiamine concentration was estimated using High Performance Liquid Chromatography (HPLC) or an equivalent validated laboratory method.
- Serum Lactate: Serum lactate was measured immediately after sample collection using an automated blood gas analyzer or enzymatic analyzer to avoid falsely elevated values.

Internal and external quality control procedures were followed throughout the study.

Statistical Methods

The collected data were entered into Microsoft Excel and analyzed using SPSS software version 26.0 (IBM Corp., USA).

- Continuous variables were expressed as Mean $\pm$ Standard Deviation (SD) or Median (Interquartile Range) depending upon data distribution.
- Categorical variables were expressed as frequency and percentage.
- Normality of continuous variables was assessed using the Shapiro-Wilk test.

- Pearson's correlation coefficient was used for normally distributed variables.
- Spearman's rank correlation coefficient was applied for non-normally distributed variables.
- Student's independent t-test or Mann-Whitney U test was used wherever appropriate.
- Chi-square test or Fisher's Exact test was used for categorical variables.
- Multiple linear regression analysis was performed to identify independent predictors of NEWS2 score.
- A p-value <0.05 was considered statistically significant with 95% confidence intervals.
- Demographic profile (age, sex)
- Presenting symptoms and duration
- Comorbid illnesses
- Source of infection
- Vital parameters
- NEWS2 score
- Laboratory investigations
- Serum Vitamin D level
- Serum Thiamine level
- Serum Lactate level
- Blood culture findings (if available)
- Requirement of ICU admission
- Requirement of vasopressor support
- Requirement of mechanical ventilation
- Duration of hospital stay
- Clinical outcome (discharge or death)

All data were verified for completeness and accuracy before statistical analysis.

Data Collection

A structured Case Record Form (CRF) was used for collecting the following information:

OBSERVATION AND RESULTS

Table 1. Demographic and clinical profile of study participants (N=100)

Variable	Category	n (%) / Mean±SD	Test of significance	95% CI	p value
Age (years)	Mean±SD	56.8±15.2	t=37.37	53.8–59.8	<0.001*
Age group	18–40 years	22 (22.0)	$\chi^2=24.76$		<0.001*
	41–60 years	39 (39.0)			
	>60 years	39 (39.0)			
Gender	Male	61 (61.0)	$\chi^2=4.84$	51.4–70.6%	0.028*
	Female	39 (39.0)			
Diabetes mellitus	Yes	46 (46.0)	$\chi^2=0.64$	36.2–55.8%	0.423
Hypertension	Yes	41 (41.0)	$\chi^2=3.24$	31.4–50.6%	0.072
Chronic kidney disease	Yes	19 (19.0)	$\chi^2=38.44$	11.3–26.7%	<0.001*
Source of infection	Respiratory	38 (38.0)	$\chi^2=15.91$		0.001*
	Urinary tract	27 (27.0)			
	Abdomen	18 (18.0)			
	Blood stream	9 (9.0)			
	Others	8 (8.0)			
NEWS2 score	Mean±SD	8.3±2.4	t=34.58	7.82–8.78	<0.001*

Table 1 presents the demographic and clinical characteristics of the 100 patients with sepsis included in the study. The mean age of the participants was 56.8 ± 15.2 years (95% CI: 53.8–59.8), which was statistically significant ($t=37.37$, $p<0.001$), indicating that the study population predominantly consisted of middle-aged and elderly individuals. Age group analysis showed that 39.0% of patients each belonged to the 41–60 years and >60 years age groups, while 22.0% were aged 18–40 years, demonstrating a significant predominance of older patients ($\chi^2=24.76$, $p<0.001$). Males constituted 61.0% of the study population compared to 39.0% females, reflecting a significant male predominance ($\chi^2=4.84$, $p=0.028$). Among the comorbidities, 46.0% of patients had diabetes mellitus and 41.0% had

hypertension; however, neither diabetes ($p=0.423$) nor hypertension ($p=0.072$) showed a statistically significant predominance. Chronic kidney disease was present in 19.0% of patients and was significantly less common than its absence ($\chi^2=38.44$, $p<0.001$). Regarding the source of infection, respiratory tract infection was the most frequent source (38.0%), followed by urinary tract infection (27.0%), abdominal infection (18.0%), bloodstream infection (9.0%), and other sources (8.0%), with the overall distribution being statistically significant ($\chi^2=15.91$, $p=0.001$). The mean NEWS2 score was 8.3 ± 2.4 (95% CI: 7.82–8.78), which was highly significant ($t=34.58$, $p<0.001$), indicating that a majority of patients presented with severe physiological derangement at admission.

Table 2. Serum vitamin D, thiamine and serum lactate levels among study participants (N=100)

Parameter	Category	n (%) / Mean±SD	Test	95% CI	p value
Vitamin D (ng/mL)	Mean±SD	17.6±6.8	$t=25.88$	16.25–18.95	<0.001*
Vitamin D status	Deficient (<20 ng/mL)	68 (68.0)	$\chi^2=38.44$		<0.001*
	Insufficient (20–30)	21 (21.0)			
	Sufficient (>30)	11 (11.0)			
Thiamine (nmol/L)	Mean±SD	58.4±18.3	$t=31.91$	54.77–62.03	<0.001*
Thiamine status	Deficient	42 (42.0)	$\chi^2=2.56$		0.109
	Normal	58 (58.0)			
Serum lactate (mmol/L)	Mean±SD	3.84±1.41	$t=27.23$	3.56–4.12	<0.001*
Lactate status	≤2 mmol/L	23 (23.0)	$\chi^2=29.16$		<0.001*
	>2 mmol/L	77 (77.0)			

Table 2 summarizes the biochemical profile of the study participants. The mean serum vitamin D level was 17.6 ± 6.8 ng/mL (95% CI: 16.25–18.95), which was statistically significant ($t=25.88$, $p<0.001$). Based on

vitamin D status, 68.0% of patients were vitamin D deficient (<20 ng/mL), 21.0% had insufficient levels (20–30 ng/mL), and only 11.0% had sufficient vitamin D levels (>30 ng/mL), demonstrating a highly significant

predominance of deficiency ($\chi^2=38.44$, $p<0.001$). The mean serum thiamine concentration was 58.4 ± 18.3 nmol/L (95% CI: 54.77–62.03), which was also statistically significant ($t=31.91$, $p<0.001$). Thiamine deficiency was observed in 42.0% of patients, whereas 58.0% had normal thiamine levels; however, this distribution was not statistically significant ($\chi^2=2.56$, $p=0.109$).

The mean serum lactate level was 3.84 ± 1.41 mmol/L (95% CI: 3.56–4.12), showing a highly significant elevation ($t=27.23$, $p<0.001$). Furthermore, 77.0% of patients had serum lactate levels exceeding 2 mmol/L, while only 23.0% had lactate levels ≤ 2 mmol/L, indicating a statistically significant predominance of hyperlactatemia ($\chi^2=29.16$, $p<0.001$).

Table 3. Correlation between NEWS2 score and biochemical markers (N=100)

Variable	Correlation coefficient (r)	95% CI	Test statistic	p value
NEWS2 vs Vitamin D	-0.63	-0.74 to -0.49	r test=-7.86	<0.001*
NEWS2 vs Thiamine	-0.49	-0.63 to -0.32	r test=-5.60	<0.001*
NEWS2 vs Serum Lactate	0.72	0.61–0.80	r test=9.43	<0.001*

Table 3 demonstrates the correlation between NEWS2 score and the evaluated biochemical markers. A strong negative correlation was observed between NEWS2 score and serum vitamin D levels ($r = -0.63$, 95% CI: -0.74 to -0.49), which was highly statistically significant (r test = -7.86, $p<0.001$). This indicates that increasing NEWS2 scores were associated with progressively lower vitamin D concentrations. Similarly, NEWS2 score demonstrated a moderate negative correlation with serum thiamine levels ($r = -0.49$, 95% CI: -0.63 to -0.32), which was also statistically significant (r test = -5.60, $p<0.001$), suggesting that higher disease severity was associated with lower thiamine levels. In contrast, a strong positive correlation was observed between NEWS2 score and serum lactate levels ($r = 0.72$, 95% CI: 0.61–0.80), which was highly significant (r test = 9.43, $p<0.001$).

Table 4. Association of biochemical markers with severity of sepsis according to NEWS2 score

Variable	Moderate NEWS2 (<7) (n=38)	Severe NEWS2 (≥ 7) (n=62)	Test	95% CI	p value
Vitamin D (ng/mL)	22.9±5.9	14.3±5.2	t=7.52	6.33–10.87	<0.001*
Thiamine (nmol/L)	67.2±17.6	53.1±16.2	t=4.08	7.25–20.95	<0.001*
Serum lactate (mmol/L)	2.41±0.81	4.71±1.16	t=10.96	1.88–2.72	<0.001*
Vitamin D deficiency	18 (47.4%)	50 (80.6%)	$\chi^2=12.19$	14.5–52.0%	<0.001*
Thiamine deficiency	10 (26.3%)	32 (51.6%)	$\chi^2=6.16$	6.0–44.7%	0.013*
Lactate mmol/L >2	20 (52.6%)	57 (91.9%)	Fisher Exact	23.1–55.4%	<0.001*

*Statistically significant ($p < 0.05$).

Table 4 compares biochemical markers between patients with moderate NEWS2 scores (<7) and those with severe NEWS2 scores (≥ 7). Patients with severe NEWS2 scores had significantly lower mean serum vitamin D levels (14.3 ± 5.2 ng/mL) compared with those having moderate NEWS2 scores (22.9 ± 5.9 ng/mL) ($t=7.52$, 95% CI: 6.33–10.87, $p<0.001$). Similarly, mean serum thiamine levels were significantly lower among patients with severe NEWS2 scores (53.1 ± 16.2 nmol/L) than among those with moderate scores (67.2 ± 17.6 nmol/L) ($t=4.08$, 95% CI: 7.25–20.95, $p<0.001$). Conversely, mean serum lactate levels were markedly higher in the severe NEWS2 group (4.71 ± 1.16 mmol/L) compared to the moderate group (2.41 ± 0.81 mmol/L) ($t=10.96$, 95% CI: 1.88–2.72, $p<0.001$). Vitamin D deficiency was significantly more frequent among patients with severe NEWS2 scores (80.6%) than those with moderate scores (47.4%) ($\chi^2=12.19$, $p<0.001$). Likewise, thiamine deficiency was observed significantly more often in the severe group (51.6%) compared to the moderate group (26.3%) ($\chi^2=6.16$, $p=0.013$). Elevated serum lactate levels (>2 mmol/L) were present in 91.9% of patients with severe NEWS2 scores compared with 52.6% of those with moderate scores, and this association was highly significant (Fisher's exact test, $p<0.001$).

DISCUSSION

Demographic and clinical profile

The present study included 100 patients with sepsis, with a mean age of 56.8 ± 15.2 years. Most patients were older than 40 years, as 39% belonged to the 41–60-year age group and another 39% were aged above 60 years. This distribution indicates that sepsis predominantly affected middle-aged and elderly patients. Advancing age is associated with immunosenescence, reduced physiological reserve, a greater burden of

chronic disease, and increased vulnerability to organ dysfunction during infection. Verma et al. (2023)^[1] similarly evaluated an adult sepsis population with a substantial proportion of older patients and demonstrated that increasing physiological derangement, measured using NEWS2, was associated with adverse outcomes. Hsieh et al. (2024)^[2], in a large cohort of more than 11,000 patients with sepsis, also observed considerable mortality and showed that NEWS2 was useful for early risk stratification. These observations support the predominance of older adults in the present study and emphasize the importance of close clinical monitoring in this age group.

A statistically significant male predominance was observed, with males constituting 61% and females 39% of the participants. Similar male predominance has been reported in many hospital-based sepsis cohorts. This may be related to differences in occupational exposure, health-seeking behaviour, smoking and alcohol use, underlying comorbidities, and sex-related variations in immune and hormonal responses. Mellhammar et al. (2019)^[3] studied patients with suspected infection and demonstrated that NEWS2 effectively identified sepsis with organ dysfunction, intensive care requirement, and infection-related mortality. Although demographic profiles vary across study settings, their adult cohort also reflected the typical mixed but predominantly older medical population encountered in emergency sepsis care.

Diabetes mellitus was present in 46%, hypertension in 41%, and chronic kidney disease in 19% of patients. Diabetes and hypertension did not show statistically significant predominance, whereas the lower frequency of chronic kidney disease was significant. Nevertheless, the relatively high prevalence of diabetes and hypertension indicates a substantial comorbidity burden. These conditions may impair immune

function, microvascular circulation, renal reserve, and cardiovascular adaptation during sepsis. Durr et al. (2022)^[4] found that NEWS was more sensitive than qSOFA for detecting sepsis and predicting ICU admission and 28-day mortality in emergency patients, supporting the need to use comprehensive physiological scores in patients with multiple comorbidities.

Respiratory infection was the commonest source of sepsis in the present study, accounting for 38%, followed by urinary tract infection in 27%, abdominal infection in 18%, bloodstream infection in 9%, and other sources in 8%. This pattern is broadly comparable with contemporary sepsis cohorts, in which pulmonary, urinary, and intra-abdominal infections constitute the leading sources. The predominance of respiratory infection may reflect the vulnerability of older patients to pneumonia, aspiration, chronic lung disease, and delayed presentation. The mean NEWS2 score was 8.3 ± 2.4 , and 62% of patients were subsequently classified in the severe NEWS2 category. This indicates that most participants had marked physiological abnormalities at admission. Verma et al. (2023)^[1] reported that NEWS2 had better discriminatory performance than qSOFA for assessing sepsis severity, while Mellhammar et al. (2019)^[3] found NEWS2 superior for detecting infection-associated organ dysfunction and adverse outcomes. Thus, the high mean NEWS2 score observed in the present study is consistent with enrolment of a clinically ill sepsis population requiring early escalation of care.

Vitamin D, thiamine, and lactate levels

The mean serum vitamin D level was 17.6 ± 6.8 ng/mL, and 68% of patients were vitamin D deficient, while a further 21% were insufficient. Only 11% had sufficient vitamin D levels. This demonstrates a high burden of hypovitaminosis D among patients with sepsis. Upala et al. (2015)^[5], in a systematic

review and meta-analysis, found a significant association between vitamin D deficiency and sepsis and suggested that inadequate vitamin D may contribute to immune dysfunction and poor outcomes. Li et al. (2020)^[6] further demonstrated that lower serum 25-hydroxyvitamin D at admission was independently associated with increased mortality among adults with sepsis, particularly in those with severe deficiency.

The high prevalence of vitamin D deficiency in the present study may be explained by poor nutritional intake, limited sunlight exposure during chronic illness, older age, renal dysfunction, inflammatory consumption, altered vitamin D-binding proteins, and reduced hepatic or renal activation. Chae et al. (2023)^[7] observed that vitamin D deficiency was common among patients with septic shock admitted through the emergency department and was associated with increased mortality despite protocol-based resuscitation. Their findings support the present observation that vitamin D deficiency was especially frequent among patients with more severe physiological disturbances.

The mean thiamine level was 58.4 ± 18.3 nmol/L, and 42% of patients were thiamine deficient. Although normal thiamine status was numerically more frequent, the difference between deficient and normal categories was not statistically significant. Thiamine deficiency in sepsis may result from reduced dietary intake, increased metabolic demand, impaired gastrointestinal absorption, renal losses, diuretic use, and depletion during prolonged systemic inflammation. As thiamine is an essential cofactor for pyruvate dehydrogenase, deficiency impairs conversion of pyruvate to acetyl coenzyme A and redirects pyruvate towards lactate formation.

Donnino et al. (2016)^[8] conducted a randomized, double-blind, placebo-controlled trial among patients with septic shock and elevated lactate. Thiamine did not

significantly reduce lactate or improve outcomes in the entire cohort; however, in the predefined subgroup with baseline thiamine deficiency, thiamine administration was associated with lower lactate levels and possible mortality benefit. This finding suggests that thiamine deficiency may be clinically relevant in a selected subset rather than in all patients with sepsis.

Woolum et al. (2018)^[9] reported that thiamine administration within 24 hours of admission in patients with septic shock was associated with more rapid lactate clearance and reduced mortality. Although that study was observational and cannot establish causality, it supports a metabolic relationship between thiamine availability and lactate metabolism. The 42% prevalence of thiamine deficiency in the present study is therefore clinically important, particularly because deficiency was more common in the severe NEWS2 group.

The mean serum lactate level was 3.84 ± 1.41 mmol/L, while 77% of patients had lactate levels above 2 mmol/L. This significant predominance of hyperlactatemia suggests widespread tissue hypoperfusion, adrenergic stimulation, mitochondrial dysfunction, impaired clearance, or accelerated glycolysis. Varis et al. (2017)^[10] found that septic-shock patients with admission lactate above 2 mmol/L had substantially higher 90-day mortality than those with lactate ≤ 2 mmol/L. Persistent hyperlactatemia at or beyond 72 hours was also associated with markedly increased mortality.

Ryoo et al. (2018)^[11], in a study of 1,060 patients with septic shock defined according to Sepsis-3, demonstrated that both absolute lactate levels and lactate clearance were useful predictors of mortality. Similarly, Lokhandwala et al. (2017)^[12] showed that a subsequent lactate concentration of at least 4 mmol/L and inadequate relative lactate reduction were associated with increased in-hospital mortality. These studies support the

present finding that serum lactate was frequently elevated in patients with sepsis and was strongly related to NEWS2-defined severity.

Correlation between NEWS2 and biochemical markers

A statistically significant strong negative correlation was found between NEWS2 score and serum vitamin D ($r = -0.63$, $p < 0.001$). This means that patients with greater physiological derangement had lower vitamin D concentrations. This relationship is biologically plausible because vitamin D contributes to innate immune defence, antimicrobial peptide production, endothelial stability, and regulation of inflammatory cytokines. However, the cross-sectional nature of the present findings does not establish whether low vitamin D contributed to more severe sepsis or occurred as a consequence of critical illness.

The inverse correlation agrees with Li et al. (2020)^[6], who showed that lower vitamin D levels were independently associated with higher mortality in adults with sepsis. Chae et al. (2023)^[7] also found vitamin D deficiency to be associated with mortality in septic shock after adjustment for other prognostic variables. The relatively strong correlation in the present study suggests that serum vitamin D may have value as an adjunctive severity marker, although it should not replace validated physiological or organ dysfunction scores.

NEWS2 demonstrated a moderate negative correlation with thiamine ($r = -0.49$, $p < 0.001$). Thus, worsening physiological severity was accompanied by declining thiamine concentrations. This may reflect increased metabolic consumption and nutritional depletion among severely ill patients. It is also possible that reduced thiamine worsened pyruvate oxidation, thereby promoting lactate accumulation and cellular energy failure. Donnino et al. (2016)^[8] found that the biochemical and

clinical effects of thiamine were most evident among patients who were deficient at baseline, while Woolum et al. (2018)^[9] observed better lactate clearance following early thiamine administration. These findings support the observed inverse relationship between thiamine and NEWS2, but interventional trials are required before routine supplementation can be recommended solely on the basis of a high NEWS2 score.

The strongest relationship was observed between NEWS2 and serum lactate, with a strong positive correlation of $r=0.72$ ($p<0.001$). Therefore, increases in NEWS2 were accompanied by marked increases in lactate. This relationship can be explained by the fact that NEWS2 incorporates respiratory rate, oxygen saturation, blood pressure, pulse rate, temperature, oxygen requirement, and consciousness all of which may deteriorate as tissue perfusion and cellular metabolism worsen.

Hargreaves et al. (2020)^[13] found that persistently elevated early warning scores and lactate identified patients with suspected sepsis who were at particularly high risk of mortality. Mortality was higher when NEWS remained ≥ 5 , and adding lactate ≥ 2 mmol/L improved risk identification. Their findings closely support the present strong positive correlation between NEWS2 and lactate and suggest that combining physiological scoring with a metabolic biomarker may improve clinical risk stratification.

Association with severity according to NEWS2

Patients with severe NEWS2 scores had significantly lower vitamin D levels than those with moderate scores (14.3 ± 5.2 vs. 22.9 ± 5.9 ng/mL, $p<0.001$). Vitamin D deficiency was also substantially more common in the severe group (80.6%) than in the moderate group (47.4%). This difference supports the possibility that vitamin D status reflects illness burden. Upala et al. (2015)^[5]

reported an association between vitamin D deficiency and sepsis, while Li et al. (2020)^[6] found that severe deficiency was particularly associated with mortality. Chae et al. (2023)^[7] similarly identified vitamin D deficiency as a mortality predictor in septic shock. Collectively, these studies are consistent with the present finding that low vitamin D was concentrated among patients with greater NEWS2-defined severity.

Mean thiamine levels were significantly lower in the severe group than in the moderate group (53.1 ± 16.2 vs. 67.2 ± 17.6 nmol/L, $p<0.001$), and thiamine deficiency occurred in 51.6% and 26.3%, respectively. The greater prevalence of deficiency among severe cases suggests that thiamine depletion may accompany increasing metabolic stress. This is clinically relevant because thiamine deficiency can aggravate lactate generation independently of tissue hypoxia. The subgroup findings of Donnino et al. (2016)^[8] and the observational results of Woolum et al. (2018)^[9] lend support to screening or empiric consideration of thiamine deficiency in selected patients with severe sepsis and persistent hyperlactatemia.

Serum lactate was markedly higher in the severe NEWS2 group than in the moderate group (4.71 ± 1.16 vs. 2.41 ± 0.81 mmol/L, $p<0.001$). Lactate above 2 mmol/L was present in 91.9% of severe cases compared with 52.6% of moderate cases. This large difference confirms that hyperlactatemia accompanies worsening physiological instability. Varis et al. (2017)^[10] demonstrated increased mortality with lactate above 2 mmol/L and persistent hyperlactatemia, while Ryoo et al. (2018)^[11] and Lokhandwala et al. (2017)^[12] confirmed the prognostic value of absolute lactate and lactate clearance. Hargreaves et al. (2020)^[13] further showed that combining lactate with an early warning score improved identification of high-risk sepsis patients.

Overall, the present study indicates that increasing NEWS2-defined sepsis severity was characterized by declining vitamin D and thiamine concentrations and increasing serum lactate. Among the evaluated biomarkers, lactate had the strongest correlation with NEWS2, whereas vitamin D demonstrated a stronger inverse relationship than thiamine. These findings suggest that simultaneous assessment of physiological severity and metabolic or nutritional biomarkers may offer a more comprehensive understanding of the patient's condition. Nevertheless, because biomarkers may be influenced by pre-existing nutrition, renal and hepatic function, fluid administration, and timing of sample collection, they should be interpreted as adjuncts rather than substitutes for clinical assessment.

CONCLUSION

The present study demonstrated that the NEWS2 score is a valuable clinical tool for assessing the severity of sepsis and shows significant correlations with important metabolic and biochemical markers. Patients with higher NEWS2 scores had significantly lower serum vitamin D and thiamine levels and significantly higher serum lactate concentrations, indicating that worsening physiological derangement is associated with nutritional deficiencies and impaired tissue perfusion. Among the evaluated biomarkers, serum lactate exhibited the strongest positive correlation with NEWS2, whereas vitamin D showed a stronger inverse correlation than thiamine. Patients with severe sepsis (NEWS2 ≥ 7) had markedly lower vitamin D and thiamine levels, a higher prevalence of vitamin D and thiamine deficiencies, and substantially elevated serum lactate compared with those having moderate NEWS2 scores. These findings suggest that combining the NEWS2 score with biochemical markers, particularly serum lactate and vitamin D, may improve early risk

stratification, facilitate prompt identification of high-risk patients, and support timely therapeutic interventions. Further large-scale multicentric prospective studies are warranted to determine whether correction of vitamin D and thiamine deficiencies can improve clinical outcomes in patients with sepsis.

LIMITATIONS OF THE STUDY

1. The study was conducted at a single tertiary care centre, which may limit the generalizability of the findings.
2. The sample size was relatively small (100 patients), reducing the statistical power for subgroup analyses.
3. The study employed an observational cross-sectional design, precluding conclusions regarding causal relationships.
4. Serum vitamin D and thiamine levels were measured only once at admission, and serial changes during treatment were not evaluated.
5. Seasonal variation, nutritional status, sunlight exposure, and dietary intake influencing vitamin D levels were not assessed.
6. Potential confounding factors such as chronic illnesses, medications, renal function, and hepatic dysfunction may have influenced biomarker levels.
7. Serum lactate was measured at baseline only, and lactate clearance was not evaluated.
8. Other inflammatory biomarkers such as procalcitonin, interleukins, and cytokines were not included for comparison.
9. Long-term outcomes after hospital discharge were not assessed.
10. The study did not evaluate the therapeutic impact of vitamin D or thiamine supplementation on clinical outcomes.

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