



General Medicine

STUDY OF CORRELATION OF SEVERITY OF SEPSIS AND ITS OUTCOME WITH VITAMIN D, THIAMINE & SERUM LACTATE LEVELS

Dr Fouzia Almas	Junior Resident, Department of General Medicine, Al-Ameen Medical College, Vijayapura.
Dr Mehboob M Kalburgi	Professor, Department of General Medicine, Al-Ameen Medical College, Vijayapura.
Dr Nasiruddin R Itagi	Assistant Professor, Department of General Medicine, Al-Ameen Medical College, Vijayapura.
Dr Raghavendra D*	Assistant Professor, Department of Community Medicine, Sri Chamundeshwari Medical College, Hospital & Research Institute, Channapatna. *Corresponding Author

ABSTRACT **Background:** Sepsis, a systemic inflammatory response to infection, poses high mortality risks, especially in cases with organ dysfunction or shock. Globally, it affects around 31 million people annually, with vitamin D deficiency—a common issue in India—linked to increased sepsis susceptibility and ICU mortality. Thiamine deficiency further exacerbates sepsis by causing lactic acidosis and impaired metabolism. This study explores associations between vitamin D, thiamine, and lactate levels with sepsis severity, aiming to enhance prognostic evaluations and therapeutic approaches. **Methods:** The study at Al-Ameen Medical College investigated the relationship between vitamin D, thiamine, and serum lactate levels in patients aged 18 and older admitted with sepsis. It included patients meeting systemic inflammatory response syndrome (SIRS) criteria with organ dysfunction. Exclusions were pregnancy, malabsorption syndromes, hepatic dysfunction, and vitamin supplement use. Demographic and clinical data were collected, and serum 25(OH)D, thiamine, and lactate levels were measured within 24 hours using chemiluminescence immunoassay (CLIA). Vitamin D deficiency was defined as <30 ng/mL, and thiamine deficiency as ≤ 9 nmol/L. Lactate levels ≥ 4 mmol/L indicated poor prognosis. **Results:** Our study investigated the association of vitamin D, thiamine, and serum lactate with sepsis severity and outcomes in 100 patients aged 18 years and above. Most participants were males (67%) and over 60 years old (57%). Common comorbidities included diabetes (34%) and hypertension (31%). Results showed a high prevalence of vitamin D insufficiency (67%) and normal thiamine levels (93%), with elevated lactate levels in 21%. Patients with higher sepsis severity had significantly lower vitamin D and thiamine levels and higher lactate levels ($p < 0.001$). Mortality predictors included age over 60, hypertension, CKD, and dialysis requirement. **Conclusion:** Our study effectively demonstrated significant associations between lower vitamin D and thiamine levels, higher serum lactate, and increased sepsis severity and mortality. These findings justify the objective by highlighting the potential role of these biomarkers in predicting sepsis outcomes, suggesting that monitoring and supplementation could enhance treatment strategies, ultimately improving prognosis and reducing mortality in sepsis patients.

KEYWORDS : Correlation, Sepsis, Vitamin D, Thiamine, Serum Lactate

INTRODUCTION:

Sepsis, a systemic inflammatory response to microbial infections, can escalate to "severe sepsis" when it leads to organ dysfunction. If severe sepsis includes hypotension unresponsive to fluid infusion, it progresses to "septic shock," marked by high mortality and morbidity.¹ Despite advancements in medical care, sepsis remains a leading cause of death in critically ill patients worldwide, with an estimated 31 million cases annually, including 19 million severe cases and 5.3 million deaths.² Infection prevention remains crucial for reducing sepsis incidence and improving outcomes.³

Vitamin D deficiency, prevalent in India despite ample sunlight, is a significant factor in sepsis prognosis. Low serum vitamin D levels impair immune response, increasing susceptibility to severe infections and mortality in ICU admissions. This deficiency underscores a public health need for vitamin D fortification in Indian foods. Patients with low vitamin D levels are at higher risk of developing sepsis, with studies confirming its essential role in immune modulation and sepsis prevention.⁴

Thiamine (vitamin B1) deficiency is common among septic patients, especially in septic shock cases. Essential for energy production, thiamine deficiency leads to increased lactate levels due to anaerobic metabolism, contributing to lactic acidosis and impaired metabolism.^{5,6} Elevated lactate levels signal tissue hypoperfusion and increased mortality risk, highlighting the potential of lactate as a prognostic marker in sepsis.⁷ This study investigates correlations between vitamin D, thiamine, and lactate levels with sepsis severity, assessing their roles in predicting outcomes, including mortality and discharge, for better clinical management.

METHODOLOGY:

Our prospective cross-sectional study was conducted in the Department of General Medicine at Al-Ameen Medical College, Vijayapura, from September 2022 to February 2024, covering an 18-

month period. The study included patients aged 18 and above, admitted to the Medicine wards or Intensive Care Unit (ICU) with sepsis, severe sepsis, or septic shock, and meeting at least two systemic inflammatory response syndrome (SIRS) criteria. Exclusion criteria encompassed patients under 18, pregnant individuals, those with malabsorption, hepatic dysfunction, on vitamin-interfering medications, or those refusing consent.

Demographic data, medical histories, and comprehensive physical examinations were conducted at admission. Routine hematologic and biochemical tests, including complete blood count, liver and renal function tests, and serum electrolytes, were performed, alongside urine and blood cultures. Serum levels of 25(OH)D, thiamine, and lactate were measured within 24 hours of admission. A qSOFA score was utilized to assess infection risk in non-ICU patients. Blood samples were collected and processed to measure vitamin D and thiamine levels using chemiluminescence immunoassay (CLIA) with a defined threshold for deficiency. Serum lactate levels were measured, with levels ≥ 4 mmol/L at 24 hours considered predictive of poor outcomes.

Data was entered into Microsoft Excel and analyzed using SPSS version 26. Categorical variables were expressed as frequencies and proportions, with chi-square or Fisher's exact test applied as appropriate. Continuous data was tested for normality and analyzed using independent t-tests or Mann-Whitney U tests for skewed distributions. A p-value < 0.05 was deemed statistically significant.

RESULTS:

In our study, 57% were over 60 years old, with a mean age of 59.2 ± 9.52 years, indicating a predominance of older adults, aligning with known vulnerability to sepsis in this age group. Males constituted 67% of the sample, suggesting a potential higher incidence or reporting of sepsis among men. Comorbidities were common, including diabetes (34%), hypertension (31%), chronic kidney disease (24%), and acute febrile illness (19%). (Table 1)

Table 1: Characteristics Of The Study Subjects

Subjects (N=100)		Frequency (N)	Percentage (%)
Age group	≤60 years	43	43.0%
	>60 years	57	57.0%
Gender	Male	67	67.0%
	Female	33	33.0%
Comorbidities	DM	34	34.0%
	HTN	31	31.0%
	CKD	24	24.0%
	AFI	19	19.0%
	None	20	20.0%

Vital signs showed 62% of subjects were febrile, with a mean pulse rate of 100.78 ± 13.88 bpm, tachycardia, and an average respiratory rate of 24.91 ± 2.39 cpm, indicating respiratory distress. Blood pressures (mean SBP 106.02 ± 10.94 mmHg, mean DBP 69.98 ± 9.34 mmHg) suggested hypotension, and an average GCS score of 12.91 ± 1.95 indicated altered mental status, highlighting sepsis-related clinical instability.

About 67% cases had vitamin D levels below 30 ng/mL, with a mean of 24.32 ± 9.52 ng/mL, ranging from 8.40 to 42.50 ng/mL, and a median of 23.10 ng/mL, highlighting a high prevalence of insufficiency potentially impacting immune response in sepsis. Thiamine levels were sufficient in 93% of subjects, with a mean of 40.35 ± 21.93 nmol/L, a range of 5.70 to 79.70 nmol/L, and a median of 39.80 nmol/L, indicating adequate metabolic function. Serum lactate levels averaged 2.66 ± 1.29 mmol/L, ranging from 1.30 to 5.50 mmol/L, with 21% exceeding 4.0 mmol/L, underscoring the importance of lactate monitoring for timely interventions. (Table 2)

Table 2: Biochemical Examination

Subjects (N=100)		Frequency (N)	Percentage (%)
Vitamin D	<30 ng/mL	67	67.0%
	≥30 ng/mL	33	33.0%
Serum Thiamine	≤9.0 nmol/L	7	7.0%
	>9.0 nmol/L	93	93.0%
Serum Lactate	<4.0 mmol/L	79	79.0%
	≥4.0 mmol/L	21	21.0%

In our study, 20% of subjects required dialysis, indicating severe renal impairment, and the mean ICU stay was 7.11 days (range 4–13, median 6), reflecting the high morbidity associated with sepsis. A survival rate of 92% demonstrates effective management, with only 8% mortality, underscoring the importance of timely, aggressive sepsis intervention to improve outcomes and reduce mortality in critically ill patients. (Figure 1)

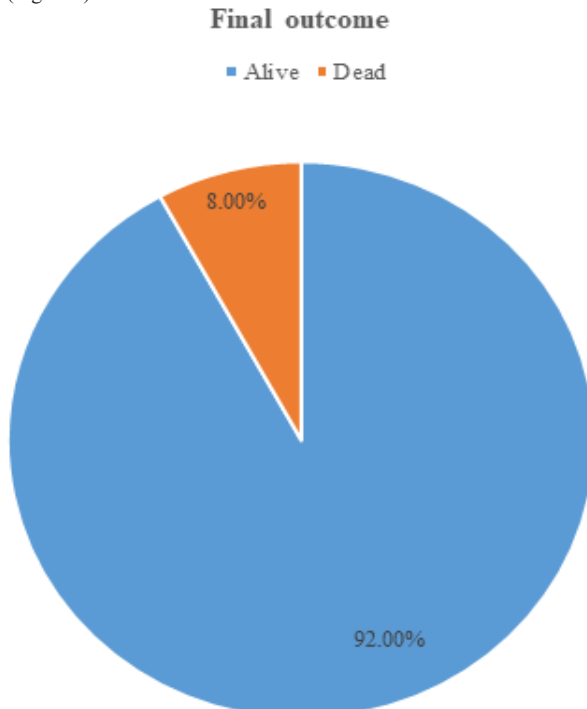


Figure 1: Final Outcome Of The Study Subjects

Analysis shows that a qSOFA score of 3 correlates with worse outcomes in sepsis, particularly among older patients (≥ 60), those with diabetes, hypertension, or chronic kidney disease, and those requiring dialysis ($p < 0.001$). These factors highlight the need for focused monitoring in severe cases. Additionally, higher qSOFA scores were linked to lower vitamin D (mean: 13.99 ng/mL vs. 29.65 ng/mL) and thiamine (16.11 nmol/L vs. 52.84 nmol/L) levels, and elevated lactate (4.34 mmol/L vs. 1.79 mmol/L), suggesting their role as biomarkers for risk assessment and prognosis in sepsis. (Table 3)

Table 3: Correlation With Severity Of Sepsis

Subjects (N=100)		qSOFA		p-value [#]
		2	3	
Vitamin D (in ng/mL)	Mean	29.65	13.99	<0.001*
	SD	7.02	2.83	
	Minimum	18.30	8.40	
	Median	30.00	14.10	
Thiamine (in nmol/L)	Maximum	42.50	18.10	<0.001*
	Mean	52.84	16.11	
	SD	15.71	6.31	
	Minimum	25.40	5.70	
Lactate (in mmol/L)	Median	52.30	17.45	<0.001*
	Maximum	79.70	24.90	
	Mean	1.79	4.34	
	SD	0.24	0.66	
	Minimum	1.30	3.40	<0.001*
	Median	1.80	4.25	
	Maximum	2.60	5.50	

Independent t-test

* Statistically significant

Mortality analysis identified key predictors: patients over 60 had a 14% mortality rate, while younger patients had none ($p = 0.010$). Hypertension and chronic kidney disease also elevated mortality risks (19.4% and 29.2%, respectively). Dialysis need was a critical predictor, with a 35% mortality rate ($p < 0.001$), and a qSOFA score of 3 correlated with a 23.5% mortality ($p < 0.001$). Survivors had significantly higher vitamin D (25.55 ng/mL vs. 10.23 ng/mL) and thiamine levels (43.17 nmol/L vs. 7.90 nmol/L), while non-survivors had elevated lactate (5.10 mmol/L vs. 2.44 mmol/L), suggesting these biomarkers' prognostic value. (Table 4)

Table 4: Correlation With Final Outcome

Subjects (N=100)		Outcome		p-value [#]
		Alive	Dead	
Vitamin D (in ng/mL)	Mean	25.55	10.23	<0.001*
	SD	8.91	1.73	
	Minimum	11.50	8.40	
	Median	24.30	9.75	
Thiamine (in nmol/L)	Maximum	42.50	13.00	<0.001*
	Mean	43.17	7.90	
	SD	20.55	2.03	
	Minimum	8.10	5.70	
Lactate (in mmol/L)	Median	42.55	7.35	<0.001*
	Maximum	79.70	11.80	
	Mean	2.44	5.10	
	SD	1.11	0.35	
	Minimum	1.30	4.40	<0.001*
	Median	1.90	5.15	
	Maximum	5.30	5.50	

Independent t-test

* Statistically significant

DISCUSSION:

This study at Al-Ameen Medical College examined adults (≥ 18 years) with sepsis, severe sepsis, or septic shock. Patients met at least two SIRS criteria, excluding those under 18, pregnant, with hepatic dysfunction, or on medications affecting vitamin D / thiamine metabolism. Within 24 hours of admission, key biomarkers—serum 25-hydroxyvitamin D, thiamine, and lactate—were measured. The quick Sequential Organ Failure Assessment (qSOFA) score was used to assess the severity of sepsis.

Characteristics Of The Study Subjects

Older adults represented a significant proportion of the cohort, with

57% aged over 60, aligning with Olejarova M et al⁸, who reported a mean age of 59.3 years among sepsis patients. Similar findings from Seok H et al⁹, Heming N et al¹⁰, and Liu Z et al¹¹ indicate that elderly patients are particularly vulnerable to sepsis due to age-related immune decline, underscoring the need for targeted management strategies for older populations in sepsis care.

Males comprised 67% of the study population, a trend consistent with Olejarova M et al⁸, Heming N et al¹⁰, and Liu Z et al¹¹, each of whom reported a higher prevalence of sepsis among males. Seok H et al⁹ observed a male predominance of 46.5%, while Donnino MW et al¹² found an equal gender distribution. These findings suggest that male patients may face heightened sepsis risks, potentially due to biological or social factors that warrant further investigation.

Diabetes mellitus (34%) and hypertension (31%) were prominent comorbidities in this study, reflecting a trend seen in other studies. Seok H et al⁹ noted similar conditions using the Charlson comorbidity index, while Heming N et al¹⁰ identified hypertension and chronic pulmonary disease as common among sepsis patients. These studies highlight chronic diseases as risk factors that exacerbate sepsis severity, emphasizing the need to manage underlying conditions to improve sepsis outcomes.

Examination Findings

Vital signs showed clinical instability, with 62% of patients febrile, a mean pulse of 100.78 bpm, and a respiratory rate of 24.91 cpm. Similar physiological stress markers were observed by Heming N et al¹⁰ (median heart rate 100 bpm, temperature 38.5°C) and Liu Z et al¹¹, who noted a correlation between elevated heart rates and sepsis severity. These findings affirm the importance of monitoring vital signs as immediate indicators of sepsis severity.

Vitamin D Levels

Vitamin D deficiency was prevalent, with 67% of subjects showing levels below 30 ng/mL. This aligns with findings by Olejarova M et al⁸, who noted widespread deficiency in sepsis patients, and Seok H et al⁹, who associated low vitamin D with increased mortality. Across studies, vitamin D deficiency appears to be a modifiable risk factor, suggesting that addressing it in clinical practice may benefit sepsis outcomes.

Serum Thiamine Levels

Although 93% of patients in this study had thiamine levels above 9 nmol/L, thiamine depletion can occur during severe illness. Heming N et al¹⁰ found lower thiamine levels among non-survivors, and Donnino MW et al¹² identified 20% of patients developing thiamine deficiency within 72 hours. This evidence underscores the importance of monitoring thiamine to prevent metabolic complications in septic patients.

Serum Lactate Levels

Elevated lactate levels were observed in 21% of patients, indicating poor prognosis. Elevated lactate has been consistently shown as a marker of sepsis severity across multiple studies, including those by Olejarova M et al⁸, Seok H et al⁹, and Liu Z et al¹¹. Lactate's utility as an indicator of hypoperfusion and predictor of mortality highlights its role as a critical biomarker in sepsis management.

Outcomes

The average ICU stay was 7.11 days, with 20% of patients requiring dialysis, underscoring the substantial morbidity associated with sepsis. Olejarova M et al⁸ reported high morbidity linked to severity markers, while Seok H et al⁹ noted ICU admissions in 60.5% of sepsis cases. These findings emphasize the need for comprehensive management, including metabolic support, for patients with severe sepsis.

The survival rate in this study was 92%, indicative of effective management protocols. Olejarova M et al⁸ similarly observed improved survival rates with sufficient vitamin D levels. Seok H et al⁹ linked vitamin D deficiency with higher mortality, reinforcing its potential role in improving sepsis outcomes. The alignment of findings across studies suggests that addressing nutritional deficiencies can contribute to better prognosis in sepsis patients.

Correlation with Sepsis Severity

The study found correlations between low vitamin D, low thiamine, and high lactate levels with sepsis severity. Studies by Olejarova M et al⁸ and Seok H et al⁹ have similarly demonstrated vitamin D's and

lactate's roles in predicting sepsis severity, while Heming N et al¹⁰ highlighted thiamine deficiency's impact. These biomarkers could aid in risk stratification, informing targeted interventions to reduce sepsis severity.

Correlation with Final Outcome

Vitamin D, thiamine, and lactate levels were linked to sepsis outcomes, reinforcing their prognostic value. Previous studies by Olejarova M et al⁸, Seok H et al⁹, Heming N et al¹⁰, and Liu Z et al¹¹ support these findings, underscoring the potential of these biomarkers as therapeutic targets. Monitoring and correcting deficiencies may guide clinical decisions to improve survival and recovery in sepsis patients.

CONCLUSION:

This study investigated the association of vitamin D, thiamine, and serum lactate with sepsis severity and outcomes in 100 patients. It found that 67% of participants had vitamin D insufficiency, while 7% had thiamine deficiency, and 21% showed elevated lactate levels. Higher qSOFA scores, indicating severe sepsis, were linked with older age, diabetes, hypertension, chronic kidney disease, and dialysis requirement. These factors correlated with increased mortality, highlighting their importance in assessing sepsis severity. Survivors had higher vitamin D and thiamine levels and lower lactate levels, emphasizing these biomarkers' potential in predicting sepsis outcomes and guiding therapeutic strategies.

Acknowledgement: We extend our sincere gratitude to the study participants for their invaluable contributions and participation in this research.

Declarations

Funding: None

Conflict of interest: None declared

Ethical Approval: The study was approved by the Institutional Ethics Committee

REFERENCES:

- Munford RS. Severe sepsis and septic shock. In: Longo DL, editor. Harrison's Principles of Internal Medicine. 18th ed. McGraw-Hill; 2012. p. 2223.
- Shojaei M, Sabzeghabaei A, Valaei Barhagh H, Soltani S. The correlation between serum level of vitamin D and outcome of sepsis patients: a cross-sectional study. Arch Acad Emerg Med. 2019 Jan 10;7(1):PMID:30847436; PMCID: PMC6377223.
- Bayat M, Gachkar L, Zahernia M, Hadavand F. Association between low serum vitamin D levels and sepsis: a single-center study in Tehran, Iran. Arch Clin Infect Dis. 2021;16(1).
- Harinarayan CV, Joshi SR. Vitamin D status in India--its implications and remedial measures. J Assoc Physicians India. 2009 Jan;57:40-8.
- Attaluri P, Castillo A, Edriss H, Nugent K. Thiamine deficiency: an important consideration in critically ill patients. Am J Med Sci. 2018 Oct;356(4):382-390.
- Kanchanasurakit S, Suthumpoung P, Santimaleworagun W, Nakaranurack C, Huynh NS, Srisawat C, et al. Effectiveness of thiamine therapy in mortality rate in patients with septic shock: a systematic review and meta-analysis. Int J Crit Illn Inj Sci. 2021 Apr-Jun;11(2):86-94.
- Filho RR, Rocha LL, Corrêa TD, Pessoa CM, Colombo G, Assuncao MS. Blood lactate levels cutoff and mortality prediction in sepsis-time for a reappraisal? A retrospective cohort study. Shock. 2016;46(5):480-485.
- Olejarova M, Dobisova A, Suchankova M, Tibenska E, Szaboova K, Koutun J, et al. Vitamin D deficiency – a potential risk factor for sepsis development, correlation with inflammatory markers, SOFA score and higher early mortality risk in sepsis. Bratisl Med J. 2019;120(4):284-90.
- Seok H, Kim J, Choi WS, Park DW. Effects of Vitamin D Deficiency on Sepsis. Nutrients. 2023;15(10):4309.
- Heming N, Salah A, Meng P, Sivanandamoorthy S, Bounab R, Chevret S, et al. Thiamine status and lactate concentration in sepsis: A prospective observational study. Medicine (Baltimore). 2020;99(7).
- Liu Z, Meng Z, Li Y, Zhao J, Wu S, Gou S, et al. Prognostic accuracy of the serum lactate level, the SOFA score and the qSOFA score for mortality among adults with Sepsis. Scand J Trauma Resusc Emerg Med. 2019;27:51.
- Donnino MW, Carney E, Cocchi MN, Barbash I, Chase M, Joyce N, et al. Thiamine deficiency in critically ill patients with sepsis. J Crit Care. 2010;25(4):576-81.