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Serum Vitamin D level in sepsis patients and its correlation with clinical outcome

Anand Singh[1], Baghel PK[2], Karan Saran Kapur[3]

[1]Resident Medical Officer, [2]Professor and Head, [3]Assistant Professor, Department of General Medicine, Shyam Shah Medical College and Associated Hospitals, Rewa, Madhya Pradesh, India

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ABSTRACT

Background: Serum Vitamin D plays an important role in sepsis; lack of Vitamin D has been linked to a higher risk for the progression of infections, as it signifies an immune system mediator. **Aims and Objectives:** In this study, our aim is to evaluate the correlation between serum levels of Vitamin D and clinical outcome in sepsis patients. **Materials and Methods:** The present prospective cohort study was performed on patients over 18 years of age suspected of sepsis presenting to an emergency department during 1 year. For all eligible patients, the blood sample was drawn for the measurement of serum level of Vitamin D3, and its correlation with outcomes such as mortality, renal failure, and liver failure was assessed. **Results:** One hundred and sixty patients with a mean age of 48.5 ± 20.587 years were studied (60.0% males). The mean serum level of Vitamin D3 in the studied patients was 32.0 ± 12.54 ng/mL. By considering 30–100 ng/mL as the normal range of Vitamin D, 70% of the patients had Vitamin D deficiency. Only age ($r = -0.261$, $P = 0.037$) and mortality ($r = -0.426$, $P = 0.025$) showed a significant correlation with mean Vitamin D. **Conclusion:** Based on the result of this study, out of 160 patients, 61.25% of patients with sepsis are Vitamin D deficient. There is a significant and inverse relationship between mortality and advanced age which were associated with serum Vitamin D3 levels. Hence, supplementing with Vitamin D appears to have potential benefits in reducing infection rates, sepsis-related deaths, and infection prevalence, particularly in the elderly.

Key words: Systemic inflammatory response syndrome; Sepsis; Patient outcome assessment; 24, 25-dihydroxy vitamin D3; Mortality

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INTRODUCTION

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection.[1] A rough estimate of the disease's burden in high-income countries is more than 31 million cases, 19 million of which are severe, and 5.3 million deaths annually.[2-4] In developing countries such as India, with a population of 1.34 billion people, the epidemiology of sepsis is poorly understood despite high mortality and morbidity rate.[5]

Sepsis is one of the main causes of death in critical illness.[6,7] Although clinical outcomes have significantly improved since the implementation of early goal-directed therapy, effective treatment still poses significant challenges and depends primarily on the prompt eradication of the pathogenic microorganism in addition to supportive care.[8]

Serum Vitamin D plays an important role in sepsis, lack of Vitamin D has been linked to a higher risk for the progression of bacterial and viral infections.[9-11] Vitamin D inhibits the over-expression of inflammatory cytokines and plays a key role in the gathering of leukocytes, the development of local inflammation, and the antibacterial reactions in innate immunity. Low serum level of Vitamin D on admission of patients to the intensive care unit (ICU) has correlated with an increase in mortality risk and increased blood infections.

Vitamin D status is a surrogate marker of mobility and outdoor activities because the majority of body stores are derived from solar ultraviolet-B (UVB) and only negligible

Address for Correspondence:
Dr. Anand Singh, Resident Medical Officer, Department of General Medicine, Shyam Shah Medical College and Associate Hospitals, Rewa - 486 001, Madhya Pradesh, India. **Mobile:** +91-7566453956. **E-mail:** dr.anandsingh0907.as@gmail.com

amounts may come from fortified, dietary sources. In higher (and lower) latitudes, endogenous Vitamin D synthesis is severely restricted during the winter months because a more oblique angle means less UVB reaches the earth. Protective clothing, air pollution, and sunscreen also impair optimal cutaneous Vitamin D production, explaining the high prevalence of Vitamin D deficiency found worldwide, even in otherwise healthy controls.[12]

Aims and objectives

1. To evaluate the correlation between serum levels of Vitamin D and outcome of sepsis patients
2. To study Vitamin D level in the study population.

MATERIALS AND METHODS

The present prospective cohort study was performed on patients suspected to sepsis presenting to the emergency department of Sanjay Gandhi Memorial Hospital Rewa. For all the eligible patients, the blood sample was drawn for measuring serum level of Vitamin D and finally, the correlation between the level of this vitamin and the studied outcomes was evaluated. Patients having collagen vascular disease malignancy, on steroids, pregnant patients, and patients having diabetes mellitus were excluded from the study.

Inclusion criteria

- Patient age >18.

Exclusion criteria

- Malignancy
- Collagen vascular disorder
- Patients on steroid
- Patients with bleeding disorder
- Pregnancy
- Diabetes mellitus
- Chronic kidney disease
- Neuroendocrine disease.

Venous blood was drawn from the median cubital vein of the patients for measuring the serum level of Vitamin D. Blood samples were kept at room temperature for 15–30 min and centrifuged (1500 rpm) for 10–15 min. Consequently, serums were separated and kept at −20°C until the time of evaluation. After completion of samples, the concentration of serum 25-hydroxy Vitamin D3 was measured.

Patients who satisfying inclusion and exclusion criteria were included in the study and a written consent was obtained from each patient. Sepsis diagnosis was confirmed after clinical examinations, meeting the required criteria and performance of laboratory tests. Patients with a history of neuroendocrine diseases, history of mental disorders, shock due to reasons other than sepsis, consumption of corticosteroid drugs, recent, and constant use of Vitamin D or other supplements including it, pregnant women, those who do not give their consent for participation in the study, and those whose sepsis diagnosis was confirmed in the end based on the mentioned criteria were eliminated from the study. Sepsis was defined as the presence of at least 2 of the symptoms of systemic inflammatory response syndrome (SIRS) with the origin of a suspected or confirmed infectious source.

RESULTS

The present study is entitled "Serum Vitamin D level in sepsis patients and its correlation with clinical outcome." The study was conducted on 160 patients of either sex between 14 and 50 and above years of age with complaints of sepsis. Patients arrived at the medicine ward and emergency department in Shyam Shah Medical College and associated Sanjay Gandhi Memorial Hospital Rewa. Recorded parameters were tabulated and appropriate statistical tests were applied. In the present study, females were 40% (64 patients) and males were 60% (96 patients), respectively. Out of 160 patients, majority 80 patients (50%) were in age of ≥51 years, and 14 patients (8.75%) of <20 years were present. The mean age was 48.5±20.587 with an insignificant P=0.0536.

The mean Glasgow Coma Scale (GCS) score of the study population was 12.59±3.80. One hundred patients (62.5%) had normal GCS score 15, 35 patients (21.875%) had 8–14 GCS score, and 25 patients (15.625%) had 3–7 GCS score with severe complications.

Majority of the patients 104 (65%) had pneumonia at the time of admission. About 12.5% of patients had urinary tract infections, 12.5% of patients had hematogenous, and 9.375% of patients had multiple source infection at the time of admission.

Out of 160 patients with sepsis, 19 patients (11.875%) had quick sequential organ failure assessment (qSOFA) score ≥II indicating poor prognosis, and rest 141 patients had qSOFA score between 0 and I (88.125%). The mean of this score was 0.5875±0.8715 with statistically significant P<0.0001 (Table 1).

Out of 160 patients, 98 patients (61.25%) had low serum Vitamin D level. 26.25% (42 patients) had deficient serum Vitamin D and 35% (56 patients) had insufficient Vitamin D level. The mean was 32.0±12.54 with a significant P<0.0001.

Out of 160 patients, 20 patients had mortality during their hospital stay. In which 14 patients (70%) had

Table 1: qSOFA score in total patients with sepsis

S. No.	qSOFA score	n	%	Mean±SD	P-value
1	0	106	66.25		
2	I	34	21.25	0.5875±0.8715	<0.0001
3	II	11	6.25		
4	III	09	5.625		
	Total	160	100		

SD: Standard deviation, qSOFA: quick sequential organ failure assessment

Table 2: Distribution of Vitamin D deficiency in total mortality

S. No.	Deficiency of Vitamin D	Mortality (20)	
		No of patients	Percentage
1	Yes	14	70
2	No	06	30
Total		20	100

Vitamin D deficiency, and six patients (30%) had sepsis with normal Vitamin D level. In the present study, three patients died who had qSOFA scores of 0 to I and 17 patients died with qSOFA score of >II with significant P<0.0001 (Table 2).

Out of 160 patients, 98 patients (61.25%) had low serum Vitamin D level. 26.25% (42 patients) had deficient serum Vitamin D and 35% (56 patients) had insufficient Vitamin D level. The mean was 32.0±12.54 with significant P<0.0001 (Table 3).

DISCUSSION

Sepsis involves the magnitude of change in different physiological, hematological, and biochemical parameters can be considered to be useful for the prediction of outcome among sepsis patients admitted to the emergency department. SOFA score is one such scoring system that takes into account different hematological and biochemical parameters to provide a comprehensive score that can be used successfully for the prediction of outcome particularly in emergency department patients which can be extended to sepsis patients too. It is thus not only complex, time-consuming, and inconvenient but also costly assessment, particularly in low-resource settings in a developing country like ours where laboratory facilities and skilled workforce is still scarce. Hence, there has always been an emphasis on the exploration and validation of such parameters that can be obtained easily and have enough applicability in clinical settings.[13]

qSOFA is one such parameter, described as "quick SOFA" criteria for early detection of patients potentially at risk of dying from sepsis which comprises three clinical indicators – systolic blood pressure, respiratory rate, and GCS for predicting the outcome in patients of sepsis. Encouraged by the outcomes reported in previous studies, the present study was carried out to access its prognostic efficacy in sepsis patients in our setup. In our study, 160 patients were included and the mean age of the patients (in years) was 48.5±20.587. About 60% of the participants were male and 40% of the participants were female. The gender ratio was 3:2. Age and gender profiles of patients in different studies have shown a considerable variability, particularly since sepsis affects almost all ages irrespective of gender. In a study by Raith et al.,[14] also from 2000 to 2015 – prognostic accuracy of the SOFA score, SIRS Criteria, and qSOFA score for in-hospital mortality among adults with suspected infection admitted to the ICU' on 1,84,875 patients with an infection-related primary admission diagnosis in 182 Australian and New Zealand ICUs from 2000 to 2015. Among 184,875 patients mean age of the patients was 62.9 years with a standard deviation (SD) of 17.4 and women comprised 44.6% of the participants in the study. Similarly in a study by Canet et al.,[15] on qS0FA as a predictor of mortality and prolonged ICU admission in emergency department patients with a suspected infection on 11,205 emergency department patients with suspected infection, the mean age of the patients was 54.16 years with a SD of 17.72 and the females comprised 49.63% of the study population. The mean age was lower in our study as compared to the previous study which can be due to ethnic and regional variability.

In the present study, 160 patients (62.5%) had normal GCS scores 15, 35 patients (21.875%) had 8–14 GCS scores and 25 patients (15.625%) had 3–7 GCS scores with severe complications. On comparing our score with the study done by Shojaei et al.,[16] we found comparable results in which 9.6% of patients had 3–7 GCS scores, 50.7% of patients had 8–14 GCS scores and 39.7% of patients had 15 GCS score. Shojaei et al.'s[16] study was done on ICU patients on the one hand; on the other hand, our study was done on ward and ICU patients.

Vitamin D deficiency has been charged with many kinds of disorders such as infections, cardiac problems, autoimmune diseases, various pulmonary diseases, and tuberculosis. Furthermore, Vitamin D deficiency may cause negative consequences such as increased infection rates, prolonged

Table 3: Gender-wise distribution of serum Vitamin D level in sepsis

S. No.	Gender	Serum Vitamin D level			P-value
		Sufficient 30–100 ng/dL	Insufficient 30–20 ng/dL	Deficient <20 ng/dL	
1	Male	50	30	16	<0.0001
2	Female	12	31	21	
Total		62	61	37	
Mean			32.0±12.54		

hospitalization in ICUs, increased hospital mortality, and increased health-care expenses. Many recent papers showed a close association between Vitamin D deficiency and some systemic diseases that have significant morbidity and mortality rates. However, Sagir Muslum et al., (2021), found no similarity in source of infection in their study. Shojaei et al.,[16] found 1.2% of patients had gastrointestinal infection, 31.1% of patients had pneumonia, 29.7% of patients showed urinary tract infection, and 21.6% of patients had pneumonia with urinary infection. In a study done by Bayat et al.,[17] they found 32% of patients had pneumonia, 13.3% of patients had urinary tract infection, and 1.3% of patients showed gastrointestinal infection at the time of admission. On comparison with previous studies, we found majority of the patients 104 (65%) had pneumonia at the time of admission. About 12.5% of patients had urinary tract infection, 12.5% of patients had hematogenous, 3.125% of patients had gastrointestinal infection, 0.625% of patients had bed sore, and 9.375% of patients had multiple source infection at the time of admission.

In our study, 21.25% of patients went on mechanical ventilation and 78.75% of patients did not require mechanical ventilation comparing with Shojaei et al.,[16] we found comparable results with our study.

Based on the National Health and Nutrition Examination Survey, the level of 25-hydroxy Vitamin D had an inverse correlation with occurrence of upper respiratory tract infection. The evidence is also indicative of the effect of Vitamin D levels on influenza and invasive pneumococcal disease. Two meta-analyses performed on observational studies have confirmed that there is a significant correlation between Vitamin D status and risk of being affected with sepsis, infection severity, and 30-day mortality.[18]

This study found organ failure patients had lower of Vitamin D level (17.0%) in which 12 patients had renal failure, nine patients had hepatic failure and 10 patients had pulmonary failure. The association between Vitamin D deficiency and insulin resistance developed through inflammation, as Vitamin D deficiency was associated with increased inflammatory markers.

In this study, out of 160 patients, 20 patients had mortality during their hospital stay. Which 14 patients (70%) had Vitamin D deficiency, and six patients (30%) had sepsis with normal Vitamin D level. The correlation between sufficient Vitamin D and reduced mortality has not been reported in all studies. In one study, the rate of mortality in sepsis patients correlated with Vitamin D level on admission, but this correlation was not significant.[19]

Limitations of the study

An important limitation present in all observational studies is also present in our study and it is not known if Vitamin D deficiency is a marker for sepsis or if it causes sepsis.

CONCLUSION

According to the current study, 61.25% of patients with sepsis are Vitamin D deficient. There is a significant and inverse relationship between mortality and advanced age which were associated with serum Vitamin D3 levels. Hence, supplementing with Vitamin D appears to have potential benefits in reducing infection rates, sepsis-related deaths, and infection prevalence, particularly in the elderly.

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Author's Contribution:
AS- Definition of intellectual content, literature survey, prepared the first draft of the manuscript, implementation of the study protocol, data collection, data analysis, manuscript preparation and submission of article; **PKB-** Concept, design, clinical protocol, manuscript preparation, design of the study, statistical analysis and interpretation; **KK-** Coordination and manuscript revision.

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Shyam Shah Medical College, Rewa, Madhya Pradesh, India.

Orcid ID:
Dr. Anand Singh- https://orcid.org/0009-0002-4771-4927
Dr. Baghel PK- https://orcid.org/0000-0001-9381-9418
Dr. Karan Saran Kapur- https://orcid.org/0000-0003-1960-7462

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