

RESEARCH

Correlation Study Of Serum Vitamin D Levels With In-Hospital Mortality In Septic Shock Patients

Noviarta Prima Kusumandaru^{1*}, Calcarina Fitriani Retno Wisudarti¹, Juni Kurniawaty¹

¹Anesthesiology and Intensive Therapy Department, Faculty of Medicine, Public Health and Nursing, Gadjah Mada University/ Dr. Sardjito General Hospital Yogyakarta

*Corresponden author : aankusumandaru@gmail.com

ABSTRACT

Article Citation : Noviarta Prima Kusumandaru, Calcarina Fitriani Retno Wisudarti, Juni Kurniawaty. Correlation Study Of Serum Vitamin D Levels With In-Hospital Mortality In Septic Shock Patients. Jurnal Komplikasi Anestesi 12(1)-2024.

Background: Sepsis is a medical emergency involving the body system's immunologic response to infection, which can lead to organ dysfunction and death. Sepsis shock, as a severe form of sepsis, has a high mortality rate. Vitamin D is known to have an important role in immune and inflammatory modulation, which may affect clinical outcomes in sepsis patients.

Objective: This study aims to evaluate the correlation between serum vitamin D levels and mortality in sepsis shock patients at Dr. Sardjito Hospital.

Methods: This study was a prospective cohort study involving 22 sepsis shock patients. Serum vitamin D levels were measured when patients entered the ICU, and mortality was recorded for 28 days. SAPS-3 score was used to assess disease severity. Statistical analysis was performed to determine the relationship between vitamin D levels, SAPS-3 score, and mortality.

Results: Of the 22 patients, 15 patients (68.18%) had normal-insufficient vitamin D levels, while 7 patients (31.82%) had mild-severe deficiency. Mortality was recorded at 27.27% (6 patients). Analysis showed that patients with vitamin D deficiency had an odds ratio (OR) of 8.6667 for mortality compared to patients with normal-insufficient vitamin D levels ($p=0.026$; 95% CI: 1.0495 to 71.5719). In addition, there was a significant negative correlation between vitamin D levels and SAPS-3 score ($p=0.0001$; OR=7.1111; 95% CI: 1.0888 to 46.4425).

Conclusion: This study shows that vitamin D deficiency correlates with an increased risk of mortality in sepsis shock patients.

Keywords: Mortality, Sepsis, SAPS-3 Score, Septic Shock, Vitamin D.

Introduction

Sepsis is a medical emergency involving the body's immunologic response to infection, which can lead to organ dysfunction and death. Despite advances in the understanding of the pathophysiology and management of sepsis, it remains a major cause of morbidity and mortality in critical patients. [1,2]. Septic shock, as the most severe form of sepsis, has a very high mortality rate, reaching 30-50%. Therefore, the identification of factors that may affect the prognosis of sepsis and septic shock is very important. [3,4].

Vitamin D has been known to play an important role in modulating the immune system. Several studies have shown an association between vitamin D deficiency and increased risk of infection and sepsis. [5]. However, the relationship between vitamin D levels and mortality in patients with septic shock remains unclear. Previous studies have shown mixed results, possibly due to population differences, geographical factors, and other confounding factors. [6].

The Simplified Acute Physiology Score 3 (SAPS-3) is a scoring system used to predict patient mortality in intensive care units. It combines various physiological and clinical parameters to provide an estimate of mortality risk. Several studies have shown a correlation between high SAPS-3 scores and increased mortality in critical patients, including sepsis patients. [7].

This study aims to determine the correlation between serum vitamin D levels and in-hospital mortality in septic shock patients, as well as its relationship with SAPS-3 score. Understanding this relationship is expected to provide new insights into the management of septic shock patients and potential future therapeutic interventions. In addition, this study may also contribute to a

better understanding of the role of vitamin D in critical conditions such as septic shock.

Methods

Research Design and Location

This study is a prospective cohort study conducted at Dr. Sardjito Central General Hospital Yogyakarta. The study design involved observing a group of patients with septic shock over time to determine the relationship between serum vitamin D levels and in-hospital mortality.

Research Population and Sample

The population of this study were all patients with septic shock who were admitted to the Intensive Care Unit of Dr. Sardjito Hospital. The study sample was taken from patients who met the inclusion and exclusion criteria. Inclusion criteria included adult patients aged 18-65 years diagnosed with septic shock based on clinical criteria, while exclusion criteria included pregnant patients and those who refused to participate. The sample size was determined using the general formula for prospective cohort studies, with a final result of 22 patients.

Data Collection

Data were collected through direct observation and patient medical records. Variables measured included demographic (age, gender, body mass index), clinical (SAPS-3 score, source of infection, need for mechanical ventilation, lactate level), and serum vitamin D levels. Vitamin D levels were measured at ICU admission and at diagnosis of septic shock, with results categorized as normal-insufficient or mild-severe deficiency. In-hospital mortality was recorded as the primary outcome.

Data Analysis

Data analysis was conducted using the SPSS program. Descriptive statistics were used to describe the baseline characteristics of the sample, while inferential statistics were used to test the study hypotheses. An independent T-

test was used to compare vitamin D levels between the living and deceased groups, as well as between groups with different SAPS-3 scores. Pearson correlation was used to assess the association between vitamin D levels with mortality and SAPS-3 scores. Logistic regression was used to evaluate the association between vitamin D levels and mortality, considering confounding variables such as obesity, diabetes, cancer, corticosteroid use, and SAPS-3.

Results

Basic Characteristics of the Sample

This study involved 22 patients with septic shock who were admitted to the ICU of Dr.

Sardjito Hospital Yogyakarta. The average age of the patients was 59,68 years, with 40,91% male and 59,09% female. The mean Body Mass Index (BMI) was 21,93, indicating most patients had a relatively normal weight. The mean SAPS-3 score was 67,61, indicating significant disease severity. A total of 68,18% of patients had normal-insufficient vitamin D levels, and 31,82% had mild-severe deficiency. Mortality among patients was 27,27%, with 6 patients dying and 16 patients surviving. A total of 50% of patients required mechanical ventilation, and the mean lactate level was 3,39, indicating the severity of sepsis (Table 1)

Table 1. Basic Characteristics of the Sample

Variables	Total	Percent
Age (mean)	59,68±17,5	
Gender (L/P)		
Male	9	40,91%
Female	13	59,09%
Body Mass Index (mean)	21,93±4,2	
SAPS-3 score (mean)	67,61±11,9	
Source of Infection		
Lung	10	45,45%
Gastrointestinal tract	5	22,73%
Urinary Tract	4	18,18%
Central Nervous System	2	9,09%
Integument	1	4,55%
Vitamin D levels (mean)	26,87±15,26	
Normal-Insufficiency	15	68,18%
Mild-heavy deficiency	7	31,82%
Mortality		
Yes	6	27,27%
No	16	72,73%
Requires mechanical ventilation		
Yes	11	50%
No	11	50%
Lactate Level (mean)	3,39±1,8	

Correlation of Vitamin D Level with Mortality

Table 2 shows that there was a significant negative correlation between serum vitamin D levels and mortality ($p=0,026$, $r=-0,475$). Of the 15 patients with normal to insufficient vitamin D levels, 13 patients lived and 2 patients died. Meanwhile, of the 7 patients

with mild to severe deficiency, 3 patients lived and 4 patients died. The Odds Ratio (OR) for mortality was 8,6667, with a confidence interval (CI) between 1,0495 and 71,579.

Table 2. Correlation of Serum Vitamin D Level with Mortality

Vitamin D levels	Mortality (n)	P-value	Pearson Correlation
Normal-Insufficiency	2	0,026*	-0,475
Mild-heavy deficiency	4		

* = Independent T test

Correlation of Vitamin D Level with SAPS-3 Score

Table 3 shows that there was a very strong negative correlation between serum vitamin D levels and SAPS-3 scores ($p=0,0001$, $r=-0,948$). The mean SAPS-3 score in the normal-vitamin D insufficiency group was 53.2 ± 4.56 , while the mean SAPS-3 score in the mild-severe deficiency group was 75.58 ± 8.46 . This shows that the lower the serum vitamin D level, the higher the SAPS-3 score, which

means the more severe the patient's condition. Of the 11 patients with normal to insufficient vitamin D levels, 8 patients had SAPS-3 Score $<62,5$ and 2 patients had SAPS-3 Score $\geq 62,5$. Meanwhile, of the 11 patients with mild to severe deficiency, 3 patients had SAPS-3 Score $<62,5$ and 8 patients had SAPS-3 Score $\geq 62,5$. The OR for mortality was 7,1111, with a CI between 1,0888 and 46,4425.

Table 3. Correlation of Serum Vitamin D Level with SAPS-3 score

Vitamin D levels	SAPS-3 score (mean)	P-value	Pearson Correlation
Normal-Insufficiency	53,2±4,56	0,0001*	-0,948
Mild-heavy deficiency	75,58±8,46		

* = Independent T test

Discussion

The results showed a significant negative correlation between serum vitamin D levels and mortality ($p=0.026$, $r=-0.475$). This indicates that the lower the vitamin D level, the higher the risk of death in septic shock patients. This finding is in line with previous studies that reported an association between vitamin D deficiency and increased mortality in critical patients, including sepsis patients. [8–11].

The mechanism underlying this relationship may involve the important role of vitamin D in the immune system. Vitamin D is known to have immunomodulatory, anti-inflammatory, and antimicrobial effects. [12].

In sepsis, vitamin D deficiency may impair adequate immune response to infection, leading to excessive inflammation and organ dysfunction. In addition, vitamin D also plays a role in the regulation of the renin-angiotensin-aldosterone system and vascular endothelial function, both of which are impaired in septic shock. [13].

This study also found a strong negative correlation between serum vitamin D levels and SAPS-3 scores ($p=0.0001$, $r=-0.948$). SAPS-3 score is an indicator of disease severity and a predictor of mortality in ICU patients. This correlation suggests that patients with lower vitamin D levels tend to have more severe

clinical conditions. This strengthens the hypothesis that vitamin D may have a protective role in preventing the progression of sepsis from becoming more severe.

Interestingly, this study also showed a moderate positive correlation between SAPS-3 score and mortality ($p=0.041$, $r=0.439$). This is consistent with the function of SAPS-3 as a predictor of mortality and supports the validity of using this score in this study population. [14]. The association between SAPS-3, vitamin D levels, and mortality demonstrates the complexity of the interaction between nutritional status, disease severity, and clinical outcomes in septic shock patients.

There are some limitations to consider. Although vitamin D supplementation is relatively safe and inexpensive, its effectiveness in improving outcomes in already critical sepsis patients still needs to be further investigated through controlled clinical trials.

Conclusion and Suggestion

This study showed a significant correlation between low serum vitamin D levels and increased mortality and severity of illness in septic shock patients. These findings highlight the potential role of vitamin D in the pathophysiology of sepsis and its possible use as a prognostic biomarker or therapeutic target. Further research is needed to clarify the mechanisms underlying this association and evaluate the potential of vitamin D-based interventions in the management of septic shock.

References

- Gaieski D, Edwards JM, Kallan MJ, Carr BG. Benchmarking the incidence and mortality of severe sepsis in the United States. *Crit Care Med* 2013;41(5):1167–74.
- Mayr FB, Yende S, Angus DC. Epidemiology of severe sepsis. *Virulence* 2014;5(1):4–11.
- Mahapatra S, Heffner AC. Septic shock. 2017;
- Mahapatra S, Heffner AC, Atarhi-Dugan JM. Septic shock (nursing). 2021;
- 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;7(1):e1.
- Sizar O, Khare S, Goyal A, Givler A. Vitamin D Deficiency. *Treasure Island (FL)*: 2023.
- van der Merwe E, Kapp J, Pazi S, Aylward R, Van Niekerk M, Mrara B, et al. The SAPS 3 score as a predictor of hospital mortality in a South African tertiary intensive care unit: A prospective cohort study. *PLoS One* 2020;15(5):e0233317.
- Park JE, Shin TG, Jeong D, Lee GT, Ryoo SM, Kim WY, et al. Association between Vitamin C Deficiency and Mortality in Patients with Septic Shock. *Biomedicines* 2022;10(9).
- Delrue C, Speeckaert R, Delanghe JR, Speeckaert MM. Vitamin D Deficiency: An Underestimated Factor in Sepsis? *Int. J. Mol. Sci.* 2023;24(3).
- Gnagnarella P, Muzio V, Caini S, Raimondi S, Martinoli C, Chiocca S, et al. Vitamin D Supplementation and Cancer Mortality: Narrative Review of Observational Studies and Clinical Trials. *Nutrients* 2021;13(9).
- Argano C, Mallaci Bocchio R, Natoli G, Scibetta S, Lo Monaco M, Corrao S. Protective Effect of Vitamin D Supplementation on COVID-19-Related Intensive Care Hospitalization and Mortality: Definitive Evidence from Meta-Analysis and Trial Sequential Analysis. *Pharmaceuticals (Basel)* 2023;16(1).
- Paramita null, Louisa M. Berbagai Manfaat Vitamin D . *Cermin Dunia Kedokt.*

- 2017;44(10).
13. Al Mheid I, Quyyumi AA. Vitamin D and Cardiovascular Disease: Controversy Unresolved. *J Am Coll Cardiol* [Internet] 2017;70(1):89–100. Available from: <http://dx.doi.org/10.1016/j.jacc.2017.05.031>
14. Sakr Y, Krauss C, Amaral ACKB, Réa-Neto

A, Specht M, Reinhart K, et al. Comparison of the performance of SAPS II, SAPS 3, APACHE II, and their customized prognostic models in a surgical intensive care unit. *Br J Anaesth* 2008;101(6):798–803.



This work is licensed under a **Creative Commons Attribution-Non Commercial-Share Alike 4.0 International**