

Factors Affecting Vitamin D Levels In Sepsis And Septic Shock

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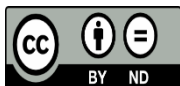


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ABSTRACT

Sepsis is a major health problem with an increasing number of incidences. Infection will trigger a more complex, varied, and prolonged host response, where pro-inflammatory and anti-inflammatory mechanisms contribute to clearance of infection and tissue recovery, but may also lead to organ dysfunction and secondary infection. Various recent studies have shown the relationship between vitamin D and sepsis. Vitamin D acts as a stimulator of antimicrobial peptide production and prevents excessive inflammation. Therefore, vitamin D insufficiency and deficiency are associated with the risk of sepsis. This cross-sectional study involved 29 subjects with sepsis and 23 subjects with septic shock. Serum vitamin D levels were measured using the ELISA (enzyme-linked immunosorbent assay) method with results in ng/ml. Vitamin D levels were found to be lower in sepsis than in septic shock ($p=0.119$) but not statistically significant. Vitamin D levels were also lower in the elderly (> 60 years) compared to < 60 years subjects, but not statistically significant ($p=0.837$). Furthermore, vitamin D levels were significantly lower in female patients than male patients ($p=0.01$). In addition, vitamin D levels were significantly lower in patients with comorbidities in both males and females than in patients without comorbidities. Vitamin D levels are not related to the severity of sepsis but are influenced by age, sex, and comorbidity factors.



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1. Introduction

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulation of the host's response to infection. Despite significant advances in understanding the pathophysiology of this clinical syndrome, as well as advances in hemodynamic monitoring tools and resuscitation measures, sepsis remains a major cause of morbidity and mortality in critically ill patients treated in the Intensive Care Unit (ICU) [1].

Research data indicate that low vitamin D levels may contribute to the development of sepsis and sepsis outcome. The incidence rates range from 38%-93% in critically ill patients which correlates with a longer

stay in the intensive care unit, as well as a higher risk of death and sepsis [2].

Vitamin D plays an important role in various physiological functions. Numerous studies have focused on the novel role of vitamin D in glucose metabolism, endothelial function, and modulation of the innate immune system by inducing antimicrobial peptides (cathelicidin and β -defensin) in epithelial cells, neutrophils, and macrophages as well as modulating adaptive immune responses. Cathelicidin and β -defensin have broad antimicrobial activity against gram-positive and gram-negative bacteria, as well as certain viruses and fungi. For adaptive immunity, vitamin D influences the proliferation and differentiation of T and B cells and modulates the production of immunoglobulins [5]. A previous study showed that patients with septic shock had significantly reduced vitamin D levels compared to patients with sepsis [3], [4]. In this study, the factors that affect vitamin D levels in sepsis and septic shock were examined.

2. Research Objectives

This study aims to determine the factors that affect vitamin D levels in sepsis and septic shock.

3. Method And Research Subject

3.1 Research Method

This cross-sectional study was conducted from December 2021 to October 2022 at Wahidin Sudirohusodo Hospital Makassar, South Sulawesi, Indonesia. The inclusion criteria for this study were sepsis patients treated at Wahidin Sudirohusodo Hospital Makassar aged ≥ 18 years, sepsis and septic shock patients who were willing to participate in the study and signed the informed consent. The sample size was 52 subjects with sepsis (n=29) and septic shock (n=23). Serum vitamin D levels were measured using the 25-Hydroxyvitamin D [25(OH)D] ELISA Kit with the enzyme-linked immunosorbent assay (ELISA) technique in ng/ml.

3.2 Statistical Analysis

The data analysis was carried out by statistical tests using SPSS version 25, which consisted of descriptive statistical calculations and frequency distribution. The types of statistical tests used were the Kolmogorov-Smirnov test to assess data normality, the Mann-Whitney test, and the Chi Square test. Statistical test results are considered significant if the p value is < 0.05 .

4. Results

The research subjects who met the criteria were 52 patients. The research variable categories (Tables 1 and 2) contained 29 subjects (55.8%) with sepsis and 23 subjects (44.2%) with septic shock. These subjects aged between 18-81 years with an average of 48.6 ± 15.5 years; 41 patients (78.8%) were < 60 years old while the remaining 11 patients (21.2%) were ≥ 60 years old. Subjects consisted of 21 men (40.4%) and 31 women (59.6%). Meanwhile, 34 subjects (65.4%) had comorbidities, whereas 18 subjects (34.6%) did not. The average vitamin D level was 16.4 ± 10.1 while the average SOFA score was 8.6 ± 2.8 . Furthermore, vitamin D status in the subjects of this study was as follows: 39 (75.0%) subjects with deficiency, 6 (11.5%) subjects with insufficiency, and 7 (13.5%) subjects with sufficiency.

Table 1. Characteristics of research subjects

Variable	Minimal	Maximum	Mean	Std. Deviation
Age (years)	18	81	48.6	15.5

SOFA Score (n=52)	3	16	8.6	2.8
Vitamin D (ng/ml)	2.90	46.64	16.4	10.1

Variable descriptive statistics (n=52); SOFA: Sequential organ failure assessment

Table 2. Distribution of research subjects

Vitamin D	Frequency	%
Deficiency	39	75.0
Insufficiency	6	11.5
Sufficiency	7	13.5
Total	52	100.0

The percentage of deficiency was found to be higher in sepsis (82.8%) than in septic shock (65.2%), but this difference was not statistically significant ($p>0.05$) (See Table 3). The percentage of deficiency and insufficiency was found to be significantly higher in women (83.9% and 16.1%) than in men (61.9% and 4.8%), with $p<0.01$ (See Table 4). As for the age category, a higher percentage of deficiency was found at age ≥ 60 years (81.8%) than at age <60 years (73.2%), but this difference was not statistically significant ($p>0.05$) (See Table 5). Furthermore, the percentage of deficiency was found higher in subjects with comorbidities, both in women (95.5%) and in men (83.3%), compared to those without comorbidities (55.6% and 33.3%), as seen in Table 6.

Table 3. Distribution of vitamin D level categories by group

Group		Vitamin D			Total
		Deficiency	Insufficiency	Sufficiency	
Sepsis	n	24	1	4	29
	%	82,8	3,4	13,8	100,0
Septic shock	n	15	5	3	23
	%	65,2	21,7	13,0	100,0
Total	n	39	6	7	52
	%	75,0	11,5	13,5	100,0

Chi Square test ($p=0.119$)

Table 4. Distribution of vitamin D level categories by sex

Sex		Vitamin D			Total
		Deficiency	Insufficiency	Sufficiency	
Female	n	26	5	0	31
	%	83.9	16.1	0.0	100.0
Male	n	13	1	7	21
	%	65.2	21.7	13.0	100.0
Total	n	39	6	7	52
	%	75.0	11.5	13.5	100.0

Chi Square test ($p=0.002$)

Table 5 Distribution of vitamin D level categories by age

Age		Vitamin D			Total
		Deficiency	Insufficiency	Sufficiency	
<60 years	N	30	5	6	41

	%	73.2	12.2	14.6	100.0
≥ 60 years	N	9	1	7	11
	%	81.8	9.1	9.1	100.0
Total	N	39	6	7	52
	%	75.0	11.5	13.5	100.0

Chi Square test (p=0.837)

Table 6. Distribution of vitamin D level categories by comorbidity and sex

Sex	Comorbid	Vitamin D			Total	
		Deficiency	Insufficiency	Sufficiency		
Female	Yes	n	31	1	2	34
		%	91.2%	2.9%	5.9%	100.0%
	No	n	8	5	5	18
		%	81.8%	9.1%	9.1%	100.0%
Male	Yes	n	10	0	2	12
		%	83.3%	0.0%	16.7%	100.0%
	No	n	3	1	5	9
		%	33.3%	11.1%	55.6%	100.0%

5. Discussion

The results of this study revealed that the percentage of vitamin D deficiency was higher in sepsis subjects (82.8%) than in septic shock subjects (65.2%), although this difference did not show a statistically significant relationship (p=0.119). This is in line with a study by [5] which found no significant difference in the proportion of vitamin D insufficiency and deficiency in the infection group without sepsis, with sepsis, and with severe sepsis, meaning that vitamin D status was not related to the severity of sepsis. However, the results of this study were not aligned with a study conducted by [6] which stated that patients with septic shock had decreased vitamin D levels significantly, compared to patients with sepsis. The insignificant results in this study were probably due to confounding factors such as age, sex, and comorbidities.

The results of the analyses to assess the factors that affect vitamin D levels, such as age, sex, and comorbidities were as follows. For the age category, the percentage of vitamin D deficiency was found higher at age ≥60 years (81.8%) than at age <60 years (73.2%), but this difference was not statistically significant (p>0.05). This is in line with [7] who argues that old age is associated with a decrease in 7-dehydrocholesterol in the skin, resulting in a decrease in vitamin D synthesis. It is reported that there is a decrease in the synthesis of vitamin D₃ by about 75% at the age of 70 years. Lack of physical activity and sun exposure are most likely the main reasons behind relevant Vitamin D deficiency in the elderly.

The percentage of vitamin D deficiency and insufficiency was found to be significantly higher in women (83.9% and 16.1%) than in men (61.9% and 4.8%), with p<0.01. This is consistent with [8] who states that women are at higher risk of experiencing vitamin D deficiency compared to men, and those who work outdoors generally have a higher concentration of 25(OH)D than those who work indoors.

As for the comorbidity category, the percentage of vitamin D deficiency was found higher in subjects with comorbidities, both in women (95.5%) and in men (83.3%), compared to those who had no comorbidities (55.6% and 33.3%). The comorbidities referred to in this study include chronic kidney disease (CKD) and malignancy. In this regard, a study carried out by [9] has found that CKD is a risk factor for vitamin D deficiency, which is common in CKD patients, especially those who have received kidney transplants and those with end-stage kidney disease. Changes in kidney function are associated with reduced renal 1- α -hydroxylase activity in addition to decreased hepatic 25-hydroxylase function in uremia.

6. Conclusion

Vitamin D levels are not related to the severity of sepsis but are influenced by age, sex, and comorbidity factors.

7. References

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