

## ORIGINAL RESEARCH

# Analysis of the Association Between Serum Vitamin D Concentration and Mortality in Severe Septic Patients at a Tertiary Care Centre

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## ABSTRACT

**Background:** Pathophysiologically, vitamin D deficiency has been related to inflammation and immune dysfunction, which may be the potential reason for the increased susceptibility of the individual to severe infection or sepsis. The present study was conducted to analyze the association between serum vitamin D concentration and mortality in severe septic patients.

**Materials and Methods:** Whole blood collected was placed into the tubes containing ethylenediaminetetraacetic acid as an anticoagulant. After completion of samples, the concentration of serum 25-hydroxy vitamin D<sub>3</sub> was measured by enzyme-linked immunosorbent assay (ELISA). SPSS version 20.0 (IBM Corp., Armonk, NY, USA) was used for data analysis. P-values less than 0.05 were considered statistically significant.

**Results:** In the present study a total of 250 patients were included in which 110(44%) were females and 140(56%) were males. The prevalence of vitamin D insufficiency in critically ill subjects with sepsis was 100% (250/250). 32% patients with non-severe sepsis, 16% with severe sepsis, and 48% with septic shock. Patients suffering from severe septic had lower levels of vitamin D compared to those with septic shock and non-severe sepsis. 12.5% patients with severe sepsis who had vit D<sub>3</sub> deficiency died and 50% patients with septic shock who had vit D<sub>3</sub> deficiency died.

**Conclusion:** 12.5% patients with severe sepsis who had vit D<sub>3</sub> deficiency died and 50% patients with septic shock who had vit D<sub>3</sub> deficiency died.

**Keywords:** Vitamin D, Mortality, Severe Septic Patients.

## INTRODUCTION

Sepsis is a clinical syndrome caused by immune response to various infections. Despite the existence of proper antimicrobial and palliative care, due to the high prevalence of multiple organ failure, being affected with sepsis is associated with a high rate of mortality.<sup>1-3</sup> Vitamin

D or cholecalciferol is a fat-soluble vitamin primarily synthesized from 7-dehydroxycholesterol in the skin by ultraviolet radiation.<sup>4</sup> A previous study showed that serum concentrations of 25-hydroxyvitamin D (25(OH)D) were related to geography and season.<sup>5</sup> Lower values were observed in the winter, whereas higher values were observed in the summer.<sup>6</sup> Additionally, a closer distance to the equator was associated with a lower magnitude of seasonal variation of 25(OH)D levels.<sup>7,8</sup> This variation in vitamin D is resemblance to that in infection as the incidence and mortality of sepsis is highest during the winter months and is associated with increased respiratory illnesses.<sup>9</sup> Previous studies showed that vitamin D deficiency, defined as lower than normal serum 25-hydroxyvitamin D (25(OH) D), is independently associated with higher incidence of sepsis in critically ill patients.<sup>10-13</sup> Vitamin D can regulate acquired and innate immune responses.<sup>14</sup> This vitamin prevents overexpression of inflammatory cytokines and is an important mediator in aggregation of leukocytes, formation of local inflammation, and anti-bacterial responses in innate immunity. Vitamin D deficiency has been linked to an increase in the risk of initiation and development of viral and bacterial infections.<sup>15-17</sup> Low serum level of vitamin D on admission of patients to the intensive care unit has correlated with an increase in mortality risk and blood infections.<sup>18</sup> Additionally, a higher risk of developing sepsis has been shown in patients who have had vitamin D deficiency before hospital admission.<sup>14,17</sup> The present study was conducted to analyze the association between serum vitamin D concentration and mortality in severe septic patients.

## **MATERIALS AND METHODS**

The present study was conducted to analyze the association between serum vitamin D concentration and mortality in severe septic patients over a period of 1 year. Before the commencement of the study ethical clearance was obtained and written consent was obtained from the patients. Patients greater than 18 years old were included if they confirmed or suspected source of infection determined by the treating clinician and having two or more criteria for the systemic inflammatory response syndrome (SIRS).<sup>19</sup> Patients were excluded if they experienced shock due to reasons other than sepsis, had neuroendocrine diseases, were in cardiac arrest on arrival, suffered from mental disorders, were under constant use of vitamin D, or were pregnant. Patient data, including demographics, comorbidities, and laboratories such as cultures and the suspected source of infection, were obtained. Whole blood collected was placed into the tubes containing ethylenediaminetetraacetic acid as an anticoagulant. Within 1 hour of collection, each sample was centrifuged at 1500 rpm for 10 minutes. The plasma was directly aliquoted and stored at -20°C. After completion of samples, the concentration of serum 25-hydroxy vitamin D<sub>3</sub> was measured by enzyme-linked immunosorbent assay (ELISA) (Immunoassays S.A., Belgium) according to the manufacturer's protocol. Vitamin D deficiency was defined as baseline serum 25-hydroxyvitamin D (25OHD) levels < 30 ng/mL.<sup>20</sup> SPSS version 20.0 (IBM Corp., Armonk, NY, USA) was used for data analysis. Categorical and continuous variables were analyzed using the chi-square test, t-test, and analysis of variance (ANOVA). P-values less than 0.05 were considered statistically significant.

## RESULTS

In the present study a total of 250 patients were included in which 110(44%) were females and 140(56%) were males. The prevalence of vitamin D insufficiency in critically ill subjects with sepsis was 100% (250/250).

32% patients with non-severe sepsis, 16% with severe sepsis, and 48% with septic shock. Patients suffering from severe sepsis had lower levels of vitamin D compared to those with septic shock and non-severe sepsis.

12.5% patients with severe sepsis who had vit D3 deficiency died and 50% patients with septic shock who had vit D3 deficiency died.

**Table 1 : The Relationship Between Mean Serum Levels of Vitamin D3 and types of sepsis**

Type of sepsis	N(%)	Vitamin D3	p-value
Non-severe Sepsis	80(32%)	17	<0.05
Severe Sepsis	40(16%)	10	
Septic Shock	120(48%)	12	

**Table 2: Mortality rate in severe septic patients**

Type of sepsis	N(%)
Severe Sepsis	5(12.5%)
Septic Shock	60(50%)

## DISCUSSION

Since vitamin D status plays an important role in the pathogenesis of sepsis and other critical diseases, limited treatment options exist to address this issue. The American Society for Parenteral and Enteral Nutrition (ASPEN) recommends 200 IU vitamin D daily for hospitalized patients.<sup>21</sup> However, further investigations have estimated that doses of 400 or 500 IU daily remained in the insufficient range for most hospitalized patients.<sup>22,23</sup>

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Rech et al. showed that vitamin D deficiency in patients with severe sepsis or septic shock was significantly associated with increase in 30-day mortality.<sup>24</sup>

In one study, the rate of mortality in sepsis patients correlated with vitamin D level upon admission, but this correlation was not significant.<sup>25</sup>

Jeng et al. found no significant differences in vitamin D concentrations in patients with sepsis compared with critically ill patients in the ICU.<sup>26</sup>

In a cohort study conducted in 2012, severe vitamin D deficiency (levels < 10ng/ml) was present in 69% of the patients with sepsis but in only 48% of the controls.<sup>27</sup>

## CONCLUSION

The present study concluded that patients suffering from severe sepsis had lower levels of vitamin D compared to those with septic shock and non-severe sepsis. 12.5% patients with severe sepsis who had vit D3 deficiency died and 50% patients with septic shock who had vit D3 deficiency died.

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