Original Research Article

Vitamin D deficiency: A potential risk factor for sepsis development and correlation with qSOFA score in patient admitted to medical ICU in MMMCH, Solan

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Abstract
Introduction: Recent studies have also revealed that vitamin D may help protect against a number of chronic diseases, including the risk of developing diabetes, cardiovascular disease, lung disease, and other chronic illnesses, such as systemic infections. The growing body of knowledge around vitamin D has started to suggest possible associations between sepsis and vitamin D insufficiency. The understanding of the relationships between these disorders is still in its infancy.
Aim: The aim of the study was to assess the role of Vitamin D deficiency as a potential risk factor for sepsis development and correlation with qSOFA score in patient admitted to Medical ICU in MMCH, Solan.
Methodology: This was a cross sectional study conducted among 120 patients diagnosed with Sepsis presenting to the Medical ICU.
Results: The mean age of the study participants was 55.87 ± 13.07. Majority of the study participants were males. The prevalence of diabetes mellitus and hypertension were 45.8% and 40% respectively. Mortality was seen among 3.3% were alive and dead respectively. 100% of the study participants with sepsis with qSOFA score of more than 2, had Vitamin D deficiency and the mean Vitamin D level was 12.21 ± 5.38. The Vitamin D level was significantly lower among those who died than those who are alive (p=0.019).
Conclusion: 100% of the sepsis patients had Vitamin D deficiency in the present study. It has been shown that this has a detrimental effect on inpatient morbidity and death. This emphasises how crucial it is for the general public to have enough vitamin D supplements.
Keywords: Vitamin D, sepsis, qSOFA sore, mortality

Introduction
Vitamin D's numerous activities in the immune system's response to infection imply that it may be an important component in the fight against sepsis. The fundamental science evidence points to vitamin D's role in the optimum functioning of the innate immune system, in part via generating AMPs like LL-37 and appearing to buffer the inflammatory cascade generated by LPS. Early clinical data on its role in infection prevention and control suggested a link, but intervention trials produced contradictory results, necessitating larger randomised controlled trials to help clarify the relationship. Furthermore, clinical data hint to a function for vitamin

D in critical illness, but further research is needed to discover a direct association between sepsis and its severity and outcomes. Some intriguing similar connections between vitamin D and seasonal and ethnic differences in sepsis are now speculative but intriguing concerns to be investigated. The current picture of vitamin D and sepsis is one of a research field in its early stages, with many critical links that provide fertile ground for future research.

Venkatram S *et al*. discovered a link between mortality and vitamin D deficiency (25(OH)D, 20 ng/mL) in 437 patients at a single centre ICU in a retrospective analysis [1]. Other research have revealed more particular information about the link between vitamin D and septic patients. Jeng L *et al*. discovered vitamin D deficiency in 100% of critically sick patients with sepsis, 92% of critically ill patients without sepsis, and 66.5 percent of healthy controls [2]. A prospective analysis of 66 surgical ICU patients revealed a non-significant tendency toward an elevated prevalence of infections and sepsis in those with low vitamin D levels (20 ng/mL) [3]. Braun A *et al*. investigated this topic in two retrospective studies on the same source population. The first was a retrospective study of 2,399 patients hospitalised to medical and surgical ICUs with a 25(OH)D drawn within the previous year. The findings revealed a 1.3- and 1.7-fold increase in all-cause mortality among vitamin D deficient and insufficient groups (30 ng/mL and 15 ng/mL, respectively), as well as a substantial increase in blood culture positivity [4].

The other study included 1,325 patients who had a 25(OH)D drawn 7 days before or after ICU admission and found a link between vitamin D deficiency (15ng/mL) and higher mortality at 30, 90 and 365 days [5]. The presence of sepsis had no effect on the vitamin D mortality association in either study [4, 5]. A prospective study by Cecchi A *et al*. identified a connection between mortality and vitamin D insufficiency among 170 patients with severe sepsis and septic shock that became insignificant following adjustment, highlighting the complexity of confounding in critically ill and septic patients [6]. A bedside prompt called the qSOFA score, also known as quick SOFA, may help identify patients with suspected infections who are more likely to have a negative outcome outside of the critical care unit (ICU). It employs three criteria and awards one point for each of the following: low blood pressure (SBP$\leq$100 mmHg), rapid breathing ($\geq$22 breaths per minute), or impaired mental status (<15 on the Glasgow coma scale).

Overall, the data supports a relationship between vitamin D deficiency and critical illness outcomes, with the link to sepsis being less obvious. Many common risk factors, such as age, socioeconomic position, obesity and chronic illness, are likely to muddle these connections. Concerning the final risk factor, chronically unwell and crippled individuals are likely to spend more time indoors, resulting in less sun exposure and vitamin D insufficiency. These confusing relationships make proving causality in critical-illness outcomes difficult. Sepsis therapy, in addition to these epidemiological facts, may confuse this association. According to one study, the hemodilutional effects of fluid resuscitation can reduce serum 25(OH)D concentrations by 35% [7].

Such research is warranted because vitamin D is inexpensive and safe to provide, and even little improvements in sepsis outcomes may be implemented on a large enough scale to have a significant public health impact. The present study was conducted with the aim to assess the role of Vitamin D deficiency as a potential risk factor for sepsis development and correlation with qSOFA score in patient admitted to Medical ICU in a tertiary care hospital, Solan. The objective of the study was to determine the Vitamin D level among the patient admitted to Medical ICU, to assess the Vitamin D deficiency as a risk factor for sepsis and to assess qSOFA score for determining sepsis severity and predicting mortality in MICU patients.

Material and Methods

This study was undertaken in the Department of General Medicine in collaboration with Department of Biochemistry, in a tertiary care hospital, Solan, Himachal Pradesh. This was a prospective cross-sectional study conducted for 1 year after ethics committee approval using convenience sampling.

Study participants
120 patients diagnosed with Sepsis presenting to the Medical ICU meeting the inclusion criteria and the exclusion criteria was taken up for the study.

Inclusion criteria
1. Age of the patient->18 years.
2. Detailed clinical History.
3. Relevant clinical investigations needed.
4. Diagnosis of Sepsis confirmed by clinically examination and investigations.
5. Vitamin D levels [According to Endocrine Society of India] (<20ng/ml-deficiency, 21-29 ng/ml-insufficiency, 30-100 Sufficient).
6. qSOFA score $\geq$ 2.

Exclusion criteria
1. Age-<18 years.
2. Pregnant females.
3. Refusal for Informed consent.
4. Vitamin D sufficient patient.
5. Patients with Uncontrolled diabetes mellitus, chronic kidney disease, immunocompromised conditions like human immunodeficiency virus and malignancies.

Data collection
After satisfying to the defined inclusion and exclusion criteria, patient was enrolled in the study and was admitted for a short period for detailed work up. A detailed clinical history was taken from each patient and recorded in the case sheet proforma. Thereafter, a thorough general and systemic physical examination was done.

Statistical analysis
Data obtained was analysed using SPSS version 26. Descriptive Statistics was expressed in frequency/percentages for categorical variable and mean/standard deviation for continuous variable. Mann Whitney U test/Chi square was used to determine the relationship between the variables and a p value of less than 0.05 was regarded as significant.

Ethical consideration
Informed and written consent (in the language they best understand) was taken from each subject before collecting data and blood sample. Only those individuals, who volunteer to participate in the study, was included and the data was kept confidential. The study won't impose any burden on the subjects and the Institute; therefore, the study was ethically justified. The proposed study was undertaken after Institutional Ethical Committee approval.

Results

The qSOFA components in the participants showed that the mean respiratory rate, systolic Blood Pressure and GCS was 24.6 ± 2.19, 84.83 ± 10.36 and 14.47 ± 1.84 respectively. 49.2% of the study participants had inotrope support.

Table 1: Profile of the study participants

S No	Variable	Frequency	Percentage
1.	**Age (years)**		
	< 25	2	1.7
	26 to 35	10	8.3
	36 to 45	13	10.8

	46 to 55	29	24.2
	56 to 65	35	29.2
	>66	31	25.8
2.	**Gender**		
	Male	69	57.5
	Female	51	42.5
3.	**Comorbidities**		
	Diabetes Mellitus	55	45.8
	Hypertension	48	40

The mean Vitamin D level was 12.21 ± 5.38. 100% of the study participants had positive CRP. 0.8% and 4.2% had Acinetobacter and CONS in blood culture. 26.7%, 37.5%, 30.8% and 5% had 4 to 10, 10 to 15, 15 to 20 and > 20 pus cells.

Table 2: Investigation findings among the study participants

S. No.	Variable	Mean	SD
1.	Total Leucocyte count	15259.16	4196.36
2.	Polymorphs	85.29	4.8
3.	Lymphocytes	9.47	4.53
4.	ESR	55.87	19.56

The mean duration of stay was 5.58 ± 1.82. Mortality was seen among 3.3% (4) of the study participants.

Table 3: Association between profile of the study participants and Vitamin D level

S. No.	Variable	Vitamin D level		P value
		Mean	SD	
1.	**Age (years)**			0.504
	< 25	12.31	0.19	
	26 to 35	14.93	6.51	
	36 to 45	13.94	6.58	
	46 to 55	12.39	5.69	
	56 to 65	11.26	4.84	
	>66	11.45	4.75	
2.	**Gender**			0.222
	Male	12.6	5.15	
	Female	11.68	5.69	
3.	**Mortality**			0.019
	No	12.36	5.37	
	Yes	6.31	0.68	

Table 4: Association between mortality and profile of the study participants

Variable	Mortality		P value
	No	Yes	
Age (years)			0.637
< 25	2(1.7)	0	
26 to 35	10(8.6)	0	
36 to 45	13(11.2)	0	
46 to 55	29(25)	0	
56 to 65	33(28.4)	2(50)	
>66	29(25)	2(50)	

Gender			
Male	66(56.9)	3(75)	0.471
Female	50(43.1)	1(25)	
Diabetes Mellitus			
Yes	51(44)	4(100)	0.027
No	65(56)	0	
Hypertension			
Yes	44(37.9)	4(100)	0.013
No	72(62.1)	0	

Discussion

Sepsis is among the main causes of mortality in critical illness. Although clinical results have significantly improved since the implementation of earlier goal-directed therapy, effective treatment is still very difficult to achieve and depends mostly on the rapid eradication of the causative bacterium in additional to supportive therapy.

This study stated the mean age of the study participants was 55.87 ± 13.07. Similar findings were found in research conducted by Trongtrakul K et al. [8], where it was determined that the study participants' average age was 59.3 15.3. In this research, men made up the majority of the study participants. Similar findings were found in research conducted by Amrein K et al. [9], which revealed that most of the study participants were men. The prevalence of diabetes mellitus and hypertension in the present study was 45.8% and 40% respectively. In research by Bohl DD et al. [10], it was revealed that the prevalence of diabetes and hypertension in the sepsis patients were 14% and 36.6% respectively.

This study revealed that 100% of the study participants with sepsis with qSOFA score of more than 2, had Vitamin D deficiency and the mean Vitamin D level was 12.21 ± 5.38. In research by Azim A et al. [11], it was shown the prevalence of Vitamin D deficiency in 80.4% of the patients. Accordingly, it was shown in research conducted by Amrein K et al. [9] that the mean Vitamin D level was 19.6 ± 11.3 ng/ml. Similar findings were found in a research by Shojaei M et al. [12], which revealed that sepsis patients had a mean Vitamin D level of 19.03 ± 13.08.

The mean Vitamin D level in the present study was lowest among those above the age of 56 years. Because of aging-related changes, elderly persons with any additional risk factors for vitamin D insufficiency are more likely to have insufficient stocks of this vitamin. Females had lower Vitamin D level than males. Similar findings were found in a study by Lagunova Z et al. [13], which demonstrated that women were more likely than men to suffer from Vitamin D deficiency. This higher risk might be explained by the custom of women minimizing sun exposure or by the fact that women use more sunscreen and sunblock products than males.

On assessing the status of the patients, 3.3% had mortality respectively. Mortality was higher among those aged more than 56 years (100%), males (75%), with diabetes (100%) and hypertension (100%). The Vitamin D level was significantly lower among those who died than those who are alive (p=0.019). There was a strong link between the mean blood level of vitamin D in sepsis patients who had died and those who survived in the research by Parekh D et al. [14]

According to research by Rech MA et al. [15], individuals with severe sepsis or septic shock who were vitamin D deficient had a considerably higher 30-day death rate. In the research by Nguyen HB et al. [16], low blood vitamin D levels were also linked to a rise in 23-day mortality among 91 sepsis patients.

Although the obstacles in the area of vitamin D and sepsis may appear formidable, the fundamental and clinical findings indicate promise. The relationship between vitamin D and the possible use of statins in the treatment of sepsis is an intriguing connection for future investigation. There is opportunity for the use of statins during sepsis even if a recent meta-analysis did not support their usefulness in avoiding infections since certain statins have been linked to an increase in vitamin D.

Furthermore, study may continue on examining the aspects of the link that are indicated by the fundamental sciences, even if it may be challenging to demonstrate mortality advantages in sepsis using vitamin D. Here, it seems that the evidence is greatest for vitamin D's capacity to prevent infections, whether they are acquired in the community or in a hospital and to lessen the severity of sepsis and the ensuing organ failure. If we're going to succeed in discovering the truth, we need to address a broad range of clinical research issues that are opened up by these areas. It may be helpful to envision and test the possible functions of vitamin D as a "primary prevention," "acute intervention," and "secondary prevention" in the design of future research.

Conclusion

In conclusion, the prevalence of vitamin D deficiency in sepsis patients was 100%. The present research lends credence to the idea that a vitamin D deficiency may play a significant role in the development of sepsis. According to the available research, taking a vitamin D supplement may help prevent infections, sepsis and the associated mortality, particularly in older people. The relationship between vitamin D and sepsis is still being studied, but there are already a number of significant connections that provide a foundation for additional study. Such research is necessary because vitamin D administration is cheap and safe, and even small improvements in sepsis outcomes might have a large public health effect.

Limitations

In observational studies like the current one, it is impossible to control every potential confounding factor, and this might have an impact on the study's results. Data generalisation is challenging since this research was a single centered study with a limited sample size. Another drawback of the research was the inability to capture certain information that may have affected the amount of vitamin D, such as cytokine levels.

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