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Research Article

A STUDY TO ASSESS VITAMIN D DEFICIENCY AND ITS ASSOCIATION WITH SEPSIS IN TERTIARY CARE CENTRE

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ABSTRACT

Objectives: The aim of the study was to evaluate the correlation between serum levels of Vitamin D and outcome of sepsis patients presenting to ED.

Methods: This cross-sectional study was performed in the Saraswathi institute of medical sciences, Hapur from October 2021 to March 2022. For all the eligible patients, 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.

Results: The mean Vitamin D level of the study subjects who get cured were 23.09±11.20, whereas those patients who died had Vitamin D level 16.12±10.60, on comparing there is significant association of Vitamin D level with outcome of study subjects, with p=0.02. On assessing Vitamin D level with thin-layer chromatography (TLC) of study subjects, on applying regression analysis we found no correlation between Vitamin D level and TLC value of the study subjects with R square 0.

Conclusion: On the basis of our study, we can conclude that there is significant association of serum Vitamin D level with outcome of sepsis in the study subjects. On comparing there is significant association of Vitamin D level with outcome of study subjects, with p=0.02, C-reactive protein increases generally in infections, it was associated with Vitamin D level, however association was statistically non-significant.

Keywords: Sepsis, C-reactive protein, Vitamin D, Thin-layer chromatography.

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INTRODUCTION

Sepsis is a clinical phenomenon characterized by infection-related signs and symptoms in the 1st month of life, with or without bacteremia. It covers a range of infant systemic diseases, including septicemia, meningitis, pneumonia, arthritis, osteomyelitis, and urinary tract infections. Newborn sepsis accounts for about 26% of neonatal fatalities worldwide, with an incidence ranging from 1 to 8 neonates per 1000 live births [1].

In sepsis a life-threatening organ failure caused by a dysregulated immunological response to infection. Multiple organ failure, which frequently accompanies sepsis, contributes to the high fatality rate. Recent research has demonstrated a link between Vitamin D deficiency and sepsis in serious infections. Vitamin D deficiency has been shown to accelerate the progression of sepsis by immune system mediator. It involves both innate and acquired immunological responses [2].

Vitamin D is a prohormone. Its primary responsibility is to control the metabolism of calcium, phosphate, and bone homeostasis. However, it also plays a role in other physiological processes such as cellular gene transcription, cellular immunological response to infection, and anti-inflammation and anti-proliferation. In addition, it guards against the danger of systemic infection, cardiovascular disease, lung disease, and diabetes, and many other chronic disorders [3]. The association between Vitamin D insufficiency and unfavorable outcomes, such as extended hospital stays, higher infection rates, and higher mortality rates, is becoming more and more clear. Sepsis and infectious infections were the leading causes of death in pediatric intensive care units. In addition, Vitamin D insufficiency has been linked to severe sepsis, sepsis-related death, and an overall rise in mortality in both adult as well as children [4]. The pleiotropic effects of 25 (OH) D on human immunity, including T-cell proliferation, immunoglobulin class switching, and cytokine production, are probably to blame for the link between 25 (OH) D deficit and infections [5].

Vitamin D also has a role in the local tissue response to infection and is essential for the generation of antimicrobial peptides, in addition to having an impact on the humoral response to sepsis (AMPs). The vital involvement of Vitamin D in the macrophage response to mycobacterium tuberculosis through the AMP cathelicidin was established in a seminal work by Liu *et al*. in 2006. It has been established that phagocytic leukocytes, mucosal epithelium, and keratinocytes all produce the cathelicidin active fragment LL-37, which is also found in mucosal secretions and plasma. In addition to direct bactericidal activity, it also disrupts Pseudomonas aeruginosa biofilms, encourages phagocytosis, and reactive oxygen species production, and chemotactically attracts other immune cells to infection sites [6]. With the aforementioned context in mind, we conducted this study to evaluate the Vitamin D insufficiency and its relationship to sepsis in study participants.

Aim and objectives

The aim of the study was to assess and evaluate correlation between serum levels of Vitamin D and outcome of sepsis patients.

METHODS

This cross-sectional study was performed in the Saraswathi Institute of Medical Sciences, Hapurfrom October 2021–March 2022. For all the eligible patients, 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 assessed. The study was carried out in accordance with the guidelines of the Helsinki Declaration with the permission of the institute's ethical committee. Patients were only included after giving their informed consent, either directly or through a relative. Only patients with proven or suspected sepsis

were included. Patients with chronic conditions such as chronic kidney disease, congenital heart disease, cerebral palsy, muscular dystrophy, malabsorption syndrome, nephrotic syndrome, severe acute malnutrition, patients taking medications that interfere with calcium metabolism, and surgical patients were excluded from our research. Fresh blood samples were taken within 24 h of admission to the patients for the purpose of measuring Vitamin D levels. Enzyme-linked fluorescent assay technique was used to measure Vitamin D levels in patient's serum. Results were examined using the biological analysis value listed below.

1. Deficiency: Below 20 ng/ml
2. Insufficiency: 20–30 ng/ml
3. Sufficiency: 30–100 ng/ml.

Baseline demographic data such as age, gender, height/length, weight, and body mass index (as defined and classified by world health organization) were recorded for each patient at the time of enrollment for this study.

We calculate sample size as per the prevalence of Vitamin D deficiency among septic patient As per the previous studies the prevalence of Vitamin D deficiency among septic patient was 51% (based on study by Ponnarmeni *et al*. [7]), the maximum error in the estimate we are willing to tolerate, say±5%, at two-sided test with 95% confidence level (α=5%) and design effect=1, expected sample size is 93 patients. Hence, a total of 100 sample size were taken.

Collected data were entered in Microsoft Excel and SSPS 20.0. For descriptive statistics percentage, mean, median, Standard deviation, interquartile range was calculated along with graphical and tabular presentation was made. For inferential statistics Chi-square was applied to find out the significant differences between the groups at 95% confidence interval where p≤0.05.

RESULTS

In this study, 100 children were included in the study. Majority of 62% children were included in the age group between 1 and 5 years and the remaining distribution was 3% in <1 years, 33% in 5–10 years and 2% in the age group more than 10 years. The minimum age was 10 months and maximum age was 11 years. The mean age was 4.21±2.83.

In our present study 58% subjects were male and 42% subjects were female.

About 34% study subjects of our study were positive for CRP whereas rest 66% subjects were negative for CRP status.

In our study, only 34% study subjects had positive CRP whereas rest 66% subjects had negative CRP. Fig. 3 shows association of Vitamin D level with thin-layer chromatography (TLC) of study subjects, on applying regression analysis we found no correlation between Vitamin D level and TLC value of the study subjects with R square 0.

Table 3 shows association of Vitamin D level with outcome of the study subjects, The mean Vitamin D level of the study subjects who get cured were 23.09±11.20, whereas those patients who died had Vitamin D level 16.12±10.60, on comparing there is significant association of Vitamin D level with outcome of study subjects, with p=0.02.

Table 4 shows association of Vitamin D level with outcome of the study subjects, the Vitamin D level in the study subjects with CRP negative study subjects was 23.0±10.66, whereas in CRP positive study subjects it was 19.97±12.51, on applying t test it was non-significant with p=0.21.

DISCUSSION

In our present study, the mean age was 4.21±2.83 years, study by Kafle *et al*. [8] shows in their study, most of children (42.85%) were below

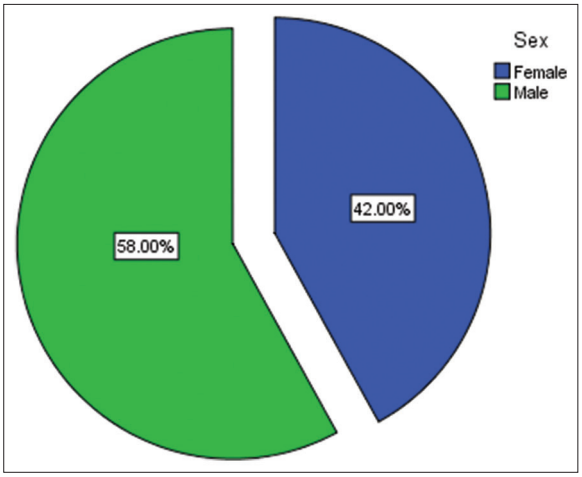

Fig. 1: Study subjects showing gender of study subjects

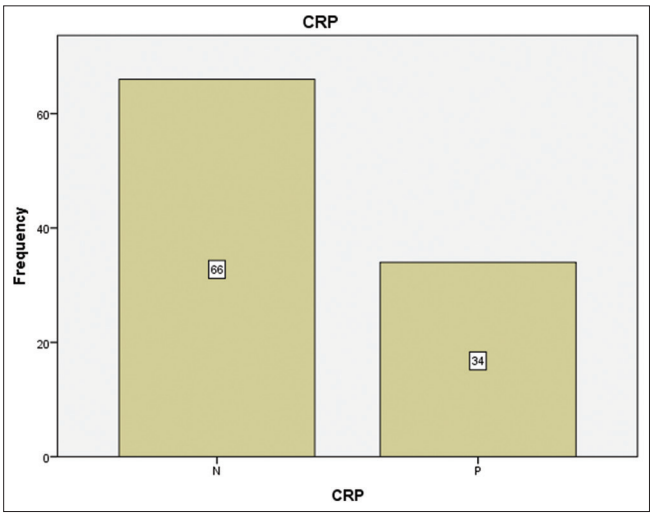

Fig. 2: Distribution of study subjects as per CRP Status

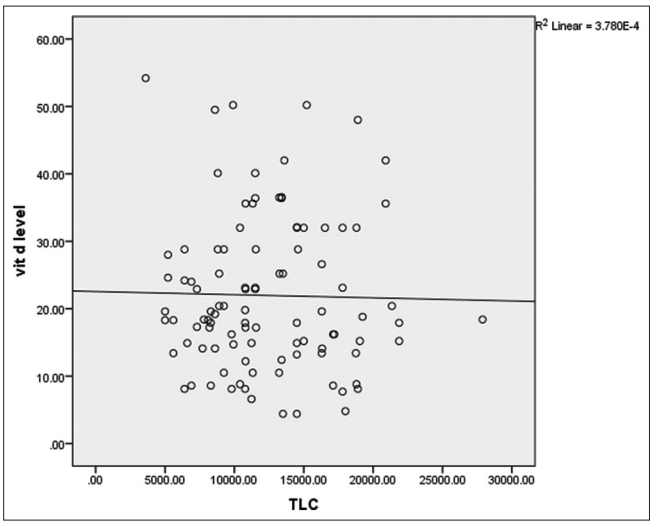

Fig. 3: Association of Vitamin D level with TLC of study subjects

5 years, study by Rajkondawar and Karde [3] shows that the mean age of patients was 41.56±13.87 years, this difference may be as it was conducted on adult population. In study by Bayat *et al*. [9] shows that patients with a mean age of 70.8±13.3 years were studied

Table 1: Distribution of children according to age group

Age group	Frequency	Percentage
<1 years	3	3
1–5 years	62	62
5–10 years	33	33
>10 years	2	2
Total	60	100

Table 2: Distribution of study subjects as per CRP Status

CRP	Frequency	Percent
Valid		
Negative	66	66.0
Positive	34	34.0
Total	100	100.0

Table 3: Association of Vitamin D level with outcome of the study subjects

Vitamin D level					
Out come	**Mean**	**n**	**SD**	**Minimum**	**Maximum**
Cured	23.0864	84	11.20362	4.80	54.20
Death	16.1188	16	10.59731	4.40	48.00
Total	21.9716	100	11.35083	4.40	54.20

T test applied, t value – 2.30, p=–0.02, significant

Table 4: Association of Vitamin D level with outcome of the study subjects

Vitamin D level					
CRP	**Mean**	**n**	**Std. Deviation**	**Minimum**	**Maximum**
Negative	23.0009	66	10.66018	8.10	54.20
Positive	19.9735	34	12.50826	4.40	50.20
Total	21.9716	100	11.35083	4.40	54.20

T test applied, t value – 1.27, p value- 0.21, non-significant

In our present study, 58% subjects were male and 42% subjects were female. In study by Bayat *et al.* [9] shows males=96 (64.0%) and females=54 (36.0%). Almost similar findings were observed in study by Bankole [10], (male 60%), however, in a study by Murdoch *et al.* [11] almost equal number of males and females were observed. In a study by Loeb *et al.* [12], 52.2% were female. There were no significant differences in the Vitamin D deficiency between males and females were reported in most of published study. However in some literature Vitamin d among males was higher than females may be because women engage in less outdoor activity, use sunscreen and wear long sleeved clothing in order to skin lighter because women consider whiter skin to be a beauty aesthetic.

In our study, only 34% study subjects had positive CRP whereas rest 66% subjects had negative CRP, Other study like Şişmanlar *et al.* [13] shows that there is no statistically significant association between Vitamin D level and CRP level. We found no correlation between Vitamin D level and thin-layer chromatography (TLC) value of the study subjects with R square 0. Other study like Şişmanlar *et al.* [13] shows that there is no statistically significant association between Vitamin D level and TLC level.

The mean Vitamin D level of the study subjects who get cured were 23.09±11.20, whereas those patients who died had Vitamin D level 16.12±10.60, on comparing there is significant association of Vitamin D level and outcome of study subjects with p=0.02. According to earlier research, Vitamin D levels and patient mortality

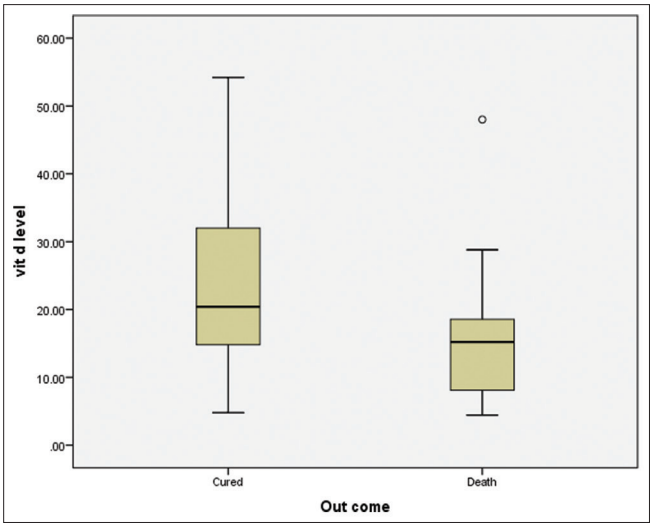

Fig. 4: Association of Vitamin D level with outcome of the study subjects

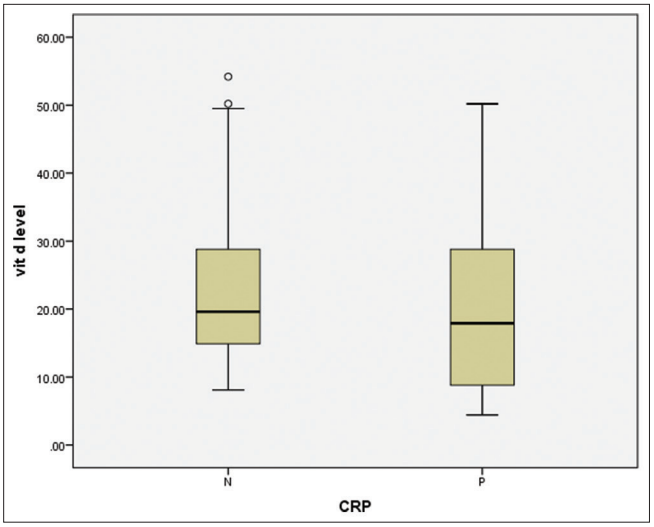

Fig. 5: Association of Vitamin D level with outcome of the study subjects

rates are correlated. This is consistent with the findings of the current study. There was a significant link between the mean serum level of Vitamin D in sepsis patients who died and those who survived in the study by Parekh *et al.* [14] In patients with severe sepsis or septic shock, Vitamin D insufficiency was substantially related with an increase in 30-day mortality, according to the findings of a research by Rechand Hunsaker [15]. In the study by Nguyen *et al.*, [16] low serum Vitamin D levels were also linked to a rise in 23-day mortality among 91 sepsis patients. The association between Vitamin D deficiency and mortality rate in critically ill patients was established in the study by Arnson *et al.* [17] Vitamin D insufficiency from 365 days before hospitalization was found to be a reliable predictor of short- and long-term mortality as well as a positive blood culture for microorganism growth in 2399 patients. Not all researchers have found association between Vitamin D level and mortality rate. According to a study by Upala *et al.*, [5] severe infection and sepsis are not the only clinical outcomes that low serum concentrations of 25 (OH) D are linked to; they also include increased mortality, longer hospital stays, and acute renal injury. The deficient Vitamin D level was also shown to be a significant predictor of 30-day death in septic patients. Innate immune dysfunction may be the pathophysiology that plays the role in the development of sepsis in Vitamin D deficiency. In addition, a decrease in 1,25 (OH)

2D may have pleiotropic effects on immunological control, mucosal function, and endothelial function at the tissue level. American society for parenteral and enteral nutrition suggests 200 IU of Vitamin D daily as supplements in sepsis patients. However, additional research has suggested that doses of 400 or 500 IU per day were still considered insufficient for the majority of hospitalized patients. These results suggest that in order to treat Vitamin D deficiency in sepsis patients, greater dosages of Vitamin D are likely required.

In our present study, Vitamin D level in CRP positive patients was lesser than CRP negative patients; however, it was not significant. Increased 25 (OH) Vitamin D levels are linked to lower CRP levels, according to research by Adrian [18], similar findings was there**.**

CONCLUSIONS

On the basis of our study, we can conclude that There is significant association of serum Vitamin d level with outcome of sepsis in the study subjects. On comparing, there is significant association of Vitamin D level with outcome of study subjects, with p = 0.02, CRP increases generally in infections, it was associated with Vitamin D level; however, association was statistically non-significant.

Limitation

There is some limitation to the current study. Due to the limited data obtained, we were unable to provide details on acute or chronic liver failure, premorbid health status, type of infection, use of vitamin D supplements, and data on the outcomes. Further studies are required to evaluate the effects of other potential medical comorbidities.

AUTHORS CONTRIBUTION

Both authors had contributed.

CONFLICT OF INTEREST

No.

AUTHORS FUNDING

No.

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