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Vitamin D as a biomarker in predicting sepsis outcome at a tertiary care hospital

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ABSTRACT

Background: Vitamin D has proven immunomodulatory effects. As per the literature, there is a vitamin D deficiency observed in critically ill sepsis patients. **Aims and Objectives:** The present study was conducted to study the association of vitamin D levels at the time of admission to the intensive care unit (ICU) with mortality and various indices of sepsis assessment like the simplified acute physiology score (SAPS II) along with the age-unadjusted Charlson Comorbidity Index (CCI) and procalcitonin. **Materials and Methods:** A single centric, observational-longitudinal study was conducted in the ICU with patients of sepsis (n = 96). Vitamin D was measured at the time of admission to the ICU. Controls were taken from age- and gender-matched patients without sepsis and with no premorbid illnesses. The objectives of the current study were to assess SAPS II and CCI scores and their predicted mortality amongst various categories of vitamin D levels at the time of admission, to correlate various categories of vitamin D levels with hospital stay and complications or hazards and to assess the sensitivity of vitamin D for prediction of sepsis outcome. **Results:** The case cohort and controls had average vitamin D levels of 15.33 ng/dL and 41.11 ng/dL, respectively. Patients with vitamin D deficiency had longer hospital and ICU stays and greater rates of morbidity. Observations showed no correlation between vitamin D and serum albumin, WBC count, total cholesterol, triglycerides, LDL, or HDL. The level of vitamin D at the time of admission to the ICU was observed to be highly sensitive (90.6%) to predicting the mortality rates in the ICU due to sepsis. **Conclusion:** Measurement of vitamin D at the time of admission may be a possible indicator for prediction of sepsis mortality and hospital and ICU length of stay for ICU-admitted patients with sepsis.

Key words: Vitamin D; Sepsis; Simplified acute physiology score II score; Charlson comorbidity score; Critical care

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INTRODUCTION

The sunshine steroid hormone vitamin D has an inhibitory effect on adaptive immunity, which is known to be beneficial in autoimmune diseases and maintaining calcium homeostasis. The association of vitamin D deficiency with immune-mediated inflammatory diseases like rheumatoid arthritis, systemic lupus erythematosis, diabetes mellitus type II, and inflammatory bowel diseases has already been emphasized in multiple literatures.[1]

Recently, studies have been trying to establish the relationship between deficient vitamin D and morbidity and mortality due to sepsis. Vitamin D can induce cathelicidine and β defensing-2-like peptides that can kill organisms, including *Mycobacterium tuberculosis*.[2] Severe sepsis patients have a higher prevalence of vitamin D deficiency. It can modulate inflammatory cytokines, viz. interleukin-6, NFκβ, and tumor necrosis factor – α. Hence, its administration has been tried for the attenuation of sepsis-related hyperinflammatory responses.[3]

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Aims and objectives

Therefore, the present study correlated serum vitamin D levels with mortality estimated at 28-day using the simplified acute physiology score (SAPS) II score (estimating 28 days mortality) and the Charlson comorbidity index (CCI) (estimating 10-year survival rates) of patients with sepsis admitted to the intensive care unit (ICU).

MATERIALS AND METHODS

This study was carried out at Kasturba Hospital, Manipal, after the receipt of approval to conduct the study from the Institutional Ethics Committee (IEC) (IEC Reg No. ECR/146/Inst/KA/2013; approval letter: 601/2014; dt: October 14, 2014). All the patients of age >18 years admitted to the ICU with a diagnosis of sepsis and ready to provide written informed content (by themselves or by 1st degree relatives) were included in the present study. Patients were categorized into survivor and non-survivor cohorts for statistical analysis. A similar protocol was followed for age- and gender-matched healthy volunteers who came for a general check-up to the hospital. An estimation of vitamin D in the leftover blood samples of cases and freshly taken samples from controls was carried out. Serum 25(OH)D within the first 24 h after ICU admission was measured using the Elecsys Vitamin D total II assay by Roche Diagnostics. At 28 days, co-morbidities using the age-unadjusted CCI for the predicted 10-year survival rate, SAPS II, and their predicted mortality rate were assessed.

According to the recommendations of the Endocrine Society for an at-risk population, subjects were distributed in 3 categories depending on their Vitamin D levels.[8]

- 25(OH)D ≤19.9 ng/mL: Deficiency
- 25(OH)D 20–29.9 ng/mL: Insufficiency
- 25(OH)D ≥30: Sufficiency.

The objectives of the current study were to assess SAPS II and CCI scores and their predicted mortality amongst various categories of Vitamin D levels at the time of admission, to correlate various categories of Vitamin D levels with hospital and ICU stays, to correlate complications or hazards (reverse of survival) in cases in different Vitamin D groups, and to assess the sensitivity of Vitamin D levels at ICU admission for prediction of sepsis outcome.

Statistical analysis

The compilation and analysis of data using appropriate statistical methods were done. SPSS 16.00 was used to plot the receiver operating characteristic (ROC) curve and Kaplan Meyer Survival Analysis for survival and hazard functions. Analysis of covariance was used to eliminate the probable confounding parameters, while assessment of other categorical variables was done using the Chi-Square tests. Statistical significance was taken at P<0.05.

RESULTS

A total of 96 patients with sepsis were recruited for the present study. There were a total of 48 patients in each group, with a mean age of 52.79 years in the survivor group and 58.15 years in the non-survivor group, and close to 50% of the population being female in both groups. The baseline median SAPS II score was 41.52 and 42 in the survivor and non-survivor groups, respective, whereas the baseline median CCI in both groups was 1. Other baseline demographic data are shown in Table 1.

As depicted in Table 2, 74% of the total study population was observed to be Vitamin D deficient, and 12.5% was Vitamin D insufficient. Only 13.5% of patients had their Vitamin D levels in the normal range. Particularly, old age patients (>70 years) were all Vitamin D deficient or insufficient. This shows the vast prevalence of Vitamin D deficiency in the hospitalized population, particularly in ICUs. 14.6% of the population who were alive had sufficient serum Vitamin D levels, whereas 13.5% of the population who died had sufficient serum Vitamin D levels (Table 3).

Serum Vitamin D levels in the study group and control group are depicted in Table 4. It was observed that the mean Vitamin D level in the study group was 15.28 ng/mL, whereas the mean value of Vitamin D was 41.11 ng/mL. (Mann-Whitney test Z-value 9.567, P<0.001) This showed the drastic difference in the levels of Vitamin D in the patients with sepsis, which was almost three times less.

Observations showed a nil correlation between Vitamin D and serum albumin (r=0.064; P=0.536), a negative correlation of Vitamin D with WBC count (r=−0.122; P=0.238), total cholesterol (r=−0.368; P=0.014), triglycerides (r=−0.301; P=0.045), LDL (r=−0.213; P=0.181), and HDL (r=−0.163; P=0.285). SAPS II scores were found to be not related to Vitamin D levels (r=0.153; P=0.970) in the case cohort. Vitamin D levels were negatively correlated with the 10-year survival rate according to the CCI (r=−0.057; P=0.581). The average SAPS II score in sepsis patients was 43.49.

The correlation of Vitamin D with age, procalcitonin (PCT) levels, ICU length of stay (LOS), hospital LOS, and mortality showed a negative correlation. PCT levels

Table 1: Baseline parameters of the case-cohort

Baseline characteristics	Overall	Survivor	Nonsurvivor
Number of subjects, n (%)	96	48 (50)	48 (50)
Age, mean (SD)	55.47 (16.09)	52.79 (15.78)	58.15 (16.13)
Male gender, n (%)	56 (58.33)	27 (48.32)	29 (51.7)
Albumin (g/dL), mean (SD)	2.95 (0.86)	3.11 (1.020)	2.79 (0.63)
TLC (/mm^3)	17,894.58 (3051.9)	21,097.5 (5992.69)	14,691.67 (1141.84)
SAPS II, median (IQR)	41.75 (25.4–57)	41.52 (21.08–49.75)	42 (30.125–69.025)
CCI, median (IQR)	1 (0–3)	1 (0–3)	1 (0–3)
PCT (ng/mL), mean (SEM)	20.46 (7.25)	24.64 (11.5)	14.88 (7.3)
ICU LOS, median (IQR)	7 (4–17)	6 (4–14)	8 (4.25–19.5)
Hospital LOS, median (IQR)	14 (7–28.75)	18 (10–34.5)	9 (5–21.75)
Duration of MV, median (IQR)	5 (3–11)	4.5 (3.10)	6 (3–11.7)
TC (mg/dL), mean (SD)	119.02 (46.85)	133.5 (47.49)	101.65 (40.67)
LDL (mg/dL), mean (SEM)	69.15 (5.44)	78.63 (8.75)	56.26 (6.34)
HDL (mg/dL), mean (SEM)	16.44 (2.26)	15.04 (3.11)	20.33 (3.70)
TG (mg/dL), mean (SEM)	190.38 (20.97)	214.16 (33.40)	136.3 (23.02)
25(OH) D (ng/dL), mean (SEM)	15.38 (1.36)	15.9 (1.68)	15.67 (2.17)
25(OH) D category (ng/dL), n (%)	96	48	48
<20	71 (71)	35	36
20–30	12 (12.5)	7	5
>30	13 (13.54)	6	7

SD: Standard deviation, TLC: Total leucocyte count, SAPS II: Simplified acute physiology score, IQR: Inter quartile range, CCI: Charlson Comorbidity Index, PCT: Procalcitonin, SEM: Standard error of mean, ICU: Intensive care unit, LOS: Length of stay, MV: Mechanical ventilation, TC: Total cholesterol, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, TG: Triglyceride, 25(OH) D: Estimated component of vitamin

Table 2: Mean levels of Vitamin D (ng/mL) in various age groups in the case-cohort

Age	Vitamin D at admission			Total, n (%)
	Deficient, n (%)	Insufficient, n (%)	Sufficient, n (%)	
30 and below	4 (100.0)	0	0	4 (100.0)
31–50	24 (77.4)	3 (9.7)	4 (12.9)	31 (100.0)
51–70	28 (63.6)	7 (15.9)	9 (20.5)	44 (100.0)
>70	15 (88.2)	2 (11.8)	0	17 (100.0)
Total	71 (74.0)	12 (12.5)	13 (13.5)	96 (100.0)

Fisher's exact test P=0.383, NS. NS: Not significant

Table 3: Mortality at 28 days of admission to ICU in the varying serum Vitamin D concentrations

Mortality at 28 days	Vitamin D at admission			Total, n (%)
	Deficient, n (%)	Insufficient, n (%)	Sufficient, n (%)	
Alive	36 (75) (50.7)	5 (10.4) (41.7)	7 (14.6) (53.8)	48 (100) (50)
Deceased	35 (72.9) (49.3)	7 (14.6) (58.3)	6 (12.5) (46.2)	48 (100) (50)
Total	71 (74) (100)	12 (12.5) (100)	13 (13.5) (100)	96 (100) (100)

χ^2=0.424, P=0.809, NS. NS: Not significant, ICU: Intensive care unit

Table 4: Vitamin D level in active as well as the control group

Groups	n	Mean (SD)	Percentile		
			25th	50th (median)	75th
Active group	96	15.38 (13.37)	4.66	11.22	20.75
Control group	96	41.11 (15.23)	29.73	38.65	52.18

Mann–Whitney test Z value: 9.567; P<0.001 (highly significant). SD: Standard deviation

had a positive correlation with SAPS II score, days of mechanical ventilation (MV), ICU LOS, and mortality. Vitamin D levels at the time of ICU admission were found to be negatively correlated with overall mortality (Table 5 and Figure 1a and b).

Also, the sensitivity of the Vitamin D level at admission was found to be excellent. Vitamin D level of <23.83 ng/dL at the time of admission was found to be 90.6% sensitive to predicting death in an ICU setting due to sepsis, as well as having a specificity of 77.1%. The same is depicted in Figure 2 with the help of the ROC curve, which showed an AUC of 0.899 with P=0.0001 and CI of (0.853–0.946).

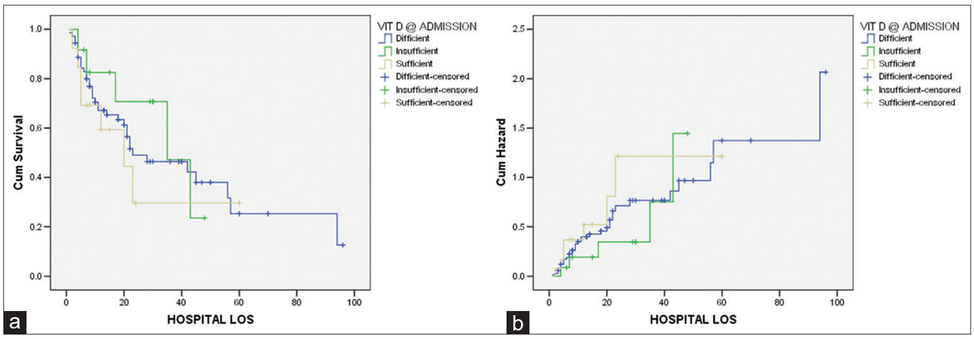

Figure 1: (a) Kaplan-Meyer Survival analysis of the cases at different categories of vitamin D levels. Patients having a deficiency of vitamin D levels had longer hospital length of stay (LOS) and intensive care unit LOS as indicated by the blue line. (b) Complications/Hazards (Reverse of survival) in cases in different vitamin D groups. Morbidity was more among the vitamin D deficient group as shown by the blue line followed by the insufficient group (green line) and then the sufficient group indicated by the yellow line

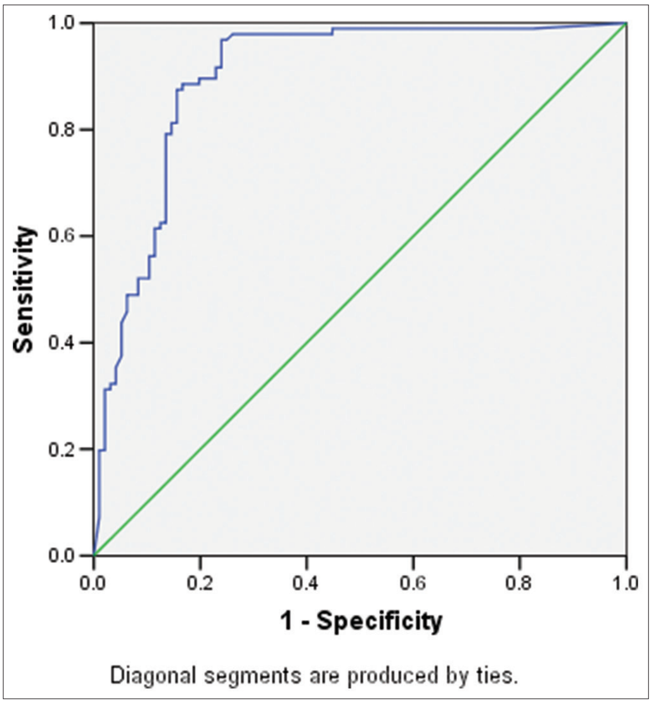

Figure 2: Receiver operating characteristic (ROC) curve showing Vitamin D levels compared between cases and controls. The cut-off (23.83 ng/dL) has a good accuracy to diagnose the patients with sepsis (Area under this ROC curve 0.899)

Table 5: Vitamin D status at admission and the hospital length of stay

Vitamin D @ admission	Mean	95% CI	
		Lower	Upper
Deficient	41.38	30.43	52.33
Insufficient	32.68	22.7	42.66
Sufficient	26.60	11.78	41.42

CI: Confidence interval

DISCUSSION

The present study evaluated the association between various parameters like Vitamin D level, SAPS II score, CCI, PCT, etc. at the time of ICU admission for patients with sepsis and mortality as the outcome in 96 patients matched with 96 controls.

The results demonstrated that 74% of patients who were admitted with sepsis had Vitamin D deficiency, 12.5% had insufficiency, and only a mere 13.5% were normal. The incidence was in close accordance with another report from India, which showed a prevalence of 67% of Vitamin D deficiency.[4] The slightly higher incidence of Vitamin D deficiency found in our study may be because of the ICU population. It might also be an indicator of prolonged disability of the patient, restricting him to the indoors before being brought to the hospital, as Indians tend to present at a later stage of the disease pathogenesis.

90% of females were Vitamin D deficient, but Vitamin D insufficiency was more prevalent among males (75%) (χ^2=9.931; P=0.007). Again, Vitamin D was deficient mostly in the 51-70 age group (39.4%). However, the same age group also showed normal Vitamin D levels (69.2%) (Fisher's exact test P=0.383). This was partly confirmed by a sizeable multicentric study conducted by Braun et al., who showed that younger age and low Vitamin D levels[5] are associated. However, most other published studies project a greater prevalence of Vitamin D deficiency in females and the elderly.[6] However, these findings can be a projection of the Vitamin D deficiency in the general population.

SAPS II scores were negatively correlated to the hospital LOS (r=−0.009; P=0.933) and ICU LOS (r=−0.044; P=0.672) but positively correlated to the MV duration (r=0.034; P=0.744), which was in accordance with the observations by Dabhi et al.,[7] Vitamin D levels had a negative correlation with the 10-year survival rate, according to the CCI (r=-0.057; P=0.581). SAPS II and CCI were possible confounding factors for mortality. Hence, we did an ANACOVA analysis and found that the Vitamin D levels between the survival and deceased groups were non-significantly different (P=0.759; NS), probably due to the limited size of the sample of the studied group. We also documented that the 10-year survival rate as predicted by CCI had a negative correlation with the SAPS II score (R=0.022; P=0.831), which was in line with the study conducted by Hsu et al.,[8] who stated that CCI along with administrative data might predict short- and long-term mortality of ICU patients as with other physiological scores.

Vitamin D deficiency and insufficient cases increased ICU LOS as well as hospital stays, as documented by Amrein et al.,[9] Still, they had no relation to the ventilatory requirement or even the number of ventilation days. Higher mortality was noted in the deficient Vitamin D (50.7%) and insufficient (41.7%) groups (85.41%) than in the sufficient group (14.6%). The important role is played by Vitamin D in the inflammatory pathway by inhibiting various cytokines responsible for it. Deficiency of Vitamin D also results in reduced levels of the cathelicidin peptide, which provides protection against various infectious agents. These mechanisms collectively play a pivotal role in the worst outcomes of Vitamin D deficiency in critical patients.[10]

The correlation between serum albumin and Vitamin D levels was studied and found not to be in correlation. This was in agreement with other studies that stated that there's an association between serum VDBP and the amount required to recover filtered 25(OH)D from urine, facilitated by *megalin* on the renal epithelium.[11] It's hypothesized that often critically ill patients have liver dysfunction leading to low albumin levels and low Vitamin D binding protein, which may not be related to low Vitamin D concentration, which might still be normal when free levels of active forms are measured.[12] Vitamin D levels had a negative correlation with WBC counts, which is a parameter for sepsis and is on par with Al Shimerty et al., who show a negative correlation of Vitamin D with TLC.[13]

The correlation of Vitamin D deficiency with higher PCT values in our study indicates more severe sepsis, which is in line with the study conducted by Wolf et al.,[14] who stated that serum Vitamin D levels measured in the first 24 h of ICU admission were in inverse relation to the 28-day mortality in sepsis patients and also their PCT levels.

The effect of Vitamin D on lipid profiles was studied, and it was found that it has a negative correlation with not only total cholesterol (TC), triglycerides (TG), and LDL but also with HDL, although not significantly. This could be because the patients with sepsis also had multiple co-morbidities as confounding factors, which is demonstrated by the fact that TC and hospital LOS had a strong positive correlation. This was confirmed by Li et al.,[15] Critical care patients with low vitamin D levels can have multifactorial causes due to interactions with multiple medications, abnormal gastrointestinal motility, and fluid resuscitation efforts.

There was a definite association between Vitamin D level at admission and mortality in the ICU-admitted sepsis patients. Vitamin D deficiency has been associated with susceptibility to a wide range of viral infections, including COVID-19.[16] The deficiency of Vitamin D in patients in medical and surgical ICUs has been shown to contributing to worse outcomes, higher morbidity, as well as mortality. In the lungs, the physiological involvement of Vitamin D is postulated as an agent that has immunomodulatory, anti-infective, and anti-inflammatory activities. The mechanism proposed for such activities of Vitamin D is via nuclear factor kappa β and mitogen-activate protein kinase inhibitors. This mechanism turns out to be of paramount importance in the management of sepsis.[3]

Furthermore, in critically ill patients, a steep fall in the serum Vitamin D level is observed because of reasons like altered metabolism, reduced production of the Vitamin D binding proteins, exaggerated vascular permeability, and an imbalance in the fluid. These factors tend to result in extravasation and renal wasting of Vitamin D, resulting in the observed steep fall.[9] This low Vitamin D level and its association with sepsis patients were confirmed by the findings of the present study. Furthermore, further analysis of the data of the present study showed an excellent sensitivity (90%) of vitamin D level of 23.83 ng/dL to predict mortality in sepsis ICU patients.

Limitations of the study

The limitation of the present study was the smaller size of the patient population. Also, the methodology was such that we included the measurement of Vitamin D level at the time of admission. Therefore, the dynamics of the fluctuation of Vitamin D levels throughout the ICU and their correlation with disease progression should be further studied to establish the involvement of vitamin D in sepsis pathogenesis.

CONCLUSION

The disease course of sepsis patients might be linked to the vitamin D reserves of the body. The deficiency of vitamin D at the time of ICU admission in sepsis patients is strongly associated with extended hospital LOS and ICU LOS and increased morbidities and mortalities.

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REFERENCES

1. Aparna P, Muthathal S, Nongkynrih B and Gupta SK. Vitamin D deficiency in India. J Family Med Prim Care. 2018;7(2):324-330.
   https://doi.org/10.4103/jfmpc.jfmpc_78_18
2. White JH. Vitamin D metabolism and signaling in the immune system. Rev Endocr Metab Disord. 2012;13(1):21-29.
   https://doi.org/10.1007/s11154-011-9195-z
3. Amrein K, Scherkl M, Hoffmann M, Neuwersch-Sommeregger S, Köstenberger M, Berisha AT, et al. Vitamin D deficiency 2.0: An update on the current status worldwide. Eur J Clin Nutr. 2020;74(11):1498-1513.
   https://doi.org/10.1038/s41430-020-0558-y
4. Siddiqee MH, Bhattacharjee B, Siddiqi UR and MeshbahurRahman M. High prevalence of Vitamin D deficiency among the South Asian adults: A systematic review and meta-analysis. BMC Public Health. 2021;21(1):1823.
   https://doi.org/10.1186/s12889-021-11888-1
5. Braun A, Chang D, Mahadevappa K, Gibbons FK, Liu Y, Giovannucci E, et al. Association of low serum 25-hydroxyvitamin D levels and mortality in the critically ill. Crit Care Med. 2011;39(4):671-677.
   https://doi.org/10.1097/CCM.0b013e318206ccdf
6. Garg R, Agarwal V, Agarwal P, Singh S and Malhotra N. Prevalence of vitamin D deficiency in Indian women. Int J Reprod Contracept Obstet Gynecol. 2018;7(6):2222-2225.
   https://doi.org/10.18203/2320-1770.ijrcog20182324
7. Dabhi AS, Khedekar SS and Mehalingam V. A prospective study of comparison of APACHE-IV and SAPS-II scoring systems and calculation of standardised mortality rate in severe sepsis and septic shock patients. J Clin Diagn Res. 2014;8(10):MC09-MC13.
   https://doi.org/10.7860/JCDR/2014/9925.5052
8. Hsu YT, He YT, Ting CK, Tsou MY, Tang GJ and Pu C. Administrative and claims data help predict patient mortality in intensive care units by logistic regression: A nationwide database study. Biomed Res Int. 2020;2020:9076739.
   https://doi.org/10.1155/2020/9076739
9. Amrein K, Papinutti A, Mathew E, Vila G and Parekh D. Vitamin D and critical illness: What endocrinology can learn from intensive care and vice versa. Endocr Connect. 2018;7(12):R304-R315.
   https://doi.org/10.1530/EC-18-0184
10. Singh S, Sarkar S, Gupta K and Rout A. Vitamin D Supplementation in Critically Ill patients: A meta-analysis of randomized controlled trials. Cureus. 2022;14(4):e24625.
    https://doi.org/10.7759/cureus.24625
11. Bikle DD and Schwartz J. Vitamin D binding protein, total and free Vitamin D levels in different physiological and pathophysiological conditions. Front Endocrinol (Lausanne). 2019;10:317.
    https://doi.org/10.3389/fendo.2019.00317
12. Sanson G, De Nicolò A, Zerbato V, Segat L, Koncan R, Di Bella S, et al. A combined role for low vitamin D and low albumin circulating levels as strong predictors of worse outcome in COVID-19 patients. Ir J Med Sci. 2023;192(1):423-430.
    https://doi.org/10.1007/s11845-022-02952-9
13. Al Shimerty DF and Al Sallami AS. The effect of Vitamin D3 and its relationship with the level of white blood cells in women spontaneous miscarriage undergoing intracytoplasmic sperm injection (ICSI) technique. Med Leg Update. 2020;20(4):164-171.
    https://doi.org/10.37506/mlu.v20i4.1789
14. Wolf TA, Wimalawansa SJ and Razzaque MS. Procalcitonin as a biomarker for critically ill patients with sepsis: Effects of Vitamin D supplementation. J Steroid Biochem Mol Biol. 2019;193:105428.
    https://doi.org/10.1016/j.jsbmb.2019.105428
15. Li Y, Tong CH, Rowland CM, Radcliff J, Bare LA, McPhaul MJ, et al. Association of changes in lipid levels with changes in Vitamin D levels in a real-world setting. Sci Rep. 2021;11(1):21536.
    https://doi.org/10.1038/s41598-021-01064-1
16. Ohaegbulam KC, Swalih M, Patel P, Smith MA and Perrin R. Vitamin D supplementation in COVID-19 patients: A clinical case series. Am J Ther. 2020;27(5):e485-e490.
    https://doi.org.10.1097/MJT.0000000000001222

Authors' Contributions:
AG- Study conceptualization, protocol preparation, literature survey, data collection, data analysis, draft manuscript preparation; **MPM**- Review concept, design and protocol, overall project guidance, manuscript; **KP**- Review manuscript, data analysis guidance; **MC, NP**- Reviewed and prepared Manuscript, Submission of manuscript, proof checking; **VSB**- Literature survey, data analysis, preparation of tables and figures.

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