

Association of vitamin D levels with severity and outcome of COVID-19 infection among inward patients at a tertiary care unit in Sri Lanka

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Abstract

Introduction: A link between vitamin D and COVID-19 infection has been expressed by many experts. In this study, we aim to investigate the association of the prevalence of vitamin D deficiency with the severity and outcome of COVID-19 infection in patients who are admitted to Teaching Hospital Batticaloa, Sri Lanka.

Methods: A retrospective cross-sectional study was conducted among COVID-19 patients over a period of one month in May 2021. All patients who tested positive for COVID-19 were included. Patients with chronic kidney disease, known vitamin D deficiency, and patients on vitamin D supplements were excluded from the study. The vitamin D deficiency was defined according to the Oxford Academic Endocrine Society guidelines. The severity of the COVID-19 was defined according to the Provisional Clinical Practice Guidelines on COVID-19 suspected and confirmed patients. Primary endpoints of this study were 'recovered from COVID-19' or 'death'. Data was analysed to report the proportion of patients with different vitamin D levels and disease severity. Chi-squared and Fisher's exact tests were used to analyse the results. A p-value of <0.05 was considered as statistically significant.

Results: Out of 141, 58% were males. Mild, moderate, and severe COVID-19 were observed in 29.8%, 48.2%, and 22.0% of patients respectively. Only 30.5% of the population had normal vitamin D levels while the rest had some degree of vitamin D insufficiency. None of the patient population had severe vitamin D deficiency status. A 52.9% in the moderate category of COVID-19 severity had insufficient levels of vitamin D levels. Those that recovered from COVID-19 were 93.6%. No significant association was observed between the severity of COVID-19 and vitamin D deficiency ($p=0.1041$). Interestingly hypoxia was significantly prevalent among those with normal vitamin D levels ($p=0.0005$). vitamin D deficiency does not impact the mortality rate among COVID-19 patients ($p=0.6559$).

Conclusions: The association of vitamin D levels with COVID-19 severity and mortality was not statistically significant.

Key words: COVID-19 severity, vitamin-D deficiency; COVID-19 mortality

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Introduction

The COVID-19 pandemic affected more than 100 million and caused nearly 3 million deaths globally.(1) COVID-19 is characterised by fever, fatigue, cough, shortness of breath, and loss of taste. It is associated with an inflammatory cytokine storm and immune dysregulation leading to life-threatening acute respiratory distress syndrome (ARDS). The COVID-19 ARDS mortality rate is more than 60%, and the major reason for mortality is respiratory failure.(2)

In the drive for potentially helpful pharmaceutical and nutraceutical therapies, studies have focused on the individual's intrinsic immune status, comorbidities, and nutritional status. Careful consideration of the pathological factors can help mitigate the cytokine storm and treat COVID-19 ARDS. vitamin D deficiency has been considered to be an important factor contributing to the severe manifestations and outcomes of COVID -19. It has been observed that vitamin D-deficient individuals have an increased COVID-19 risk and mortality.(3) vitamin D modulates both innate as well as adaptive immunity. It may potentially prevent or mitigate the complications associated with respiratory tract infections (RTIs) by inhibiting the production of pro-inflammatory cytokines and enhancing the production of anti-inflammatory cytokines. Only a few interventional studies have discovered the link between vitamin D and RTIs with conflicting evidence. There is a need for larger intervention trials.(4)

There are no studies that evaluate the association between vitamin D status and COVID-19 severity in Sri Lanka. In this study, we aim to investigate the association of vitamin D deficiency (VDD) with COVID-

19 infection in patients who are admitted to teaching Hospital Batticaloa (THB), Sri Lanka.

Methods

A retrospective cross-sectional study was conducted among COVID-19 patients admitted to a tertiary care hospital during a period of one month in May 2021. All patients who tested positive for COVID-19 infection by rapid antigen test (RAT) or Polymerase chain reaction (PCR) were included. Patients with known chronic kidney disease (CKD) or vitamin D deficiency, or patients on vitamin D supplements were excluded from the study.

Sample size estimation: Sample size was calculated considering a prevalence rate of 50%. With a 10% margin of error, the minimum sample size was estimated to be 97.

Vitamin D deficiency was defined according to the Oxford Academic Endocrine Society guidelines as follows.(5)

- Normal: 30 – 100 ng/mL
- Insufficiency: 21-29 ng/mL
- Moderate deficiency: 11 – 20 ng/mL
- Severe deficiency: ≤ 10 ng/mL

The severity of the COVID-19 infection was defined according to the Provisional Clinical Practice Guidelines on COVID-19 suspected and confirmed patients in Sri Lanka (published in March 2020).(6)

Data were analysed using SPSS 24 statistical package. All the significant tests were performed at a 95% confidence interval. Chi-square and Fisher's exact tests were used to analyse the results.

Table 1 - Severity of COVID-19 infection

Parameter	Level of severity (one or more)		
	Mild	Moderate	Severe (Critical)
Respiratory Rate (RR/min)	12 - 20	21 – 30	≥ 31
Heart Rate (HR/min)	≤ 100	101 – 120	≥ 121
O ₂ Saturation on room air (% by Pulse Oximeter)	≥ 94	90 – 93	≤ 89

Results

Total study population was 141. Among them, 58% (82) were males and 42% (59) were females. Mild, moderate, and severe COVID-19 were observed in 29.8% (42), 48.2% (68), and 22.0% (31) of patients respectively. vitamin D deficiency status is shown in table 2.

Table 2 - Vitamin D deficiency status

Vitamin D deficiency levels	Patient Population n (%)
Normal	43 (30.5)
Insufficiency	70 (49.6)
Moderate deficiency	28 (19.9)
Severe deficiency	0
Total	141(100)

Out of COVID-19 patients, 93.6% (132) recovered and 6.4% (9) died. The mean duration of hospital stay was nearly one month.

A higher proportion of female patients (32.2%) with COVID-19 infection had a moderate deficiency status

of vitamin D compared to the male population (11%) (Figure 1).

Some degree of low vitamin D levels were found in 77.9% (53) and 51.6% (16) of moderately-severe and severe COVID-19 infection respectively. However, no significant association was found between the severity of COVID-19 and the status of vitamin D ($p=0.1041$). Hypoxia was found to be significantly more prevalent in patients with normal vitamin D levels ($p=0.0005$). vitamin D deficiency did not seem to have an impact on the mortality rate of COVID-19 patients ($p=0.6599$) (Table 3).

Discussion

Mild, moderate, and severe COVID-19 were observed in 29.8%, 48.2%, and 22.0% of patients respectively. In the study population, 30.5% had normal vitamin D levels while 69.5% had some degree of vitamin D insufficiency. The association between the severity of COVID-19 and vitamin D deficiency was not statistically significant.

Sri Lanka experienced a high number of COVID-19 cases during the period from 2020-2021. The limited vaccine coverage rate in the country has persuaded COVID-19 patients to switch to alternative products, including vitamin supplements that can enhance immunity.(7) Several studies conducted worldwide have shown heterogeneity in the results regarding the susceptibility to COVID-19 infection in vitamin D-deficient individuals.(8)

Studies based on the Sri Lankan population have reported vitamin D insufficiency in the range of 31.4%

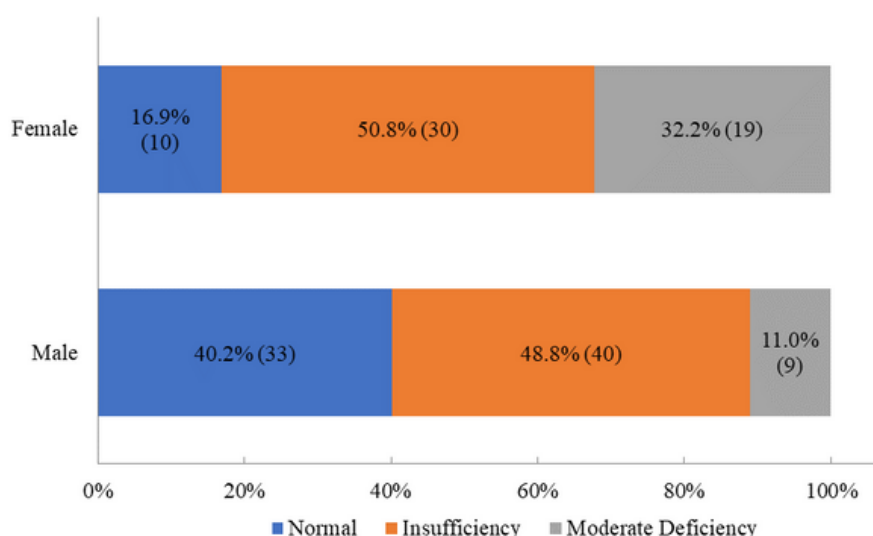


Figure 1 - Gender-wise distribution of vitamin D levels

Table 3 - Distribution of the study population based on vitamin D levels

		Status based on vitamin D levels			p-value
		Normal n (%)	Insufficiency n(%)	Moderate Deficiency n(%)	
The severity of COVID-19	Mild (n = 42)	13 (31.0)	22 (52.3)	7 (16.7)	0.1041
	Moderate (n = 68)	15 (22.1)	36 (52.9)	17 (25.0)	
	Severe (n = 31)	15 (48.4)	12 (38.7)	4 (12.9)	
Oxygen Concentration in room air	Normal (n = 120)	29 (24.2)	65 (54.1)	26 (21.7)	0.0005#
	Mild to severe hypoxia (n = 21)	14 (66.7)	5 (23.8)	2 (9.5)	
Outcome/Primary end points	Recovered (132)	39 (29.5)	66 (50.0)	27 (20.5)	0.6599
	Dead (9)	4 (44.4)	4 (44.4)	1 (11.1)	

The mild to severe hypoxia group was merged to have a non-zero value. This is to avoid having a 100% probability that is statistically deemed irrelevant and practically impossible to measure.

- 45.6% and vitamin D deficiency in the range of 13.2% - 58.8% among different age groups.(9,10) Several reasons have been postulated for high vitamin D deficiency levels, including lack of proper education, lower income, lack of milk in the diet, and insufficient outdoor activity.(9) Corresponding to the enormity of the vitamin D deficiency among the Sri Lankan population, we also observed that 70% of the study population with COVID-19 had insufficient or deficient vitamin D status. However, our study findings did not observe a significant association between the severity of COVID-19 and vitamin D deficiency which is in concordance with other studies. (11,12)

Although studies have associated the status of vitamin D insufficiency and deficiency with hypoxia (13), severity (14), and mortality of COVID-19 infection (15,16), a meta-analysis study after analysing 31 observational studies, found no correlation between the status of vitamin D and the severity of COVID-19. (17) Another meta-analysis conducted with 76 studies found no associations between vitamin D deficiency/insufficiency and mortality in COVID-19, when studies with a high risk of bias or studies reporting unadjusted effect estimates were excluded. (8) In concordance with the above meta-analyses, our study found no significant association between the status of vitamin D and the severity of COVID-19, and

between the status of vitamin D and COVID-19 mortality. Although a significant association was found between the prevalence of hypoxia and the status of vitamin D levels, a significantly higher prevalence of hypoxia was observed in patients with normal vitamin D status as opposed to those with vitamin D insufficiency or deficiency. Vitamin D deficiency did not seem to have an impact on the mortality rate of COVID-19 patients. However, a recent study has suggested that vitamin D deficiency may be considered as a predictor of COVID-19 mortality rather than a side effect.(15)

Studies regarding the correlation between vitamin D and COVID-19 are scanty, and the status of the relationship still remains unclear and needs further studies.(18) Larger, population-size retrospective studies can be conducted using data previously collected during outbreaks to further explore the relation between COVID-19 severity and vitamin D.

Conclusion

Despite the high prevalence of low vitamin D levels (69.5%) among COVID-19 patients, we found no significant association between vitamin D deficiency and COVID-19 severity or outcome of COVID-19 infection.

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