The role of vitamin D as a preventive strategy in COVID-19 infections: evidence from South Asia

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Research Article

Keywords: COVID-19, deficiency, risk factors, Sri Lanka, urban, vitamin D

Posted Date: March 28th, 2024

DOI: https://doi.org/10.21203/rs.3.rs-3964082/v1

Additional Declarations: No competing interests reported.

Abstract

Background

Regional evidence on prevention of COVID-19 and its sequalae by vitamin D remains inconclusive and sparse.

Aim/Objective

This study aimed to determine the association between COVID-19 and Vitamin D deficiency among adults in Colombo District, Sri Lanka.

Methods

A sex-matched case-control study was conducted among 104 RT-PCR-confirmed COVID-19 patients and 104 RT-PCR negative adults recruited from community. Non-fasting blood samples were analysed for serum 25(OH)D using chemiluminescence assay and vitamin D deficiency identified (< 50.0nmol/L).

Results

Cases (34.2; SD = 15.4nmol/L) had significantly lower 25(OH)D compared to controls (39.8; SD = 17.8nmol/L) (p = 0.02) which persisted after adjustments (p = 0.02), along with Sinhalese ethnicity (p < 0.001). VDD was significantly more prevalent in cases (83.7% vs. 71.2%; crude odds ratio (OR) = 2.1; 95%-CI:1.1,4.1), although not an independent COVID-19 predictor (adjusted OR = 1.9; 95%-CI:0.6,5.7). A significantly lower 25(OH)D level was observed in moderate/severe cases (39.7; SD = 12.3nmol/L) vs mild (32.9; SD = 15.8nmol/L) (p = 0.015). Neither low serum concentrations nor deficiency showed an independent relationship with severity (p > 0.05). Diabetes was the sole predictor of COVID-19 severity (p = 0.022).

Conclusions

Vitamin D has potential as a cost-effective primary, but not secondary, preventive strategy.

1. Background

Vitamin D is traditionally recognized for its role in maintaining bone health across all age groups [1]. However, recent studies have revealed its critical influence on the immune system, particularly its capacity in modulating immune responses against respiratory viruses [2–4]. Vitamin D has also been found to decrease the production of inflammatory cytokines, potentially reducing the morbidity and mortality from such infections [2–4].

The emergence of COVID-19 pandemic has brought vitamin D deficiency (VDD) or lower serum 25(OH)D levels to the forefront of medical research, highlighting its strong link with COVID-19 infection [5–7]. Numerous studies [5–7] have evaluated the impact of VDD, predominantly in Caucasian populations experiencing severe forms and death from COVID-19 [5], highlighting the potential importance of vitamin D as a secondary preventive strategy to mitigate disease [8]. Vitamin D has also shown promise in preventing COVID-19 but not received attention to the same extent.

The COVID-19 pandemic has revealed a disproportionate excess of deaths in ethnic minority groups, particularly in Northern US States [9], notably among Black Americans and those of South Asian origin [5]. This disparity has been linked to lower vitamin D levels among them, compared to those with lighter skin [10], supporting the hypothesis that VDD contributes to a disproportionately higher risk of COVID-19. The magnitude of this risk could even be greater among South Asians living close to the equator, whose dark skin tones produce lesser vitamin for the same exposure time. In further exploration, a study from India reported a higher risk of VDD associated with the severity of COVID-19 [11], however the evidence remains inconclusive on the prophylactic benefit of vitamin D for primary prevention of COVID-19.

VDD is currently identified as a major public health problem in South Asia [10], including Sri Lanka [12]. Therefore, this study intended to assess the magnitude of the risk of lower concentrations or deficiency related to vitamin D in the development and progression of COVID-19 in a South Asian country. This evidence would be of value particularly in resource-limited settings, to reduce the burden on over-whelmed healthcare systems, against the less affordable treatment facilities including vaccines available for the ever-changing virus variants [8]. The findings from this study may serve as a foundation for further investigations into the role of vitamin D in combating novel respiratory diseases which could be widely transmitted through airborne routes, especially in countries with poor housing and sanitation.

2. Methods

A matched case-control study was conducted among adults aged 35–74 years residing in the district of Colombo, Sri Lanka during January-August 2021. The cases were RT-PCR confirmed COVID-19 patients admitted to the two major hospitals that were designated as COVID-19 treating centres in Sri Lanka (National Institute of Infectious Diseases (NIID) and Colombo East Base Hospital, Mulleriyawa) [13]. Controls were apparently healthy adults residing in the catchment area of the two hospitals, without a diagnosis of COVID-19 based on a negative RT-PCR. Those who had been living abroad within the past three months were excluded from the study.

The required sample size was 95 participants per group, as per calculated for a matched case control study [14], in order to estimate an odds ratio (OR) of 2.42 for the risk of VDD associated with COVID-19 reported among South Asians in the United Kingdom [6], probability of an exposure-discordant pair of 50.9%, proportion in the control arm of 47.4% based on the prevalence of VDD in Sri Lanka [12], 10% nonresponse, Z value of 1.96, type II error of 0.2, and 5% precision. During recruitment, controls were matched 1:1 by the sex of each case. Cases were recruited consecutively from the hospital inward registers, after checking their eligibility and willingness for participation. Controls were recruited consecutively, each one matched by the sex of the corresponding case, from the register that was maintained by the public health staff of the area for COVID-19 contacts who have been released from their 14-day quarantine period following a negative RT-PCR.

Data were collected by MBBS qualified doctors and trained nurses working in the two designated COVID-19 treating hospitals. An interviewer-administered questionnaire was used to assess the basic characteristics including the information on potential confounders, such as comorbidities (presence of hypertension, diabetes, hypercholesterolemia, cardiovascular and chronic respiratory diseases confirmed by documental evidence, such as diagnosis cards and clinic records), smoking status and alcohol consumption. Body weight and height were measured using standard protocols to determine the body mass index (BMI). The severity of COVID-19 status was determined in cases using the standard classification [15].

A non-fasting venous blood sample of 4 mL was obtained from cases upon hospital admission and from controls upon release from their 14-day quarantine period. It was collected into a plain tube under aseptic conditions and transported at room temperature to the laboratory. Serum 25(OH)D level was measured in nmol/L by a chemiluminescence method using 'DiaSorin LIAISON 25-OH D, Stillwater, Minnesota, USA assay'. This is a direct competitive immunoassay which detects total vitamin D2 and D3 levels; and is shown to be valid and reliable (intra-assay coefficient of variation (CV) of 4.9% and inter-assay coefficient of 5.4%, indicating acceptable level (< 10%); dynamic range between 4–150 ng/mL; sensitivity of ≤ 4 ng/mL and specificity of 100% for both vitamin D2 and D3 [16]. The tests were performed by trained medical laboratory technicians under the supervision of an expert on medical laboratory accreditation. Individuals having serum vitamin D < 50 nmol/L were identified as having 'VDD' and others as 'no VDD' [1].

2.1 Data analysis

The Statistical Package for Social Sciences (SPSS) version 22 was used for data analysis. Data normalcy was assessed using the Kolmogorov-Smirnov test. Normally distributed continuous data were presented as mean and standard deviation (SD) and non-normally distributed data as median and interquartile range (IQR). Categorical data were presented in percentages.

In univariate analysis, significance of the differences between cases and controls in relation to vitamin D level (nmol/L) and other continuous variables was assessed using Mann-Whitney U test; and the differences in relation to VDD and other categorical variables using Chi-squared test and crude OR. To assess the independent relationship of vitamin D level with COVID-19 status, a conditional logistic regression model with adjustments for covariates (age, ethnicity, BMI, smoking and alcohol status, presence of co-morbidities) was applied to determine adjusted p values. The dependent variable was the case/control status. Also, to assess the independent predictors of COVID-19, adjusted ORs were calculated for VDD with adjustments for the same variables in another model. To assess the relationship of vitamin D with severity of the disease, a binary logistic regression model was applied to cases in the same manner, with disease severity (moderate/severe versus mild) as the dependent variable. The models were run using backward likelihood (LR) method and were evaluated using Nagelkerke R, Omnibus test and Hosmer-Lemeshow goodness-of-fit test.

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Review Committee of the Faculty of Medicine, University of Colombo (protocol number EC-20-EM18 approved on 17.12.2020). Informed written consent was obtained from all participants after providing them with an information sheet in the language of their preference. The participation in the study was voluntary and the right of the participant to withdraw from the study at any time without penalty and effect on medical care or loss of benefits was informed and their rights were respected. Privacy and confidentiality were ensured. Blood collection was carried out by a trained nurse as per the World Health Organization Guidelines on best practices in phlebotomy. Those who were found to have low vitamin D levels were referred to the closest Endocrine clinic of state sector hospital and were advised on locally available vitamin D-rich food that can be consumed and sensible sun exposure.

3. Results

A total of 104 cases and 104 sex-matched controls participated in the study. As shown in Table 1, the majority in both groups were educated up to grade 6–11, employed and consuming tobacco and alcohol at the time of recruitment. Cases were predominantly of Sinhalese ethnicity, while the controls had fewer persons with co-morbidities. In both groups, stroke and chronic respiratory conditions were present in less than 5%.

Table 1
Demographic and clinical characteristics of the cases and controls

Characteristics	Cases (n = 104)	Controls (n = 104)	Total
Age (years), Mean (SD)	55.2 (11.9)	46.5 (8.8)	50.8 (11.3)
Age (years), Median (IQR)	55.5 (21.0)	44.0 (14.0)	49.5 (18.8)
Age groups, No. (%)			
< 50 years	37 (35.6)	67 (64.4)	104 (50.0)
50–64	39 (37.5)	34 (32.7)	73 (35.1)
≥ 65	28 (26.9)	3 (2.9)	31 (14.9)
Ethnicity, No. (%)			
Sinhalese	76 (73.1)	31 (29.8)	107 (51.4)
Tamil	16 (15.4)	37 (35.6)	53 (25.5)
Muslim	12 (11.5)	36 (34.6)	48 (23.1)
Highest educational level, No. (%)			
Grade 1–5	16 (15.2)	11 (10.5)	27 (12.9)
Grade 6–11	59 (57.1)	76 (72.4)	136 (64.8)
Grade 12–13	20 (19.1)	17 (16.2)	37 (17.6)
Degree/ Diploma/University education	9 (8.6)	1 (0.9)	10 (4.7)
Current employment status			
Employed	71 (68.3)	95 (91.3)	166 (79.8)
Not employed	33 (31.7)	9 (8.7)	42 (20.2)
Monthly income (LKR ’000), median (IQR)	35 (20)	25 (15)	30 (20)
Co-morbidity status, No. (%)[a]			
Hypertension	34 (32.7)	7 (6.7)	41 (19.7)
Diabetes	38 (36.5)	7 (6.7)	45 (21.6)
Hypercholesterolemia	27 (26.0)	6 (5.8)	33 (15.9)
Myocardial infection	15 (14.4)	3 (2.9)	18 (8.7)
Stroke	5 (4.8)	0 (0.0)	5 (2.4)
Bronchial asthma	22 (21.2)	4 (3.8)	26 (12.5)

Characteristics	Cases (n = 104)	Controls (n = 104)	Total
Chronic obstructive pulmonary disease	4 (3.8)	0 (0.0)	4 (1.9)
Bronchiectasis	0 (0.0)	0 (0.0)	0 (0.0)
Obesity	17 (16.3)	7 (6.7)	24 (11.5)
One or more co-morbid conditions	67 (64.4)	19 (18.3)	86 (41.3)
Smoking status, No. (%)			
Never	31 (29.8)	19 (18.3)	50 (24.0)
Not within last 6 month	50 (48.1)	70 (67.3)	120 (57.7)
Within last 6 months	23 (22.1)	15 (14.4)	38 (18.3)
Alcohol consumption, No. (%)			
Not within last 6 months	27 (25.9)	15 (14.4)	42 (20.2)
Within last 6 months	24 (23.1)	11 (10.6)	35 (16.8)
Body mass index, Mean (SD)	25.2 (5.1)	24.3 (4.4)	24.8 (4.7)
Body composition, No. (%)			
Underweight	10 (9.6)	10 (9.6)	20 (9.6)
Normal	18 (17.4)	25 (24.1)	43 (20.7)
Overweight	59 (56.7)	62 (59.6)	121 (58.2)
Obese	17 (16.3)	7 (6.7)	24 (11.5)

[a] Percentages calculated out of the total number of cases and controls.

3.1 Relationship of vitamin D with the COVID-19 status

Serum 25(OH)D level in the sample ranged between 7.5–97.5 nmol/L, with a median value of 30.0 nmol/L (IQR = 21.2) among cases and 35.9 nmol/L (IQR = 28.3) among controls. The cases presented with a lower mean vitamin D level (34.2 nmol/L; SD = 15.4) compared to the controls (39.8 nmol/L; SD = 17.8) (Fig. 1).

This difference was statistically significant (p = 0.02). When adjusted for confounders, this relationship retained its significance in the regression analysis (p = 0.02) (Table 2).

Table 2
Potential risk factors of COVID-19 infection

Parameter	Cases	Controls	p value*	
	(n = 104)	(n = 104)	Unadjusted	Adjusted
Age, mean (SD)	55.16 (11.9)	46.5 (8.8)	*< 0.001***	0.063
Sinhalese ethnicity, No. (%)	76 (73.1)	31 (29.8)	*< 0.001*	*< 0.001*
Presence of co-morbidities, No. (%)				
Diabetes mellitus	38 (36.5)	7 (6.7)	*< 0.001*	0.151
Hypertension	34 (32.7)	7 (6.7)	*< 0.001*	0.985
Asthma	22 (21.2)	4 (3.8)	*< 0.001*	0.197
Hypercholesterolemia	27 (25.9)	6 (5.8)	*< 0.001*	0.751
Myocardial infarction	15 (14.4)	3 (2.9)	*0.003*	0.221
Stroke	5 (4.8)	0 (0.0)	*0.024*	-***
Chronic obstructive pulmonary disease	4 (3.8)	0 (0.0)	*0.043*	-***
Body mass index, mean (SD)	25.2 (5.1)	24.3 (4.4)	0.1**	0.851
Tobacco use - past 6 months, No. (%)	23 (22.1)	15 (14.4)	0.15	0.558
Alcohol use - past 6 months, No. (%)	24 (23.1)	11 (10.6)	*0.016*	0.374
Serum 25(OH)D levels (nmol/l)	34.2 (15.4)	39.8 (17.8)	*0.02***	*0.026*

*Significant p values in italics; **Mann-Whitney U test applied; *** Not considered in the conditional logistic regression model as 1 cell has 0 value.

The other factors significantly associated with COVID-19 status were (Table 2) older age, Sinhalese ethnicity, presence of co-morbidities, namely diabetes mellitus, hypertension, asthma, hypercholesterolemia, myocardial infarction, stroke and chronic respiratory pulmonary disease, and history of tobacco and alcohol consumption during last six months ($p < 0.05$). Of these, only Sinhalese ethnicity ($p < 0.001$) remained significant in the regression analysis, along with lower vitamin D level.

With regards to the relationship of VDD with COVID-19 status (Table 3), a higher proportion of those with VDD were seen among cases (n = 87; 83.7%) compared to the controls (n = 74; 71.2%). This difference was statistically significant ($p = 0.031$). When adjusted for confounders, it was not significant as an independent predictor, however, those aged 55 and above ($p < 0.001$) and Sinhalese ethnicity ($p < 0.001$) were identified as significant predictors.

Table 3
Significant predictors of COVID-19 infection

Predictor	Unadjusted			Adjusted		
	OR [a]	95% CI [b]	p value	OR	95% CI	p value*
Age ≥ 55 years	3.7	2.0-6.7	*< 0.001*	1.1	1.04–1.18	*0.001*
Sinhalese ethnicity	6.4	3.5–11.7	*< 0.001*	9.1	2.7–30.6	*< 0.001*
Presence of co-morbidities						
Diabetes mellitus	7.9	3.4–18.9	*< 0.001*	3.5	0.9–12.9	0.06
Hypertension	6.7	2.8–16.1	*< 0.001*	1.4	0.3–7.6	0.7
Asthma	6.7	2.2–20.2	*<0.001*	2.6	0.4–17.5	0.32
Hypercholesterolemia	5.7	2.3–14.6	*< 0.001*	1.1	0.1–8.9	0.95
Myocardial infarction	5.7	1.6–20.2	*0.003*	14.7	1.1-204.8	0.05
Obesity/overweight	1.4	0.8–2.5	0.29	1.6	0.5–5.1	0.4
Tobacco use - past 6 months	1.7	0.8–3.4	0.15	1.5	0.3–7.5	0.6
Alcohol use – past 6 months	2.5	1.2–5.5	*0.016*	1.4	0.2–7.9	0.7
Vitamin D deficiency status	2.1	1.1–4.1	*0.031*	1.9	0.6–5.7	0.14

[a] OR indicates odds ratio.

[b] CI denotes confidence interval.

*Significant p values are in italics

3.2 Relationship of vitamin D with the severity of COVID-19

Among the cases, the moderate/severe forms of COVID-19 presented with lower serum 25(OH)D levels (32.9 nmol/L; SD = 15.8) compared to the mild forms (39.7 nmol/L; SD = 12.3) (Fig. 1).

This difference was statistically significant (p = 0.01) (Table 4). However, when adjusted for other potential risk factors, the relationship was not significant. The only risk factor that was significant in the regression analysis was diabetes (42.4% among those with moderate/severe form versus 10.5% among mild form) (p = 0.022).

Table 4
Potential risk factors for the severity of COVID-19 infection

Parameter	**Severity status**		**p value***	
	Mild **(n = 19)**	**Moderate/ severe (n = 85)**	**Unadjusted**	**Adjusted**
Age, mean (SD)	52.9 (11.6)	55.7 (11.9)	0.3**	0.5
Sinhalese ethnicity, No. (%)	14 (73.7)	62 (72.9)	0.95	0.7
Presence of co-morbidities, No. (%)				
Diabetes mellitus	2 (10.5)	36 (42.4)	*0.009*	*0.022*
Hypertension	5 (26.3)	29 (34.1)	0.51	0.8
Asthma	0 (0.0)	22 (25.9)	*0.013*	0.9
Hypercholesterolemia	4 (21.1)	23 (27.1)	0.59	0.6
Myocardial infarction	3 (15.8)	12 (14.1)	0.85	0.8
Stroke	1 (5.3)	4 (4.7)	0.92	0.9
Chronic obstructive pulmonary disease	0 (0.0)	4 (4.7)	0.34	0.3
Body mass index, mean (SD)	25.9 (5.4)	25.0 (4.9)	0.8**	0.4
Tobacco use - past 6 months, No. (%)	4 (21.1)	19 (22.4)	0.9	0.9
Alcohol use - past 6 months, No. (%)	4 (17.4)	20 (23.5)	0.82	0.8
Serum 25(OH)D levels (nmol/l)	39.7 (12.3)	32.9 (15.8)	*0.015***	0.2
*Significant p values in italics				
**Mann-Whitney U test applied				

4. Discussion

In our case-control study, a significantly lower concentration of 25(OH)D was noted among COVID-19 cases compared to the sex-matched controls. This relationship persisted even after adjusting for age, BMI and co-morbidities. In contrast, VDD, though significantly more prevalent in cases, was not an independent predictor of COVID-19 infection. Similarly, low serum concentrations nor deficiency showed an independent relationship with the severity or mortality of COVID-19, despite a significantly lower

25(OH)D level observed in moderate/severe cases compared to those with mild forms. This suggests that vitamin D may serve as a primary preventive strategy, but not as a secondary preventive strategy in COVID-19 infection.

Observational studies, including a few notable studies conducted in Asia [11, 17–20] and elsewhere have investigated the relationship between vitamin D and COVID-19. Early studies using population-level databases suffered from time-lag bias, with the actual vitamin D status not reflected well in the participants, as it was measured before the COVID-19 testing [5, 17, 21]. Subsequent case-control studies [6], included healthy individuals from population-based cohorts who were not screened for a negative diagnosis of COVID-19 as controls, leading to misclassification bias. Recent studies conducted in non-Caucasian populations in Saudi Arabia [18], China [20] and India [11] aimed to address these methodological issues, using hospitalized patients with minimum selection bias. Our study provides both supporting and contrasting evidence in this global context.

Our study emphasized that lower vitamin D levels were associated with a higher risk of COVID-19. The difference was significant at both unadjusted and adjusted p values ($p = 0.02$). The findings align with other case-control studies [6, 8, 11, 18], except one study from India showing no difference between the cases and controls ($p = 0.757$) [11]. Furthermore, of the traditionally known risk factors of COVID-19 [22], only ethnicity ($p < 0.001$) was retained in our final model, while none of the pre-existing chronic conditions and BMI exhibited the expected associations. As suggested by some studies, the risk for COVID-19 may be multifactorial and related to the clustering of risk factors rather than individual factors [23]. Nevertheless, when interpreting results, it is important to note that all these studies face a common challenge in ascertaining the temporal relationship, where the vitamin D levels were assessed only after the disease onset. Assuming that vitamin D levels remain stable and unaffected by acute viral infections [24], the current evidence favours vitamin D in preventing COVID-19 infection.

Despite having vaccines with modest success, additional preventive strategies remain important, particularly in resource-limited settings, where the availability of and access to vaccines are major challenges during epidemics. In this backdrop, our study emphasizes the potential of vitamin D supplementation, particularly in countries like Sri Lanka, where there are no routine supplementation programmes. Despite being a tropical country with an abundance of sunlight, there are less opportunities for sun exposure, especially in urban areas, due to sedentary jobs and societal preferences for fair skin, thus contributing to VDD [10]. This justifies the need for supplementation, at least for vulnerable groups, such as the elderly and those with immuno-suppressive conditions like diabetes. However, recommendations for supplementation should be made cautiously, as there is currently no national consensus on dosage and route of administration, which could lead to irrational use, such as over-dosing and toxicity, over-prescribing and exploitations by pharmaceutical companies.

Vitamin D supplementation has demonstrated immune modulation properties, reducing the risk of acute respiratory infections by 32–60%, and its preventive and safe impact [25]. This suggests that it could be a cost-effective preventive strategy not only for COVID-19, but also for other respiratory viruses in future pandemics. During the COVID-19 pandemic, healthcare resources in Sri Lanka were primarily directed towards preventing the spread of the disease. Human resources were mobilized for island-wide contact tracing, quarantine and providing isolation facilities to patients [13], while many health institutions were converted to quarantine centres or isolation wards, leaving long-term care for chronic diseases neglected in the country.

With regards to VDD, studies from China [20] and India [11] have shown a strong relationship with COVID-19, using extreme cut-off values such as 62.5 nmol/L [20] and 30 nmol/L [11]. In comparison, our study demonstrated a two-fold risk of VDD for COVID-19 but failed to show it as an independent predictor (OR = 1.9; 95% CI: 0.6–5.7; p = 0.14). This could be due to disease development taking place at much lower vitamin D levels in Sri Lankans. This warrants further exploration, especially when determining target groups for vitamin D supplementation.

Our study did not support the growing evidence linking vitamin D levels or deficiency to the severity of COVID-19 [26, 27]. Though significant in univariate analysis, vitamin D lost its significance when adjusted for confounders. Instead, diabetes emerged as the sole predictor of disease severity (p = 0.022), highlighting the bigger role played by it than vitamin D in determining the severity. This was in line with other case-control studies [28]. Changes in glucose homeostasis, immunological status and inflammation are possible pathogenetic links with diabetes mellitus [29]. Given the high prevalence of diabetes in the country [30], controlling diabetes becomes a critical secondary preventive strategy for COVID-19 in Sri Lanka.

Our study did not assess mortality as an outcome due to the absence of deaths among the cases. Sri Lanka reported exceptionally low mortality rates during the pandemic, further highlighting the role of vitamin D in primary prevention.

There were some strengths of this study. Controls were matched by sex of each case, eliminating a major confounder in interpretations. Misclassification bias related to controls, which was a major limitation in previous studies, was minimized by identifying apparently healthy, non-infected controls with a negative COVID-19 diagnosis confirmed at the end of 14-day quarantine period. Vitamin D was measured using valid and reliable assays with standard protocol and cut-off values. There were some limitations. Mortality could not be studied due to 100% survival among cases. Also, the findings apply to hospitalized patients with pre-existing conditions and not to the general community, thus leading to selection bias.

5. Conclusions and Recommendations

Serum vitamin D level was significantly lower in COVID-19 patients compared to non-COVID-19 healthy controls, along with ethnicity that is known to influence the development. VDD, however, was not an independent predictor of COVID-19. Though significantly higher in moderate/severe cases compared to mild cases, lower serum vitamin D did not assume an independent relationship with disease severity. Instead, diabetes emerged as the sole predictor of severity. Our study underscores the potential of vitamin D as a cost-effective primary preventive strategy, but not as a secondary preventive strategy, especially in regions with high vitamin D deficiency. However, clinical trials are needed to validate these findings and explore the full benefit of vitamin D supplementation.

Declarations

Funding: This research was funded by the World Bank (https://www.worldbank.org/en/home) through the COVID-19 Emergency Response and Health System Preparedness (ERHSP) Project of the Ministry of Health, Sri Lanka (LK-MoH-224251-NC-RFQ) awarded to CA. The funders had no role in data collection and analysis, decision to publish, or preparation of the manuscript.

Competing interests: The authors declare that there is no conflict of interest.

Data availability statement: The datasets generated during and/or analysed during the current study are not publicly available because no prior permission has been granted from the participants, hospital authorities or the Ethics Review Committee, Faculty of Medicine, University of Colombo for uploading raw data files in order to preserve individuals' privacy but are available from the corresponding author on reasonable request. A non-author point-of-contact that can field data access queries is Chairperson, Ethics Review Committee, Faculty of Medicine, University of Colombo, Sri Lanka (ethicscommitteemfc@gmail.com).

Code availability: Not applicable.

Author Contributions: C.A., N.G. and D.A. conceptualized the study. C.A. was the principal investigator involved in methodology, analysis and drafting the manuscript. S.W. contributed to laboratory testing. R.S. was involved in data collection, analysis and drafting the manuscript. All authors contributed to interpretation of the data. All authors have read and approved the final manuscript.

Compliance with Ethical Standards: The study was conducted in accordance with the 1964 Declaration of Helsinki and approved by the Ethics Review Committee of the Faculty of Medicine, University of Colombo (protocol number EC-20-EM18 approved on 17.12.2020). Data collection commenced from January 2021 to August 2021. Informed written consent was obtained from all participants after providing them with an information sheet in the language of their preference. The participation in the study was voluntary and the right of the participant to withdraw from the study at any time without penalty and effect on medical care or loss of benefits was informed and their rights were respected. Privacy and confidentiality were ensured. Blood collection was carried out by a trained nurse as per the World Health Organization Guidelines on best practices in phlebotomy. Those who were found to have low vitamin D levels were referred to the closest Endocrine clinic of state sector hospital and were advised on vitamin D-rich food that can be consumed and sensible sun exposure. The authors have no conflict of interest and the World Bank, which funded the study, had no role in data collection and analysis, decision to publish, or preparation of the manuscript.

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Figures

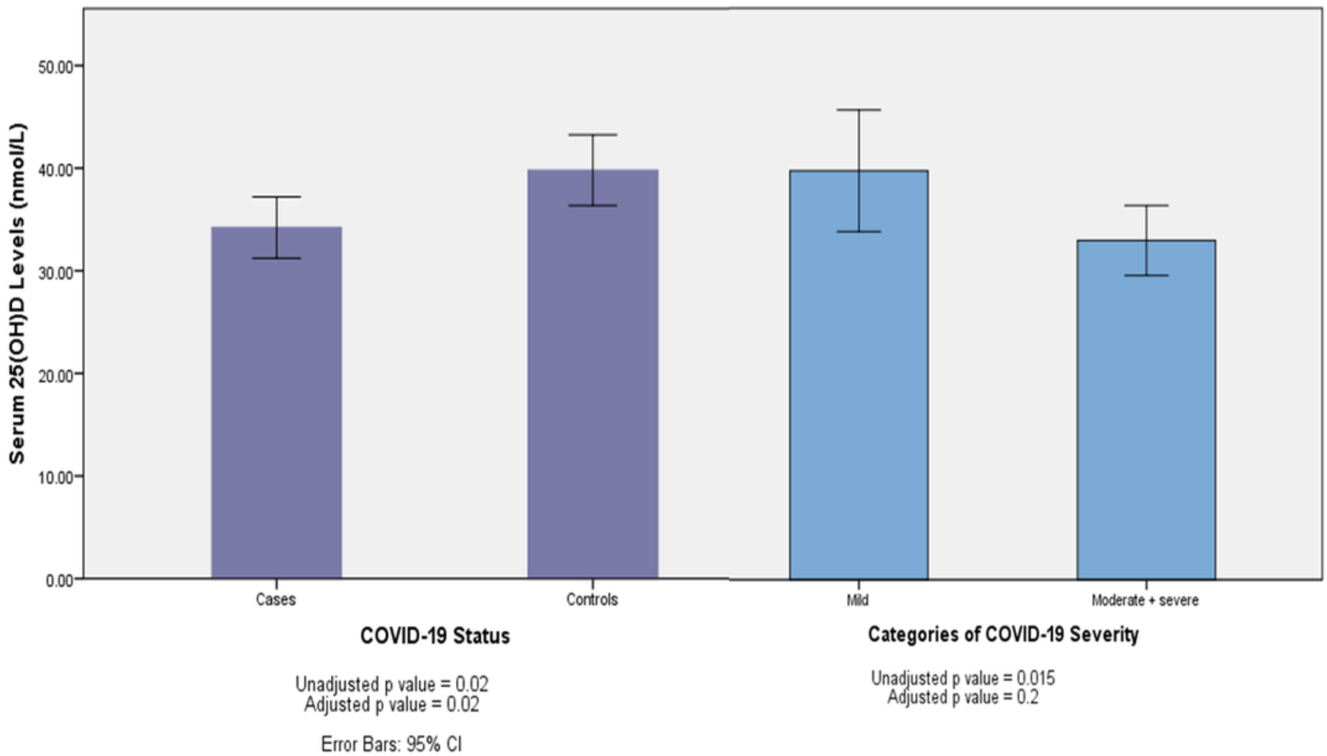

Figure 1

Serum 25(OH)D levels in cases and controls and according to COVID-19 disease severity status