

# Vitamin D Status and Severe COVID-19 Disease Outcomes in Hospitalized Patients

Journal of Primary Care & Community Health  
Volume 12: 1–7  
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DOI: 10.1177/21501327211041206  
journals.sagepub.com/home/jpc



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## Abstract

**Background:** Vitamin D deficiency may increase the risk of severe COVID-19 disease. **Objectives:** To determine if 25-hydroxyvitamin D [25(OH)D] levels in patients hospitalized for COVID-19 were associated with the clinical outcomes of days on oxygen, duration of hospitalization, ICU admission, need for assisted ventilation, or mortality. **Methods:** We conducted a retrospective study of 92 patients admitted to the hospital with SARS-CoV-2 infection between April 16, 2020 and October 17, 2020. Multivariable regression was performed to assess the independent relationship of 25(OH)D values on outcomes, adjusting for significant covariates and the hospitalization day the level was tested. **Results:** About 15 patients (16.3%) had 25(OH)D levels <20 ng/mL. Only 1 patient (3.4%) who had documented vitamin D supplementation prior to admission had 25(OH)D <20 ng/mL. Serum 25(OH)D concentrations were not significantly associated with any of our primary outcomes of days on oxygen, duration of hospitalization, intensive care unit (ICU) admission, need for mechanical ventilation, or mortality in any of the adjusted multivariable models. Adjusting for the hospital day of 25(OH)D sampling did not alter the relationship of 25(OH)D with any outcomes. **Conclusion:** Vitamin D status was not related to any of the primary outcomes reflecting severity of COVID-19 in hospitalized patients. However, our sample size may have lacked sufficient power to demonstrate a small effect of vitamin D status on these outcomes.

## Keywords

25-hydroxyvitamin D, severe acute respiratory syndrome coronavirus 2, COVID-19, critical care

Dates received: 1 June 2021; revised: 2 August 2021; accepted: 4 August 2021.

## Introduction

Symptomatic COVID-19, caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can manifest as mild to severe illness.<sup>1</sup> Clinical manifestations can vary but most commonly involve fever and respiratory symptoms.<sup>2,3</sup> It has been hypothesized that vitamin D deficiency may increase the risk of severe SARS-CoV-2 infection.<sup>4–6</sup> The original basis for this hypothesis was based on pre-COVID-19 observational studies that showed an inverse association of lower vitamin D levels with upper respiratory tract infections.<sup>7,8</sup> Additionally a meta-analysis reviewing 25 randomized double blind placebo controlled trials with 11 321 participants completed by the end of 2015 found that vitamin D supplementation reduced the risk of acute respiratory tract infections, particularly in those with 25-hydroxyvitamin D [25(OH)D] levels <10 ng/mL (25 nmol/L).<sup>9</sup>

Specific to COVID-19 disease, vitamin D has been implicated in modulating both the innate and adaptive immune response pathway, both of which are involved in the immune response to SARS-CoV-2.<sup>10,11</sup> Vitamin D facilitates immunocompetence through activating the innate immune system when antigens present to respiratory epithelial cells which in turn convert 25(OH)D to 1,25-dihydroxyvitamin D [1,25(OH)<sub>2</sub>D]. This in turn activates antigen presenting macrophages to recruit neutrophils and T cells to the infection site, as a part of the “intracrine” non-endocrine mechanism of vitamin D. Sufficient 1,25(OH)<sub>2</sub>D

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is important for promotion of the synthesis of a number of proteins (cathelicidin, beta-defensin2, nucleotide-binding oligomerization domain-containing protein 2 [NOD2]) and suppression of hepcidin, which enhances microbial killing through increased induction of proinflammatory cytokines, migration of immune cells to the site of infection and clearance of respiratory pathogens through induced apoptosis and autophagy of infected epithelial cells.<sup>10</sup> Additionally, it has been hypothesized that cytokine storm may contribute to severe COVID-19 in some patients and 1,25(OH)<sub>2</sub>D has been shown to reduce cytokines associated with cytokine storm in acute viral infections.<sup>10,12</sup>

A cohort study in Switzerland found that 25(OH)D levels were significantly lower in PCR-positive COVID-19 patients versus PCR-negative controls.<sup>13</sup> A case control study in Belgium of PCR-positive COVID-19 patients compared to seasonally matched controls found similar 25(OH)D levels in females but significantly lower levels in males with COVID-19 infection compared to seasonally matched controls.<sup>14</sup> Early in the pandemic, Ilie et al<sup>15</sup> compared the incidence and mortality from COVID-19 in 20 European countries with previously published data on mean 25(OH)D levels and found an inverse correlation between 25(OH)D levels and incidence of COVID-19 cases and mortality from COVID-19. Similarly, an analysis of subjects from 20 European countries, also done early in the pandemic, found that countries with lower average vitamin D levels had increased rates of COVID-19 cases, although there was no correlation between mean vitamin D levels and mortality from COVID-19.<sup>16</sup> In contrast, a review of biobank participants did not show any link between 25(OH)D concentrations and the risk of COVID-19 infection. This correlation, however, was based on 25(OH)D levels obtained from stored samples taken 10 to 14 years prior to the pandemic.<sup>17</sup>

Therefore, our aim was to determine if 25(OH)D levels in patients hospitalized for COVID-19 were associated with the clinical outcomes of days on oxygen, duration of hospitalization, ICU admission, need for assisted ventilation, or mortality. These endpoints were chosen as potential markers of severity of illness.

## Methods

We conducted a retrospective study of a random selection of 92 patients admitted to the hospital with a SARS-CoV-2 infection between April 16, 2020 and October 17, 2020. Serum samples were collected through the Mayo Clinic COVID-19 Biobank. 1,25(OH)<sub>2</sub>D is the biologically active form of vitamin D but has a relatively short half-life; thus 25(OH)D was measured to assess vitamin D status.<sup>18</sup> We compared 25(OH)D levels in blood samples obtained during hospitalization for the primary outcomes of days on oxygen,

duration of hospitalization, ICU admission, need for assisted ventilation and mortality.

Secondary outcomes of Acute Physiology and Chronic Health Evaluation IV (APACHE IV) scores (for patients admitted to the ICU), need for oxygen supplementation, and need for vasopressors were also evaluated. Demographic and patient specific data collected included age, sex, vitamin D supplement in the outpatient medication list pre-hospitalization, and underlying medical conditions listed by the Centers for Disease Control (CDC)<sup>19</sup> as increasing the risk for severe COVID-19 infection. For this study, vitamin D deficiency was defined as a 25(OH)D level <20 ng/mL as designated by the Institute of Medicine.<sup>20</sup>

This study was approved by the Mayo Clinic Institutional Review Board. Only patients who had a valid research authorization on file were included in this study.

## Statistical Analysis

JMP 14.1.0 (SAS Institute Inc., Cary, NC) was used to perform statistical analysis. Because many of the continuous variables had skewed distributions, they were reported as medians with inter-quartile ranges and compared with non-parametric Wilcoxon/Kruskall-Wallis tests. Proportions were compared with the chi-square test or Fisher exact test, as appropriate. Unadjusted analysis comparing vitamin D deficiency versus sufficiency with our primary and secondary outcomes was performed.

Linear regression was performed to assess the relationship between continuous variables. Multivariable linear regression was performed to assess the independent relationship of 25(OH)D values on outcomes of duration of hospitalization and number of days requiring oxygen, while adjusting for other variables. Multivariable logistic regression was performed to evaluate the independent relationship of 25(OH)D values on outcomes of mortality, ICU admission, and need for assisted ventilation, while adjusting for other variables. *P* values <.05 were considered significant.

Multivariable analyses included variables that were significantly related with the outcome in bivariate analyses as independent variables in the adjusted models. 25(OH)D was included as a continuous variable in all models to determine if adjusting for other variables would result in 25(OH)D being independently associated with outcomes.

## Results

Demographics, comorbidities, and outcomes for the total cohort as well as for vitamin D sufficient and deficient patients are shown in Table 1.

Fifteen patients (16.3%) had 25(OH)D levels <20 ng/mL, though only 2 patients had levels <10 ng/mL. Twenty

**Table 1.** Subject Characteristics and Vitamin D Status of 92 Patients Hospitalized for Covid-19.

Characteristic	Total	25 (OH)D		P value
		≥20 ng/mL N=77	<20 ng/mL N=15	
Median age (years, IQR)	61 (50-74)	63 (52-77)	48 (36-61)	<.01
Male sex (n, %)	52 (56.5)	45 (58.4)	7 (46.7)	.4
Race <sup>a</sup>				
White (n, %)	64 (69.6)	58 (75.3)	6 (40)	<.01
Non-white	28 (30.4)	19 (24.7)	9 (60)	
Medications				
Dexamethasone (n, %)	68 (73.9)	58 (75.3)	10 (66.7)	.48
Remdesivir (n, %)	69 (75.0)	58 (75.3)	11 (73.3)	.87
Tocilizumab (n, %)	10 (10.8)	9 (11.7)	1 (6.7)	.57
Vitamin D supplement as outpatient (n, %)	29 (31.5)	28 (36.4)	1 (6.7)	.02
Median 25(OH)D (ng/mL, IQR)	36 (26-43)	38 (31-45)	15 (11-16)	<.001
25(OH)D < 20 ng/mL (n, %)	15 (16.3)			
Median serum sample hospital day (IQR)	4 (3-6)	4 (3-6)	4 (4-6)	.39
Median CRP (mg/L, IQR)	49 (11-70)	52 (13-730)	34 (5-63)	.13
Comorbidities				
Asthma (n, %)	22 (23.9)	19 (24.7)	3 (20)	.70
Obesity (n, %)	33 (35.9)	28 (36.4)	5 (33.3)	.82
Diabetes (n, %)	29 (31.5)	26 (33.8)	3 (20)	.29
Hypertension (n, %)	56 (60.9)	53 (68.8)	3 (20)	<.001
Coronary artery disease (n, %)	23 (25)	23 (30)	0	.01
Cardiomyopathy (n, %)	3 (3.3)	3 (3.9)	0	.44
Congestive heart failure (n, %)	9 (9.8)	9 (11.7)	0	.16
COPD (n, %)	14 (15.2)	13 (16.9)	1 (6.7)	.31
Chronic kidney disease (n, %)	16 (17.4)	16 (20.8)	0	.05
Pulmonary fibrosis (n, %)	16 (17.4)	14 (18.2)	2 (13.3)	.65
Sickle cell disease (n, %)	1 (1.1)	1 (1)	0	.66
Solid organ transplant (n, %)	8 (8.7)	8 (10.4)	0	.19
Outcomes				
Required supplemental oxygen (n, %)	88 (95.7)	74 (96.1)	14 (93.3)	.63
Median days on oxygen (IQR)	5 (4-8)	5 (3-8)	6 (4-12)	.33
ICU admission (n, %)	63 (68.5)	54 (70.1)	9 (60)	.44
Assisted ventilation (n, %)	12 (13.0)	8 (10.4)	4 (26.7)	.09
Vasopressors utilized (n, %)	6 (6.6)	4 (5.3)	2 (13.3)	.25
Median APACHE IV hospital death prediction (%; IQR) <sup>b</sup>	7.6 (4.6-13.7)	7 (5-14)	6 (5-7)	.19
Median length of hospital stay (days, IQR)	7 (5-9)	7 (5-9)	6 (5-12)	.74
Median length of ICU stay(days, IQR) <sup>b</sup>	6.9 (5-9.1)	6.9 (5-9.4)	5.9 (5.1-9)	.71
Mortality (n, %)	7 (7.6)	6 (7.8)	1 (6.7)	.88

Abbreviations: 25(OH)D, 25-hydroxyvitamin D3; APACHE IV, acute physiology and chronic health evaluation IV; CRP, C-reactive protein; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; IQR, interquartile range.

<sup>a</sup>Fisher's exact test.

<sup>b</sup>Limited to 63 patients admitted to ICU.

nine patients (31.5%) had vitamin D listed in their outpatient medication list. Of these patients, only 1 patient had a 25(OH)D concentration <20 ng/mL.

In a bivariate analysis (Table 1), non-whites and those not taking vitamin D supplementation were more likely to have 25(OH)D levels <20 ng/mL. The median age for patients with 25(OH)D levels <20 ng/mL was significantly

lower than those with levels in the sufficient range. Median 25(OH)D levels in deficient patients were 15 ng/mL compared to a median level of 38 ng/mL in those who were sufficient. Patients with a diagnosis of hypertension and coronary artery disease were more likely to be vitamin D sufficient than deficient. In our univariate analysis we found no relationship of any of our outcomes (days on oxygen,

duration of hospitalization, ICU admission, need for assisted ventilation and mortality) with 25(OH)D status. Additionally, in ICU patients there was no difference in median APACHE IV scores or need for vasopressors between those with and without vitamin D deficiency. Vitamin D deficiency was also not associated with need for supplemental oxygen. Serum 25(OH)D values were not related with CRP values ( $r = -.01$ ;  $P = .91$ ).

Table 2 shows the association of primary outcomes with clinical variables. Documented outpatient vitamin D supplementation prior to hospitalization was not associated with better outcomes, despite improved vitamin D status. Multivariable analyses of the relationship of 25(OH)D levels with outcomes were performed, adjusting for the day of 25(OH)D sampling and significant variables in the univariate analyses (Table 3). Serum 25(OH)D concentrations were not independently associated with any of the primary outcomes in the adjusted analyses. We also explored the effect of age and the interaction of age and 25(OH)D levels on primary outcomes. In adjusted analyses, the interaction of age with 25(OH)D level was not significant for any outcome. Model outcomes did not materially change with use of 25(OH)D as a continuous or binary variable with 20 ng/mL as a cut point.

A retrospective power analysis showed that for comparison of 2 groups above and below the median 25(OH)D level, our sample size would have 80% power to detect a difference in length of hospital duration of 3.4 days (SD 5.8 days) and length of use of oxygen of 3.5 days (SD 6.0 days) between the 2 groups with 95% confidence.

## Discussion

Vitamin D status, as measured by 25(OH)D concentrations, was not associated with COVID-19 severity in hospitalized patients, as measured by days of oxygen use, duration of hospitalization, need for ICU admission, need for mechanical ventilation, APACHE IV score (in ICU patients) or mortality. Our results were similar with analysis of 25(OH)D as a continuous variable or as a dichotomous variable. Vitamin D supplementation prior to hospitalization was associated with a lower risk of vitamin D deficiency but was not associated with better outcomes.

The accumulating literature for the potential contribution of vitamin D in SARS-CoV-2 infection, largely originating outside of the US, has had mixed results. In a hospitalized cohort of patients in Belgium with COVID-19, lower median 25(OH)D levels on admission were associated with greater mortality. Their study population was older than ours, and fewer comorbidities were included in the adjusted analysis.<sup>14</sup> Hospitalized patients in Spain with 25(OH)D levels  $< 20$  ng/mL on admission had a longer length of hospitalization. However, 25(OH)D status was unrelated to ICU admission, need for assisted

ventilation, or in-hospital death.<sup>21</sup> Vitamin D deficiency (defined as levels  $< 12$  ng/mL) in patients hospitalized with COVID-19 in the United Arab Emirates was significantly associated with the need for ICU admission and mortality.<sup>6</sup> All of these studies had a greater proportion of patients with vitamin D deficiency (59%, 82%, and 66%, respectively) compared with our population, where only 16% were vitamin D deficient.<sup>6,14,21</sup>

Several investigators have evaluated the role of vitamin D supplementation in COVID-19 disease and severity. A retrospective study of older patients hospitalized for COVID-19 in France found that those who were given regular bolus vitamin D<sub>3</sub> supplementation (20 000-50 000 IU/month) had a lower likelihood of mortality at day 14 compared to those who did not (7% vs 31%).<sup>4</sup> Additionally, a non-peer reviewed, open label, randomized trial in Spain found that hospitalized COVID-19 patients supplemented with oral calcifediol had a 55% decrease in mortality and were less likely to require ICU admission compared with untreated patients.<sup>20</sup> Randomization was done by ward, with the treated cases having less men and higher baseline 25(OH)D levels in comparison to the control group.<sup>22</sup> As male gender is recognized as a potential risk factor for ICU admission and mortality from COVID-19 this difference between groups has the potential to affect results.<sup>23</sup> In a randomized controlled trial in patients hospitalized with moderate to severe COVID-19 in Brazil, a single dose of 200 000 IU of vitamin D<sub>3</sub> had no effect on the primary outcome of duration of hospitalization nor secondary outcomes of in-hospital death, ICU admission or need for assisted ventilation.<sup>24</sup> Notably, prior to the COVID-19 pandemic, a randomized controlled trial of bolus vitamin D supplementation in critically ill patients with baseline 25(OH)D levels  $< 20$  ng/mL, showed no benefit of vitamin D supplementation on mortality.<sup>25</sup>

Our study results are limited by the observational study design, which is subject to confounding by unmeasured variables that may be related to both vitamin D status and disease outcome. If we had found an association between vitamin D status and COVID-19 outcomes, it would have been difficult to determine if the vitamin D status was the cause or the effect of the disease outcome. For example, 25(OH)D levels may be suppressed by inflammation and acute illness.<sup>26,27</sup> However, we found no relationship between CRP and 25(OH)D concentrations or any of the hospital outcomes. The 25(OH)D measurements were done on biobank samples obtained at varying time points during hospitalization, and the duration of illness itself may have altered vitamin D status. Most samples were drawn between hospital days 3 and 6, and we found no significant relationship between 25(OH)D values and the serum sample hospital day. The serum sample hospital day was not significantly associated with any of our primary outcomes and adjusting for the sample hospital day in multivariable analyses did not

**Table 2.** Association of Subject Characteristics with Outcomes in 92 Patients Hospitalized for Covid-19.

Characteristic	Mean length of stay difference (d)	Oxygen duration difference (d)	ICU admission	ICU ventilation	Death
			Odds ratio	Odds ratio	Odds ratio
Age (years, $\beta$ )	.02 (-.05, .09)	.009 (-.06, .08)	-.01 (-.04, .01)	0.0 (-.04, .04)	-.085 (-.16, -.03)**
Male sex	1.5 (-.9, 3.9)	1.9 (-.6, 4.4)	1.1 (.45, 2.6)	1.1 (.32, 3.7)	5.1 (.59, 44)
Non-White race	1.3 (-1.3, 3.9)	-.70 (-2.1, .65)	.96 (.37, 2.5)	2.6 (.77, 9.1)	.91 (.17, 5.0)
Medications					
Dexamethasone	2.3 (-.4, 5.0)*	2.6 (-.2, 5.4)**	4.9 (1.8, 13)**	1.9 (.38, 9.4)	2.2 (.25, 20)
Remdesivir	4.2 (1.5, 6.8)***	4.4 (1.6, 7.1)***	4.3 (1.6, 12)**	1.8 (.36, 8.8)	.82 (.15, 4.5)
Tocilizumab	1.9 (-1.5, 6.2)	3.8 (-.1, 7.8)	1.1 (.26, 4.5)	1.8 (.33, 9.7)	8.4 (1.5, 45)*
Vitamin D supplement as outpatient	1.3 (-1.5, 3.7)	.1 (-2.6, 2.8)	1.3 (.50, 3.5)	1.1 (.30, 4.0)	1.7 (.36, 8.2)
25(OH)D (ng/mL, $\beta$ )	.002 (-.04, .04)	.007 (-.03, .05)	-.002 (-.02, .01)	.02 (-.01, .06)	-.001 (-.02, .04)
25(OH)D < 20 ng/mL	.44 (-2.8, 3.7)	-.67 (-2.4, 1.0)	.64 (.20, 2.0)	3.1 (.81, 12)	.85 (.09, 7.6)
Serum sample hospital day (d, $\beta$ )	.97 (.52, 1.4)***	.58 (.09, 1.07)*	-.05 (-.26, .13)	-.48 (-.81, -.21)**	-.040 (-.29, .32)
CRP (mg/L, $\beta$ )	.02 (-.006, .04)	.01 (-.01, .03)	.000 (-.008, .008)	-.005 (-.01, .005)	-.007 (-.02, .005)
Comorbidities					
Asthma	2.7 (-.1, 5.5)	1.8 (-1.1, 4.7)	.58 (.21, 1.6)	2.6 (.74, 9.4)	10 (1.8, 56)**
Obesity	.03 (-2.5, 2.6)	.2 (-2.4, 2.8)	.57 (.23, 1.4)	.56 (.14, 2.2)	.28 (.03, 2.4)
Diabetes	1.0 (-1.5, 3.6)	.9 (-1.8, 3.6)	.65 (.26, 1.7)	1.1 (.30, 4.0)	1.7 (.36, 8.2)
Hypertension	-1.4 (-3.9, 1.1)	-2.3 (-4.8, .2)*	1.1 (.47, 2.8)	.60 (.18, 2.0)	4.2 (.48, 36)
Coronary artery disease	1.3 (-1.4, 4.1)	.2 (-2.7, 3.1)	1.4 (.49, 4.1)	1.0 (.25, 4.1)	4.6 (.95, 23)
Cardiomyopathy	1.3 (-5.5, 8.1)	-.9 (-8.0, 6.1)		3.5 (.30, 42)	6.9 (.55, 88)
Congestive heart failure	1.7 (-2.3, 5.8)	1.5 (-2.7, 5.7)	1.7 (.33, 8.7)	2.1 (.38, 11)	4.5 (.73, 27)
COPD	4.9 (1.7, 8.1)	3.7 (.3, 7.1)	.39 (.12, 1.3)	2.1 (.49, 8.9)	10 (1.9, 51)**
Chronic kidney disease	1.5 (-1.7, 4.7)	.1 (-3.2, 3.4)	1.5 (.43, 5.0)	.94 (.19, 4.8)	4.2 (.83, 21)
Pulmonary fibrosis	2.2 (-1.0, 5.4)	1.8 (-1.5, 5.1)	1.0 (.32, 3.2)	.94 (.19, 4.8)	17 (2.9, 98)**
Sickle cell disease	-3.5 (-15, 8.2)	-3.9 (-16, 8.1)			
Solid organ transplant	3.9 (-.3, 8.1)	3.3 (-1.1, 7.7)		.95 (.11, 8.5)	1.9 (.19, 18)
Outcomes					
Required supplemental oxygen	2.8 (-3.1, 8.7)		7.2 (.7, 72)		
Days on oxygen (d, $\beta$ )	.88 (.79, .96)***		-.31 (-.51, -.14)**	-.17 (-.29, -.08)**	-.09 (-.17, .01)
ICU admission	4.3 (1.8, 6.7)***	4.5 (1.9, 7.0)***			1.2 (.21, 6.4)
Assisted ventilation	9.3 (6.2, 12)***	8.0 (4.7, 11)***			12.8 (2.4, 68)**
Vasopressors utilized	12 (7.3, 16)**	10.6 (6.0, 15)*			8.0 (1.2, 55)*
Length of hospital stay (d, $\beta$ )		.94 (.85, 1.0)***	-.35 (-.58, -.16)**	-.21 (-.35, -.11)***	-.09 (-.18, .02)
Mortality	4.5 (0, 8.9)	4.8 (.2, 9.4)	1.2 (.21, 6.4)	13 (2.4, 68)**	

Abbreviations: 25(OH)D, 25-hydroxyvitamin D3; CRP, C-reactive protein; COPD, chronic obstructive pulmonary disease.

Values are shown with 95% confidence intervals in parentheses. Linear or logistic regression parameter estimates ( $\beta$ ) are shown for relationships with continuous independent variables.

\* $P < .05$ , \*\* $P < .01$ , \*\*\* $P < .001$  by nonparametric Wilcoxon/Kruskall-Wallis test, or chi-square test for categorical variables and linear or logistic regression for continuous variables.

alter the results. Another potential limitation in our study design is that our study population was comprised of Mayo Clinic COVID-19 Biobank patients and it is possible that patients who declined participation in the Biobank study may have differed from those that agreed to participate. Finally, our sample size may have lacked sufficient power to demonstrate an effect of vitamin D status on our measured outcomes, particularly those occurring with a low frequency, like mortality and the need for mechanical ventilation. Our study population had a lower incidence of vitamin D deficiency than we anticipated based on other published reports which likely adversely affected the power

of our study.<sup>6,14,21</sup> However, if our sample size led to inadequate power to detect a small but important benefit of vitamin D, we feel our findings could still be helpful for future authors interested in performing a meta-analysis to further study the potential role of vitamin D in severity of COVID-19 disease.

## Conclusion

Vitamin D status was not related to any of the primary outcomes reflecting severity of COVID-19 in hospitalized patients. A greater sample size or meta-analysis of multiple



**Table 3.** Multivariable Models<sup>a</sup> Assessing the Association of 25(OH)D Levels on Outcomes.

Characteristic	Length of stay (d)	Oxygen duration (d)	ICU admission	ICU ventilation	Death
			Odds ratio	Odds ratio	Odds ratio
Age >65 years					9.3 (.78, 111)
Dexamethasone			4.9 (1.8, 14)		
Remdesivir	1.83 (.72, 2.95)	2.4 (1.1, 3.6)			
25(OH)D (ng/mL, $\beta$ )	.011 (-.02, .04)	.017 (-.018, .053)			
Serum sample hospital day (d, $\beta$ )	.42 (-.02, .86)	.10 (-.35, .55)	-.002 (-.20, .20)	.46 (.16, .76)	.09 (-.31, .49)
25(OH)D < 20 ng/mL			.71 (.21, 2.4)	2.8 (.58, 13)	1.6 (.10, 27)
Hypertension		-1.4 (-2.5, -.32)			
Pulmonary fibrosis					12.5 (2.0, 78)
Assisted ventilation	2.0 (.10, 4.0)				
Vasopressors utilized	3.6 (1.0, 6.2)	5.5 (3.3, 7.7)			

<sup>a</sup>Multivariable linear regression was performed for outcomes with continuous variables; multivariable logistic regression was used for binary outcomes. Serum 25(OH)D values <20 ng/mL and age >65 years were included in the logistic regression models for ease of interpretation.

studies could better clarify the role of vitamin D status in COVID-19 hospital outcomes. However, more definitive conclusions regarding the benefit of vitamin D supplementation in COVID-19 await further results of randomized controlled trials.<sup>28</sup>


### Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

### Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: Mayo Clinic benefactor funding

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