

# **Vitamin D supplementation could possibly improve clinical outcomes of patients infected with Coronavirus-2019 (Covid-2019)**

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*To the Editor:*

The rapid spread of Covid-2019 in many areas of the world calls for preventive health measures. Although basic guidelines on infection control are recommended, treatment has remained the best choice to avert mortality. However, for the time being, there are no known vaccines for the disease. This has driven several researchers in the world to assess the effectiveness of previously used treatments for severe acute respiratory syndrome (SARS) such as lopinavir.<sup>1</sup> Clinical trials for these vaccines could take more time, hence, palliative drugs have been developed to alleviate the severity of the disease.

Vitamin D has been proven to reduce risk of getting common cold.<sup>2</sup> It also enhances cellular immunity,<sup>3</sup> modulates adaptive immunity,<sup>4</sup> and enhances expression of antioxidation-related genes.<sup>5</sup> Hence, several authors proposed Vitamin D supplementation to prevent and treat Covid-2019.<sup>6,7,8</sup> To the best of my knowledge, no clinical trials have been conducted yet to determine the potency of Vitamin D in suppressing SARS-CoV-2 strain. A statistical analysis of the association between Vitamin D levels and clinical outcomes of Covid-2019 patients has not been described. In this paper, I used multinomial logistic regression to predict clinical outcomes of patients infected with Covid-2019 based on 25-hydroxyvitamin D [25(OH)D] levels, the barometer for Vitamin D status.

Using the database of three hospitals in Southern Asian countries, I conducted a retrospective multicentre study of 212 cases with laboratory-confirmed infection of SARS-CoV-2. Data pertaining to clinical features and serum 25(OH)D levels were extracted from the medical records. No other patient information was provided to ensure confidentiality. I classified the cases as follows: (1) mild – mild clinical features without pneumonia diagnosis, (2) ordinary – confirmed pneumonia in chest computer tomography with fever and other respiratory symptoms, (3) severe

– hypoxia (at most 93% oxygen saturation) and respiratory distress or abnormal blood gas analysis results ( $\text{PaCO}_2 > 50$  mm Hg or  $\text{PaO}_2 < 0$  mm Hg), and (4) critical – respiratory failure requiring intensive case monitoring. Classification was based on a previous work.<sup>9</sup> I also classified the vitamin D status of the cases based on their serum 25(OH)D level: (1) normal - 25(OH)D of  $> 30$  ng/ml, (2) insufficient - 25(OH)D of 21-29 ng/ml, and (3) deficient - 25(OH)D of  $< 20$  ng/ml. A previous report guided this classification.<sup>10</sup> For statistical analysis, I used Mann-Whitney U and  $\chi^2$  tests to compare differences in the clinical outcomes. Multinomial logistic regression was used to explore the association between serum 25(OH)D level and clinical outcomes of the cases. Frequency and percentage were used for categorical variables. Mean was used for continuous variables. A p-value below 0.01 was considered statistically significant. Ethics approval was considered exempt owing to the nature of the study and open-access data used. All names were originally hidden by the health governing bodies to ensure patient confidentiality.

Table 1. Descriptive statistics

Variables	Overall N (%)	Clinical Outcomes				p-value
		Mild	Ordinary	Severe	Critical	
Overall N (%)	212 (100.0)	49 (23.1)	59 (27.8)	56 (26.4)	48 (22.6)	
Serum (OH)D, ng/ml	23.8	31.2	27.4	21.2	17.1	<0.001
Vitamin D status						
Normal	55 (25.9)	47 (85.5)	4 (7.3)	2 (3.6)	2 (3.6)	<0.001
Insufficient	80 (37.7)	1 (1.3)	35 (43.8)	23 (28.8)	21 (26.3)	
Deficient	77 (36.3)	1 (1.4)	20 (26.0)	31 (40.3)	25 (32.5)	

Table 2. Multinomial logistic regression analysis

Predictor	Mild	OR	p-value
Serum (OH)D, ng/ml	Ordinary	0.614	0.007
	Severe	0.126	<0.001
	Critical	0.051	<0.001

Note: OR = odds ratio associated with the effect of a one standard deviation increase in the predictor.

Of the 212 (100.0%) cases of Covid-2019, 49 (23.1%) were identified mild, 59 (27.8%) were ordinary, 56 (26.4%) were severe, and 48 (22.6%) were critical (Table 1). Mean serum (OH)D level was 23.8 ng/ml. Serum (OH)D level of cases with mild outcome was 31.2 ng/ml, 27.4 ng/ml for ordinary, 21.2 ng/ml for severe, and 17.1 ng/ml for critical. Serum (OH)D levels were statistically significant among clinical outcomes ( $p < 0.001$ ). A total of 55 (25.9%) cases had normal Vitamin D status, majority of which (85.5%) were identified mild. A total of 80 (37.7%) cases had insufficient Vitamin D status, majority of which (43.8%) were ordinary. Cases identified as Vitamin D-deficient were 77 (36.3%), majority of which were severe (40.3%). Vitamin D status is significantly associated with clinical outcomes ( $p < 0.001$ ). A multinomial logistic regression analysis reported that the odds of having a mild clinical outcome rather than an ordinary outcome were approximately 1.63 times ( $OR = 0.614$ ,  $p = 0.007$ ) for each standard deviation increase in serum (OH)D (Table 2). Also, for each standard deviation increase in serum (OH)D, the odds of having a mild clinical outcome rather than a severe outcome were approximately 7.94 times ( $OR = 0.126$ ,  $p < 0.001$ ) while interestingly, the odds of having a mild clinical outcome rather than a critical outcome were approximately more than 19.61 times ( $OR = 0.051$ ,  $p < 0.001$ ).

More generally, the odds of having a mild clinical outcome increase when serum (OH)D level increases. Alternatively, the odds of having a critical outcome increase when serum (OH)D level decreases. This means that serum (OH)D level in the body could account for the clinical outcomes of the patients infected with Covid-2019. An increase in serum (OH)D level in the body could either improve clinical outcomes or mitigate worst (severe to critical) outcomes. On the other hand, a decrease in serum (OH)D level in the body could worsen clinical outcomes of Covid-2019 patients. In this case, Vitamin D supplementation may play an important role to raise 1,25-dihydroxyvitamin D [ $1,25(OH)_2D$ ], the biologically active form of Vitamin D in the blood.

In conclusion, this study provides substantial information to clinicians and health policy-makers. Vitamin D supplementation could possibly improve clinical outcomes of patients infected with Covid-2019 based on increasing odds ratio of having a mild outcome when serum (OH)D level increases. Further research may conduct randomized controlled trials and large population studies to evaluate this recommendation.

### **Declaration of Competing Interests**

The author declares no conflict of interest.

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