

## ORIGINAL ARTICLE

# Role of Vitamin D in the Management of COVID-19 Patients Regarding Morbidity and Mortality

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## ABSTRACT

**Aim:** To determine the role of vitamin D in the management of COVID-19 patients regarding morbidity and mortality.

**Study Design:** Prospective/Observational

**Place and Duration:** Departments of Medicine & Pulmonology, Allama Iqbal Memorial Teaching Hospital, Sialkot and Department of Medicine, Sughra Shafi Medical Complex Narowal from 1<sup>st</sup> November 2020 to 30<sup>th</sup> April 2020.

**Methodology:** One hundred and sixty patients of both genders diagnosed to have COVID-19, were enrolled. Patient's ages were ranging from 17 to 70 years. The detailed demographics such as age, sex, and body mass index were recorded. 5 ml blood samples were taken from all the patients to check their vitamin D levels. Severe Vitamin D deficiency was defined as 25(OH)D <25 nmol/L (10 ng/dl). Association between mortality and morbidity was examined.

**Results:** Ninety (56.25%) were males while 70 (43.75%) were females with mean age 40.15±17.37 years. Mean body mass index of patients was 24.16±7.26 kg/m<sup>2</sup>. Severe vitamin D deficiency was observed in 80 (50%) patients. Mortality found in 30 (18.75%) patients. Frequency of morbidity was among 66 (41.25%) patients. Patients with severe vitamin D deficiency had high rate of mortality 20 (25%) and morbidity 50 (62.5%) as compared to patients with no vitamin D deficiency had 10 (8%) mortality and 16 (20%) morbidity. A significant association was observed between severe vitamin D deficiency regarding morbidity and mortality among patients with covid-19 disease with p-value <0.05.

**Conclusion:** The vitamin-D has strongest relationship among patients with covid-19 disease to reduce mortality and morbidity.

**Keywords:** Morbidity, COVID-19, Vitamin D, Mortality

## INTRODUCTION

COVID-19 was declared a worldwide pandemic by the World Health Organization as a source of SARS-CoV-2. Protective factors can exist, but they aren't well understood. In the case of COVID-19, we can distinguish between anti-infective agents that could protect against infection and factors that enhance the outcome once infection has occurred.<sup>1</sup> Cannell et al<sup>1</sup> also showed in an observational study that low serum 25-hydroxyvitamin D was related to susceptibility to acute airway infections. Martineau et al<sup>2</sup> found that vitamin D protects against acute respiratory tract inflammation in a systemic study and a meta-analysis of 25 randomised controlled studies. Gruber-Bzura<sup>3</sup> reported that possible role of Vitamin D in the prevention of influenza virus infection and found the findings raise questions and controversy.

A strong influence on the ACE2/Ang(1-7)/MasR axis is calcitriol (1,25-dihydroxyvitamin D<sub>3</sub>), which increases ACE2 expression.<sup>4</sup> SARS-CoV-2 infection is caused by the ACE-2 receptor of the host cell. It can indicate an increased risk of infection from this point of view. However, past research showed a link between higher ACE2 levels and

improved health outcomes for coronavirus diseases. Lungs have shown to be safe from acute lung injury with the antioxidant enzyme, ACE2<sup>5,6</sup>.

Moreover, COVID-19 is most common during the cold winter season, when concentrations of serum 25(OH)D-calcidiol or calcifediol and ultraviolet B (UVB) - are lower, with lower numbers on the Southern Hemisphere close to the end of the summer<sup>7-10</sup>.

Vitamin D can reduce the risk of infections and, according to various biological/molecular pathways, can down regulate the immune/inflammatory response in general. In both B and T lymphocytes, and more in monocytes/macrophages, vitamin D receptors (VDRs) are strongly expressed, indicating that both the innate and adaptive immune responses have a role to play<sup>11-13</sup>.

The aim of the study was to determine the role of vitamin D in the management of COVID-19 patients regarding morbidity and mortality.

## MATERIALS AND METHODS

This prospective/observational study was conducted at Departments of Medicine & Pulmonology, Allama Iqbal Memorial Teaching Hospital, Sialkot and Department of Medicine, Sughra Shafi Medical Complex Narowal from 1<sup>st</sup>

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November 2020 to 30<sup>th</sup> April 2020. A total of 160 patients of both genders diagnosed to have severe covid-19 were enrolled in this study. Patient's ages were ranging from 17 years to 70 years. After receiving written consent, detailed demographics such as age, sex, and body mass index were registered. Patients taking vitamin D supplements and those who did not give their consent were excluded. To diagnose COVID-19 illness, all of the patients underwent real-time PCR. All of the patients had a 5 mL blood sample taken to check their vitamin D levels. 25(OH)D 25nmol/L (10 ng/dL) was considered severe Vitamin D deficiency. Association between mortality and morbidity was examined. The data was analyzed through SPSS-24. The correlation between the role of vitamin D in the management of COVID-19 patients regarding morbidity and mortality was investigated using the Chi-square test. P-value <0.05 was taken as significant.

## RESULTS

There were 90(56.25%) were males while 70(43.75%) were females with mean age  $40.15 \pm 17.37$  years. Mean BMI of patients was  $24.16 \pm 7.26$  kg/m<sup>2</sup> (Table 1). Severe vitamin D deficiency was observed in 80 (50%) patients. Mortality found in 30 (18.75%) patients. Frequency of morbidity was among 66 (41.25%) patients. Patients with severe vitamin D deficiency had high rate of mortality 20 (25%) and morbidity 50 (62.5%) as compared to patients with no vitamin D deficiency had 10 (8%) mortality and 16 (20%) morbidity. A significant association was observed between severe vitamin D deficiency regarding morbidity and mortality among patients with COVID-19 disease with p-value <0.05 (Table 2).

Table 1: Demographic details of the patients (n=160)

Variables	No.	%
<b>Gender</b>		
Male	90	56.25
Female	70	43.75
Mean age (years)	40.15±17.37	
Mean BMI (kg/m <sup>2</sup> )	24.16±7.26	

Table 2:

Variable	Severe vitamin D deficiency		P value
	Yes	No	
<b>Mortality</b>			
Yes	20 (25%)	10 (12.5%)	<b>0.03</b>
No	60 (75%)	70 (87.5%)	
<b>Morbidity</b>			
Yes	50 (62.5%)	16 (20%)	<b>0.05</b>
No	30 (27.5%)	64 (80 %)	

## DISCUSSION

COVID-19 has a wide range of clinical symptoms, ranging from asymptomatic or symptomatic types to acute illness marked by respiratory failure requiring ICU mechanical ventilation.<sup>14</sup> Other severe COVID-19 manifestations that include ICU admission include multiple organ dysfunction syndromes (MODS), sepsis, and septic shock. According to research, about 10-15% of cases progress to severe illness. Even among people in the same age group who do not have any coexisting conditions, there is a wide range of clinical seriousness.<sup>6-8</sup> Pakistan is one country where the

corona-virus is spreading at an alarming rate, owing to sloppy human behavior and a failure to obey standard operating procedures for life-threatening diseases. Vitamin D deficiency is a worldwide problem that is affecting people not only in the North, but also in the South. COVID-19 is an emerging pandemic with a wide range of seropositivity in population, and no formula suits well with a satisfactory reduction in the likelihood of error<sup>15</sup>.

In the present study, majority 56.25% patients were males and maximum number of patients was ages between 27 years to 45 years. These results showed similarity to many of previous studies in which male patients were predominant 60% and majority of patients were ages above 40 years.<sup>16,17</sup> In the case of COVID-19 acute lung injury, the available evidence suggests that an unregulated immune response in the host is the key mechanism that contributes to the so-called 'cytokine storm,' with the net result of significant tissue damage and defective coagulation<sup>18,19</sup>.

In this study, 80(50%) of patients had significant vitamin D deficiency, while 80(50%) of patients had vitamin D levels greater than 25nmol/L. According to the Seneca study, elderly people in Spain have a mean level of 26nmol/L in serum vitamin D, of 28nmol/L in Italy and of 45nmol/L in the north<sup>20</sup>. The average level of vitamin D in nursing homes is 23nmol/L, while 76% of women over 70 in Italy have levels of circulation below 30nmol/L. The highest risk of morbidity and mortality in SARS-CoV2 are the countries with most COVID-19 cases. In the late winter of 76% of Italian women over 70 years of age Isaia et al<sup>21</sup> discovered circulating levels of 25(OH)D less than 12 ng/ml (30nmol/L). The vitamin D deficiency is a major public health concern for people of all ages worldwide.<sup>22,23</sup> However, due to a decrease in sun exposure and cutaneous synthesis, vitamin D status deteriorates with age, in particular after 70s.<sup>24</sup> Much worse, with extreme vitamin D deficiency (SERUN 25(OH)D 25nmol/L) in 75% institutionalizing persons<sup>20</sup>.

Mortality in 30(18.75%) patients was identified in our sample. Among 66 patients (41.25%) the frequency of morbidity was high. Extreme vitamin D deficient patients were high in 20(25%) and 50(62.5%) deaths compared with 10(8%) and 16(20%) morbidity in 10(8%) vitamin D deficiency patients. Important links have been observed in the patients with extreme vitamin D deficiency in morbidity and death. According to a retrospective cohort study by the University of Chicago, the levels of COVID-19 were higher in the vitamin D-deficient group than in the vitamin D-sufficient group<sup>25</sup>. Vitamin D deficiency is a pandemic according to Kara et al<sup>26</sup>, particularly in Europe, where 40% of the population are deficient in vitamin D and 13% have a major deficiency. A four-fold association between COVID-19 occurrence, vitamin D deficiency and latitude has been found in the most frequently affected countries. This may be because vitamin D comes mainly from sunlight and there is very little sunlight in many European countries during the year.

Biesalski<sup>15</sup> conducted a meta-analysis to look at vitamin D interaction and COVID-19 morbidity and mortality in twenty European countries, and they found potential links between vitamin D levels, SARS-CoV-2 infections, and mortality.

## CONCLUSION

Vitamin D plays an important role in the prevention of any severe illness. The vitamin-D has strongest relationship among patients with covid-19 disease to reduce mortality and morbidity. Patients with severe Vitamin D deficiency had high rate of mortality and morbidity as compared to patients with vitamin D level >25nmol/L.

## SUGGESTIONS

1. Regular vitamin D levels should be measured to pre hand reduction of prevalence and burden of disease.
2. If at any stage ,vitamin D levels fall significantly, immediately rule out any pathological cause and should be corrected by supplementation
3. By taking these simple measures and by keeping the levels of vitamin D within normal limits, we can reduce the prevalence and burden of disease in our community.
4. Further elaborated study with large number of samples should be conducted for more comparative reliability of the reduced vitamin D levels and covid-19 disease.

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