Prevalence of vitamin D deficiency among COVID-19 patients: A cross-sectional study

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Abstract---To determine the prevalence of Vitamin D deficiency among COVID-19 patients. The present study was conducted at Rural Tertiary Care Centre Designated COVID Care Hospital, MMIMSR Mullana Ambala, Haryana, India. The duration of the study was 1.5 months (Aug 2020 to Sep 2020). Those who tested positive in RT-PCR were taken from the wards and Flu clinic of the hospital. To calculate the sample size for cross-sectional study, enough literature for Vitamin D and COVID-19 in India was not available. Therefore, all patients were enrolled consecutively over 1.5 months. Data were collected on a pre-validated Case Recording Form. The demographic data of all the COIVD-19 patients were recorded. Comorbid conditions like diabetes and hyper- tension were also recorded. History of alcohol consumption and smoking was recorded. The sample for Vitamin D along with routine investigations was sent and the level of Vitamin D was estimated using chemiluminescence-based immunoassay analyzer. To understand the Vitamin D status among the different groups, deficiency, and insufficiency were calculated separately and

compared. This study included 200 COVID-19 patients. Among total patients, males (57.5%) were represented more than females (42.5%). The mean age of the patients was 45.56 ± 26.23 years. More than 30% of the patients of the cases were obese, while 37% had normal BMI. 26% were consuming alcohol and 23.5% were smokers. Concerning co-morbid conditions, 14.5% had diabetes and 20.5% had hypertension. On the categorization of patients based on severity, 142 (71%) were mild, 38 (19%) were moderate and 20 (10%) were severe. Out of 200 patients, 107 (53.5%) patients had deficient vitamin D levels, 55 (27.5%) had insufficient vitamin D levels, and 38 (19%) had normal levels of vitamin D. It can be concluded from this study that vitamin D deficiency and insufficiency are quite prevalent among COVID-19 patients. In many countries people are taking a diet which is deficient and lacks micronutrients. Its role in COVID-19 patients should not be underestimated and supplementation with Vitamin D among patients can prevent worsening of disease severity.

Introduction

COVID-SARS-2 pandemic has struck and spread at light speed, reaching 6 continents within 3 months, transforming our societies globally [1]. The developed and developing countries are facing the burden equally and no proven treatment options available. The COVID-19 pandemic has become a global threat, with an inexplicable course of action and suboptimal response to the multitudes of therapies being tried. The pandemic has not affected only health but also had a great economic burden on the lives of entire world. Researchers are finding ways and measures by which we can control the risks and can reduce the death tolls which are a greater and clinical important aspect [2]. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the new strain of coronavirus that causes coronavirus disease 2019 (COVID-19) [3,4]. Due to the high infectivity and transmissibility of this novel virus, COVID-19 quickly became a global pandemic that has already affected at least 219 countries since its emergence from Wuhan, China in December 2019 [4,5]. The most common clinical manifestations of COVID-19 include fever, fatigue, anorexia, myalgia, cough, sputum production, and dyspnea [6,7].

Although the majority of patients with COVID-19 are either asymptomatic or develop only mild respiratory symptoms, a significant number of patients develop severe complications that result in morbidity and mortality, including acute respiratory distress syndrome (ARDS), arterial and venous thrombosis, multi-organ failure, and septic shock, among others [6,7]. Factors known to be associated with increased susceptibility to severe outcomes are advanced age, cancer, immunocompromised state, chronic kidney disease, chronic respiratory disease, cardio-metabolic disorders and smoking [8]. The elderly, African Americans, patients with obesity, and nursing home residents [8,9] have disproportionately higher rates of infection, morbidity, and mortality from COVID-19. These populations are also known as being at high risk for vitamin D

deficiency [11-14]. Thus, vitamin D deficiency could potentially contribute to higher COVID-19 positivity, morbidity, and mortality rates appreciated in these populations.More importantly studies also shows vit d deficiency can be associated with severe respiratory infection.

Vitamin D insufficiency, a serum 25-Hydroxy vitamin D [25(OH)D] between 20 and 50 nmol/L (8–20 ng/mL), causes calcium malabsorption, secondary hyperparathyroidism, accelerated bone loss, osteoporosis and fractures in adults [15]. Deficiency, a serum 25(OH)D < 20 nmol/L, decreases the serum calcium-phosphate product, and leads to rickets in children and osteomalacia in adults [15]. Both can be prevented with daily supplements of 400–800 IU of vitamin D, provided calcium intake is adequate. In elderly or institutionalized subjects, vitamin D at doses of 800–2000 IU/day, co-administered with calcium, reduces the risk of hip fractures by 15–30%, and of other non-vertebral fractures by 20% [15-17]. These doses are within ranges recommended by major organizations pre-COVID times. With the observation that the groups of people with Vitamin D deficiency are also the same group suffering from more complications and higher mortality from COVID-19, then Vitamin D deficiency might be an important risk factor for COVID-19. Vitamin D plays important role in maintaining health and prevents disease. It is well known that Vitamin D deficiency impairs bone health and cause osteoporosis.Studies also shown efficacy of vitamin D in diabetic neuropathy [18]. In the light of above observations the present study was initiated to find out the prevalence of Vitamin D deficiency among COVID-19 patients.

Materials and Methods

The present study was conducted at Rural Tertiary Care Centre. The duration of the study was 1.5 months (Aug 2020 to Sep 2020). Those who tested positive in RT-PCR were taken from the wards and Flu clinic of the hospital. To calculate the sample size for cross-sectional study, enough literature for Vitamin D and COVID-19 in India was not available. Therefore, all patients were enrolled consecutively.

Inclusion criteria

- Those who tested positive (RT-PCR) for SARS-CoV-2 from Flu clinic and COVID ward were included.
- Exclusion criteria:
- Those who were taking Vitamin D supplements or having taken them in the last 6 months were excluded.

Methodology

Data were collected on a pre-validated Case Recording Form. The demographic data of all the COIVD-19 patients were recorded. Comorbid conditions like diabetes and hyper- tension were also recorded. History of alcohol consumption and smoking was recorded. Patients were classified into different groups according to their serum 25(OH) Vitamin D levels. Serum 25(OH) Vitamin D level >30 ng/mL was classified as normal. Vitamin D insufficiency and deficiency were defined as serum 25(OH) Vitamin D levels of 20–30 ng/mL and <20 ng/mL, respectively [19]. COVID-19 patients were also classified into three groups based

on severity. The classification of the patients was based on the guidelines of the Ministry of Health and Family Welfare, India [20]. As per the guideline, the classification of the patients was based on clinical parameters as following:

- Mild case: Without evidence of breathlessness or hypoxia (normal saturation)
- Moderate case: the presence of clinical features of dyspnea and/or hypoxia, fever, cough, including SpO2 <94% (range 90–94%) on room air, Respiratory Rate more or equal to 24 per minute
- Severe case: clinical signs of Pneumonia plus one of the following; respiratory rate >30 breaths/min, severe respiratory distress, SpO2 <90% on room air.

The sample for Vitamin D along with routine investigations was sent and the level of Vitamin D was estimated using chemiluminescence-based immunoassay analyzer. To understand the Vitamin D status among the different groups, deficiency, and insufficiency were calculated separately and compared.

Results

This study included 200 COVID-19 patients. Among total patients, males (57.5%) were represented more than females (42.5%). The mean age of the patients was 45.56 ± 26.23 years. More than 30% of the patients of the cases were obese, while 37% had normal BMI.Concerning co-morbid conditions, 14.5% had diabetes and 20.5% had hypertension.

Table1
Demographic details and systemic history of the patients

Variables		Cases (%) N=200
Gender	Male	115 (57.5)
	Female	85 (42.5)
Age group (in years)	20–29	54 (27)
	30–39	51 (25.5)
	40–49	36 (18)
	≥50	59 (29.5)
	Mean Age, SD	45.56 + 26.23
BMI Classification	Underweight [<18.5 kg/m^2]	21 (10.5)
	Normal [18.5–22.9 kg/m^2]	74 (37)
	Overweight [23–24.9 kg/m^2]	45 (22.5)
	Obese [≥ 25 kg/m^2]	60 (30)
Alcohol consumption	Consuming alcohol	52 (26)
	Not consuming alcohol	148 (74)
Smoking	Smoker	47(23.5)
	Non-smoker	153 (76.5)
Diabetes	Diabetic	29 (14.5)
	Non-diabetic	171 (85.5)
Hypertension	Hypertensive	41 (20.5)
	Non-hypertensive	159 (79.5)

On the categorization of patients based on severity, 142 (71%) were mild, 38 (19%) were moderate and 20 (10%) were severe. Out of 200 patients, 107 (53.5%) patients had deficient vitamin D levels, 55 (27.5%) had insufficient vitamin D levels, and 38 (19%) had normal levels of vitamin D. Out of 107 vitamin D deficient patients, 69.6% were under mild, 19.6% were moderate, and 11.2% were from severe category. Out of 55 vitamin D deficient patients, 76.4% were from mild, 18.2% were moderate, and 5.4% were from severe category. Out of 38 patients who had normal levels, 68.4% were from mild, 18.4% were moderate, and 13.2% were from severe category.

Table 2
Association of vitamin D among cases based on the severity

COVID Severity	Deficient (Vit D <20 ng/mL)	Insufficient (Vit D 20–30 ng/ mL)	Normal (Vit D >30 ng/ mL)	P value
Mild (142, 71%)	74 (69.6)	42 (76.4)	26 (68.4)	0.7695 (>0.05)
Moderate (38, 19%)	21 (19.6)	10 (18.2)	7 (18.4)	
Severe (20, 10%)	12 (11.2)	3 (5.4)	5 (13.2)	
Total	107 (53.5%)	55 (27.5%)	38 (19%)	

Discussion

Since the 1930s, Vitamin D has been used for the treatment and prevention of acute respiratory infections [21]. Studies reported in the last era revealed Vitamin D protective effects although these effects showed substantial heterogeneity and were of modest size [22-26]. The risk factors for Vitamin D deficiency overlap strikingly with severe COVID-19 including, but not limited to, obesity, age, ethnic origin [26]. A study by Cannell et al. revealed that those who were taking Vitamin D supplement were less likely to have respiratory infections [27]. The Vitamin D might have a pleotropic effect on multiple organs and plays an important role as immunomodulator, antiviral and anti-inflammatory [28, 29]. Vitamin D also promotes the degradation of SARS-CoV-2 through autophagy mechanism via acidification process of endolysosomes [28].

In the present study, on the categorization of patients based on severity, 142 (71%) were mild, 38 (19%) were moderate and 20 (10%) were severe. Out of 200 patients, 107 (53.5%) patients had deficient vitamin D levels, 55 (27.5%) had insufficient vitamin D levels, and 38 (19%) had normal levels of vitamin D. A study by Kun ye et al. also reported higher percentage of patients among severe/critical disease with Vitamin D deficiency compared to mild/moderate disease [30]. A cross sectional study among COVID-19 patients from India reported 58.97 % of Vitamin D deficiency [31]. A regression analysis, including all potential risk factors as independent variables, indicate statistically significant difference between Vitamin D deficiency and COVID-19 (OR, 3.29; 95 % CI, 1.25–8.68) in the present study. Similar type of case control study reported significant association between Vitamin D deficiency and critical/severe COVID-19 (OR, 15.18; 95 % CI, 1.23–187.45) [32-34].

A study conducted to assess the inflammatory response and lung involvement, found that Vitamin D deficiency was associated with altered inflammatory response and higher lung involvement [35]. Vitamin D insufficiency was also linked to high infection rates and death from COVID-19 in European countries [36]. Other research from Indonesia discovered that 90 % of COVID-19 patients had Vitamin D insufficiency [37]. Metabolites of Vitamin D support innate antiviral effector mechanisms such as induction of autophagy and antimicrobial peptides [38]. There is limited information on the correlation between blood picture and laboratory findings of Vitamin D and COVID-19 [39], but it has also been reported that biologically active steroid hormone Vitamin D metabolite 1,25-dihydroxy Vitamin D (1,25 (OH)2D) exhibited antiviral inhibitory effect in human nasal epithelial cells infected with COVID virus [40]. A recent review and meta-analysis showed that Vitamin D supplementation taken daily or weekly reduces ARI (acute respiratory infection) by 32% to 60%, thus having a protective effect and safe. The review done by Nurshad Ali concluded that a negative correlation between Vitamin D and COVID-19 was found among European countries, while retrospective studies found a correlation between Vitamin D and COVID-19 after adjusting the confounders [41].

Conclusion

It can be concluded from this study that vitamin D deficiency and insufficiency are quite prevalent among COVID-19 patients. In many countries people are taking a diet which is deficient and lacks micronutrients. Its role in COVID-19 patients should not be underestimated and supplementation with Vitamin D among patients may prevent worsening of disease severity. Further studies are required to findout whether supplementation with vitamin Dwould improve outcome.

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