Vitamin D Deficiency Among Patients with COVID-19 : Case Series and Recent Literature Review

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Abstract

Background The world is now challenging the pandemic of COVID-19 infection. Previous studies showed the plausibility of Vitamin D prophylaxis and therapy for COVID-19, particularly in settings where hypovitaminosis D is frequent. Recent study from Indonesian showed that prevalence of vitamin D deficiency were 23.0%. The examination of Vitamin D status is not a routine in Indonesian clinical setting.

Methods This study is a Case Series from confirmed cases of COVID-19 in Bethesda hospital Yogyakarta Indonesia. The data of clinical symptoms, clinical signs, and laboratory examination were obtained from electronic medical record. The vitamin D status was measured by standardized laboratory method. We searched PubMed and Google Scholar for studies that included terms for Vitamin D and COVID-19.

Results The data was obtained from 10 participants consist of 50% male and 50% female. The mean of age was 49.6 years. The prevalence of vitamin D deficiency in this case was 90% and 10% of insufficiency. Patients in this case had various symptom and also had various chronic disease as comorbidity.

Conclusions The prevalence of vitamin D deficiency in this case series in Bethesda hospital Yogyakarta, Indonesia is 90% and 10% vitamin D insufficiency. We found no clinical evidence that vitamin D supplements are beneficial in preventing or treating COVID-19. Randomized controlled trials need to determine and evaluated this recommendation.

Background

The world is now challenging the pandemic of coronavirus (CoV) infections, the disease that called COVID-19. A new CoV infection epidemic began in Wuhan, China, in late 2019 [1]. This is the third and most extensive pandemic after the first severe acute respiratory syndrome (SARS)-CoV, which started in China in 2002 [2].

Indonesia is a tropical country with abundant sun exposure, as it lies within the equatorial zone. Previous study showed that the prevalence of 25(OH)D deficiency among Indonesian elderly women in institutionalized care is about 35.1% [3]. Recent study from Indonesian showed that prevalence of vitamin D deficiency were 23.0% [4].

Vitamin D has been proven to enhance expression of anti- oxidation-related genes, modulates adaptive immunity, and improves cellular immunity [5,6]. The protective effect of vitamin D against COVID-19 is related to suppression of cytokine response and reduced severity/risk for ARDS. The evidence from a meta-analysis that regular oral vitamin D2/D3 intake (in doses up to 2000 IU/d without additional bolus), is safe and protective against acute respiratory tract infection, especially in subjects with vitamin D deficiency [7]

There were no proven therapy for COVID-19 yet. Previous studies showed the plausibility of Vitamin D prophylaxis and therapy for COVID-19, particularly in settings where hypovitaminosis D is frequent. The examination of Vitamin D status is not a routine in Indonesian clinical setting. The aim of our study was report case series of Vitamin D status in patients with confirmed COVID-19 and review recent literature on the role of Vitamin D on COVID-19.

Methodology

Case series from confirmed cases of COVID-19 in Bethesda hospital Yogyakarta, Indonesia. The data of clinical symptoms, clinical signs, and laboratory examination were obtained from electronic medical record. The data were analyzed descriptively. This study obtained EC and permission from Bethesda hospital Yogyakarta, Indonesia.

The vitamin D status was measured by standardized laboratory method. The Vitamin D examination was used VIDAS 25OH Vitamin D (bioMerleux Marcy l'Etolie France) for Vitamin D2 and DE3 with Enzyme Linked Fluorescence Assay. Measurement of 25(OH) vitamin D serum were done by enzyme immunoassays for the quantitative measurement of total serum 25(OH) vitamin D levels. The levels < 10 ng/dL is deficiency, 10-29 ng/ dL is in-sufficiency, and 30-100 ng/ dL is sufficiency.

We searched PubMed and Google Scholar for studies that included terms for Vitamin D and COVID-19. We found no trials of Vitamin D in COVID-19 that have reported results. We did find several studies that are registered, but have not yet reported. None seemed to be masked comparisons to placebo.

Results

Herein we report that there were 10 participants with COVID-19 consisting of 50% (5 patients) Male and 50% (5 patients) Female. All the patients had either positive serological and real time PCT test for COVID-19. The average age of participants was 49.6 years. Symptoms felt by patients vary and some with asymptomatic. For comorbidities that are owned by patients also vary; 40% have a history of hypertension, 10% patients with diabetes, 10% patients with COPD, and 10% post stroke.

Based on laboratory tests, 90% (9 patients) had vitamin D deficiency status (vitamin D levels <20ng / mL) where 3 out of 10 patients had vitamin <8.1 ng / mL and 10% (1 patient) had vitamin D insufficiency status (vitamin D levels 20 - 29ng/mL) and there were no patients with normal or adequate vitamin D levels. The results of other blood tests can be seen in Table 1.

Table 1 Demographics, Clinical Characteristics on Admission and Laboratory Results of 10 patients cases with COVID-19 Infection

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10
Demographics										
Age (years)	49	51	17	40	65	73	14	54	69	64
Mean of age = 49.6 years										
Gender	Female	Male	Male	Male	Female	Male	Female	Female	Female	Male
Clinical Findings on Admission										
Symptom	Fatigue(close contact)	Fever, diarrhea	No symptoms (close contact)	Fever, fatigue, dry cough	Fever, fatigue, headache	Fever, fatigue, dry cough,	No symptoms, (close contact)	Fatigue, non specific headache	Fatigue, dry cough	Fever, dry cough
Comorbidity	-	Diabetes	-	-	Hypertension	Hypertension, COPD	-	-	Hypertension	Post Stroke, Hypertension
SARS-CoV IgG	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Negative
SARS-CoV IgM	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive
Laboratory Results										
Vitamin D Levels (ng/mL)	<8.1	10.6	20.5	11.9	11.6	12.4	8.3	10.1	<8.1	<8.1
Vitamin D Status	Deficiency	Deficiency	Insufficiency	Deficiency	Deficiency	Deficiency	Deficiency	Deficiency	Deficiency	Deficiency
Hemoglobin(g/dL)	12.4	16	17.6	14.3	12.6	13.5	14.6	12.2	10.7	12.4
White Blood Cell (10^3/µl)	6.80	7.14	6.81	6.94	7.62	5.62	5.64	7.07	5.97	9.84

Red Blood Cell (10^6/µl)	3.94	5.14	6.21	5.11	4.21	4.38	5.01	4.31	3.34	4.18
Platelets (10^3/µl)	451	174	289	384	542	184	290	190	312	327
Lymphocyte(%)	24.0	16.8	29.7	30.1	25.9	24.2	20.7	16.5	19.9	17.4

Discussion

Here we report our findings in 10 patients with confirmed COVID-19 infection hospitalized patients from Bethesda Hospital, Yogyakarta Indonesia. Patients in this case were conducted from 50% (5 patients) male and 50% (5 patients) female with an average age of 49.6 years. The incubation period for COVID 19 in this case is 2-14 days. Our study showed that elderly and female tends to have lower vitamin D status. This is relevant with the facts on vitamin D and COVID-19. Serum 25(OH)D concentrations tend to decrease with age [8]. In COVID-19 case-fatality rates (CFRs) increase with age [9].

We found out that COVID-19 patients in this case had several comorbidities which are chronic diseases such as hypertension, diabetes, COPD, and post stroke. Some studies report that people with chronic disease co-morbidities have lower 25(OH)D than healthy people [10]. Case Fatality Rate (CFR) in China is 6%-10% for those with cardiovascular disease, hypertension, diabetes, and chronic respiratory diseases [9].

In this case series, we evaluated vitamin D status in 10 patients with COVID-19. Examination of vitamin D levels was carried out by blood tests in the laboratory. From 10 patients, we found 90% (9 patients) with vitamin D deficiency and 10% (1 patient) with vitamin D insufficiency. Some of the patients have very severe deficiency. Similar to our findings, previous studies reported COVID-19 patients among ICU subjects, 11 (84.6%) had Vitamin D insufficiency vs 4 (57.1%) of floor subjects. Surprisingly, 100% of ICU patients who are less than 75 years old have Vitamin D Insufficiency (n = 11). Among these, 64.6% (n = 7) had very low 25(OH)D levels <20 ng / mL and three had 25(OH)D levels <10 ng / mL [11].

Recent study from Martineau, et al. were performed a meta-analysis from 25 randomized controlled trials (10.933 participants). There was a statistically significant reduction found from vitamin D supplementation in the risk of having acute respiratory infection. In subgroup analysis, they found a protective effect in daily or weekly supplementation but not in bolus doses. There was a strong protective effect in those with 25(OH)D levels <10 ng/mL and there was no significant effect in those with serum 25(OH)D >10 ng/mL. There were an inverse relationship between serum vitamin D levels and risk of acute respiratory tract infection [7]. It means, low vitamin D levels may contribute to increased risk of respiratory infection including COVID-19 [12].

Previous report have speculated that people with low serum vitamin D might be at higher risk of infection with COVID-19, or will be worsen when infected [13]. There is an overlap between groups at high risk of Vitamin D deficiency and groups at high risk of severe COVID-19. Examples include people with chronic disease, and elderly. Our studies showed that some of the COVID-19 cases were elderly, and have chronic disease.

The seasonality of many viral infections, one of them is a respiratory viral infection, is associated with a low concentration of 25(OH)D, as result a UVB doses are low because of winters in temperate climates and rainy seasons related in tropical climates [14]. Our study showed that all patients have deficient and insufficient status of vitamin D. The surprising facts in tropical country that very rich with sun.

Vitamin D have possible beneficial effects in the immune system especially in COVID-19 patient. For example, vitamin D will increase the production of various peptides by the innate immune system, which has anti-viral, anti-microbial and anti-fungal activity [15]. Vitamin D has been proven to not only reduce the production of proinflammatory Th1 cytokines but also to increase the expression of anti-inflammatory cytokines by macrophages. This may be worth bearing in mind the proinflammatory cytokine environment observed in patients infected with COVID-19 and how the "cytokine storm" that leads to acute respiratory distress syndrome [16].

We found no trials of Vitamin D in COVID-19 that have reported results. We did find several studies that are registered, but have not yet reported. One trial is testing whether a single oral dose of 25,000 IU (625 μg) of vitamin D will improve mortality in patients who are infected with SARS-CoV-2 but do not have severe symptoms, compared with usual care [17]. Another RCT will compare single doses of vitamin D3, 50,000 IU to 200,000 IU (1250 Vs 5000 μg) in people with COVID-19 pneumonia who are over 75 years of age, or over 70 with low oxygen saturations; the primary outcome measure is mortality at 14 days [18].

We found no clinical evidence that vitamin D supplements are beneficial in preventing or treating COVID-19. We would need evidence from well-masked randomized trials to determine if there are effects, before recommending vitamin D3 supplements for treating or preventing COVID-19 infection. The hypothesis that vitamin D supplementation can reduce the risk of influenza and COVID-19 incidence and death should be investigated in trials to determine the appropriate doses, serum 25(OH)D concentrations, and the presence of any safety issues.

People at risk of vitamin D deficiency should in any case take supplements in line with current guidance. In our case series we treat all our patient with 2000 IU oral supplementation. As clinicians, we should continue to treat people with vitamin D deficiency, but not because of any possible association with respiratory infection.

Conclusion

The prevalence of vitamin D deficiency in this case series in Bethesda Hospital Yogyakarta, Indonesia is 90% and 10% vitamin D insufficiency. Hypothetical review showed that Vitamin D supplementation may be benefit for COVID-19. We found no clinical evidence that vitamin D supplements are beneficial in preventing or treating COVID-19.

Abbreviations

COVID: Corona Virus Disease, SARS: Severe Acute Respiratory Syndrome, MERS: Middle East Respiratory Syndrome, CFR: Case Fatality Rate , RCT: Randomized Controlled Trial.

Declarations

Availability of data and materials

Study's data can be accessed from RTP after permission and approval from the Bethesda Hospital Yogyakarta Indonesia.

Ethics approval and consent to participate

We declare that this study was carried out after obtaining an Ethical clearance certificate was obtained from Bethesda Hospital Yogyakarta as an institution that grants research permission. Ethical clearance certificate number 18 (EC/18/2020) Bethesda Hospital Yogyakarta, Indonesia. Authorization from Bethesda Hospital was obtained to conduct this study.
All patients' privacy and confidentiality were strictly observed throughout the study. We have also give informed consent and obtained the consent of the patients involved in this study.

Consent for publication

The manuscript does not contain any identifying individual personal data in any form.

Competing interests

All authors declare no conflict of interest.

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