

# The role of Vitamin D in the prevention of Coronavirus Disease 2019 infection and mortality

Petre Cristian Ilie (✉ [dr.cristianilie@gmail.com](mailto:dr.cristianilie@gmail.com))

The Queen Elizabeth Hospital Foundation Trust, King's Lynn

Simina Stefanescu

University of East Anglia

Lee Smith

Anglia Ruskin University

---

## Short Report

**Keywords:** COVID-19, SARS-Cov2, Corona virus, vitamin D, cholecalciferol, calcitriol

**Posted Date:** April 8th, 2020

**DOI:** <https://doi.org/10.21203/rs.3.rs-21211/v1>

**License:** © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

---

**Version of Record:** A version of this preprint was published on May 6th, 2020. See the published version at <https://doi.org/10.1007/s40520-020-01570-8>.

# Abstract

**Background/Aims:** WHO declared SARS-Cov-2 a global pandemic. The aims of this paper are to assess if there is any association between mean levels of vitamin D in various countries and cases respectively mortality caused by COVID-19.

**Methods:** We have identified the mean levels of vitamin D for 20 European Countries for which we have also got the data regarding the morbidity and mortality caused by COVID-19.

**Results:** The mean level of vitamin D (average 56nmol/L, STDEV 10.61) in each country was strongly associated with the number of cases/1M (mean 295.95, STDEV 298.73  $p=0.004$ , respectively with the mortality/1M (mean 5.96, STDEV 15.13,  $p < 0.00001$ ).

**Discussion:** Vitamin D levels are severely low in the aging population especially in Spain, Italy and Switzerland. This is also the most vulnerable group of population for COVID-19.

**Conclusions:** We believe, that we can advise Vitamin D supplementation to protect against SARS-CoV2 infection.

## Background/aims

WHO declared SARS-Cov-2 a global pandemic. Little is known about the potential protective factors. Previous studies identified associations between higher levels of ACE2 and better coronavirus disease health outcomes. In the lung, ACE2 protects against acute lung injury [1]. Calcitriol (1,25-dihydroxyvitamin D3) exerts pronouncedly impacts on ACE2/Ang(1-7)/MasR axis with enhanced expression of ACE2 [2].

We hypothesize that vitamin D may play a protective role for SARS-Cov2 infections.

The primary aims of this study are to assess if there is any association between the mean levels of vitamin D in various countries and the mortality caused by COVID-19. The secondary aim was to identify if there is any association between the mean vitamin D levels in various countries and the number of cases of COVID-19.

## Materials And Methods

To test this hypothesis and to limit confounding bias (latitude, etc), we focused on European countries only. We searched the literature for the mean levels of vitamin D in each country [3]. We searched the number of cases of COVID-19/1M population in each of the countries and mortality caused by this disease/1M population (20March, 16.00GMT) (table 1)[4]. Statistical analyses were carried out (t-test calculator).

## Results

We found very significant correlation between the mean vitamin D levels (average 56.79 nmol/L, STDEV 10.61) and the number of cases of COVID-19/1M population (average 259.95, STDEV 298.732,  $t$ -value = -3.03947;  $p$ -value = 0.004274), and between the mean vitamin D levels and the number of deaths caused by COVID-19/1M (Figure 1) (average 5.963936, STDEV 15.13207,  $t$ -value = 12.29871;  $p$ -value < 0.00001) (table 1).

## Discussion

We acknowledge that this cross-sectional analysis has limitations. The number of cases/country is affected by the number of tests performed. We believe that mortality is a better outcome to demonstrate the potential protective role of vitamin D.

The Seneca study showed a mean serum vitamin D of 26nmol/L in Spain, 28 nmol/L in Italy and 45 nmol/L in the Nordic countries, in older people [3]. Severe deficiency is defined as a serum 25(OH)D lower than 30nmol/L [3]. In Switzerland, mean vitamin D levels are 23(nmol/L) in nursing homes and in Italy 76% of women over 70 years of age have been found to have circulating levels below 30nmol/L [3]. These are countries with high number of cases of COVID-19 and the aging people is the group with the highest risk for morbidity and mortality with SARS-Cov2.

Martineau AR et al concluded in a meta-analysis that vitamin D supplementation was safe and protective against acute respiratory tract infections. They described that patients who were severe vitamin D deficient experienced the most benefit [5].

In conclusion, we found significant relationships between vitamin D levels and the number COVID-19 cases and especially the mortality caused by this infection. The most vulnerable group of population for COVID-19 is also the one that has the most deficit in Vitamin D.

Vitamin D has already been shown to protect against acute respiratory infections and it was shown to be safe. We believe, that we can advise Vitamin D supplementation to protect against COVID-19 infection.

## Declarations

### Ethical Statement

This study is compliant with the ethical standards. Petre Cristian Ilie, Simina Stefanescu and Lee Smith do not have any conflict of interests. No source of funding was used. Considering the design of the study no informed consent was necessary.

## References

1. Kuka K, Imai Y, Penninger JM. Angiotensin-converting enzyme 2 in lung diseases. 2006 Jun;6(3):271-6. Epub 2006 Apr 3, available from: < 1.

<https://www.sciencedirect.com/science/article/pii/S1471489206000579?via%3Dihub> [Accessed 20 March 2020]

2. Cui C, Xu P, Li G, et al. Vitamin D receptor activation regulates microglia polarization and oxidative stress in spontaneously hypertensive rats and angiotensin II-exposed microglial cells: Role of renin-angiotensin system. *Redox Biol.* 2019;26:101295. doi:10.1016/j.redox.2019.101295
3. Lips, P, Cashman, K., Lamberg-Allardt, C., Bischoff-Ferrari, H., Obermayer-Pietsch, B., Bianchi, M., Stepan, J., El-Hajj Fuleihan, G., and Bouillon, R. (2019). Current vitamin D status in European and Middle East countries and strategies to prevent vitamin D deficiency: a position statement of the European Calcified Tissue Society. *European Journal of Endocrinology* 180, 4, P23-P54, available from: <<https://doi.org/10.1530/EJE-18-0736>> [Accessed 21 March 2020]
4. <https://www.worldometers.info/coronavirus/#countries>. Accessed 20th March 17.1
5. Martineau Adrian R, JolliffeDavid A, Hooper Richard L, Greenberg Lauren, Aloia John F, Bergman Peter et al. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data *BMJ* 2017; 356 :i6583

## Table 1

Not provided with this version of the manuscript.

## Figures

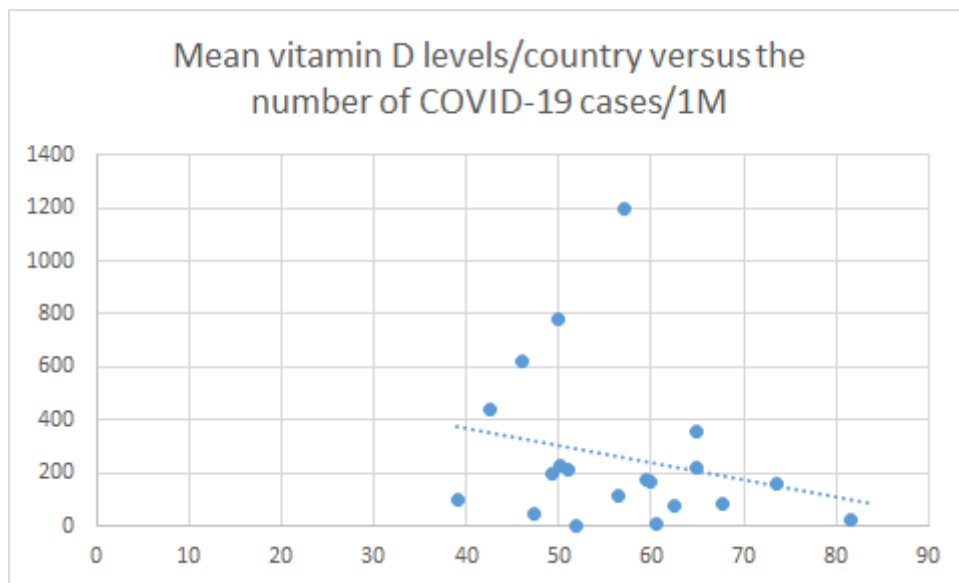
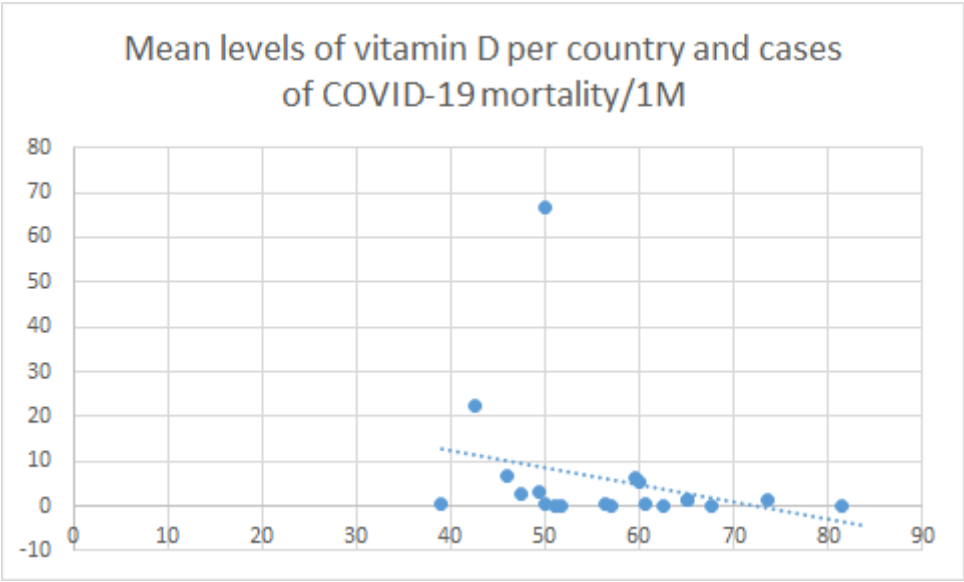


Figure 1

Mean vitamin D levels/country versus the number of COVID-19 cases/1M



**Figure 2**

Mean levels of vitamin D per country and cases of COVID-19 mortality/1M