Vitamin D and COVID-19 Infection

Amru Ainine, MBChB, Elliot Heward, MBChB, John Rocke, MBChB, Roomana Kapasi, MBChB, Denise Darby, MBChB, Nirmal Kumar, FRCS, Abdul Ashish, FRCS

Wrightington, Wigan & Leigh Teaching Hospital NHS Foundation Trust, United Kingdom

ABSTRACT

Introduction: The COVID-19 pandemic has prompted the medical world to look at factors that may influence outcomes. There have been connections made between vitamin D and COVID-19, as vitamin D has previously been shown to play a role in the maintenance of immune homeostasis.

Materials and Methods: We performed a prospective cohort study on 103 patients at Wigan Wrightington and Leigh NHS Foundation Trust looking at serum vitamin D levels of patients with positive COVID-19 swabs. Results were collated and correlations were made to compare vitamin D levels with age; severity of illness; hospital outcomes; and frailty. Comparisons were also made between frailty and outcome.

Results: The results showed that there was a significant statistical difference between vitamin D levels and severity of infection: those who were treated in the intensive care units (ICU) (severe symptoms) had lower vitamin D levels than those treated on the ward (p=0.0446). There was also a correlation between vitamin D levels and frailty: those who were more frail had higher vitamin D levels than fitter patients (P=0.005). Vitamin D and frailty had no effect on hospital outcomes of COVID-19 infection.

Conclusion: Ultimately, we concluded that low vitamin D can increase susceptibility of contracting COVID-19, increase severity of infection but does not affect mortality.

INTRODUCTION

The COVID-19 pandemic has stimulated the medical community to investigate factors which could affect outcomes.

Coronavirus Disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which has led to hundreds of thousands of deaths globally. During the infection, it is thought to use the immune evasion process followed by hyper reaction and cytokine storm as a pathogenic process of acute respiratory disease syndrome (ARDS). To enter the alveolar and intestinal epithelial cells, it uses the angiotensin-converting enzyme 2 as the host receptor, which in turn causes dysregulation of the system, thus excess cytokine production ultimately causing ARDS.[1]

There have been many hypothesises on what can affect the replication of the virus; one thought is that vitamin D has a significant role in maintenance of immune homeostasis by stimulating exhibition of antimicrobial peptides or by directly interfering with the viral replication.[2]

It is known that deficiency in vitamin D can lead to promotion of the renin-angiotensin system leading to ARDS and chronic cardiovascular disease.[3] This may explain why susceptibility to COVID-19 is increased.

Vitamin D, known as calciferol, is a fat-soluble steroid hormone that can be produced endogenously by the effect of ultraviolet radiation on the skin or it can be absorbed from food and dietary supplements. Due to changes in our lifestyle with increased working hours, more sedentary life and imbalanced diet, there has been a reduction in vitamin D levels.[4] Vitamin D deficiency is widely linked to skeletal disorders, such as rickets or osteoporosis. It can also be attributed to other health conditions such as certain cancers, cardiovascular disease, inflammatory bowel diseases, psychological disorders as well as autoimmune diseases and infections.

Previous studies have found that Vitamin D has an immunomodulatory role, increasing innate immunity by secretion of antiviral peptides, which improves mucosal defences.[1] Some studies have also linked vitamin D insufficiency to respiratory tract infections including epidemic influenza and one meta-analysis showed those with low serum vitamin D levels had 64% more risk of developing community acquired infections.[5-8]

We aimed to further understand the relationship between vitamin D deficiency and COVID-19 outcomes.

In order to answer the hypotheses of whether vitamin D levels have any correlation with outcome or severity of COVID-19 infection, a prospective cohort study on patients admitted with positive viral swabs was undertaken to compare levels with length of stay, mortality and clinical frailty scoring (Rockwood score).

MATERIALS AND METHODS

A prospective cohort study was undertaken between March 2020 and May 2020 of patients admitted to Wrightington, Wigan and Leigh NHS Foundation Trust. Patients were tested routinely for both COVID-19 and serum vitamin D levels on admission to hospital. Information was collected from electronic patient records concluding on 21/05/2020. The audit was registered with the local audit department, ethics approval was not required.

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Corresponding Author: Dr Amru Ainine
Email: aainine@doctors.org.uk

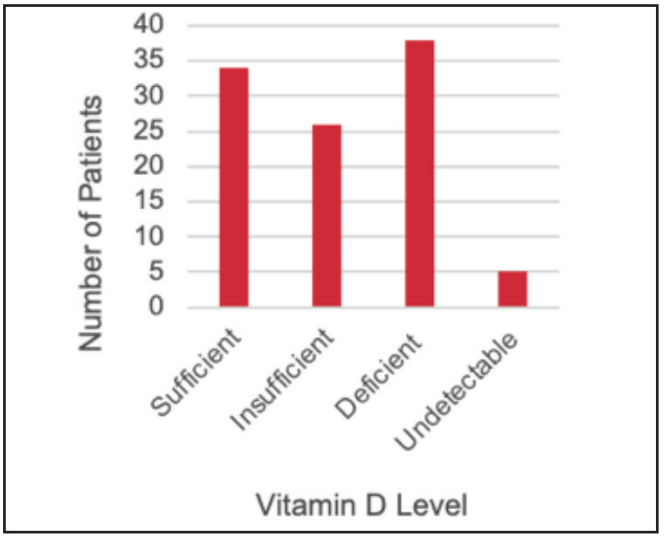

Fig. 1: Vitamin D levels of cohort.

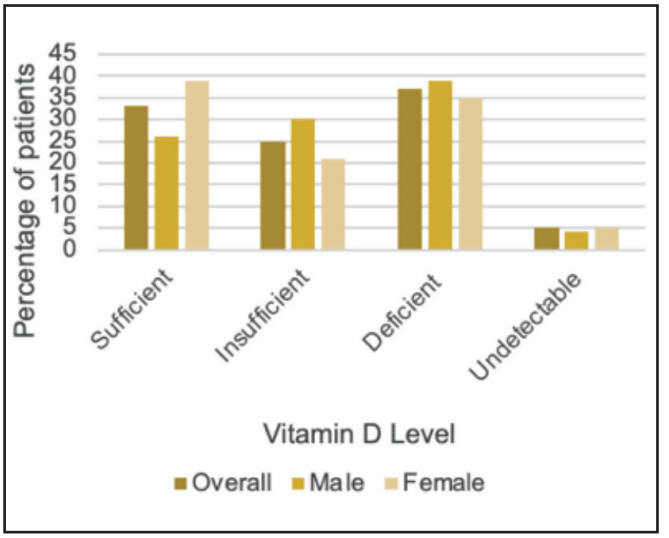

Fig. 2: Vitamin D levels in relation to gender.

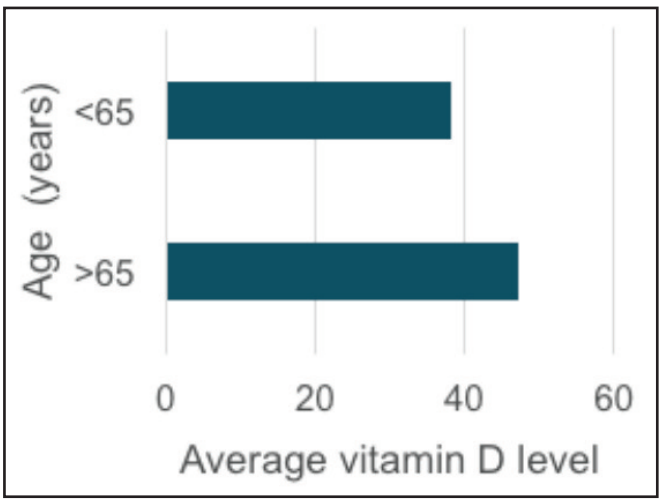

Fig. 3: Average vitamin D in relation to age.

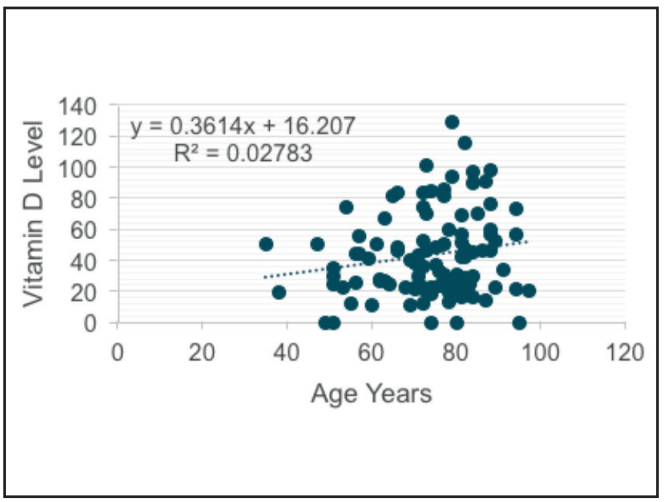

Fig. 4: Vitamin D in relation to age in linear regression.

The National Institute of Health and Care Excellence (NICE) classifies those with serum 25-hydroxyvitamin D (25[OH] D) levels >50nmol/L to have adequate vitamin D levels. Those with 25[OH] D levels between 25 and 50 are insufficient and those with levels less than 25 are deficient of vitamin D.9

Statistical analysis was performed (graph pad prizm). Unpaired T test was used to compare groups. A statistically significant difference was considered when the $p<0.05$.

RESULTS

Of the 103 patients who were COVID-19 swab positive, there were 57 females (55%), there was a mean age of 73.6 years (range: 35-97 years). The majority of the patients identified as White British 95 (92.2%), one Indian, one Arab, and six had not declared their ethnicity. The mean length of stay of the all patients was 15.3 days. At the time of data collection, 10.7% of patients were still admitted, 41.7% patients were discharged, and 47.6% died. Of the cohort, 17 patients (16.5%) were admitted to ICU; of which, 13 (76.5%) died, the remaining 4 (23.5%) were still admitted.

Vitamin D and age

For patients who were older than 65 (n=79), the average vitamin D level was 47.4. However, for those younger than 65 (n=24), the average vitamin D level was 38.4 (Figure 3). An unpaired t-test revealed p=0.1854. Linear regression – p=0.1140 (Figure 4)

Vitamin D and severity of illness

Those who required intensive care treatment had a mean vitamin D level of 27.6 nmol/L as opposed to the average of those treated at ward level care being 45.6nmol/L (p=0.0446).

Vitamin D levels and hospital outcomes

Those who were discharged had mean vitamin D level of 45.2nmol/L compared to 41.0 nmol/L for those who died (p=0.5297). Of those discharged; 15 patients were sufficient, 11 insufficient, 16 deficient, 1 undetectable. Of those who died; 14 were sufficient, 13 insufficient, 19 deficient and 3 undetectable. (Figure 5)

Vitamin D and frailty
Out of the 103 patients, 87 patients (85%) had a documented Rockwood Clinical Frailty Score (CFS). Those with sufficient vitamin D levels had a higher mean Rockwood score (5.7) than patients with insufficient levels (4.9), deficient patients (4.3) or undetectable vitamin D levels (4.5). Comparing those with sufficient versus those with low Vitamin D levels (insufficient, deficient and undetectable) the average CFS was 5.7 versus 5.4 with a p-value of 0.005. (Figure 6)

Frailty and outcome
Comparing the CFS with patient outcome, those who were discharged had a CFS average of 4.97 compared to those who died with an average of 5.1, p=0.39.

DISCUSSION

Understanding how to improve the outcomes for COVID-19 patients is currently a worldwide endeavour. Our results show that most patients who were COVID-19 positive had deficient vitamin D levels. Moreover, 40.2% of patients had vitamin D levels less than 25nmol/L which is deficient. According to the National Diet and Nutrition Survey; 24% of men and 21.7% of women between the ages of 19 and 64 years old had vitamin D concentration below 25nmol/L, this was also true for 16.9% of men and 24.1% of women aged 65 years and over.[10] This suggests that patients admitted with COVID-19 had in fact had significantly lower levels of vitamin D than the general population. Our patient cohort contained mainly patients of a White British background (92%) in comparison to 80.5% average of the United Kingdom population.[11]

The overall outcomes of patient treatment were not greatly affected by the concentration of vitamin D, patients who died had a marginally lower vitamin D level than those who were discharged. This was not a statistically significant difference.

It has to be noted that whilst vitamin D levels had no effect on final outcomes, the severity of illness did correlate to vitamin D levels. Those who required intensive care had a significantly lower concentration of vitamin D (27.6nmol/L) as opposed to those not requiring ICU treatment (45.6nmol/L) p=0.0446.

There was also a correlation between vitamin D concentration and Rockwood clinical frailty scores. Interestingly, those with sufficient vitamin D had a statistically significantly higher Rockwood score than those with low levels. This means that patients who were frailer (higher CFS) had better vitamin D levels than those who were fitter. A suggestion to explain this could be that the elderly/frail population are generally more investigated, i.e., regular bloods and therefore, vitamin D may have been monitored and replaced as necessary. We recommend further studies to explore the relation of vitamin D levels and clinical frailty. Patients who died compared to those who were discharged had no significant difference in their frailty scores, thus suggesting there was no effect of frailty on outcome of COVID-19 infection.

There were a few limitations to this study: this is a single centre study with limited numbers which wasn't adequately powered to look at the effects of corrected Vitamin D levels on hospital outcomes.; there was no control group to compare the levels of vitamin D of those with COVID-19 infection against the normal population; there was also no data on the comorbidities to compare patients who required treatment in ICU against those who received ward level care.

CONCLUSION

The Coronavirus pandemic has caused the death of hundreds of thousands of people worldwide. It is thought that lower vitamin D levels may increases the severity of COVID-19 infections and potentially increase susceptibility to contracting COVID-19. Our data suggests that lower vitamin D levels do not affect mortality. We found that low vitamin D levels potentially can lead to more severe disease requiring ICU level care. We therefore suggest that Vitamin D levels should be measured and corrected in those hospitalised with COVID. Studies that investigate the effect of Vitamin D correction on COVID outcomes are required.

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