

# Vitamin C and D to Decrease the Risk and Severity of COVID-19 Symptoms. Is Cortisol Reduction the Mechanism Behind Lowering the Severity of COVID-19 Symptoms? A Commentary on The Available Evidence

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## Keywords

COVID-19, Vitamin C, Vitamin D,

## Introduction

According to the World Health Organization, there has been over 3 million deaths reported in the world due to COVID-19. In spite of an increasing number of vaccinated people across the world it is important to keep evaluating the pathophysiology of this disease and the mechanism of action for all the interventions that show improvement. Cortisol is a hormone produced by the adrenal gland that causes sequestration and apoptosis of eosinophils, monocytes and lymphocytes which lead to lymphopenia, eosinopenia and overall immunosuppression.

Lymphocytes in particular form part of both the acquired and innate immune system. In 2020, Ramezani, et al. designed a study of 30 patients with COVID-19 within 7 days of their first symptom. This study revealed that the levels of cortisol in patients who died of COVID-19 were significantly higher in comparison with surviving patients [1]. Another study in 2020 by Tan, et al. including 403 patients with COVID-19 showed that a doubling of cortisol concentration was associated with a significant 42% increase in the hazard of mortality. Patients with COVID-19 whose baseline cortisol concentration was equal to or less than 744 nmol/L had a median survival of 36 days whereas, patients with COVID-19 whose cortisol value was more than 744 nmol/L had a median survival of 15 day [2]. This commentary will evaluate some nutritional supplements that may decrease the severity of symptoms associated with COVID-19.

## Nutritional Supplementation to Reduce the Risk and Severity of COVID-19

### Vitamin D

#### Role in COVID-19

The role of vitamin D has been evaluated not only for COVID-19 in terms of positive correlation relationship between vitamin D deficiency and severity of COVID-19 symptoms. In 2020, Pereira, et al. conducted a meta-analysis and systematic review of 27 articles. This study found that vitamin D concentration insufficiency increased hospitalization (odds ratio = 1.81) and mortality (odds ratio= 1.82) from COVID-19 [3]. Three other studies took place in 2021. The first study was by Liu, et al. who carried out systematic review and meta-analysis of 10 articles involving over 360,000. This study indicated that vitamin D deficiency or insufficiency was associated with an increased risk of COVID-19 (odds ratio = 1.43) [4]. The second study was by Petrelli, et al. who performed a meta-analysis and systematic review of 43 observational studies. This study revealed that in subjects with deficient vitamin D values, risk of COVID-19 infection was higher compared to those with replete values (OR = 1.26). Moreover, vitamin D deficiency was also associated with worse severity and higher mortality than in nondeficient patients (OR = 2.6 and 1.22 respectively) [5]. The third study was by Jeshome, et al. published a systematic review and meta-analysis of 14 articles. This study indicated that vitamin D deficient individuals were at higher risk of COVID-19 infection as compared to vitamin D sufficient patients. The pooled analysis showed that individuals with Vitamin-D deficiency were 80% more likely to acquire COVID-19 infection as compared to those who have sufficient Vitamin D levels (OR = 1.80) [6].

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### Effect on cortisol

In 2016, Dujali, et al. conducted a randomized placebo-controlled single-blinded parallel trial of 15 patients who received 2000 IU (50 µg) vitamin D3 per day or placebo. This study showed that at day 14 urinary free cortisol levels and cortisol/cortisone ratio were significantly reduced from 162.65 nmol/day and 2.22 to 96.4 and 1.04 respectively [7].

In 2020, Ramezani, et al. carried out a double-blind, placebo-controlled, randomized controlled trial of 46 patients who were assigned to vitamin D3 supplement (2000 IU/day) or placebo for 12 weeks. This study indicated that the serum cortisol levels were reduced significantly only in subjects with vitamin D deficiency ( $p = 0.042$ ) [8].

### Vitamin C

#### Role in COVID-19

Vitamin C is commonly used as a supplement to boost the immune system for the common cold among other conditions. In 2019, Hemila, et al. performed a meta-analysis of 18 controlled trials involving over 2000 participants. In 12 trials with vitamin C reduced the length of ICU stay on average by 7.8%. Moreover, in six trials, orally administered vitamin C in doses of 1-3 g/day reduced the length of ICU stay by 8.6%. Finally, in three trials in which patients needed mechanical ventilation for over 24 hours, vitamin C shortened the duration of mechanical ventilation by 18.2% [9]. Hemila, et al. also published a meta-analysis in 2020 of 8 trials involving over 600 subjects. This study found that in five trials including 471 patients requiring ventilation for over 10 h, a dosage of 1-6 g/day of vitamin C shortened ventilation time on average by 25% [10].

### Effect on cortisol

In 2001, Brody, et al. conducted a randomized double-blind, placebo-controlled 14-day trial of sustained-release ascorbic acid (3 x1000 mg/day) including 60 participants. This study revealed that treatment with high-dose sustained-release ascorbic acid palliates cortisol response [11]. In 2008, Carrillo, et al. carried out a double-blind, randomized controlled trial of 12 subjects who consumed 3x500 mg tablets of vitamin C for 12 days. This study revealed a significant linear trend in postexercise cortisol attenuation in the vitamin C group, 21.7nmol/L at baseline, to 13.5 at acute, to 7.6 after a short term [12].

### Discussion

Based on the aforementioned studies evaluated in this commentary it seems like vitamin D plays a role in the prevention of COVID-19 and may reduce the severity of symptoms in COVID-19 patients. Vitamin D appears to play a role in the risk of acquiring COVID-19 as well as in reducing the severity of symptoms of infected patients and mortality. In the systematic review by Yisaki, et al. nine studies were reviewed, and they concluded that seven (77.8%) showed that COVID-19 infection, prognosis, and mortality were correlated with vitamin D status [13].

On the other hand, the studies that were evaluated in this commentary for vitamin C were very specific in terms of reducing the length of stay in the intensive care unit and shortening mechanical ventilation time. Vitamin C is an antioxidant and water soluble so any excess can be eliminated through urine.

Based on the introduction increased cortisol is correlated with a high risk of mortality. As discussed in the introduction cortisol can suppress the immune system by reducing white blood cells like lymphocytes which play a critical role in viral infections.

### Conclusion

Vitamin C appears to be effective in reducing the length of stay in ICU and decreasing the mechanical ventilation time in COVID-19 infected patients. Moreover, Vitamin D appears to reduce both the severity and mortality of COVID-19 infected patients. It seems feasible that both Vitamin C and D can reduce the severity of COVID-19 symptoms by means of cortisol reduction as the main mechanism since cortisol suppresses the immune system. Well-designed studies measuring cortisol levels during treatment with Vitamin C and D for COVID-19 infected patients are warranted.

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