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Vitamin C and COVID-19

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Corona disease has killed at least 5 million people globally since it started in Wuhan, China in December 2019 (World Health Organization, 2021). The disease is caused by SARS-COVID-19, and is transmitted from person to person by respiratory droplets (Baladia *et al.*, 2020, Ejaz *et al.*, 2020). Although the early symptoms of COVID-19 include fever, weariness, headache, sore throat, cough, dizziness, vomiting, diarrhea, and lung involvement (Shakoor *et al.*, 2021), it can cause long-term risks, such as chronic lung disorders, Alzheimer's, Parkinson's, and multiple sclerosis (Wang *et al.*, 2020)

The absence of a definite preventive or therapy for COVID-19 viral infection is the most significant difficulty humans face. Despite the fact that many vaccinations have been created in this sector, none of them have resulted in total protection of the person against this virus (Galmés *et al.*, 2020). Diabetes, cardiovascular disease, and obesity may impair the immune system's capacity, resulting in increased disease severity and mortality risk (Zabetakis *et al.*, 2020). As a result, it is required to evaluate the elements affecting the strength of an individual's immune system. Previous studies have shown that a person's diet before and throughout the illness has a significant impact on the severity of COVID-19, recovery time, complications, and death (Mentella *et al.*, 2021).

The European Food Safety Authority (EFSA) has classified six vitamins, including D, A, C, folate, B6, B12, and four minerals (zinc, iron, copper, and selenium), as well as their beneficial effects required for the correct functioning of the immune system. It has been seen in the course of COVID-19, (Galmés *et al.*, 2020). Meanwhile, vitamin C, the most significant water-soluble antioxidant with anti-inflammatory and anti-thrombotic effects, may help the immune system operate better and reduce oxidative stress levels (Carr and Rowe, 2020, Colunga Biancatelli *et al.*, 2020). Infection may reduce vitamin C levels in the blood and enhance oxidative stress and inflammation. As a result, during infections, the requirement for vitamin C rises, and this vitamin

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may help to lower the severity of the sickness by enhancing phagocytosis and promoting microbial killing (Di Renzo *et al.*, 2020). According to studies, many risk factors for COVID-19 overlap with vitamin C insufficiency, so that the elderly, males, African Americans, people with diabetes and hypertension, and those with COPD are more likely to have severe COVID-19 levels. They had reduced vitamin C levels in their blood (Holford *et al.*, 2020). In patients with severe coronavirus disease, there is also a clear link between hospitalization in the intensive care unit (ICU) and vitamin C insufficiency (Hemilä and Chalker, 2020b). As a result, vitamin C is thought to be effective in preventing and treating coronavirus disease.

People in the top quartile of baseline plasma vitamin C concentrations were 30% less likely to develop pneumonia, according to a prospective research of 19,357 men and women conducted over a 20-year period. Vitamin C supplementation has been shown to reduce the risk of pneumonia in those who are deficient in the vitamin (Hemilä and Chalker, 2020a). Another study conducted on patients with severe corona disease reported that up to 82%of the patients had inadequate vitamin C levels (Tomasa-Irriguible and Bielsa-Berrocal, 2021). Although 0.1 g of vitamin C per day is sufficient to maintain normal plasma vitamin C levels in a healthy individual, substantially greater dosages (about 1 to 4 g per day) are required to raise plasma vitamin C levels in critically ill patients (Hemilä and Chalker, 2020b). In general, the therapeutic impact of vitamin C in the course of infections has been debated, and various and often conflicting findings have been recorded during investigations on respiratory infections and critically ill patients (Milani *et al.*, 2021).

The benefits of intravenous vitamin C on the symptoms of COVID-19 were investigated in 214 patients in a clinical trial research in Shanghai, China. For 7 to 10 days, patients with coronavirus disease received an intravenous daily dose of 10 g vitamin C, while those with severe coronavirus disease received a dose of 20 g vitamin C. In patients with moderate symptoms of COVID-19, high doses of intravenous vitamin C were administered to avoid cytokine storm. The study found that prescribing vitamin C to 50 patients with moderate to severe COVID-19 improved their condition. The intervention group hospital stay decreased to 3 to 5 days, and no fatalities were recorded. Infection with COVID-19 induces an overproduction of pro-inflammatory cytokines, resulting in a cytokine storm, severe lung injury, and adult respiratory distress syndrome. Vitamin C therapy lowered the production of proinflammatory cytokines, cytokine storms, and tissue damage caused by inflammation (Cheng, 2020). Treatment with zinc gluconate, vitamin C, or a combination of these two supplements did not significantly reduce the duration of symptoms in outpatients with SARS-CoV-2 infection in a randomized clinical study compared to the control group (Boudreault *et al.*, 2011). High doses of vitamin C have been shown to minimize the usage of corticosteroids, antibiotics, and antiviral medicines, all of which may weaken the immune system, cause depression, adrenal suppression, and toxicity, and ultimately aggravate the illness process (Szklarczyk *et al.*, 2019).

There are various findings on the impact of a high vitamin C intake on the death rate of COVID-19 patients. While some studies have shown no link between the vitamin intake and mortality, others have found this vitamin to be useful in decreasing death rate (Carr *et al.*, 2017). According to a recent meta-analysis research, vitamin C supplementation lowers the length of time a patient spends in the ICU by 8% and the duration of mechanical breathing in ICU patients (Hemilä and Chalker, 2019). Another clinical trial study done in three Chinese hospitals reported that injecting large doses of vitamin C (50 mm of vitamin C every 12 hours for 7 days) increased the pao2/fio2 ratio but failed for days, and for 28 days, increased forceful mechanical ventilation (Zhang *et al.*, 2021).

The period of vitamin C delivery is also significant; some studies have indicated greater outcomes when vitamin C is given for at least 7 days, and meta-analyses have revealed that the

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duration of vitamin C treatment for COVID-19 is optimal. When the condition lasts for more than 3 to 4 days, and you use it for less than 3 days, the efficacy reduces (JamaliMoghadamSiahkali *et al.*, 2021).

There are concerns regarding the risks and negative effects of consuming too much vitamin C. Vitamin C consumption of up to 2 grams per day has been certified safe in the United States, while 3 to 4 grams per day has been described as the lowest risk of gastrointestinal adverse effects by European food safety experts. Diarrhea produced by excessive oral consumption is one of the risks linked with high dosages of vitamin C. The incidence of diarrhea as a consequence of in-hospital oral treatment or intravenous administration of vitamin C has been recognized and recorded. However, diarrhea seldom occurs at doses less than three grams per day. Another problem associated with high doses of intravenous vitamin C is kidney stones. According to a study conducted at the Kidney Stone Research Laboratory of the University of Cape Town, high doses of vitamin C did not increase the risk of kidney stones. However, people with a history of kidney stones or kidney dysfunction should take high doses of oral and intravenous vitamin C under the supervision of a physician (Auer *et al.*, 1998).

Vitamin C may decrease fatigue and accompanying symptoms, such as sleep disturbances, loss of focus, depression, and pain, in addition to reducing inflammation. It may also be useful in reducing psychological issues in patients with COVID-19 (Gao *et al.*, 2021).

Finally, given the advantages of vitamin C and its beneficial effects on acute respiratory infections, it is believed that taking a vitamin C supplement, particularly in individuals at risk of insufficiency, would be successful in the treatment of COVID-19.

Authors' contribution

All of authors were equally contributed to the searching and writing of the manuscript and approved it.

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