



The therapeutic, preventive, and immune-boosting effects of some minerals and vitamins in COVID-19: A narrative review

Afagh Hassanzadeh Rad¹ , Amirhossein Fakhre Yaseri^{2*}

Abstract

Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), which produces COVID-19, is the most deadly coronavirus ever identified. Essential treatments and nutrition are crucial for improving the immune system against viral infection. As studies recommended checking the nutritional state of COVID-19-infected individuals before treatment, we aimed to review the therapeutic, preventive, and immune-boosting effects of some minerals and vitamins on COVID-19. This review emphasizes the possible therapeutic, preventive, and immune-boosting effects of some minerals such as zinc, selenium, iron, calcium, phosphorus, potassium, and magnesium and vitamins C, D, and E on COVID-19 patients. Regarding the evidence that shows the preventive effects of vitamins and minerals on serious COVID-19, it seems that clinicians have to consider these factors precisely.

Keywords: Vitamin, Mineral, COVID-19, Immunomodulation, Therapy, Prevention

Please cite this paper as: Hassanzadeh Rad A, Fakhre Yaseri A. The therapeutic, preventive, and immune-boosting effects of some minerals and vitamins in COVID-19: a narrative review. *J Parathyr Dis.* 2022;10:e9151.

Copyright © 2022 The Author(s); Published by Nickan Research Institute. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Introduction

Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), which produces COVID-19, is the most deadly coronavirus ever identified (1). Essential treatments and nutrition are crucial for improving the immune system against viral infections such as coronavirus. Several model systems and human investigations have repeatedly demonstrated that poor diet weakens the immune system. Furthermore, before administering general medications, they recommended checking the nutritional state of COVID-19-infected individuals (2).

A hectic lifestyle, obesity, viral infections, and diabetes directly impact the status of nutrients and have all been scientifically proven to cause the body to become deficient in nutrients, minerals, and vitamins when the body fights against infections. The expression of immune cell genes and aiding in developing immune cells are some of their beneficial roles—for instance, vitamins E and C act as potent antioxidants in the fight against free radicals (3). This review emphasized the possible therapeutic, preventive, and immune-boosting effects of some minerals such as zinc, selenium, iron, calcium, phosphorus, potassium, and magnesium in addition to vitamins C, D, and E on COVID-19 patients.

Methods

In this narrative review, we evaluated the probable effects

of some vitamins and minerals on COVID-19. We searched and extracted relevant English publications from the Web of Science, PubMed, Scopus, and Google Scholar using keywords such as COVID-19, zinc, selenium, iron, calcium, phosphorus, potassium, magnesium, vitamin C, vitamin D, and vitamin E.

COVID-19

The pneumonia of unknown causes was detected in Wuhan city (China) in December 2019, and it was called coronavirus (COVID-19). This virus spread rapidly and caused a global pandemic in March 2020. Thus, various countries adopted extreme public health measures to control it (4).

The clinical characteristics of COVID-19 are categorized into five distinct types as follows (5):

1. Asymptomatic/presymptomatic infection; no symptoms/no findings in chest imaging
2. Mild illness; fatigue, malaise, fever, cough, headache, muscle pain, anorexia, sore throat, nausea, vomiting, dyspnea, and nasal congestion/No shortness of breath/no abnormal findings on chest imaging
3. Moderate illness; mild symptoms/mild abnormalities on chest imaging due to lower respiratory tract infection (LRTI)
4. Severe illness; various signs of the LRTI with some of the following features:

Received: 17 July 2022, Accepted: 22 August 2022, ePublished: 11 September 2022

¹Pediatric Diseases Research Center, Guilan University of Medical Sciences, Rasht, Iran.

²Faculty of Medicine, Qazvin University of Medical Sciences, Qazvin, Iran.

*Corresponding author: Amirhossein Fakhre Yaseri, Email: Ahfyaseri@gmail.com

■ Implication for health policy/practice/research/medical education

This review emphasizes the possible therapeutic, preventive, and immune-boosting effects of some minerals such as zinc, selenium, iron, calcium, phosphorus, potassium, and magnesium and vitamins C, D, and E on COVID-19 patients.

- Oxygen saturation $\leq 93\%$ at rest on room air
 - $\text{PaO}_2/\text{FiO}_2 \leq 300$ mm Hg + marked tachypnea
 - $\text{RR} \geq 30$ breaths/min/lung infiltrates $>50\%$.
 - Shortness of breath.
5. Critical illness; septic shock, acute respiratory distress syndrome, mechanical ventilation, necessitates intensive care unit treatment, and multiple organ failure (5).

COVID-19 is not independent and can be associated with different underlying diseases. Even comorbidities such as diabetes can be the risk factors for COVID-19. Therefore, understanding the pathophysiology of COVID-19 helps improve comorbidity management (6).

Since it is a severe contagious disease that can quickly spread, new care methods are required to reduce the likelihood of face-to-face contact between patients and healthcare providers. Thus, the telemedicine application can be an alternative method for in-person visits to stop the virus spread (7). The previous studies highlighted the importance of nutritional supplements. Indeed, these studies helped COVID-19 patients by possibly lowering the viral load and preventing hospitalizations (8). In the next section, the authors investigated the effects of minerals and vitamins on COVID-19.

Zinc and COVID-19

Zinc is a component of various enzymes, and the growth and improvement of immunological and other cells depend significantly on zinc. The deficiency of zinc makes people more vulnerable to viral infectious diseases by impairing cellular and humoral immunity (9). Moreover, it has antiviral effects and is a substantial component of the immune defense against viral infections such as H1N1 influenza (10). Since zinc deficiency decreases cell-mediated immunity, its supplementation is suggested for improving several viral infections. In addition, zinc intake impacts many cellular immune processes, including releasing interferon- γ (IFN- α) and interleukin-2 (11).

The previous studies demonstrated that older people taking zinc supplements produced more IFN- α from their leukocytes in vitro than others. This situation can be beneficial for preventing and treating viral infections such as COVID-19. However, long-term zinc therapy raises the possibility of immune system suppression. Maywald et al revealed that excessive zinc supplementation could decrease the IFN- α production and some essential cytokines for the immune system (12). Furthermore, they reported that raising intracellular zinc levels could

effectively prevent coronaviruses (13). Therefore, its potential impact cannot be ignored on COVID-19.

Selenium and COVID-19

Selenium is the most trustworthy trace element. This issue is due to its anti-inflammatory and antiviral capabilities. The immune system, made up of selenocysteine, is generally regulated by several sets of selenoproteins. Besides, selenium deficiency created significant viral infection risk factors (14). It affects pathogens, especially viruses, and the immunological response. A viral genome changes by dietary selenium deficit, and a mild virus becomes more severe and virulent under oxidative stress (14).

The selenium deficiency not only dysfunctions the host immune system but also transforms coronaviruses from benign to virulent forms. Moreover, it helps collect enzymes that inhibit the production of free radicals and prevent oxidative damage to cells and tissues (15).

An overactive inflammatory response accompanies a compromised antioxidant defense even without active infection. Besides, its efficient operation needs at least 100 μg of selenium per day (16). The previous studies demonstrated that Selenium was in charge of the antiviral properties of glutathione peroxidase. In addition, glutathione peroxidase counterbalances the inflammation induced by COVID-19 (17).

The obtained data demonstrated the critical role of Selenium-based mechanisms in coronavirus infection. Consequently, Selenium considerably impacts COVID-19.

Iron and COVID-19

Anemia, iron overload, and perhaps neurodegenerative disorders are a few clinical symptoms of iron metabolism disorders. These are classified as the most widespread diseases affecting people. In the biological system, iron has several different functions. It is an oxidant that contributes to creating hemoglobin and red blood cells (18). The previous studies showed that both the host and virus needed iron. Although iron excess leads to oxidative stress and the spread of dangerous viral mutations, the iron shortage weakens the immune system (19).

Calcium and COVID-19

Calcium helps fight against viral infections. This procedure is performed by cleaning them out of the cells. Thus, calcium not only gives protection against the simple common cold but also prevents breast cancer and promotes health by adding calcium to vitamin D as a supplement. The patient's calcium level in the blood is adversely correlated with the disease severity. A combined study showed that patients with severe COVID-19 had lower calcium concentrations than patients with mild and moderate diseases. Hypocalcemia (e.g., decreased plasma potassium and sodium levels) indicates COVID-19 infection (20).

This retrospective clinical analysis demonstrated that people with COVID-19 had a relatively high rate of hypocalcemia. The imbalances of 25-hydroxy-vitamin D and parathyroid hormone (PTH) levels are related to hypocalcemia. Besides, the lower serum calcium levels were associated with poorer clinical outcomes, higher rates of septic shock, and death (21). Hence, it is assumed that blood calcium levels are related to the severity and prognosis of individuals with COVID-19.

Phosphorus and COVID-19

The low amounts of phosphorus (hypophosphatemia) are directly correlated with COVID-19 severity, and thus tracking the blood phosphorus level in patients with severe COVID-19 is helpful for prognosis (22). Hypophosphatemia raises the risk of susceptibility to coronavirus infection. Since few minerals are available, phosphorus primarily impairs immune responses, which makes it impossible to repair the harm imposed on cells and tissues and promotes the disease spread. It sheds light on the potential function of phosphorus in reducing COVID-19 causalities (23).

Potassium and COVID-19

Patients with COVID-19 may have potassium problems. The proportion of hypokalemia is higher than hyperkalemia. However, both of them are subject to a poor prognosis and consequences. Serious arrhythmias can be prevented, especially in severely COVID-19 patients. This procedure is conducted through the early diagnosis and control of potassium abnormalities and regular electrocardiogram monitoring (24).

A study showed that potassium level in patients with severe COVID-19 was considerably lower than in mild or moderate patients. In this case, potassium variability was significantly less than sodium variability. The decreased plasma potassium and sodium levels are a coronavirus infection sign (25).

Magnesium and COVID-19

Mg supplements may be quite helpful in reducing the stress brought on by post-traumatic stress disorder due to the COVID-19 pandemic that would affect survivors of COVID-19, medical professionals, and the general public. Controlling several processes, including immune cell adhesion, immunoglobulin production, binding of immunoglobulin M lymphocytes, and cytolysis, also play a crucial role in immune function (23).

However, a previous study revealed that blood magnesium levels may be negatively correlated with White blood cells, neutrophil, and lymphocyte cell concentrations and that high magnesium levels may contribute to or be a consequence of infection with COVID-19 (26). Another study discovered an association between magnesium levels and pneumonia. The mortality

rate in hospitalized patients with hypermagnesemia and even normomagnesemia were higher than in the hypomagnesemia group (27).

Vitamin C and COVID-19

Vitamin C is recognized as an antioxidant because of its potential effect to eliminate harmful reactive oxygen species. It guards the cells and tissues against oxidative harm and malfunction. The levels of vitamin C could drop during infection regarding the need for vitamin C. Therefore, in severe circumstances, vitamin C should be administered intravenously to reach normal levels in the body (28). Based on established research, people that received vitamin C supplements showed considerably reduced rates of pneumonia, which raises the possibility that, under some circumstances, vitamin C may lessen the risk of lower respiratory tract infections. Therefore, Vitamin C can be beneficial in respiratory tract infections due to COVID-19 and is an effective option for treating COVID-19. Additionally, sepsis due to pneumonia, also observed in COVID-19, is influenced by vitamin C. Evidence shows that people with severe COVID-19 may benefit from high dosage vitamin C treatment. To help prevent and promote immunological responses, vitamin C supplementation makes sense for people who are micronutrient deficient and at risk of contracting COVID-19 (29).

Vitamin D and COVID-19

Vitamin D has antioxidant and anti-inflammatory effects, and calcium-phosphorus metabolism is supported by it. Our body may create vitamin D by using sunlight, which besides functions as a hormone. It helps to accelerate the development of numerous cells, including immune cells. Studies have shown that vitamin D prevents the upregulation of inflammatory cytokines, including tumor necrosis factor- α and Interleukin-1 (30). Xu et al showed that calcitriol (the agonist of vitamin D) protects against acute lung damage. Calcitriol regulates the expression of ACE2 (angiotensin-converting enzyme 2) in lung tissue, which is the pathophysiology of COVID-19. A high dosage of between 250 and 500 thousand IU had notable outcomes in several trials (31). According to the previous meta-analysis, people using vitamin D supplements had a lower chance of developing acute respiratory tract infections than those with low baseline vitamin D levels. Hence, it may be beneficial in COVID-19 patients because it is a common complication of coronavirus infection (32). The prospective cohort study showed the level of vitamin D could be the prognostic tool for coronavirus infections. Furthermore, vitamin D insufficiency might be linked to poorer outcomes from COVID-19 (33). There seems to be a link between nations with a higher prevalence of vitamin D insufficiency and greater COVID-19 incidence and death.

Vitamin E and COVID-19

Vitamin E is crucial in lowering oxidative stress through its ability to bind to free radicals as an antioxidant (34). Vitamin E has a role in the immune system besides having antioxidant and anti-inflammatory effects, and it is said to be critical against COVID-19 (35). Vitamin E levels are inversely associated with the number of oxidative stress metabolites. Vitamin E derivatives' antioxidant capabilities, which enhance cell membrane and the immune system against respiratory tract infections, are considered one of vitamin E's possible mechanisms of action against COVID-19 (36).

Folic acid, vitamin E, or a combination of the two, improved blood indices more efficiently. The hemoglobin and hematocrit may considerably increase, especially in acute hemolysis. Therefore, it might be helpful for COVID-19 patients who have acute hemolysis (37).

Taking vitamin E could help COVID-19 patients' neurological damage be partially controlled. In COVID-19 patients, supplemental vitamin E could also act as a therapeutic medicine and reduce damage to several organs, including the heart, lungs, kidneys, liver, gut, and neurological system. According to some research, it causes viral eradication and the elimination of inflammation through modulating T cells (38).

Conclusion

Previous studies showed that vitamin and mineral supplements prevented serious COVID-19 or expedited the recovery rate from COVID-19 complications. Therefore, adding nutritional supplements into the diet is an adopted approach for prevention and treatment processes against infections, especially for those at risk of coronavirus infection.

Clinicians must consider these factors precisely regarding the preventive effects of vitamins and minerals on serious COVID-19.

Authors' contribution

Conceptualization: AHR and AFY. Methodology: AHR and AFY. Validation: AHR and AFY. Investigation: AHR and AFY. Resources: AHR and AFY. Data Curation: AHR and AFY. Writing—Original Draft Preparation: AHR and AFY. Writing—Review and Editing: AHR and AFY. Supervision: AHR and AFY. Project Administration: AHR and AFY.

Conflicts of interest

The authors declared no conflict of interest.

Ethical issues

Ethical issues (including plagiarism, data fabrication, and double publication) have been completely observed by the authors.

Funding/Support

None.

References

- Chen Y, Liu Q, Guo D. Emerging coronaviruses: Genome structure, replication, and pathogenesis. *J Med Virol.* 2020;92:418-23. doi: 10.1002/jmv.25681.
- Zhang L, Liu Y. Potential interventions for novel coronavirus in China: A systematic review. *J Med Virol.* 2020;92:479-90. doi: 10.1002/jmv.25707.
- Gombart AF, Pierre A, Maggini S. A Review of Micronutrients and the Immune System-Working in Harmony to Reduce the Risk of Infection. *Nutrients.* 2020;12:236. doi: 10.3390/nu12010236.
- Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med.* 2020;382:1199-207. doi: 10.1056/NEJMoa2001316.
- Hu B, Guo H, Zhou P, Shi ZL. Characteristics of SARS-CoV-2 and COVID-19. *Nat Rev Microbiol.* 2021;19:141-54. doi: 10.1038/s41579-020-00459-7.
- Hashemipour M, Zamanfar D, Hashemian H, Hassanzadeh Rad A, Shahrokhi M, Dalili S. COVID-19 and Diabetes in Children: A Narrative Review. *Journal of Pediatrics Review.* 2022;10:397-402. doi: 10.32598/jpr.10.SpecialIssue.584.3.
- Badeli H, Nejad AT, Hassanzadeh Rad A. Utilizing Telemedicine for Managing COVID-19. *Journal of Pediatric Nephrology.* 2020;8:1-3. doi: 10.22037/jpn.v8i2.30046.
- Shakoor H, Feehan J, Mikkelsen K, Al Dhaheri AS, Ali HI, Platat C, et al. Be well: A potential role for vitamin B in COVID-19. *Maturitas.* 2021;144:108-11. doi: 10.1016/j.maturitas.2020.08.007.
- Maares M, Haase H. Zinc and immunity: An essential interrelation. *Arch Biochem Biophys.* 2016;611:58-65. doi: 10.1016/j.abb.2016.03.022.
- Sandstead HH, Prasad AS. Zinc intake and resistance to H1N1 influenza. *Am J Public Health.* 2010;100:970-1. doi: 10.2105/ajph.2009.187773.
- Prasad AS. Zinc: role in immunity, oxidative stress and chronic inflammation. *Curr Opin Clin Nutr Metab Care.* 2009;12:646-52. doi: 10.1097/MCO.0b013e3283312956.
- Maywald M, Rink L. Zinc supplementation induces CD4(+) CD25(+)Foxp3(+) antigen-specific regulatory T cells and suppresses IFN- γ production by upregulation of Foxp3 and KLF-10 and downregulation of IRF-1. *Eur J Nutr.* 2017;56:1859-69. doi: 10.1007/s00394-016-1228-7.
- te Velthuis AJ, van den Worm SH, Sims AC, Baric RS, Snijder EJ, van Hemert MJ. Zn(2+) inhibits coronavirus and arterivirus RNA polymerase activity in vitro and zinc ionophores block the replication of these viruses in cell culture. *PLoS Pathog.* 2010;6:e1001176. doi: 10.1371/journal.ppat.1001176.
- Guillin OM, Vindry C, Ohlmann T, Chavatte L. Selenium, selenoproteins and viral infection. *Nutrients.* 2019;11:2101. doi: 10.3390/nu11092101.
- Harthill M. Review: micronutrient selenium deficiency influences evolution of some viral infectious diseases. *Biol Trace Elem Res.* 2011;143:1325-36. doi: 10.1007/s12011-011-8977-1.
- Alehagen U, Alexander J, Aaseth J, Larsson A. Decrease in inflammatory biomarker concentration by intervention with selenium and coenzyme Q10: a subanalysis of osteopontin, osteoprotegerin, TNFr1, TNFr2 and TWEAK. *J Inflamm (Lond).* 2019;16:5. doi: 10.1186/s12950-019-0210-6.
- Seale LA, Torres DJ, Berry MJ, Pitts MW. A role for selenium-dependent GPX1 in SARS-CoV-2 virulence. *Am J Clin Nutr.* 2020;112:447-8. doi: 10.1093/ajcn/nqaa177.
- Abbaspour N, Hurrell R, Kelishadi R. Review on iron and its importance for human health. *J Res Med Sci.* 2014;19:164-74.
- Wessling-Resnick M. Crossing the Iron Gate: Why and How Transferrin Receptors Mediate Viral Entry. *Annu Rev Nutr.* 2018;38:431-58. doi: 10.1146/annurev-nutr-082117-051749.
- Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo

- E, Villamizar-Peña R, Holguin-Rivera Y, Escalera-Antezana JP, et al. Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. *Travel Med Infect Dis.* 2020;34:101623. doi: 10.1016/j.tmaid.2020.101623.
21. Sun JK, Zhang WH, Zou L, Liu Y, Li JJ, Kan XH, et al. Serum calcium as a biomarker of clinical severity and prognosis in patients with coronavirus disease 2019. *Aging (Albany NY).* 2020;12:11287-95. doi: 10.18632/aging.103526.
 22. Xue X, Ma J, Zhao Y, Zhao A, Liu X, Guo W, et al. Correlation between hypophosphatemia and the severity of Corona Virus Disease 2019 patients. *MedRxiv.* 2020. doi: 10.1101/2020.03.27.20040816.
 23. Ni W, Yang X, Yang D, Bao J, Li R, Xiao Y, et al. Role of angiotensin-converting enzyme 2 (ACE2) in COVID-19. *Crit Care.* 2020;24:422. doi: 10.1186/s13054-020-03120-0.
 24. Noori M, Nejadghaderi SA, Sullman MJM, Carson-Chahhoud K, Kolahi AA, Safiri S. Epidemiology, prognosis and management of potassium disorders in Covid-19. *Rev Med Virol.* 2022;32:e2262. doi: 10.1002/rmv.2262.
 25. Lippi G, South AM, Henry BM. Electrolyte imbalances in patients with severe coronavirus disease 2019 (COVID-19). *Ann Clin Biochem.* 2020;57:262-5. doi: 10.1177/0004563220922255.
 26. Anuk AT, Polat N, Akdas S, Erol SA, Tanacan A, Biriken D, et al. The Relation Between Trace Element Status (Zinc, Copper, Magnesium) and Clinical Outcomes in COVID-19 Infection During Pregnancy. *Biol Trace Elem Res.* 2021;199:3608-17. doi: 10.1007/s12011-020-02496-y.
 27. Nasser R, Naffaa ME, Mashiach T, Azzam ZS, Braun E. The association between serum magnesium levels and community-acquired pneumonia 30-day mortality. *BMC Infect Dis.* 2018;18:698. doi: 10.1186/s12879-018-3627-2.
 28. Carr AC, Rosengrave PC, Bayer S, Chambers S, Mehrtens J, Shaw GM. Hypovitaminosis C and vitamin C deficiency in critically ill patients despite recommended enteral and parenteral intakes. *Crit Care.* 2017;21:300. doi: 10.1186/s13054-017-1891-y.
 29. Cheng RZ. Can early and high intravenous dose of vitamin C prevent and treat coronavirus disease 2019 (COVID-19)? *Med Drug Discov.* 2020;5:100028. doi: 10.1016/j.medidd.2020.100028.
 30. Hughes DA, Norton R. Vitamin D and respiratory health. *Clin Exp Immunol.* 2009;158:20-5. doi: 10.1111/j.1365-2249.2009.04001.x.
 31. Xu J, Yang J, Chen J, Luo Q, Zhang Q, Zhang H. Vitamin D alleviates lipopolysaccharide-induced acute lung injury via regulation of the renin-angiotensin system. *Mol Med Rep.* 2017;16:7432-8. doi: 10.3892/mmr.2017.7546.
 32. Martineau AR, Jolliffe DA, Hooper RL, Greenberg L, Aloia JF, Bergman P, et al. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. *BMJ.* 2017;356:i6583. doi: 10.1136/bmj.i6583.
 33. Baktash V, Hosack T, Patel N, Shah S, Kandiah P, Van den Abbeele K, et al. Vitamin D status and outcomes for hospitalised older patients with COVID-19. *Postgrad Med J.* 2021;97:442-7. doi: 10.1136/postgradmedj-2020-138712.
 34. Galmés S, Serra F, Palou A. Vitamin E Metabolic Effects and Genetic Variants: A Challenge for Precision Nutrition in Obesity and Associated Disturbances. *Nutrients.* 2018;10:1919. doi: 10.3390/nu10121919.
 35. Calder PC, Carr AC, Gombart AF, Eggersdorfer M. Optimal Nutritional Status for a Well-Functioning Immune System Is an Important Factor to Protect against Viral Infections. *Nutrients.* 2020;12:1181. doi: 10.3390/nu12041181.
 36. Jovic TH, Ali SR, Ibrahim N, Jessop ZM, Tarassoli SP, Dobbs TD, et al. Could Vitamins Help in the Fight Against COVID-19? *Nutrients.* 2020;12:2550. doi: 10.3390/nu12092550.
 37. Darbandi B, Zarezadeh S, Rosha A, Hassanzadeh Rad A, Baghersalimi A. The efficacy of vitamin E and folic acid on the acute hemolysis caused by glucose-6 phosphate dehydrogenase. *Iranian Journal of Pediatric Hematology and Oncology.* 2017;7:232-6.
 38. Tavakol S, Seifalian AM. Vitamin E at a high dose as an anti-ferroptosis drug and not just a supplement for COVID-19 treatment. *Biotechnol Appl Biochem.* 2022;69:1058-60. doi: 10.1002/bab.2176.