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## Opinion Paper

# The key role of zinc in elderly immunity: A possible approach in the COVID-19 crisis

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## SUMMARY

**Background & aims:** The COVID-19 infection can lead to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), mainly affecting patients aged 60 and older. Preliminary data suggest that the nutritional status can change the course of the infection, and on the matter, zinc is crucial for growth, development, and the maintenance of immune function. In the absence of treatment for this virus, there is an urgent need to find alternative methods that can contribute to control of disease. The aim of this paper is to establish the relation between zinc and COVID-19.

**Methods and results:** From the prior scientific knowledge, we have performed a review of the literature and examine the role of zinc in immune function in the infection by COVID-19. Our findings are that the zinc as an anti-inflammatory agent may help to optimize immune function and reduce the risk of infection.

**Conclusions:** Zinc supplementation can be a useful strategy to reduce the global burden of infection in the elderly, there is a need the increased reporting to improve our understanding of COVID-19 and the care of affected patients.

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## 1. Introduction

The Corona Virus Disease 2019 (COVID-19) started in Wuhan, the largest city of the Chinese province of Hubei, in the second half of 2019. The infection can lead to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), mainly affecting patients aged 60 and older [1,2]. Epidemiological data have shown that the mortality rate increases with both age and occurrence of underlying diseases, being especially combined with hypertension, cardiovascular diseases, diabetes mellitus, smoking, and chronic obstructive pulmonary disease [3].

Indeed, aging is associated with declines in adaptive and innate immunity [4]. Infections, cancer, and autoimmune diseases occur more frequently in the elderly; the coexistence of multiple chronic diseases in the elderly is strongly related to aging. Although many factors, including nutrition, contribute to this the age-related changes in the structure and function of the immune system, termed immunosenescence, play the main role [5,6] in insufficient production of naïve immune cells and amplified oligo-clonal

expansion of memory immune cells. The other important aspect of aging is the occurrence of inflammation, with elevated self-reactivity, increased levels of circulating pro-inflammatory cytokines (e.g., TNF- $\alpha$ , IL-1, and IL-6) and low-grade chronic inflammation [6–8].

Nutritional interventions, including the supplementation of vitamins and minerals, thereby accede to potential therapeutics for novel COVID-19, acting also about of the symptoms of infection such as diarrhea [9]. Recently, the European Society for Clinical Nutrition and Metabolism (ESPEN) published a guidance for nutritional management of COVID-19 patients by proposing diverse practical recommendations, among them, require special focus and consideration the identification of risk and presence of malnutrition in hospitalised patients, highlighting that the nutritional supplementation may be necessary [10].

## 2. Literature search methodology

A literature research was conducted using relevant keywords (MeSH terms: zinc, immunity, aging, and COVID-19). Specially, we considered review manuscripts, but also randomized-clinical trials and case-series reports.

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### 3. Discussion

Vitamins A, C, D, E, B2, B6, and B12, folic acid, iron, selenium, and zinc are some of the main micronutrients essential for a normal capacity to develop an immune response (immunocompetence). Micronutrient deficiencies are a global problem and may predispose an individual to certain infections. Immune function may be improved by restoring deficient micronutrients to appropriate levels, thereby enhancing resistance to infection and supporting a faster recovery when infected. Diet alone may be insufficient and micronutrient supplementation could be necessary, based on the individual characteristics of the target group [11,12].

In this respect, the different mechanisms of immune response depend on specific micronutrients for their adequate performance. Thus, although the mechanisms involved are not yet fully clear, the total presented body of evidence suggests that supplementing the diet with a wide of selected micronutrients with effective immune function may help to optimize immune function and reduce the risk of infection. The efforts to fight the current pandemic scenario of COVID-19, in which there is still no vaccine or specific drug, create a need to achieve the most effective treatment possible for infected patients. There still is not a consensus for nutrition therapy of these patients, but specialists add efforts to reach the best clinical outcome, and the nutritional intervention a key element in this process.

Zinc has the potential to increase the cytotoxic activity of NK cells, which are capable of attacking cells that exhibit abnormal or unusual proteins in the plasma membrane. When NK cells kill infected cells, the microorganisms inside are released and destroyed through phagocytosis by neutrophils and macrophages, which migrate to infected areas. The zinc also acts as an anti-inflammatory agent, maintaining immune tolerance as it induces the development of Treg cells and mitigates the development of pro-inflammatory Th17 and Th9 cells, besides being involved in antibody production, particularly IgG. Microarray analysis of T-lymphocyte population changes in moderate zinc deficiency has indicated alterations in the expression of various genes related to the proliferation, survival, and response of T-cells [11,13–16]. Zinc deficiency is very common, particularly within the elderly population, and there are difficulties in the diagnosis because of the lack of clinical signs and reliable biochemical indicators, as well as the absence of a specific and reliable biomarker of zinc status [17,18].

The recommended daily intake of zinc depends on several factors such as age, sex, weight, and phytate content of diet. Those recommended values differ, the US Food and Nutrition Board/Dietary Reference Intakes (DRI) recommended intake for the adult of 11 mg/day for males and 8 mg/day for females. However, besides of reduced zinc dietary intake, some age-related factors including intestinal absorption, drug interactions, subcellular processes, among others, may jeopardize his activity. Zinc supplementation must be assessed individually, considering cases of zinc deficiency, low dietary intake, and related diseases. According to the studies that evaluated zinc supplementation with different doses and duration, 20–40 mg/day appears to be a safe and effective dosage [19,20]. It is worth mentioning that there is no consensus on these values.

### 4. Conclusion

Therefore, it is worth to investigate the efficacy of zinc supplements - especially because they have relatively low cost, low toxicity, and the potential to reduce the global burden of infection,

as well as to suggest strategies to support clinical nutrition services within a multidisciplinary team. It is important to point out the complementary role that the various micronutrients play, not acting in isolation, but being mutually dependent instead.

### Statement of authorship

Poliana Guiomar de Almeida Brasiel carried out the study and the whole writing of the manuscript.

### Statement and funding sources

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### Declaration of Competing Interest

No conflict of interest to declare.

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