

# Nutritional Interventions for COVID-19

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The coronavirus infection (COVID-19) conveys a serious threat globally to health and economy because of lack of vaccines and specific treatments. A common factor for conditions that predispose for serious progress is a low-grade inflammation, as seen e.g. in metabolic syndrome, diabetes and heart failure to which micronutrient deficiencies may contribute. The aim of the present article is to explore the usefulness of early micronutrient intervention, with focus on zinc, selenium and vitamin D, to relieve escalation of COVID-19.

Methods: We have conducted an online search for articles published in the period 2010-2020 on zinc, selenium and vitamin D and corona and related virus infections.

Results: There were a few studies providing direct evidence on association between zinc, selenium and vitamin D and COVID-19. Adequate supply of zinc, selenium, and vitamin D, is essential for resistance to other viral infections, immune function and reduced inflammation. Hence, it is suggested that nutrition intervention securing an adequate status might protect against SARS-CoV2, and mitigate the course of COVID-19.

Conclusion: We recommend initiation of adequate supplementation in high risk areas and/or soon after the time of suspected infection with SARS-CoV-2. Subjects in high-risk groups should have high priority as regards this nutritive adjuvant therapy, which should be started prior to administration of specific and supportive medical measures.

Keywords: COVID-19 ; corona virus ; nutritional ; therapy ; micronutrients ; selenium ; zinc ; vitamin D ; coenzyme Q10

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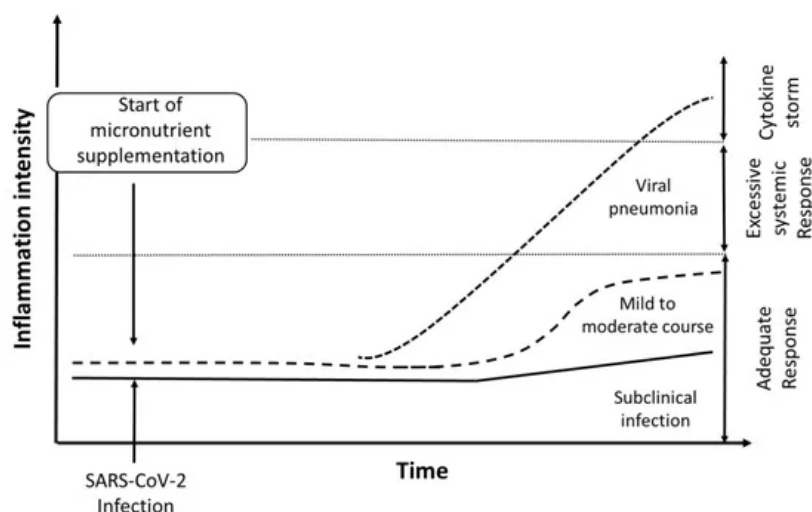
## 1. Introduction

The novel coronavirus SARS-CoV-2 (Severe Acute Respiratory Syndrome-coronavirus-2), causing COVID-19, is by far the most dangerous coronavirus ever identified, capable of infecting not only animals, but also humans across the globe. The severity of the COVID-19 pandemic has dramatically surpassed the prevalence of acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV), which were distributed to more limited regions in 2003 and 2012, respectively. A single-stranded RNA comprises the genomic structure of SARS-CoV-2 <sup>[1]</sup>. In severe cases, COVID-19 is accompanied by excessive activation of the innate immune system with progressive inflammation and a cytokine storm from activated cells, particularly in the airways <sup>[2]</sup>, leading to the cytokine release syndrome <sup>[3][4]</sup>. Unfortunately, in spite of their anti-inflammatory effects, corticosteroids have been observed to worsen the clinical status of patients with SARS or related virus infections <sup>[5][6]</sup>. Use of convalescent plasma has been tried as a possible approach, but the experiences with this strategy are limited <sup>[7]</sup>. Except for the use of convalescent plasma, there is at present no approved treatment or vaccine for COVID-19. Therefore, it is an urgent need for public health measures, not only to limit the spread of the virus, but also to implement preventive approaches to alleviate severe COVID-19, e.g., by reduction of the excessive inflammation. The metabolic status of the host, as influenced by advanced age, current medical condition, and lifestyle, appears to determine the clinical severity of COVID-19 <sup>[8]</sup>. In critically ill patients, coexisting diseases include type 2 diabetes, hypertension, and heart disease <sup>[9]</sup>. The elderly are more prone to severe respiratory infection than young people, apparently due to connections between old age and deficient nutrition and immunity <sup>[10]</sup>. Clinical and subclinical micronutrient deficiencies common in older adults are known to contribute to decreased immune function and age-related diseases <sup>[11]</sup>, implying that nutritional management is essential to reduce the risk of severe infection <sup>[12]</sup>. In view of a lack of clinical data on preventive and/or therapeutic efficiency of the nutritive adequacy of selenium, zinc, and vitamin D in COVID-19, we, in the present narrative review, discussed recent clinical data on the role of these micronutrients in the protection against bronchopulmonary infections, as well as the existing indications of their impact on COVID-19. Although the status of other nutrients, such as vitamins C and A, may also play a role, they were not focused upon in the present article. We did a literature search for the period 2010–2020 on PubMed, Medline, and Google Scholar with the keywords of SARS, SARS-CoV-2, COVID 19, coronavirus, micronutrients (zinc,

selenium, vitamin D), immune system, inflammation, prevention, and treatment. Based on the information retrieved, we here discussed the role of the nutritional status of certain trace elements and vitamin D in the perspective of principles for implementing preventive measures against RNA viruses.

## 2. Discussion and Findings

The direct evidence that the micronutrients zinc, selenium, and vitamin D might be involved in the course and outcome of the COVID-19 disease is observational and weak. However, based on experiences from treatments of SARS and other viral infections, we here underscored observations showing that nutritive supplements administered at an early stage of the infection were important for enhancing host resistance against RNA viral infections, which might also include severe COVID-19. We hypothesized that, in particular, increased resistance toward escalation of COVID-19 into the life-threatening cytokine release syndrome might be obtained (Figure 1). The nutritional status of the host has yet not been considered a crucial factor in severe viral infections, because the efficacy of nutrient supplementation when administered at the stage of advanced illness has been disappointing. Nevertheless, it is conceivable that a good nutritional status, if achieved in vulnerable population segments before escalation of the disease, would have immuno-enhancing and anti-inflammatory effects [13]. We are aware of the alleged therapeutic role of megadoses of vitamin C (6–8 g/day) in viral infections [14][15], but, as this would be a pharmacological approach, we did not further discuss this in the present article. We considered the proposed intervention with, i.a., proteins and multivitamin solutions, given immediately after hospital admission to relieve the COVID-19 infection [16] to represent an interesting modification of our approach. However, further research and clinical trials are requested both on therapeutic and preventive roles of nutritive supplements. Based on the available literature, a reasonable presumption is that the pre-infectious status of zinc, selenium, and vitamin D might be of especial importance for the resistance against a progressive course of COVID-19.



**Figure 1.** Hypothesized effect of supplements (Zn, Se, and vitamin D) on intensity of inflammation in patients with COVID-19: A severe course of the disease, which may occur in cases with pre-infectious low-grade inflammation and inadequate status of micronutrients, is characterized by an escalation of the inflammation into a cytokine storm (dotted line). Supplementation with Se, Zn, and vitamins when given at an early stage after infection is anticipated to act protectively by improving immune reactivity and supporting adequate inflammatory response, leading to lower risk of cytokine storm and less severe course of COVID-19, as indicated by the dashed line.

## 3. Recommendations

Our recommendations are early outpatient nutritional intervention in SARS-CoV-2 exposed or high-risk subjects, preferably before specific and supportive treatment. It is tempting to suggest that that early nutritional interventions will be of particular significance for vulnerable segments of populations in developing countries. Such an approach is simple, cheap, and harmless. While high doses of the micronutrients might be needed to restore deficiencies, it is advisable to follow recommended upper tolerable intake levels for long-term intakes of the micronutrients. Parallel to any of the nutritional approaches, controlled studies on the efficacy of anti-viral and anti-inflammatory measures are of importance. To obtain general immunity, a COVID-19-related vaccine is highly warranted.

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