

# Nutrition and COVID-19

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Contributor: Maria Chiara Mentella

SARS-CoV-2, the cause of the COVID-19 disease, is posing unprecedented challenges. In the literature, increasing evidence highlights how malnutrition negatively affects the immune system functionality, impairing protection from infections.

COVID-19

SARS-CoV-2

nutritional status

malnutrition

obesity

undernutrition

nutrients deficiencies

older adults

## 1. Introduction

The contemporary severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), responsible for coronavirus disease 2019 (COVID-19), was first observed in December 2019 in the city of Wuhan, China <sup>[1]</sup>. Then, the fast diffusion of the disease led the World Health Organization (WHO) to declare a status of international health emergency, considering the effects the virus could have all over the world and in particular in underdeveloped countries with lower-quality health infrastructure <sup>[2]</sup>. The COVID-19 outbreak has deeply changed human life and brought new challenges to worldwide healthcare systems, which are currently allocating significant efforts in the development of vaccines, in the identification of therapeutic solutions and in the containment of the infection through restrictive measures such as social quarantine. Clinical manifestations of SARS-CoV-2 range from asymptomatic infection to the onset of serious pneumonia, acute respiratory syndrome, acidosis, coagulation dysfunction, organ failure, and death <sup>[3][4]</sup>. In such a multifaceted spectrum of clinical manifestations, it is crucial to identify predictive factors associated with mild, severe, or critical outcomes.

## 2. Malnutrition in the COVID-19 Pandemic

The retrospective assessment of data of the Spanish flu in 1918, which killed an estimated 50 million victims worldwide, suggested that disease severity resulted from an articulated interaction between viral, societal and individual factors <sup>[5]</sup>. According to recent clinical evidence in the COVID-19 pandemic scenario, several aspects have been correlated with more critical patients' admissions to hospital, higher rate of complications, longer recovery time, and even higher mortality rate. In particular, recent studies have reported how malnutrition is one of the crucial elements that may be predictive of slower recovery, or no recovery at all, for the affected subjects <sup>[6]</sup>. Malnutrition refers to the incorrect intake of both energy and macronutrients (carbohydrates, proteins, fats), as well as to micronutrient (minerals and vitamins) deficiency. In the case of shortage of energy intake, the food energy fails to meet the individual's needs, whereas micronutrient deficiency refers to a lack of vitamins and minerals

which are needed, in small amounts, for healthy growth and development. Although it might seem contradictory, individuals might be overfed in terms of energy but be deficient in one or more micronutrients in their routine diet. Inadequate intake of these nutrients is currently largely diffuse, leading to an impaired resistance to infections and, consequently, to an increase in disease seriousness [7].

In January 2016, the major clinical nutrition societies organized the Global Leadership Initiative on Malnutrition (GLIM) to agree on shared key criteria for the classification of malnutrition in adult people in clinical contexts [8]. These allow defining malnutrition by first screening for malnutrition risk, and then assessing for diagnosis and severity classification. The main criteria involve assessing three parameters concerning clinical manifestation (reduced body mass index, involuntary weight loss, and low muscle mass) and two etiologic parameters (low food intake or assimilation, inflammation or any burden related to the disease). Malnutrition is diagnosed when at least one clinical manifestation and one etiology criterion are present. Malnutrition may be staged as moderate (Stage 1) or severe (Stage 2) according to phenotypic parameters, and fall within one of four categories concerning its etiology, by considering if it is caused by a chronic disease, distinguishing if inflammation is either present or absent, by an acute inflammatory disease, or by starvation (even when related to socio/economic or environmental causes implying food shortage or hunger).

## Malnutrition, COVID-19 Infection, and the Immune System

Nutrition is pivotal in supporting the immune system. Immune homeostasis is indeed well-regulated by a balanced nutrition. Calder et al. reported that an adequate nutrition regimen is key in the defense against viral threats [9]. In the current scenario, in which the changes in dietary and lifestyles habits, largely due to social distancing, might have significantly contributed to a deprived nutritional status, immune system functionality might be undermined. The immune response could indeed be impaired even by minor deficiencies or insufficiencies of some micronutrients [9][10]. Importantly, this can be reversed by correcting the patient's nutritional status.

The European Food Safety Authority (EFSA) scientific panel has highlighted how the healthy maintenance of the immune system strictly depends upon vitamins D, C, A (including  $\beta$ -carotene), and those of group B (particularly B6, B12 as well as folate). Zinc, copper, iron, and selenium are given similar roles. Taking this into account, Galmés et al. [11] have published an updated report on the relevance of nutrition as an immune-enhancing factor. Results from their review demonstrate the importance of preserving a well-balanced level of these ten nutrients, emphasizing the key role played by vitamin D as well as iron as far as the current pandemic is concerned. Relevant micronutrient intake levels—especially those of iron and vitamins B12, C and D—have been found to present an inverse correlation with higher disease incidence and fatality rate, especially in populations showing genetic predisposition to poorer micronutrient status. On the other hand, the wide prevalence of malnutrition and trace element deficiency all over the world will likely affect the global COVID-19 outcomes [12].

## 3. Conclusions

Here, we discussed the relevance of nutritional status in COVID-19 patients, confirming the existing relationship between nutrition status, immune response, and disease clinical manifestations severity. In COVID-19, this relationship has shown to be crucial across the disease phases, particularly in people at risk for a poor prognosis, including obese, undernourished, and older patients. Malnutrition is largely recognized to be both a cause and a consequence of immune system dysfunction. Even prolonged stay in an intensive care unit is a known risk factor for malnutrition, often causing dramatic muscle mass loss and physical function impairment. The altered inflammatory response consequent to the SARS-CoV-2 infection may aggravate catabolic processes and cachexia. These aspects may, in turn, worsen malnutrition and contribute to slow recovery, loss of independence in the daily life, depression, disability, and generally to a decreased quality of life after ICU discharge.

According to ESPEN recommendations, programs addressing the care of COVID-19 patients should integrate nutritional screening, assessment, and therapy. Obesity is a negative prognostic risk factor in COVID-19 disease progression, its effect also being independent of patient age or gender, or the presence of comorbidities. Underfeeding in individuals with COVID-19 should be carefully avoided, and ad hoc nutrition protocols and practical indications should be largely adopted in hospitals. Moreover, research will soon shed light on the possible benefits that ad hoc nutrient supplementation may provide to patients. In this pandemic scenario, community efforts should focus on promoting healthy eating and active living habits, thus preventing overweight, obesity or nutrient deficiency. In this respect, following guidelines for a healthy diet is highly recommended to prevent malnutrition in all its forms. Healthcare services should define and implement cost-effective strategies focused on increasing population awareness on the importance of balanced nutrition regimens, also considering the no imminent end of pandemic.

A multidisciplinary approach is likely to bring the highest benefit to patients. Unfortunately, most of the current knowledge is based on evidence that is mainly retrospective and observational or on previous investigations concerning other populations affected by infectious diseases; thus, it is not possible to draw robust conclusions and further recommendations. Future research should focus on investigating how malnutrition relates to the COVID-19 course and prognosis through rigorous, ad hoc clinical studies.

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