

## Nutrition Importance in preventing COVID-19 pandemic disease

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### Abstract

COVID-19 pandemic was causing havoc across the world. Businesses, education, people's lifestyle, and many more have been severely affected. As humans are adapting to their new environment, many wonders about nutrients and supplements as some believe that certain substances can help reduce and even prevent the symptoms of COVID-19. Currently, only vitamin C has been proven to help boost immune system to fight against COVID-19. Even though it is not proven that certain diets can help the immune system against COVID-19, one should always have a balanced nutritional diet as it can help boost the immune system against many more diseases. A proper diet can ensure that the body is in the proper state to defeat the virus. However, along with the dietary management guidelines the food safety management and good food practices are compulsory. This article explores the importance of nutrition to boost immunity and gives some professional and authentic dietary guidelines about nutrition and food safety to withstand COVID-19. The discussion of the most recent pertinent literature aims to lay the foundations for making reasonable assumptions and evaluations of different types of nutrition, their functions, their mechanism of action, key targets, and their contribution against COVID-19.

**Keywords:** COVID-19, nutrition, pandemic, immune system, nutrition

### Introduction

Coronaviridae is a type of virus that infects mammals and birds, it can cause them to have symptoms like common cold to

severe acute respiratory syndrome (SARS). A new type of coronaviridae emerged in 2019, causing a pandemic across the globe. Ultimately, the virus is now known as COVID-19. It is currently causing a worldwide pandemic across the globe, affecting many people's lives (1). In the current situation, COVID-19 has provided many hardships for humans to have a balanced diet. Self-isolation, social distancing and lockdown are crucial precautions to reduce the infectivity of the disease, these precautions ultimately change one's lifestyle. The act of staying indoors has huge impacts on one's lifestyle, including changes in sleeping habits, eating habits and activities. It would cause sedentary behaviours that affect physical and mental health. This leads to a high chance of obesity (2). The pandemic also caused concerns in people's minds, which caused changes in eating habits leading to unhealthy eating habits and less tendency to eat.

Currently, researchers are developing a vaccine. Even though a vaccine was made, there is a high chance that the virus will mutate, and a new strain of viruses will spread in society (3). Nutritional status is crucial to having a healthy immune system against the virus (4). The efficiency and functionality of the immune response is an important factor in defending against viral infections. Different types of nutrients are a necessity for the body to improve the immune system. Besides, nutritional supplements have positive impacts towards boosting the immune system against infections. For example, taking vitamins A and D supplements raises the strength of immunity

of paediatric patients after having influenza vaccination (5). An unhealthy diet and infections can cause a person to have malnutrition (6).

In terms of COVID-19, it is important to show the data relating to the immune response to disease. Current research shows that COVID-19 shows influenza like viral infections. Therefore, nutrients for the prevention and therapy of COVID-19 are recommended (7). Correspondingly, the purpose of this study was to give a supportive overview of the available scientific literature of using different nutrients in boosting the immune system under the COVID-19 pandemic. Prominence is directed on the supplementation of phytogetic, protein rich food, probiotics, vitamins, and minerals. The negative effects of the COVID-19 pandemic may be mitigated if health and nutrition professionals create individualised nutrition plans that consider nutritional risk and underlying diseases (8).

### **Material and Methods**

A literature search was performed on the PubMed database between June 10 and July 10, 2023, using search terms such as SARS-CoV-2, COVID-19, nutritional status, older adults, obesity, malnutrition, undernutrition, nutrient deficiency, and supplementation. All types of articles related to humans were included for evaluation. Articles for which full text was not available and articles that were not in English were excluded. From the articles retrieved in the first round of searches, additional references were identified by a manual search among the cited references. Studies were critically appraised, and the findings were analysed.

### **Results and Discussion**

#### **Minerals**

Minerals are important to maintain body's health and wellbeing to function properly. Thus, enough minerals are needed for the immune system to function optimally. Individuals who are having mineral deficiency could be dangerous and this happens when

the body does not get enough amounts of mineral that are needed for proper functioning. Therefore, minerals are one of the important nutrition that can help in preventing COVID-19 pandemic disease.

#### **Zinc**

Zinc is a necessary mineral that can be obtained from fruits, vegetables, meats, legumes, some shellfish, some fortified cereals, and whole grain (9). It has an important role in maintaining and growing innate and adaptive immune cells (10). Zinc deficiency will lead to dysfunction of the immune system that increases the chances of getting diseases and infections. Many studies emphasized that zinc could help to prevent respiratory tract infections (11). It has been recorded that supplementation of zinc given to children who have zinc deficiency and are infected with measles has been proven to reduce the lower respiratory tract infections mortality and morbidity rate. Besides, supplementation of zinc in cases of human papilloma virus (HPV) and hepatitis C infection has also shown to have clinical improvement. Current studies also show that the increase in concentration of intracellular zinc has marked the reduction in replication of a variety of RNA viruses. It also reported that the combination of low concentration of zinc-ionophores and zinc will slow down the in vitro replication of SARS-CoVs (12).

On the other hand, the targeting of ACE-2 receptors is another way for the treatment of COVID-19. This is because SARS-CoV-2 enters host cells through ACE-2 receptors. Thus, they are thought to be potential therapeutic sites. The activity of human recombinant ACE-2 in the lungs of rat has been reduced when exposing to zinc (100  $\mu$ M) (13). It was observed that there is a significant improvement in 4 patients diagnosed with COVID-19 when they are being treated with zinc salt at high dose in a current case study. COVID-19 related symptoms can also be relieved by taking zinc supplements (14).

Zinc has an antioxidant effect that acts as a primary defense mechanism which helps to defend against viral and bacterial infections.

Adequate amounts of zinc that are present inside the body will have protection against reactive oxygen species (ROS) that exert oxidative stress. Deficiency of zinc will stimulate pro-inflammatory cytokines production which is related to the inflammatory modification of lung that is predisposed to fibrosis. Zinc supplementation in moderate doses has an effect by correcting pro-inflammatory cytokines overproduction in elderly which is due to zinc deficiency. The removal of foreign substances and prevention of infections are stimulated by the proliferation of immune cells that are having this function. Zinc also has a structural role in the body that maintains the integrity of skin and membranes. It controls the function and development of immune cells. Zinc also involves adaptive immunity through the participation of development of T lymphocytes through promoting the binding action of some regulatory enzyme to T cells (15).

#### **Iron**

Iron is a necessary mineral which contributes to the development of immunity. It can be obtained from dried fruits, eggs, shellfish, legumes, red meat, grains, fish, and poultry (16). Deficiency of iron will destroy host immunity because many immune cells require iron for development and growth. However, high dose of iron will cause oxidative stress which creates an appropriate environment that will cause harmful viral mutations (17). During the current COVID-19 pandemic, it could be useful to maintain an adequate level of iron as deficiency of iron will increase the chance of acute respiratory tract infections reoccurrence. Iron will contribute to up-regulation of immune response while dysregulating homeostasis of iron which regulates the production of pro-inflammatory cytokine. It also controls enzyme synthesis which is important for generation of immune cells. This includes ribonucleotide reductase that carries out DNA synthesis. Iron will help neutrophils to kill bacteria and viruses by generating hydroxyl radicals. It also stimulates ROS synthesis that will destroy pathogens as well as induce T lymphocytes differentiation (18).

In a retrospective investigation of patients being hospitalized due to COVID-19, it was indicated that most the patients that suffer from functional iron deficiency are associated with continuous inflammation and results in prolonged staying in hospitals (19).

#### **Selenium**

Selenium is a crucial element that is only required in small amounts in the body. The content of selenium present in food depends on the quantity of selenium contained in soil. Therefore, the quantity of the same food will be different in separate locations. The primary sources of selenium are mushrooms, fish, bread, nuts, seafood, whole grains, meat, and dairy products. It involves mammalian redox reaction by acting as enzyme cofactor. The nutritional condition in a host is important to protect against virus infections, thus nutrients deficiency will affect the immune reaction and viral infection (20).

The deficiency of selenium in diet will lead to an increase of body's oxidative stress. This may result in the mutation of viral genome, and it is also possible to transform a benign virus into a more infectious pathogen and highly virulent. Low levels of selenium have been shown to increase the pathogenicity of coxsackievirus, influenza virus, and COVID transforming their genome from non-virulent virus to virulent virus. The mutation of genome will change the function of some enzymes which control the regulation of oxidative stress level in body and lead to tissue as well as organ impairment (21).

Selenium has been reported to cause the up regulation of reaction to a live infectious coronavirus vaccine against avian coronavirus (IBV) in the chickens when it is taken along with ginseng saponins. Current study shows that selenium has a role in inhibiting ACE, which is beneficial against COVID-19. Another study suggests that pre-infectious levels of selenium and zinc may have particular significance in resisting the progression of COVID-19 (22). These findings had shown that using selenium supplements is helpful in the COVID-19 treatment. The immune effect of

selenium is due to its role in selenoproteins (selenium-dependent enzymes) that control oxidative stress level in the body. Selenoprotein will mediate the defense system of antioxidants which helps in controlling the function of leukocytes. It also involves in production of immunoglobulins and proliferation of T lymphocytes which will protect the body against diseases and infections (23).

#### **Vitamin A**

Vitamin A is a potent anti-inflammatory which plays a remarkable role in enhancing the immune system by strengthening the functions of cell immune response and humoral immune response (24). It plays a relatively crucial characteristic in immune capability of mucosa and integrity of epithelial cell. The immune system can be improved, and inflammation can be reduced by  $\beta$ -carotene (provitamin A carotenoids), a powerful antioxidant found in vegetables and fruits. It increases lymphocytes which are the disease-fighting cells in the body (25). Therefore, vitamin A is believed to maintain a healthy immune system and fight against SARS-CoV-2 infections.

Bioavailability of vitamin A is around 17% if consumed in a mixed diet. The bioavailability of vitamin A is affected by food-preparation techniques, dose of  $\beta$ -carotene and the number of carotenoids in the diet (26). Vitamin A sources from vegetables include green leafy vegetables like tomatoes, carrots, spinach, pumpkins. Vitamin A sources from fruit include  $\beta$ -carotene rich fruits like oranges, papayas, apricots, grapefruits. Vitamin A sources from animals include retinol-rich food like cream, cheese, liver, kidney, halibut fish oil (27).

#### **Vitamin B6**

Vitamin B6 is to sustain the homocysteine level in blood. The normal range of homocysteine level is between 5 to 15 mmol/L. Increased level of homocysteine will increase the risk of getting cardiovascular disease. Vitamin B6 consists of 3 derivatives which are pyridoxal, pyridoxamine and

pyridoxine. All these derivatives can be converted to pyridoxal phosphate coenzyme which is essential for most biological activities in the body. It is involved in carbohydrates, protein, fat metabolism and many other reactions in the body. Recently, there is a research study about bananin (BAN), one of the derivatives of vitamin B6. They found out that BAN can inhibit the function of SARS-helicase enzyme that is required for viral replication process (28).

Bioavailability of vitamin B6 is around 75% if consumed in a mixed diet. The bioavailability of vitamin B6 is affected by temperature and food-preparation techniques. It will be destroyed by high temperatures. The sources of vitamin B6 include liver, fishes, chickens, potatoes, oats, peanuts, and starchy vegetables.

#### **Vitamin B12**

Vitamin B12 is for the proper development of nervous system, red blood cells and DNA synthesis. Besides, it is also an essential immune modulator for cell immune response. Vitamin B12 combines with folate which helps to maintain homocysteine levels in blood. According to one of the studies, combination of vitamin B12 and folate is believed to have crucial responsibility on a healthy immune system. The studies found out that this combination enhances protein and nucleic acid formation as well as inhibits metabolism and activity of immune cells. Thus, the immune response improved drastically (29).

Bioavailability of vitamin B12 in adults with healthy gastrointestinal tract is around 50% absorbed. Absorption is impaired by an inadequate number of intrinsic factors in the stomach. The bioavailability of vitamin B12 is affected by temperature and food-preparation techniques. It will be destroyed by high temperature and prolonged cooking. The sources of vitamin B12 include poultry, fish, meats, eggs, and milk.

#### **Vitamin C**

Vitamin C is the most essential scavenger for the healthy functioning of the immune system, especially in fighting viruses.

It is an antioxidant which fights against the oxidative free radicals produced by viruses by stimulating skin removal activity. Therefore, the role of epithelial barriers against microbes is enhanced. As evidence, a high dose of vitamin C is given intravenously for the treatment of serious infections such as acute respiratory distress syndrome. Most of the patients have improved signs and symptoms. Vitamin C is crucial in cancer prevention and wound healing. This is because cancerous cells are highly susceptible to free radicals, so vitamin C can protect the body cells from free radicals.

Besides, it also maintains the well-functioning of cell immune response and humoral immune response. Vitamin C can stimulate chemotaxis phagocytosis by assembling in neutrophils. Therefore, all the microbes are killed. It also decreases tissue damage and necrosis by stimulating neutrophil removal and apoptosis from the site of infection.

Moreover, due to gene-regulating activities, vitamin C enhances cell differentiation and proliferation in B and T lymphocytes. B lymphocytes mature in bone marrow and are involved in innate immune response while T lymphocytes are mature in thymus gland and involved in adaptive immune response. Thus, inflammation is increased, sensitivity towards infections is increased and causes immune system impairment in vitamin C deficiency. However, there are studies that have proven that vitamin C supplement can prevent and heal respiratory and systemic diseases (30). So, vitamin C seems to be essential in reducing risk of getting COVID-19 by preventing irritation of immune cells and diseases. A clinical trial carried out in the USA revealed that sepsis-induced acute respiratory distress syndrome (ARDS) death rate reduced by vitamin C given intravenously. This is helpful for COVID-19 patients because most mortality is due to serious progression of ARDS.

The amount of consumption of vitamin C affects the level of absorption.

Bioavailability of vitamin C is around 70-90% being absorbed when intake is less than 1000mg/day and around 50% when intake is more than 1000 mg/day. The bioavailability of vitamin C is affected by food-preparation techniques, storage time and surrounding conditions. It will be destroyed by high temperature and oxidation by oxygen. The sources of vitamin C include green leafy vegetables and citrus fruits like oranges, lemons, and grapefruits.

### **Vitamin D**

Vitamin D has two derivatives which are Vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol). It is synthesized in the skin from cholesterol-derived precursors when exposed to sunlight. Vitamin D is a powerful scavenger of pro-inflammatory cytokines in the body. This can help to minimise the risk of viral infections as well as respiratory tract diseases. Since the role of immune cells is influenced by vitamin D receptors, it is highly related to innate and adaptive immune responses against infections. It also blocks the renin-angiotensin system (RAS) and thus prevents hypertension.

There are studies showing that high levels of vitamin D in the blood can prevent some chronic diseases such as cardiovascular disease, acute respiratory distress syndrome and hepatitis which are patients that are highly susceptible to COVID-19. However, the intensity of vitamin D supplements in minimising the risk of respiratory tract infections varied. According to the research, among individuals with respiratory tract infections, patients with influenza had lesser sign and symptoms but only with high dose of vitamin D which is more than 1000 IU can recover faster (31). Therefore, the efficacy of vitamin D is more effective on people with vitamin D deficiency. According to another studies, it is proven that vitamin D increases cathelicidin and  $\beta$ -defensin levels or activates the Toll-like receptors (TLRs) in innate immunity. Vitamin D also decreases the pro-inflammatory cytokines production and antibodies secretion from plasma cells in adaptive immunity (32). Thus, vitamin D

supplements are crucial to prevent and treat COVID-19. The sources of vitamin D are mainly from sunlight. The natural food sources of vitamin D include egg yolks, liver, fortified food like cereals and oily fish like salmon and mackerel.

### **Vitamin E**

Vitamin E is the most powerful antioxidant among all the vitamins. It is always said to be a cancer preventing agent. This is because it protects the cells against free radicals and maintains the integrity of cell membrane and thus aids in regulating immune response. Therefore, deficiency in vitamin E alone will weaken immune response in our body especially in elderly (33). Vitamin E is a fat-soluble vitamin. High fat meals can increase the absorption of vitamin E. So, people who are on diet have irregular intake of green leafy vegetables and edible oil, they will have relatively increased chances of getting vitamin E deficiency. The sources of vitamin E include green leafy vegetables like broccoli and spinach, edible oil like sunflower oil and wheat germ, avocados, sunflower seeds as well as nuts.

### **Proteins**

Protein-rich foods are essential in boosting our body immune system which can get from fish, milk, and eggs. A low carbohydrate diet is also known as a protein-rich diet where aids in keeping our body fit (34). Proteins are the building blocks of cells and every tissue which leads to the build-up of organs, systems, and organisms. Proteins also represent enzymes and hormones which control functions of various body systems. Protein is mainly composed of carbon, hydrogen, oxygen, and nitrogen which are essential for the formation of natural and acquired immunities against any infectious agents. Dietary protein can be obtained from two sources, which are animals or plants. Animal sources of protein are responsible for the pro-inflammatory aspects whereas plant derived proteins in charge of the anti-inflammatory properties (35).

Malnutrition of proteins leads to essential amino acids deficiency which causes immune dysfunction. Thus, it shows that amino acids are beneficial and important towards immune modulatory effects to stimulate the body immunity. Besides, a low pool of available proteins leads to reduction of functional active immunoglobulins and gut-associated lymphoid tissue (GALT). GALT is responsible for producing secretory IgA which prevents the adhesion of pathogens to the intestinal surface which prevents the damage of gut.

Dietary intake of certain proteins is crucial to produce antibodies optimally. Villous morphology is maintained by branched chains of amino acids besides the rise in intestinal immunoglobulin levels which enhance the gut barrier and response. Furthermore, certain amino acids act as the modulator in metabolism and the body immune system. For example, T-cell response and number of T-helper cells increase with the consumption of arginine supplementation by playing roles in prolonged or repeated infection. The most abundant amino acids, glutamine is performing an essential role in cell proliferation which divides cell such as reticulocytes, lymphocytes, and fibroblasts rapidly (36). In common situations, glutamine is synthesised by the body itself by catabolism. However, when the body is facing acute stress, the endogenously synthesised glutamine is unable to meet the high requirement of glutamine during acute stress. Therefore, a dietary supplement of glutamine is needed to maintain the glutamine level.

Fish, fish oil and various marine protein sources contain omega-3 polyunsaturated fatty acids (PUFA) which are also known as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). EPA and DHA involve several cellular mechanisms such as incorporation into cellular membranes to stimulate the anti-inflammatory response. EPA and DHA also involve in the pro-resolving lipid mediator's synthesis such as protectin and maresins by acting as the substrates in that mechanism. These lipid mediators suppress influenza to replicate and have influence in the

inflammatory manifestations of respiratory viral disease.

### Probiotics

Studies recommend that the utilisation of probiotics shows a positive impact on the prevention and treatment of COVID-19. Probiotics fight against viral infection at three different levels. Firstly, probiotics play an essential role in the body immune system by regulating the immune cells in response to the pathogens or ant infectious agents which attack the mucosa or epithelium cell in intestine. Probiotic cultures inhibit the virus from entering cells by acting in the ACE receptor region. It also produces a synergistic immune response between the gastrointestinal and lung microbiome (37).

Some studies have proved that probiotic bacteria have potential in reducing the incidence of bacterial and viral infections of airways. With administration of antibiotics, increase of predisposition of airways viral infection is observed due to the change in gut microbiome under influence of antibiotics (38). *Lactobacillus* and *Bifidobacterium* also show decrease the case of infection and able to improve the outcome of viral infection (39). In India, a well-organized randomized controlled trial is conducted with 5,000 infants. Those infants are treated with lactobacillus plantarum strain and prebiotics and showing a reduction in level of sepsis and lower respiratory tract infections (LRTI) (40). Probiotics response to airway viral infection via pattern recognition receptors like the toll-like receptors (TLR) (41). TLRs receptors connect natural immunity to acquired immunity. They recognize the pathogen-associated molecular patterns (PAMPs) then initiate the downstream signalling cascades like nuclear factor- $\kappa$ B (NF- $\kappa$ B) which induces expression of the antiviral gene. Furthermore, in the expression of TLRs, antigen-presenting cells (APC) such as macrophage and dendritic cells perform a vital role after being activated by probiotics. The activated APCs induce the activation of natural killer (NK)

cells. NK cells will then release interferon-gamma and are responsible for the antiviral defense (42).

### Phytogetic/ Phytochemical

Phytochemicals are a biologically active nutrient chemical from plant foods such as vegetables, fruits, and grains. Phytochemicals improve health beyond basic nutrition needed to give protection against major chronic disease in relation to their content of active substances such as polyphenols and secondary metabolites (43). Dietary polyphenols are reported to exert an anti-inflammatory, immunomodulatory, antioxidant and anti-allergic microbial activity. Suppression of neuraminidase and hemagglutinin activity by polyphenols is the major important mechanisms that affect the entry, adhesion, replication and hemagglutination of virus into host cell (44). Polyphenols also act as a immune system modulator by binding to the cellular receptor which then alters the cellular pathways and gene transcription factor thereby regulates the host immune response.

Moreover, curcumin inhibits the release of proinflammatory cytokine TNF- $\alpha$  by inhibition of nuclear factor-kappa  $\beta$  (NF- $\kappa$  $\beta$ ) signalling cascades. NF- $\kappa$  $\beta$  is a proinflammatory protein complex which express the proinflammatory genes to produce various inflammatory substances such as chemokine and cytokines [Lawrence et al., 2009]. Curcumin performs important roles in the immune cell proliferation and activation too like B-lymphocytes and T-lymphocytes which are responsible for innate immunity. In consequences, the level of antibody increases thereby stimulating and enhancing the immune response by rising of leukocytes level and phagocytes activation. The enhanced function of B-lymphocytes, T-lymphocytes, and various immunologic agents such as macrophage and neutrophils will then suppress the inflammatory response (45).

### Conclusion

When the COVID-19 pandemic started, scientists wanted to find a vaccine to cure this disease. Even if a vaccine is

delivered, the human immune system will still need to defend the body against COVID-19-infected bodies. Proper nutrition diets can help in maintaining immune systems as the front line of defence. Based on the studies conducted, all nutrition contributes towards boosting the immune system. Minerals such as zinc can maintain and grow innate and adaptive immune cells. It also acts as an antioxidant agent. Iron can upregulate immune response while dysregulating homeostasis of iron which regulates the production of pro-inflammatory cytokines. Selenium contributes towards mammalian redox reaction by acting as an enzyme factor. Vitamins such as vitamin A, vitamin B6, vitamin B12, vitamin C, vitamin D and vitamin E all perform different roles in maintaining the immune system such as strengthening the functions of cell immune response and humoral immune response, sustain homocysteine level in blood, development of nervous system, acting as an antioxidant and as pro-inflammatory cytokines. Proteins on the other hand represent enzymes and hormones which control functions of various body systems while probiotics inhibit viruses from entering the cell by acting in ACE receptor region. Lastly, phytochemicals improve health beyond basic nutrition needed to give protection against major chronic disease in relation to their content of active substances.

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#### Conflict of Interest

The authors declare no conflict of interest.

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