



# Nutrition Strategies Pre-infection, during, and Post-infection with Coronavirus Disease

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## Abstract

Coronavirus disease is a serious viral infection that is characterized by severe inflammation and lymphopenia. The virus attacks many organs causing acute respiratory distress and malfunctioning of the organs leading to death. Through strengthening of the innate immune system, a balanced diet plays a critical role in defense against bacterial and viral diseases. A healthy diet before, during and after an infection can lessen the severity of the symptoms and speed up the recovery of damaged cells. Due to the Mediterranean diet's high concentration of bioactive polyphenols, which have antioxidant, anti-inflammatory, and antithrombotic properties, numerous studies have suggested that it is a preventative dietary strategy against many diseases including coronavirus disease. Nutrition and herbal plants play a key role to enhance the immunity of people to protect and fight against coronavirus. Diet rich in antioxidants and phytochemicals represents perfect barrier to the virus through elevation of the innate immunity of the body. In addition, gut microbiota including prebiotics, probiotics, and synbiotics were found to enhance immunity to reduce the symptoms of the disease during infection. Protein-rich foods and honey bee products reported significant role during and post-coronavirus infection. This review presents updated information from original pre-clinical and clinical researches, and review articles as well to expose the nutritive strategies including breastfeeding benefits to infants pre-infection, during, and post-infection with coronavirus.

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## Introduction

The World Health Organization (WHO) has stated that the infections of the respiratory system in humans are considered from the highly ranked causes of mortality worldwide with special regard to the infections of the lower respiratory tract that comes to the 4<sup>th</sup> ranking [1]. Coronavirus represents one of the most infectious viral infections that inhabit bats and birds, and then extends its infection to humans causing severe damage of the respiratory tract [2], [3]. Coronavirus is a single-stranded ribonucleic acid (RNA) virus that belongs to the family *Coronaviridae* which was firstly discovered in 1960 and the first infected human case reported in Wuhan, China in 2019 [4]. Among RNA-viruses, coronavirus contains the biggest RNA genome as previously published [5]. In mammals, coronavirus can be transferred from bats in the form of alpha- and beta-coronavirus strains, while gamma- and delta-coronavirus strains infect birds [2]. The immune system plays key role in protecting the body against infectious

pathogens. Immunity includes innate and adaptive immunity, innate immunity acts as barrier against the entrance of pathogenic subjects to inside the body through the fast inflammatory responses of specific cells [6]. In addition, acquired immunity responds to the infection by killing viral-infected cells using antibody-secreting cells related to the antigens produced by the pathogen [7].

Balanced diet plays crucial role in protection against bacterial and viral diseases through reinforcement of the innate immune system. In addition, balanced nutrition during and after infection can reduce the severity of symptoms and accelerate healing of damaged cells as well [8]. Recently, studies have shown that following the pandemic, food consumption in many countries changed, and shifted to immune-boosting foods [9]. Many articles exposed the role of nutrition in coronavirus pandemic. Mediterranean diet (MD) was reported by many studies for its protective nutritive strategy against diabetes and cardiovascular diseases in addition to its high contents of bioactive polyphenols that possess antioxidant, anti-inflammatory,

and anti-thrombic activities. Therefore, MD was recommended for coronavirus patients to reduce the severity of inflammation and thrombosis [10]. Idelson, Rendina, and Strazzullo, in 2021, have reported that excess alcohol and salts, and lack of vitamin D can negatively weaken the immune system especially in elder people who became easily susceptible to coronavirus infection. Another recent study published that dietary supplementation with nutrients rich in micronutrients, folate, vitamins, and omega-3 fatty acids are effective in stimulating the immune system to reach its optimum working level against influenza virus and coronavirus [7]. A recently published study detailed the role of synbiotics, probiotics, prebiotic, and postbiotics in protecting the body against coronavirus infection and accelerated treatment during the infection [11]. Ismail *et al.*, in 2022, have speculated that during infection with coronavirus, liquids are highly recommended such as juice, soup, water, and teas. In addition, dietary protein-rich foods are needed for healing damaged tissues and meals rich in vitamins and minerals are able to elevate the degree of immunity inside the body enhancing recovery period. It has been recently revealed that honeybee and bee products such as royal jelly and bee bread proven to be good therapy in reducing the possibility of infection with coronavirus disease through their boosting potential to the immunity [12]. Further, breastfeeding was highly recommended by many studies as immunity-boosting strategy for infants during the first 6 months of their lives especially post-vaccination of mothers through the development of high concentration of antibodies to coronavirus in the milk of vaccinated lactating mother [13], [14], [15], [16].

## Database Search

The search of literature was carried out between July 2022 and October 2022, using database of PubMed, Web of Science, Google Scholar, Scopus, and Science direct. The following keywords were used to address the search terms: "Coronavirus," "COVID-19," "COV-19," "severe acute respiratory syndrome coronavirus 2 (SARS-COV-2)," "viral infection," "microbial infection," "influenza," "nutrition," "clinical study," "*in vitro*," "pre-clinical," "double-blind study," "MD," "prebiotic," "probiotic," "symbiotic," "β-glucans," "inulin," "diet," "immunity-boosting food," "antioxidants," "vitamins," "proteins," "minerals," "breastfeeding," "liquid foods," "honey bee products," "fructo-oligosaccharides," "galacto-oligosaccharides," "vaccination," "treatment," "prevention," "patients," "protection," "lactating mother," "gut microbiota," "gut flora," "bacteria," "respiratory tract," "intestinal flora," "inflammation," "inflammatory response," "cytokines," "cytokine storm" "innate and adaptive immunity," and "pandemic." Original research and review articles written in English were only included

in the search. Studies that exclusively examined the functions of the different food constituents without administering pharmaceutical medicines concurrently were excluded from the search. A total of 117 articles were found using the mentioned database searching strategies, while 20 studies were disregarded owing to their lack of relevance. Finally, 97 studies were included in this study and further examined to give a comprehensive summary of the field's advancement. For each paper, the following information was summarized and narratively described: author, year of publication, type of study, key findings, mechanism of interaction, and the methods used to determine interaction.

## Discussion

Natural defense was able to defeat numerous past epidemics by boosting immunity before medicinal science and health organizations working for population health care were able to manufacture and use many medications for the treatment of infectious diseases [17]. The available information from recent studies showed that nutrition has a significant impact on people's immune systems and susceptibility to disease. Many studies have shown that there is synergistic interaction between immunological health and diet [18], [19], [20]. It has been suggested that certain foods or combined nutrients may influence the immune system by activating cells, altering the synthesis of signaling molecules, and changing gene expression [21].

### ***Nutrition strategies in protection and treatment of coronavirus disease***

#### *Nutritional recommendations pre-COVID-19 infection*

#### MD

One of the healthiest food habits in the world, the MD is renowned for its evident and significant positive impact in heart diseases and type-2 diabetes across many investigations [22], [23]. It is characterized by the inclusion of chiefly plant-based vital nutrients, such as fruits, wild fruits [24], vegetables, grains, nuts, and olive oil, which are all rich in health-promoting factors as polyphenols and high quality micronutrients [25]. Due to their potent activity against oxidative stress, inflammation, and atherosclerosis, polyphenols, especially flavonoids and their derivatives, have modulatory and health-promoting benefits, notably in heart and metabolic illnesses [26], [27]. A study conducted on Italian people using online questionnaire during COVID-19 lockdown revealed that approximately 74% of the respondents shifted their dietary practices to MD and were mainly 18–30 years

age [28]. An online international questionnaire was applied to study in different languages (Italian, Arabic, Hebrew, Russian, English, French, and Spanish) during the pandemic COVID-19 in 2020. Based on the MD-screener performed in the mentioned study, those MD-adhered participants recorded inverse correlation to weight increase and anxiety [29]. Figure 1 illustrates the main constituents of MD along with its potential against COVID-19.

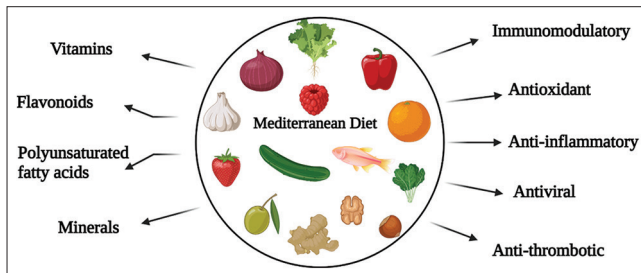


Figure 1: The main constituents of MD and its potential against COVID-19 infection. Vitamins, flavonoids, polyunsaturated fatty acids, and minerals play crucial role as immunomodulatory, antioxidant, anti-inflammatory, antiviral, and anti-thrombotic activities

### Antioxidants-rich foods

Antioxidants are well-known compounds in protecting the body against many diseases such as cancer [30], liver damage [31], and gastric disorders [32]. Numerous studies have revealed that the pathogenesis of respiratory viral infections, such as COVID-19 infection, is significantly influenced by the generation of excessive reactive oxygen/nitrogen molecules and an imbalanced milieu between these oxidant species and cellular antioxidants [33], [34]. Antioxidant phytochemicals may be good choice in boosting the immune system pre-infection, protecting against the spread of coronavirus disease during infection, and preserving health balance post-infection.

### Immunity-boosting foods

In humans, coronaviruses are causing common cold and, recently, SARS. This presents a major threat to public health. The novel coronavirus has spread rapidly to multiple countries and has been declared a pandemic by the WHO. COVID-19 is usually caused by a virus to which most probably the people with low immunity response are being affected. Herbal plants increase the intestinal beneficial bacteria which are helpful and make up the immune system. In addition to the well-known personal hygiene and preventive measures against the new coronavirus (COVID-19), we can also follow some simple recommendations regarding our nutrition that strengthen our immune system and could better prepare us for an epidemic. The virus rapidly infected too many people within a short period of time. Good nutrition is crucial for health, particularly in times when the immune system might need to fight back. It

can also potentially lead to an increased consumption of highly processed foods, which tend to be high in fats, sugars and salt. Nonetheless, even with few and limited ingredients, one can continue eating a diet that supports good health. Numerous researches looked into the possibility that the bioflavonoid quercetin with the potent antioxidant glutathione could protect a range of infections, including COVID-19. In short, nutrition and herbal plants play important role in elevating the natural immunity of individuals against COVID-19 disease [35].

Consumption of plant-based foods is crucial in boosting people's defences against COVID-19 as well as the viral family that produces the common cold and the SARS [36]. In addition, beneficial gut bacteria, which were boosted by plant-based diets, are responsible for about 85% of the immunity. By drinking plenty of water, supplementing with minerals such as zinc and magnesium, micronutrients, foods high in vitamins C, D, and E, and leading a better lifestyle, one can strengthen their resistance against the COVID-19 infection [37].

### Prebiotics

Prebiotics are chemicals that promote the development of commensal bacteria in the gut and the production of microbial metabolites. Prebiotics come in a wide variety, and they have all been thoroughly researched for their ability to improve health through gut microbiota modification and stimulation of commensal bacterial metabolic synthesis. Dietary fibres, inulin, fructans, glucans, and arabinoxylan are examples of common prebiotics [38].

Although the prebiotic galacto-oligosaccharides cannot be digested in the human intestines, it can be fermented by the gut microbiota increasing their abundance and protecting against pathogens as pre-clinically and clinically reported by researchers [39], [40]. It is conceivable that galacto-oligosaccharides and fructo-oligosaccharides could improve the effectiveness of COVID-19 vaccinations. A previous study revealed that maternal fructo-oligosaccharides supplementation improved child responses to oral vaccine, as observed by elevated levels of interferons, immunoglobulin-A, and butyrate that are critical in both innate and adaptive immunity against pathogens [41].

#### Inulin

Inulin as one of the prebiotics found in many plants such as garlic, wheat, asparagus, and onion has reported anti-influenza activity in experimental animals. Mice fed on inulin had decreased systemic monocytes, more activated macrophages, and less chemokine attractant ligand-1 to immune cells (CXCL1) production in the respiratory system. Collapse in the level of CXCL1 has led to reduced neutrophil translocation to the respiratory system and, hence, restrained inflammation and anti-influenza activity [42]. *In vitro* study on fermentation of inulin and fructo-oligosaccharides



using the fecal microbiota of infants for 26 h revealed significant reduction in the production of pro-inflammatory cytokines in the immature dendritic cell line [43].

### $\beta$ -glucans

$\beta$ -glucans are another prebiotic polymers identified as class of polysaccharides found as component of the cell wall of many microorganisms as well as fungi. Researchers consider  $\beta$ -glucans as promising therapeutic strategy against coronavirus infection for its mechanistic stimulation to the trained immunity of the body on supplementation [44].  $\beta$ -glucans were reported for its amelioration to both innate and adaptive immunity of experimental animals through its enhancement to the intestinal bacteria *Lactobacillus* and *Bifidobacterium* that secrete butyrate and propionate and accordingly control gut viral infection [45]. In addition, studies reported that the immunoglobulin IgG1 levels are greatly stabilized and antibodies are significantly produced by B-lymphocytes when  $\beta$ -glucans are taken orally, preserving anti-infectious immunity [46]. An *in vitro* study on the respiratory alveolar type II A549 cell line showed that  $\beta$ -glucans extracted from the mushroom species *Lentinus edodes* reported significant amelioration of the cytokine storm and oxidative stress demonstrating pulmonary cytoprotection and immunomodulation [47]. Figure 2 represents illustration for the mechanism of prebiotics in enhancing the immune response of the body against coronavirus disease.

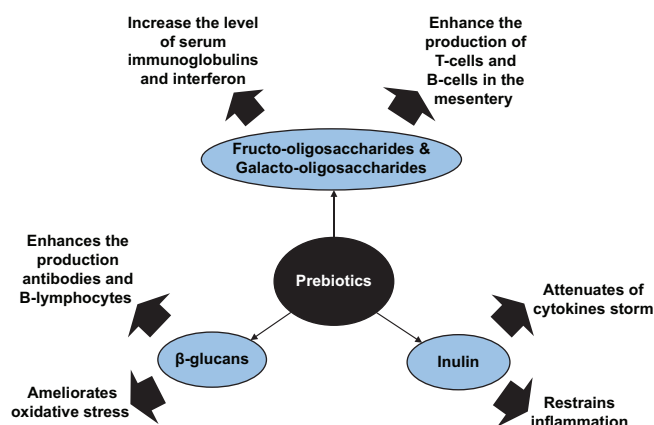


Figure 2 The mechanism of prebiotics in enhancing the immune response of the body against Coronavirus disease. Enhancement of immune cells production by fructo- and galacto-

### Probiotics

Live bacteria known as probiotics can help the host's health when given in sufficient quantities (Food and Agricultural Organization/WHO 2002) [48]. The usage of probiotics to improve human health has long been researched, initially as ingredients in foods and later as cultural preparations. Probiotics have primarily been studied for their potential to prevent and treat gastrointestinal infections and

diseases, but other potential effects have also been investigated, including nutritional effects, prevention and treatment of oral infections, diarrhea brought on by a diverse range of factors, irritable bowel syndrome, *Helicobacter pylori* infections, allergic diseases, antitumor effects, and decrease in serum cholesterol [49]. The numerous bacteria, fungi, viruses, protozoans, and other microorganisms that make up the human gut microbiome are crucial for maintaining human health. The majority of the bacteria in the gut microbiota work in symbiotic relationships with the host [50]. Different aspects, including nutrition, antibiotics, location, culture, and environment, possibly have an effect on the type of bacteria in the gut [51]. Probiotic use on a regular basis helps to keep the gut's composition healthy and ward against various disorders [52]. Compared to persons who do not engage in any aerobic fitness, those who regularly exercise had a highly healthy gut constitution [53]. Excessive use of antibiotics modulates the gut microbiota and responsible for many diseases, it is found out that giving antibiotics in the early life of infants could alter their gut microbiota development. In addition, unhealthy sleep-wake cycle also affects the gut microbiota [54].

### Synbiotics

The integration of probiotics with prebiotics in the same product, referred to as "synbiotics," has a high potential since it implies synergy, in which a prebiotic component specifically promotes the growth and activity of a probiotic microorganism. The knowledge of advanced synbiotics' modified bioactive profile, metabolic function, and possible health advantages holds promise that can be commercially used to satisfy consumer needs [55]. A recent study demonstrated that inulin boosted the intestinal persistence of the synbiotic bacteria *Lactobacillus plantarum* Lp900, which consumes inulin [56].

### Protein-rich foods

A well-balanced diet can strengthen the immune system to fight against COVID-19 [57]. For people at high risk of infection, protein requirements should be calculated appropriately and high protein and energy food sources should be consumed [58]. Glutamine makes about 60% of the body's entire supply of free amino acids, making it the most prevalent amino acid. Skeletal muscle, lungs, and adipose tissue are the primary sources of plasma glutamine. The potent antioxidant glutathione, which is generated endogenously inside body cells, is also a precursor to glutamine which is the most extensively studied amino acids in relation to several facets of medical nutritional therapy. N-acetylcysteine (NAC) is a supplement form of cysteine that can be found in a

variety of protein-rich foods including chicken, turkey, yogurt, cheese, eggs, sunflower seeds, and legumes.

#### Honey bee products

There are several medicinal and nutritional values associated with honeybee products (honey, propolis, pollen, bee bread, bee venom, and royal jelly) which have been investigated for years for different therapeutic purposes. Honey is famous for its healing properties, but many people are unfamiliar with the other products. Honey is composed of several bioactive chemicals, phenols, polyphenols, vitamins, bioflavonoids, and sugars [59]. Bee pollen is used by humans as a functional food with many biological properties, including sports performance, antioxidant, and antimicrobial properties [60]. Many of the bioactive compounds (polyphenols) present in pollen and bee bread have promising activity against COVID-19 [59]. Bee venom is well known to have antimicrobial properties [61]. A recent study by Yang *et al.* showed that bee venom might enhance the immune system and reduce susceptibility to infection with the COVID-19 [62]. Propolis has a wide spectrum of pharmacological properties and is a dietary supplement that is commonly consumed by both healthy and sick people as a preventative precaution and for treatment. It is also used in veterinary medicine, due its antibacterial, antifungal, antiviral, antiparasitic, hepatoprotective, and immunomodulatory activities [63], [64].

#### Liquid foods

Among traditional medicines, green tea (*Camellia sinensis*) is known for its antioxidant properties. Polyphenols in green tea are able to interact with reactive oxygen species (ROS) by scavenging free radicals [65]. Epigallocatechin gallate (EGCG) is one of the most abundant poly-phenolic catechin found especially in green tea [66]. The antiviral properties of EGCG have been experimented against various viruses and have been found to have a greater potential than synthetic chemical drugs for treating viral infections [67]. It is recognized as a multi-functional bioactive molecule exhibiting activities against tumors, inflammation, bacteria, oxidative stress, and cell proliferation in addition to its antiviral effects [68]. The aflavins (TFs) are category of polyphenols found in considerable percentage in black tea. The bioactive properties of TFs are being researched, and they have been shown to have antitumor, antiviral, anti-inflammatory, antioxidative, and antibacterial activities [69].

#### Breastfeeding and coronavirus disease

Mothers and babies develop a strong bond through breastfeeding, which not only provides the infant with an optimal source of nutrients and strength against

infection but also lays the foundation for their physical and psychological development [70]. All dimensions of health care have been affected by the COVID-19 pandemic, including exclusive breastfeeding assurance and promotion. Due to the risk of possible COVID-19 transmission through breast milk, future mothers and those who are already breastfeeding are concerned about the consequences of the pandemic [71]. By breast-feeding, the baby receives microbiota, nutrients, diverse white blood cells, prebiotics, hormones, and antibodies, which provide short-and long-term immunological protection against a variety of infectious, gastrointestinal, and respiratory diseases.

#### Nutritional recommendations during COVID-19 infection

##### MD

In light of the elevated inflammatory and pro-thrombotic milieu linked to COVID-19 acute disease, these aspects have become increasingly important [10]. Pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF- $\alpha$ ), interleukin-6 (immunoglobulin-6), and C-reactive protein were found to play important role in inflammation producing cytokine storm during COVID-19 infection [72]. In addition, platelet-activating factor (PAF) plays key role in thrombosis process associated with COVID-19 infection [73]. Hence, effective therapeutic methods depend mainly on suppressing inflammation and boosting immunity of the patient. These therapeutic mechanisms could be attained by following the MD which is rich in polyunsaturated fatty acids, vitamins, antioxidants, fibers, and minerals [74]. Highly-adhered and positively diagnosed COVID-19 patients to MD reported considerably less chance of developing the disease to severe status compared to those of MD-intermediate and MD-low adhered patients in the project study of Segimiento University of Navarra [75].

##### Antioxidants-rich foods

The highly complicated pathophysiology of COVID-19 involves the inhibition of the host's innate and antiviral immune systems, the development of oxidative stress followed by an excessive inflammatory response known as a "cytokine storm," which results in pneumonia, fibrosis, and severe lung damage [76]. In addition, severe infection may also be more likely to occur in people with pre-existing disorders such as hyperglycemia, hypertension, lung, heart, and kidney disease, according to recent findings [77]. It has been proposed that a number of micronutrients can serve in modulating immunity against COVID-19 [78]. Their mechanism of action depends mainly on the suppression of PAF and thrombosis [25]. A recent molecular docking study found that curcumin, the active ingredient of ginger rhizomes, *Curcuma longa*

[79] has greater receptor binding capabilities and may prevent the invasion of the COVID-19 virus through its binding to the characteristic glycoprotein receptor of COVID-19 virus and accordingly prevent the entry of the virus [80]. Docking studies reported that some essential oils such as anethole from basil leaves, cinnamaldehyde from cinnamon spices, carvacrol from oregano and thyme, and geraniol from peach, raspberry, watermelon, lemon, and orange all showed antiviral activity through their inhibitory activity to COVID-19 spike-S-glycoprotein [81]. In addition, cinnamaldehyde was reported for its anti-inflammatory efficacy in alleviating the hyper-inflammation of the lung during SARS-CoV-2 infection through down-expression of the inflammatory cytokines nuclear factor kappa of activated B-cells nuclear factor kappa-light-chain-enhancer of activated B cells (NF- $\kappa$ B) and TNF- $\alpha$  [76]. Figure 3 shows that some natural antioxidant ingredients in foods have role in suppressing COVID-19 infection.

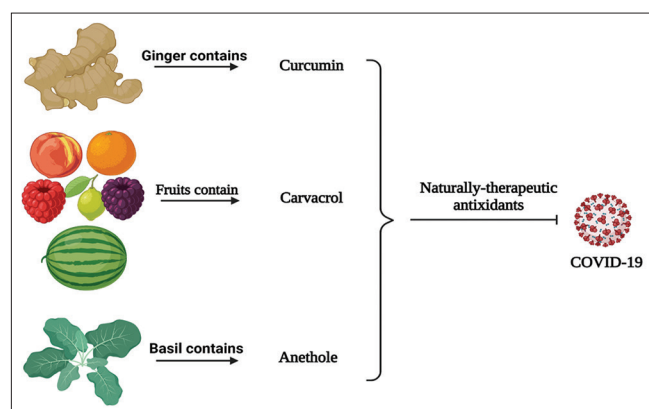


Figure 3: Some natural antioxidants that were proved for their possible role in suppressing COVID-19 infection. Curcumin, the active ingredient compound of ginger rhizomes; carvacrol, the active ingredient in many fruits such as orange, berries, lemon, apricot, and watermelon; anethole, the active ingredient of basil

### Prebiotics

Prebiotics may be useful in lowering the severity of the COVID-19 infection due to their unique abilities to influence the intestinal flora. Prebiotics have been used in a number of pre-clinical models as well as clinical cases with COVID-19 [45].

Fructo-oligosaccharides and galacto-oligosaccharides

Galacto-oligosaccharide is a galactose polymer, whereas fructo-oligosaccharide is a fructose polymer with <10 fructose residues. Both polymers' prebiotic capabilities have been recently demonstrated [45]. In an experimental influenza vaccine model, it was postulated that combined treatment of fructo-oligosaccharides and galacto-oligosaccharides has elevated the immune reactions inside the body of mice through the increased level of serum immunoglobulin-1 and immunoglobulin 2a and stimulated the activity of B-cells and T-cells in the

lymph nodes of mesentery resulting in hypersensitivity of mice to influenza vaccination [82].

### $\beta$ -glucans

A double-blind study conducted on 50 (age 50–70) adults reported that daily supplementation of  $\beta$ -glucans for 90 days in winter could reduce the symptoms of the upper respiratory tract infection through the stimulation of the innate immunity of the older patients [83]. Similar report published by Dharsono *et al.*, 2019 that the daily intake of  $\beta$ -glucans at a dose of 900 mg for 16 weeks in adults showed reduction of the severe symptoms related to upper respiratory tract infection along with elevation of the weak immune response and mood [84].

### Probiotics

Patients with COVID-19, which is brought on by SARS-CoV-2, have a variety of clinical symptoms, including gastrointestinal involvement. Commensal gut bacteria can support the body's protection against potential infections by promoting favorable immunological interactions. Interventions targeting the gut microbiota may have systemic antiviral effects in SARS-CoV-2 infection. Infections with SARS-CoV-2 reduced the health of the gut microbiota, and this was correlated with the severity of the illness. The prognosis for SARS-CoV-2 infection was worse in subjects with concurrent comorbidities who had increased gut permeability and lower gut microbiome variety [85]. During the SARS-CoV-2 infection, dietary microorganisms, such as probiotics or specific prebiotics of Chinese origin, demonstrated antiviral effects against other types of coronavirus and could enhance host immune activities [86]. Extensive researches are looking into how probiotics can help protect against and lessen the risk of SARS-CoV-2 infection in patients, household members, and health-care personnel. A strategy to improve gut health during the COVID-19 pandemic and reduce pro-inflammatory conditions by eating a more varied diet [85].

At the clinical level, there have not been many studies involving the use of probiotics in COVID-19 patients, but the main findings included shortening of the disease's duration and reducing the severity of symptoms such as fatigue, olfactory dysfunction, difficulty in breathing, and gastrointestinal symptoms. However, individuals receiving corticosteroid therapy who are immune-compromised are not advised to take probiotics. A clinical trial revealed that oral administration of 2.4 colony-forming unit including bacterial species of *Streptococcus*, *Lactobacillus*, *Lactocaseibacillus*, *Levilactobacillus*, *Bifidobacterium*, and *Lactocaseibacillus* to hospital-admitted patients with COVID-19 for a therapeutic time of 14 days has significantly reduced the symptoms related to infection [87]. Another American double-blinded randomized clinical trial proved that oral administration



of 1132 COVID-19 patients with the probiotic bacteria, *Lactocaseibacillus rhamnosus* for 28 running days has revealed obvious reduction in the symptoms of the disease [88]. Gutiérrez-Castrellón *et al.*, in 2021, conducted another randomized clinical trial on 300 (18–60 years age) patients who were diagnosed positive COVID-19 infection and given daily oral intake of probiotics for a month. The intervention resulted in reduction of symptoms in more than 50% of patients [89]. A Chinese clinical trial study used intervention therapy of multiple probiotic strains of bacteria to COVID-19 patients (n = 800). The study showed disappearance or reduction of disease-related symptoms [90]. Future perspectives suggest that probiotic, prebiotic, synbiotic, and postbiotic modification of the gut microbiota represents a promising adjuvant strategy for enhancing the health of patients with COVID-19 [11].

### Synbiotics

Intestinal dysbiosis in COVID-19 patients may refer to an elevated pro-inflammatory milieu in the intestines with the cytokine storm, according to a recent study [91]. This might be explained by decreased production of metabolites produced by commensal microorganisms. Therefore, altering the gut microbiota and adding commensal bacterial metabolites could lessen the hyperinflammation status in people with severe COVID-19. Both commensal bacteria and fermentation substrates are necessary for the development of commensal gut microbiota. To enhance the creation of commensal bacterial metabolites, synbiotics fulfil both requirements [45]. In a clinical trial, a synbiotic combination that included a mixture of *Bifidobacterial*, *Enterococcus*, *Lactobacillus* strains, called Omni-Biotic® 10 AAD was used for COVID-19 treatment. The prebiotics used were starch isolated from maize, inulin, and fructooligosaccharide, while the synbiotic formula contained trace elements, manganese sulphate, and potassium chloride [45].

### Protein-rich foods

Glutathione is crucial in regaining immunity and recovery after infection [92]. Several viral infections, including COVID-19, produce ROSs that are inhibited by glutathione in cellular proteins. Excessive ROS production depletes defending proteins and worsens COVID-19 patients' conditions. Glutathione is the main defensive antioxidant synthesized from three amino acids involving cysteine, glycine, and glutamic acid, which acts as a barrier to prevent ROS from damaging cellular components [93]. Hence, protein-rich foods provide the main amino acids for producing glutathione which is beneficial in enhancing the immune response in viral infections [94]. The supplement NAC is a well-known mucolytic agent in respiratory infections due to

its thiol-containing free-radical scavenger and its role as a precursor of glutathione [95].

### Honey bee products

Honeybee products are used in traditional medicine to treat viral respiratory diseases. Arentz *et al.*, in 2021, showed the potential action of honey against SARS-CoV-2 [96]. Salama *et al.*, in 2022, explained that the physical properties of honey might help to disinfect COVID-19 before passing to the lungs. Royal jelly as one of bee products has shown enhanced antioxidant and immunomodulatory activities through the release of antioxidant markers in the liver and kidney [30]. In fact, bee propolis and some of its active compounds have recently been shown to have suppressive mechanism to many active in the pathophysiology of the disease activated by COVID-19, such as reducing transmembrane protease, serine 2 expression, and reducing angiotensin-converting enzyme (ACE2) anchorage, potentially facilitating virus entry, reducing transcription factors NF- $\kappa$ B and cell-signaling pathway, and blocking serine/threonine-protein kinase 1, which determine inflammatory activities and fibrosis in a COVID-19 infected body [97]. In addition, propolis has recently been studied for its effectiveness against SARS-CoV-2, the pathogen responsible for COVID-19 and has been used to treat viral infections for a long time [97]. Moreover, modifying a number of pathogenic and antiviral pathways, propolis, and its constituents have shown potential efficacy against SARS-CoV-2. In the search for honeybee products as new natural remedies to treat COVID-19 disease, the molecular docking method was used to identify the binding forms and preferences of 40 propolis derivative compounds against five viral receptors and one human receptor. The targets revealed RNA-dependent RNA polymerase (RdRp), non-structural protein helicase, 3C-like protease, receptor-binding domain of the spike protein, the viral target ACE2, and the papain-like protease (PLpro) [98].

### Liquid foods

Caffeine as an active ingredient in green tea and coffee attracted the attention of scientists in treating viral infection. An important focus should be placed on caffeine's immunomodulatory effects in the treatment of COVID-19 infections. The presence of caffeine at high concentrations and for a prolonged period has proved promoting activity to natural killer (NK) cells in human body. Studies showed that NK cells and lymphocytes play a critical role in the pathogenesis of COVID-19 infection because they are the first cells to activate in response to a viral threat [99]. During times of COVID-19, orange juice consumption has gained increased attention, because it is perceived to boost immunity [100]. Several micronutrients are

present in orange juice, including vitamin C, folate, and polyphenols (such as hesperidin), all of these are believed to be significant contributors to the preventive effects of orange juice against COVID-19 [101].

### Breastfeeding and coronavirus disease

Based on the limited evidence available, breast milk only rarely transmits COVID-19, it has been discarded as the source of contagion [102]. Two reviews on breastfeeding and COVID-19 have been published in 2020. Both recommended breastfeeding among infected mothers [103], [104]. There is no significant increase in COVID-19 infection rate when a baby is born vaginally, breastfed, or allowed contact with the mother. Therefore, the United Nations International Children's Emergency Fund guideline strongly recommends breastfeeding for all babies, including preterm and sick babies [104].

### Nutritional recommendations post-COVID-19 infection

#### Ketogenic diet

It has been conclusively shown that the SARS-CoV-2 can harm tissues and organs besides the lung, such as the heart [105], liver, and gut [106], [107], as well as the central nervous system [108], either by direct infection or by facilitating the spread of other infections. In addition, research demonstrates that the acute phase of COVID-19 and the post-COVID syndrome both have an impact on the skeletal muscles [109]. High-fat diets known as ketogenic diets are distinguished by a noticeable carbohydrate limitation. Recent studies have demonstrated that very low calorie ketogenic diets, in particular, can significantly reduce body weight in patients with obesity and type 2 diabetes mellitus, both of which are risk factors for a negative result from SARS-CoV-2 infection [110]. In recent years, it has been clear that ketogenic diets have a positive effect on maintaining lean body mass. According to Merra and colleagues' pilot double-blind trial findings, very low calorie ketogenic diets was very effective at reducing body weight without causing the loss of lean body mass [111]. Ketogenic diet is thus an effective strategy for post-COVID patients to maintain skeletal muscle mass [110].

#### Prebiotics

Luo *et al.*, in 2020, also reported that altering the gut microbiota would protect against subsequent infections by preventing the migration of microorganisms to the gut [112]. Recently, studies reported that MD and Ketogenic diet play crucial role in maintaining gut microbiome post-COVID infection [110].

#### $\beta$ -glucans

A double-blind controlled study performed on 175 children aged 2–5 years released that

supplementation of children with imunoglukan syrup formula syrup that contains a synergistic combination of pleuran  $\beta$ -glucan and vitamin C has remarkably protected the participant children from repeated respiratory tract infection when orally administered every day for 12 months on empty stomach [113].

## Conclusion

Taken together, the present review displayed the nutritional recommendation strategies for pre- and during COVID-19 infection through the intake of MD, antioxidants-rich foods, immunity-boosting foods, prebiotics, probiotics, synbiotics, protein-rich foods, honey bee products, liquid foods, and breastfeeding performance for infants. In addition, the article showed the efficacy of MD and ketogenic diets in reducing the complications resulted from acute infection with COVID-19 through the decrease in body weight, maintaining skeletal muscles and improving gut microbiota which accordingly enhance immune responses post-COVID-19 infection.

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