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Impact of therapeutic diet and dietary nutrients on covid-19 - A review

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Abstract
Coronavirus is spreading from animal market of Wuhan in central China. There are several types of coronavirus but all are not dangerous but this new coronavirus is very dangerous. It is a group of RNA viruses that cause a variety of disease in animal and animal to human. The world health organization (WHO) announced that coronavirus 2019 (COVID-19) is a pandemic. As of 7th April 2022, almost 493,392,853 confirmed cases of COVID-19 including 6,165,833 deaths have been reported to the World Health Organization. The SARS-CoV-2 pandemic represents a potential threat to patients and healthcare systems worldwide. Patients with the worst outcomes and higher mortality are reported to include older adults, polymorbid individuals, and malnourished people in general. Mild symptoms of coronavirus are cough, shortness of breath and severe problems are pneumonia, kidney failure and death also. Basically corona virus effects on immune systems and decrease the immune power. There are no specific treatments or vaccines for this disease still now. Hence in this condition, people have to maintain immunity and should increase immune power to fight against coronavirus. Only washing hand and wearing a mask are not enough to fight against this virus, people have to modify their daily diet. This article summarizes the immune boosting therapeutic diet and dietary nutrients on COVID-19.

Keywords: coronavirus 2019 (covid-19), immune system, therapeutic diet, immunonutrition

Introduction
Corona virus is a positive sense single standard RNA (ssRNA), which is enveloped by a spike glycoprotein, which appears like a crown under a 2D-electron microscope, and hence it is generally called a coronavirus (Iddir *et al*., 2020). Seven coronaviruses can cause infection in people around the world, but only four human coronaviruses are usually transmitted by men: 229E, NL63, OC43, and HKU1. These typically cause respiratory infection ranging from the common cold to more severe illnesses such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS), and the most recent coronavirus (COVID-19) causes infectious disease. Coronavirus is a member of the coronaviridae family and has a close connection with severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). Coronavirus structure consists of four major proteins including spike glycoprotein, nucleoprotein (attached with RNA), membrane protein, and an envelope protein, which plays a key role in replication (division). SARS-CoV2 can use angiotensin-converting enzyme 2 (ACE2) as a receptor and enter host cells and start to divide and finally cause COVID-19 (Mrityunjaya *et al*., 2020; Wiersinga *et al*., 2020) [13, 32]. This coronavirus pandemic has impacted the economy and health care system all over the world (Kozlov *et al*., 2021) [10]. This coronavirus spreads from human to human via respiratory and airborne droplets as well as through direct contacts. The biggest threat of the coronavirus is that most of the infected patients are asymptomatic and few develop severe symptoms like fever, dry cough, fatigue loss of smell/taste, and headache. If COVID-19 is not treated properly it can result in high mortality and morbidity and also its long-term effects are not clear (Kazemi *et al*., 2021; Syed, 2020) [9, 20]. Especially, elderly people, people with comorbid conditions (Cardiovascular, diabetes mellitus, cancer, and hypertension), immunosuppressed subjects, and heavy smokers are highly susceptible to Coronavirus infection (Subedi *et al*., 2021) [19]. Recently, WHO has announced four major variants/ genera of COVID-19 virus including α, β, γ, δ till date (out of 11 known variants). Out of all these coronavirus variants the δ (delta) is one the deadliest with a high transmissibility rate (Reproductive number) and contributed to high mortality and morbidity globally in recent times (Alizon *et al*., 2021; Liu *et al*., 2021). Several doctors and researchers have already attempted to use herbal medicines on clinical trials against SARS-CoV-2.5 The longstanding use of dietary therapy and herbal medicine to prevent and treat diseases cannot be overemphasized, as several herbs exhibit antiviral activity. Using dietary therapy and herbal medicine to prevent SARS-CoV2 infections could be

a complementary COVID-19 therapy, while drugs remain under development. Therapeutic diet is a diet which is given to the patient who is suffering from any type of disease condition (Tewari, 2019).

Symptoms of COVID-19

Maximum number of virus-infected patients will suffer common cold and flu while few will remain asymptomatic. 80 percent of patients will experience mild disease symptoms. Adult has the strongest immune power to combat the infection but the demerit is that they are more likely to transmit the infection. A recent research of nearly patients (140 case studies) at Wuhan University's Zhongnan Hospital reported different types of symptoms, contributing to a disease known as COVID-19. Ninety-nine percent of patients reported severe high-temperature fever, while over half felt dry cough and fatigue. One-third of the patient experienced dry cough and breathing difficulties (Bendix, 2020) [4].

Modified Lifestyle Pattern to Lower the Risk of Covid-19

The common recommendation from various expert includes regular exercise (indoor or outdoor), maintaining social distancing, wearing a mask and washing hands (hygienic lifestyle) as well as limiting smoking and alcohol consumption (Ismail *et al*., 2021; WHO, 2020) [7, 24]. Moreover, the vaccine can only help to improve or boost the immune response against coronavirus (produce antibodies). However, the individual immune system should be strong enough to produce enough antibodies (plasma/memory cells) to fight against the coronavirus (Ahn *et al*., 2020) [1]. Hence, consumption of a healthy balanced diet would help to boost the host immune system and thereby mitigate the harmful health impacts associated with coronavirus. Along with vaccination, few anti-viral drugs and micronutrients are recommended for treating Covid-19 but following a healthy lifestyle (healthy food) would be the best choice to help combating this pandemic (Lordan *et al.*, 2021) [11].

Protein Rich Foods

Milk, Egg, tofu, meat and fish these are a complete protein, helps maintain immunity. Under plant foods pulses, oil seeds and nuts are good source, which is beneficial for this pandemic situation. Soyabean is the richest source containing 40 % protein (Srilakshmi, 2016) [5].

Essential Trace Elements and COVID-19

Trace elements are fundamental for the correct functioning of our bodies, and they are especially important in disease states. There are no specific recommendations about how to supplement trace elements in individuals with COVID-19, but here is some evidence about the benefits of these minerals and their importance in the proper functioning of the body; these minerals should be supplemented in case of deficiency. Key dietary components such as vitamins A, C, D, E, iron, zinc, selenium, and copper have well-established immunomodulatory effects, with benefits in infectious disease. Some of these nutrients have also been shown to have a potential role in the management of COVID-19(Enrique *et al.*, 2020).

Zinc

Zinc is after iron the most abundant trace element in the human body. This metal possesses strong immunogenic properties, being also known to bind to a number of proteins and modulating their activities. The importance of zinc for the development and function of the immune system has been demonstrated in a number of studies conducted in various species. Moreover, zinc has been also used in viral infections control. Zinc has the potential to increase the cytotoxic activity of NK cells, which can attack 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. 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. Studies show that chloroquine along with Zn supplementation may show a better anti-corona virus activity by inhibiting the attachment and subsequent multiplication of the SARS-CoV2 virus (Pal *et al*., 2020; Ishida, 2019) [28], however, this subject is somewhat controversial, especially in light of false claims related to hydroxychloroquine. In addition, Zn is reported to lower the production of pro-inflammatory cytokines via inhibiting the TLR and NFkB signalling pathways (Hamid and Thakur, 2021) [26]. A clinical trial, conducted by Prasad *et al*. (2007) [25] has shown that zinc supplementation in elderly subjects for one year could significantly decrease the incidence of viral infection through lowering of cytokines production and oxidative stress. Their data show that low levels of Zn (Zn deficiency) are associated with high susceptibility of viral infection especially COVID-19. The author strongly suggested that all subjects (especially elderly people) maintain the normal Zn levels and in this way lower the risk of Covid infection and its severity. Meat, poultry, eggs and dairy products are the best sources of Zn. Outer layer of grains also contribute to zinc. Fruits and most vegetables are fair sources.

Selenium

Selenium is an essential trace element for mammalian redox biology. The nutritional status of the host plays a very important role in the defense against infectious diseases. Dietary selenium deficiency, which causes oxidative stress in the host, can alter a viral genome so that a normally benign or mildly pathogenic virus.

Selenium is usually incorporated as selenoprotein and used by cells for various biological functions especially for lowering oxidative stress (Chiu *et al*., 2021) [29]. The proposed mechanism of Selenium against COVID-19 includes possible enhancement of glutathione family antioxidants, and thus effectively lowering oxidative stress. Se can promote the production and proliferation of NK cells and thus play a major role in innate immunity (Avery and Hoffmann, 2018) [30]. Selenium administration can also downregulate various pro-inflammatory cytokines production (Mrityunjaya *et al*., 2020) [13, 32]. Previous studies have indicated that Selenium supplementation could significantly lower the inflammatory response in respiratory distress syndrome patients (ARDS) as well as lowering the production of various pro-inflammatory cytokines (Mahmoodpoor *et al*., 2019) [31]. The *above*-mentioned antioxidant, anti-inflammatory, and immune-modulatory (innate immunity) activities of Se recommend it as a good choice for fighting against COVID-19 and its related complications. Other minor minerals like iron (Fe), and copper (Cu) have also been found to show some positive impact against COVID-19 infection and severity. Iron supplementation showed lower inflammatory cytokines and altered immune cell activation as well as oxidative status (Wu *et al*., 2019) [33].

Bae and Kim (2020) [1] reviewed the roles of vitamins C and D, as well as that of selenium in the immune system. The beneficial effects of these micronutrients to reduce the risk of infectious diseases in general, and COVID-19 in particular, were also reviewed. Brazil nuts, fish, ham, chicken, cottage cheese, sunflower seeds are the good sources of selenium.

Copper

Copper is another essential trace element that plays a key role in immune function and free-radical defense. This metal is essential for both, pathogens and the hosts, in viral infections. Therefore, copper has been clinically used to reduce the risks of bacterial and viral contamination. Copper, as other transition metals, has a notable affinity for biological ligands and redox properties. This makes it ideal to drive biochemical reactions involving redox and oxygen chemistry. However, these same chemical properties, which make copper a superb enzymatic cofactor, render the metal potentially toxic, being especially notorious for unicellular microbes. Thus, the antimicrobial properties of copper make it useful as effective biocides for pathogens from COVID-19 to eukaryotic pathogens (Culbertson and Culotta, 2020). Recently, Cortes and Zuniga, (2020) reviewed the scientific literature about the use of copper to prevent the potential transmission of influenza viruses and SARS-coronaviruses.

Some of the rich sources of copper are seafoods like oysters, crabs and lobster, meat sources followed by nuts and dried legumes like almonds, sesame, sunflower and soya bean contain 12-37 microgram per gram, Chocolate is also rich in copper. In seeds and other grains, most of the copper is present in the brain and germ (Srilakshmi, 2016) [5].

Vitamins

It is now known that patients with nutritional deficiencies are at the highest risk for ventilatory complications. Part of the general treatment for viral infections is vitamin supplementation to improve the outcome of the disease

Vitamin A

Many host defenses depend on the adequate supply of this vitamin, and it has been reported that vitamin A supplementation reduces the morbidity and mortality of different infectious diseases. It has also been reported that supplementation with vitamin A offers some protection against the complications of other life-threatening infections.

Vitamin A or retinol is present in some animal foods like butter, ghee, whole milk, curd, egg yolk, liver etc. The liver oils of certain fish like cod, halibut and shark and saw fish are some of the richest known natural sources of the vitamin. Vitamin A is not present as retinol in vegetable foods. These foods contain yellow pigments called carotenes which are converted into vitamin A in the body. There are different types of carotenes alpha, beta and gamma.

The rich sources of beta carotene is green leafy vegetables, spinach, amaranth, coriander, drumstick leaves, curry leaves, mint, radish leaves etc. Ripe yellow fruits such as mangoes, papaya and tomatoes are also rich in carotene. Among other vegetables carrots and yellow pumpkin are good sources (Srilakshmi, 2016) [5].

Vitamin C

Vitamin C is known as an essential antioxidant and enzymatic co-factor for physiological reactions, such as hormone production, collagen synthesis, and immune potentiation, also improves vasopressor synthesis, improves endovascular function, and exerts epigenetic immunologic modifications. Vitamin C may also function as a weak antihistamine agent to provide relief from flu-like symptoms such as sneezing, a runny or stuffy nose, and swollen sinuses. Humans are unable to synthesize vitamin C; therefore, they must acquire vitamin C from dietary sources. The therapeutic use of vitamin C to prevent inflammatory hyperactivation in myeloid and lymphoid cells has been explored. High doses of vitamin C act as a prooxidant for immune cells.

Rich sources of vitamin C are Amla, guava lemon and orange. Green leafy vegetables like drumstick leaves and agathi are good sources of vitamin C. (Srilakshmi, 2016) [5].

Vitamin D

In addition to its role in maintaining bone integrity, vitamin D also stimulates the maturation of many cells, including immune cells. Several reviews have considered the way in which vitamin D reduces the risk of microbial infection and death, and those mechanisms can be grouped into three categories: physical barrier, cellular natural immunity, and adaptive immunity. Vitamin D helps maintain tight cell junctions, gap junctions, and adherence junctions. There are good reasons to postulate that vitamin D favourably modulates host responses to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), both in the early viraemic and later hyperinflammatory phases of COVID-19. Furthermore, previous investigations have demonstrated that high-dose supplementation of vitamin D (250,000– 500,000 IU/day) is safe and effective in improving the health status of mechanically ventilated critically ill patients (enhancing the capacity of blood for oxygen transport and increasing haemoglobin levels), which resulted in shorter hospital stays Vitamin D is found in fish oil, sun light, Cod liver oil, liver and fortified milk. (Srilakshmi, 2016) [5].

Vitamin E

Vitamin E is a lipid-soluble vitamin that plays an important role in reducing oxidative stress by binding to free radicals as an antioxidant. Vitamin E is a major fat-soluble antioxidant that scavenges peroxyl radicals and terminates the oxidation of polyunsaturated fatty acids (PUFAs).

Many studies have provided evidence that the immunostimulatory effects of vitamin E confer improved resistance to infections. However, the magnitudes of the effects were rather small, and in some studies, positive effects were only observed in subgroups of participants. A recent study found a lower incidence of pneumonia among participants taking 50 mg/day of vitamin E for a median of 6 years.

Vegetable oils, nuts and whole grams are the richest sources of vitamin. Wheat germ oil contains 120mg vitamin E per 100 g oil (Srilakshmi, 2016) [5].

Polyunsaturated Fatty Acids

Long-chain polyunsaturated fatty acids (PUFAs) are important mediators of inflammation and adaptive immune responses. Omega-3 and omega-6 PUFAs predominantly promote anti-inflammatory and proinflammatory effects. They are precursors of resolvins /protectins and prostaglandins/leukotrienes, respectively. They are of 2 types, namely Omega-3 and omega-6 fatty acids. Omega-3 fatty acid-rich foods help to increase immunity. Omega-3 rich fishes are Coldwater fish like salmon, mackerel, sardines and tuna (Srilakshmi, 2016) [5].

Proposed Health Benefits and Hygienic Guidelines (Food Safety)

Consumption of fruits and vegetables can improve overall health status especially lower oxidative stress and enhance immune system and thus lowering the risk of Covid 19. Wash hands before handling food (before eating or cooking). Wash vegetables/fruits before cooking. Maintain social distancing and wear a mask (outdoor activities).

Therapeutic Diet against Corona Virus

Therapeutic diet is a diet which is given to the patient who is suffering from any type of disease condition (Tewari, 2019).

There are different types of immune-boosting foods are present, which helps to increase immunity and helps to fight against different virus infection. The most important pharma-therapeutic foods are garlic, turmeric, neem leaves and tulsi leaves, green tea, high anti-oxidant fruits and vegetables.

Garlic and Its Immunomodulatory Properties

Garlic (Allium sativum) is one of the good pharma-therapeutic immune-boosting spices. Garlic has pharmacological properties against microbial infection and also helps to prevent inflammation. Recently garlic has been considered as an immunomodulatory spices. Immunomodulators are medicines which are used to regulate or normalize the immune system. Several researches have been studied out in animal models to examine the effects of garlic compound as an immunomodulator (Arreola, *et al*., 2015) [2].

Turmeric

Turmeric is a natural polyphenolic compound, which helps to protect from infection of coronavirus (Zahedipour *et al*., 2020) [37].

Zorofchian Moghadamtousi. (2014) [38] reported that turmeric has inhibitory potential activities against various viral infections. Virus- like stomatitis virus, parainfluenza virus type-3, respiratory syncytial virus and simplex virus.Turmeric may have beneficial effects against infection with COVID-19 as it has the ability to modulate the various molecular targets that lead to the attachment and internalization of SARS-COV-2 in many organs such as the liver, kidney, and heart.

Neem Leaves

Neem is a traditional ancient medicinal plant that has beneficial effects on various viral diseases (Biswas *et al*., 2002) [6].

Many researchers have been studied that neem has a biologically active compound, that acts as an antiviral, anti-inflammatory, antiseptic, and antifungal. Isopropenoids and non-isoprenoids are two important compounds which are found in neem extract.

Tulsi Leaves

In India, Tulsi is the oldest traditional medicinal plant, which has broad beneficial effects on human health for preventing viral fever and cough etc. According to Charaka Samhita (Claus, 2003) Tulsi helps to maintain balance various mechanism and increases the life span.

Pattanayak *et al*., (2010) [16] noted that Tulsi is being used for the management of pain, diarrhoea, cough and fever. Tulsi leaves have beneficial effects on various normal fever to malaria fever. Singh *et al*., (2010) reported that for controlling pneumonia, Tulsi leaves with the addition of cow ghee are the best medicine. Tulsi leaves have inhibitory effects on various deadly viruses like vaccinia virus, infections, Bursal Disease virus and Newcastle Disease virus (Prakash and Gupta, 2005) [17]

Green Tea and Its Potential Health Benefits

The green tea has physiological and pharmacological health benefits. Steinmann *et al*., (2013) [22] reported that the main component of green tea is epigallocatechin-3-gallate (EGCG) that is very helpful for the controlling infection and others viral fever, because it has anti-infective and anti-viral properties.

Lee *et al*., (2012) [12] reported that green tea has Epigallocatechin-3-gallate (EGCG) compound that has beneficial effects on Chikungunya virus (CHIKV). It is a transmitted alphavirus that causes chikungunya fever. Researchers also noted that green tea has antiviral properties that are helpful for the prevention of viral infection and fever.

High Omega-3 Fatty Acid Rich Foods

Omega-3 fatty acid-rich foods help to increase immunity. Omega-3 rich fishes are Coldwater fish like salmon, mackerel, sardines and tuna.

Anti-oxidant rich fruits and vegetables.

Vegetables and fruits are important human sources of abundant vitamins, minerals, and fibres. Fruits are well known to be abundant in various antioxidants including ascorbic acid, carotenoids and phenolics (Arshiya, 2013) [3].

Some studies indicate the bioavailability of the antioxidants found in some fruits and vegetables (Parashar *et al*., 2008) [18]. Many fruits and vegetables can also be used as an excellent source of natural antioxidants. It is possible to speculate that increased consumption of these fruits would intentionally increase the intake of natural antioxidants which can provide an alternative in the involvement of the ageing process by protecting against oxidative harm.

Some of the Nutrient Antioxidants are found in green leafy vegetables, Ripe yellow fruits and vegetables like papaya, musk melon, mango, pumpkin, carrots, orange, lemon, sweet lime, guava, berry etc. (Srilakshmi, 2016) [5].

Conclusion

In this paper, we reviewed the scientific literature regarding the role of zinc, selenium, copper and iron, as well as the development and prognosis of COVID-19 in infected subjects. The deficits of zinc and selenium seem clearly to play a negative role in COVID-19 patients, being their supplementation recommended in many cases. On contrary, the supplementation of copper and iron to COVID-19 patients is not obvious. Anyhow, the role of these trace elements is clearly linked to the immune system of the COVID-19 patients, which is crucial in this disease.

In this pandemic condition, researchers are trying to discover appropriate vaccine or medicine to control coronavirus spreading, but still now there is no appropriate vaccine or medicine. So, people have to maintain their daily diet to maintain immunity because initially corona virus effects on our immunity and decrease the immune power. Within this study, we have also attempted an overview of therapeutic diet against COVID-19, which may be helpful to increase immunity. Garlic, turmeric, neem, tulsi, green tea, high antioxidant-rich fruits are most abundant immune-boosting foods, plant and spices to boost immunity, people can add these items as a therapeutic diet in daily diet. Different studies have been conducted to determine the effects of garlic compounds on immune system cells and these studies have shown that garlic compounds can maintain immunity through their immunomodulatory activities. Turmeric can have beneficial implications against infection with COVID-19. Neem is an ancient herbal medicinal plant with beneficial effects on various viral diseases.

It has been observed by several researchers that neem has a biologically active compound that functions as an antiseptic, antiviral, anti-inflammatory and antifungal. Isopropenoids and non-isoprenoids are two important compounds which are found in neem extract. To sum up, this review shows that Immune-boosting therapeutic diet can be helpful for both prevention and treatment of new emerging coronavirus. However, well-designed clinical trials are needed to demonstrate the potential efficacy of Immune-boosting therapeutic diet against SARS-CoV-2 infection and its ensuing complications.

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