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IMPORTANCE OF NUTRIENTS IN COMBATING WITH COVID-19

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AUTHOR'S CONTRIBUTION

The sole author designed, analysed, interpreted and prepared the manuscript.

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Review Article

ABSTRACT

In present scenario COVID-19 pandemic is the leading challenge across the globe. This new coronavirus disease is declared to be a global pandemic by the World Health Organization. At present, we are dependent upon lifesaving drugs/vaccines. In addition to the drugs, the essential advisories are to be followed to prevent the spread of COVID-19 like maintaining personal hygiene, physical distancing, respiratory hygiene, vaccination, healthy and balanced nutrition and strong immune system. Our immune system protects against diseases and maintains health. Good healthy nutrition increases the immunity and controls the diseases. We need to pay attention to the importance of nutrition in curing the covid 19. This can help us to understand the relation between disease and our dietary intake. A number of vitamins (A, B6, B12, folate, C, D and E) and trace elements (zinc, copper, selenium, iron) help in maintaining the human immune system and prevent the infections. Vitamin A controls dendritic cell and CD4+ T lymphocyte maturation. Vitamins B6, B12 and folate are useful for proper functioning of natural killer cells and CD8+ cytotoxic T lymphocytes. Vitamin C fights against infection and helps in phagocytosis and bacterial killing, natural killer cell activity, T lymphocyte function and antibody production. Vitamin D improves cellular immunity. Vitamin E helps in cell-mediated immune responses. Trace amount of zinc increases the proliferation of CD8+ cytotoxic T lymphocytes and provides antiviral defence. Trace elements like copper has antiviral properties. Iron is also important for maintaining the immunity. In additions to these nutrients gut micro bacterias are found to be protective against respiratory infection. In this article the role of specific nutrients in the immune system, with regard to antiviral defences have been summarised .

Keywords: COVID-19; pandemic; coronavirus; vaccines; respiratory hygiene; immunity and nutrition.

1. INTRODUCTION

COVID-19 is the disease caused by a new coronavirus called SARS-CoV-2. This new virus with cluster of cases of 'viral pneumonia' was noticed first time on 31 December 2019, in Wuhan, China. The virus was identified as a novel coronavirus and officially named by the WHO as 2019-nCoV, the new coronavirus in 2019 [1].

In the month of January, other countries like Thailand, Japan, and Korea also confirmed the human infection with 2019-nCoV from China [2]. In India the Kerala was the first state where first confirmed case of coronavirus was detected in the end of January 2020. In April 2020, more than 154,000 people have died, 2.2 million have been affected. and at least 185 countries have been affected by the coronavirus. In 2002–2003 severe acute respiratory syndrome

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(SARS) was noticed with coronavirus first time and in 2011, Middle East respiratory syndrome (MERS) showed the presence of coronavirus for the first time. In both cases SARS-CoV and MERS-CoV, newly identified coronaviruses of zoonotic origin belong to genus Beta coronavirus [3]. Coronaviruses are a large group of single stranded RNA viruses that are common among mammals and birds. Coronaviruses cause respiratory and, less frequently, gastrointestinal diseases [4,5]. It is mainly transmitted through droplets of infected person which comes in coughs, sneezes, or exhales.

Presently, there are other alternative means to control COVID-19 infection and for preventing transmission. There are many guidelines which include isolation of known cases, quarantine of persons at high risk of exposure and closing regional and country borders and restricting movement and travel and screening of travellers [6,7]. At last the community had been forced to complete lockdown [8]. Vaccination is major tool to fight with this virus. But in spite of all efforts, this disease is not under control and widely transmitting to urban and rural areas. In addition to all measures we need to improve our health status by concentrating on our immune system. Our immune system, maintains our health and kills the pathogens. A number of vitamins A, B6, B12, C, D and E, folates and some trace elements like zinc, copper, selenium, iron assist the human immune system and prevent from infections. Other essential nutrients including other vitamins and trace elements, amino acids and fatty acids also assist the immune system. Deficiencies of micronutrients can affect both innate and adaptive immunity.

2. AIM

The main objective of this review article is to analyse the role of specific nutrients in the immune system, with regard to antiviral defence.

3. METHODOLOGY

Many research papers were studied thoroughly and analysed to review them. Research articles published up to April 2021 with keywords like immune system, immunity, specific nutrients, importance of vitamins, role of diet in immunity, micronutrients, vitamins, respiratory infection ,corona virus etc. were searched on pubmed. Elsveir and springer journlas were also accessed.

4. DISCUSSION

4.1 Immune System

Our immune system, plays a main role in maintaining the health. It protects the body from harmful substances, germs, and cell changes. Immune system work at three levels innate immunity which is rapid response, adaptive immunity which is slow response and passive immunity. Passive immunity is of two types: natural immunity, received from the maternal side, and artificial immunity received from medicine. Innate immunity is an immediate defence that is not as specific whereas adaptive immunity is specific to T and B cells. These cells recognize specific antigens on the invading microorganism and kill the pathogen by producing antibodies. Immune system acts as a barrier to prevent pathogens from entering the body. It eliminates the pathogens like bacterias, viruses and other microorganisms and generates an immunological memory. Dendritic cells (DCs) stimulate the activation of T-lymphocytes and B-lymphocytes. T cells, CD4+ T cells, and CD8+ T cells show antiviral role. CD4+ T cells promote the production of virus-specific antibodies by activating T-dependent B cells. However, CD8+ T cells are cytotoxic and can kill viral infected cells. Neutrophils, macrophages and natural killer cells help in phagocytising of the foreign particles like microbes. Deficiencies of micronutrients can affect both innate and adaptive immunity, causing immunosuppression and thus increasing the susceptibility to infections.

4.2 Role of Nutrients in Immunity

According to the World Health Organization, healthy foods and hydration are vital. A well-balanced diet are healthier with a strong immune system and have a reduced risk of chronic illness, infectious diseases. Patients affected with COVID-19 become serious cases if already affected by malnutrition and thus proper nutrition should be provided [9].

4.3 Nutrient Rich Dietary Sources

Vitamin A: Good sources of vitamin A are milk and cheese, eggs, liver, oily fish, cereals, green vegetables e.g., carrots, pumpkin, spinach, many fruits like apricots, peaches, papaya, mango etc. Vitamin A is useful in normal differentiation of epithelial tissue. It helps in maturation of immune cells, CD4+ T lymphocyte maturation and their functioning. Vit. A controls the dendritic cells and maturation of neutrophils. It promotes bacterial killing by phagocytic activity.

Deficiency of vitamin A altered the immune responses and increases the susceptibility to many infections. Vitamin A deficiency can lead to respiratory infections, diarrhoea and severe measles. It has been noticed that deficiency of vitamin A increases the blood neutrophil, but phagocytic function of neutrophils to ingest and kill bacteria is impaired.

Vitamin A deficiency would impair antiviral defences as Natural killer cell activity is diminished and its deficiency alters the balance between T helper 1 and T helper 2 lymphocytes.

Retinoic acid promotes survival and proliferation CD8+ T lymphocyte. It is also required for normal functioning of B lymphocytes. Retinoic acid promotes movement of T lymphocytes to the gut-associated lymphoid tissue. Some gut associated immune cells are able to synthesize retinoic acid.

It is found in the research that vitamin A deficiency can impair the response to vaccination [10]. Vitamin A and some other retinoids also shows important immunomodulatory properties and increases the efficiency of actions of type 1 interferons (IFN-I). Interferon (IFN-1) is an important antiviral cytokine released by the innate immune system against viral infections. Studies show that coronaviruses similar to SARS-CoV-2 can suppress the host IFN-I-based antiviral response [11].

Vitamin B6: Main source of vitamin B are fish, poultry, meat, eggs, whole grain cereals, fortified cereals, many vegetables and fruits, soya beans, yeast extract etc.

Vitamin B12: It is found in meat, milk and cheese, eggs, cereals, yeast extract, fish and some shellfish etc.

Folate: Main sources of folate are broccoli, sprouts, green leafy vegetables spinach, cabbage peas, chick peas and fortified cereals. B vitamins regulate the intestinal immune system act as gut barrier. Vitamins B6 and B12 and folate all support the activity of natural killer cells and CD8+ cytotoxic T lymphocytes, effects which would be important in antiviral defence.

Deficiency of folic acid leads to thymus and spleen atrophy, and decreases circulating T lymphocyte numbers. Vitamin B12 deficiency decreases phagocytic and bacterial killing capacity of neutrophils. Vitamin B6 deficiency causes thymus and spleen atrophy and lowers the number of the T lymphocytes. Proliferation of lymphocyte and T lymphocyte-mediated immune responses are impaired. One of the study shows that patients with vitamin B12 deficiency had low blood numbers of CD8+ T lymphocytes and low natural killer cell activity [12].

Vitamin C: Main source of Vitamin C are oranges, red and green peppers, strawberries, kiwi, broccoli, sprouts and potatoes etc. Vitamin C is essential for collagen biosynthesis and for maintaining epithelial integrity. It plays important role in providing immunity and fight against infections. It helps in leucocyte migration to sites of infection, phagocytosis, natural killer cell activity and bacterial killing. Vit C helps in proper functioning of T lymphocyte particularly of CD8+ cytotoxic T lymphocytes and antibody production. Deficiency of Vitamin C increases susceptibility to a variety of infections [13]. Vitamin C deficiency leads to severe respiratory infections such as pneumonia. A meta-analysis reported that vitamin C supplementation, in individuals with low dietary intakes helped in reducing the risk of pneumonia [14]. Vitamin C gives protection against flu-like symptoms [15].

Vitamin D: Vitamin D can be found in sunlight. Other sources of Vitamin D are oily fish, liver, eggs, fortified foods and cereals. Vitamin D enhances epithelial integrity and induces antimicrobial peptide synthesis in epithelial cells and macrophages directly enhancing host defence [16,17].

Vitamin D helps in differentiation of monocytes to macrophages. It increases phagocytosis and bacterial killing by innate immune cells. In immune system Vit D promotes antigen processing by dendritic cells whereas antigen presentation is impaired. Vitamin D inhibits T-cell proliferation and production of cytokines by T helper 1 lymphocytes and of antibodies by B lymphocytes. Vitamin D increases regulatory T lymphocytes but have little impact on CD8+ T lymphocytes. Vitamin D can improve cellular immunity by reducing the cytokine storm induced by the innate immunity. In a research it is found that insufficient vitamin D and vitamin E can lead to coronavirus infection [18]. Vitamin D supplementation could reduce the production of pro-inflammatory cytokines, increase the expression of anti-inflammatory ones, and enhance the expression of genes related to the antioxidant system [19]. Other studies also reported that individuals with low vitamin D status have a higher risk of viral respiratory tract infections [20]. Many studies showed that vitamin D supplementation can reduce the risk of respiratory tract infections [21-24].

Vitamin E: The main sources of vitamin E are shellfish, meat, cheese, cereals, grains and seeds. Vitamin E helps in cell-mediated immune responses and in interaction between dendritic cells and CD4+T lymphocytes. Vitamin E deficiency also increases susceptibility of animals to infectious pathogens. Studies show that Vitamin E supplementation for the elderly increases the immunity [25-28]. Another studies show that Vitamin E supplementation improves cell-mediated immunity, lymphocyte

proliferation, IL-2 production and vaccination responses [29,30].

Zinc: Main sources of zinc are shellfish, meat, cheese, some grains and seeds, cereals, seeded or wholegrain bread. Zinc influences the antioxidant activity of some proteins and optimal levels of zinc acts as an anti-inflammatory compound. It helps in optimizing the immune responses and reduces the risk of infection [31]. Zinc maintains the numbers of T and B lymphocyte. Zinc helps in proliferation of CD8+ cytotoxic T lymphocytes, which are key cells in antiviral defence. Zinc deficiency leads to immune dysfunction and increases susceptibility to infectious diseases and may cause lower respiratory tract infection and diarrhoea. Moreover, its deficiency is also associated with impaired NK cell activity and neutrophil, macrophage phagocytosis activity, T-cell mediated antibody response, and abnormalities in complement activity [32]. Deficiency of zinc affects the acquired immunity causing decreased B lymphocyte and antibody production. Circulating CD4+ T lymphocyte numbers and function e.g, IL-2 and IFN-γ production are decreased. Most of the *in vitro* immune effects of zinc are prevented by zinc chelation [33].

Zinc deficiency affects bone marrow, decreasing the number immune precursor cells, naive B lymphocytes, naive T lymphocytes which causes thymic atrophy. Zinc deficiency also impairs innate immunity affecting phagocytosis and natural killer cell activity. Improving zinc deficiency lowers the likelihood of diarrhoea and of respiratory and skin infections. Recent study proved the role of zinc in antiviral immunity [34]. Zinc inhibits the RNA polymerase required by RNA viruses, like coronaviruses, to replicate, and hence zinc may play a key role in host defence against RNA viruses [35]. Zinc also releases the neutrophil extracellular traps for microbes [36].

Essential amino acids: Meat, poultry, fish, eggs, milk and cheese, soya, nuts and seeds, pulses are rich source of proteins. It is recommended that food rich in protein should be the top priority because it has immune properties (immunoglobulin production) and potential antiviral activity [37–39].

Iron: Iron is found in Meat, liver, beans, nuts, dried fruit (eg, apricots), wholegrains (eg, brown rice), fortified cereals, most dark green leafy vegetables spinach etc. Iron deficiency induces thymus atrophy, reducing output of naive T lymphocytes, and has multiple effects on immune function in humans. The effects include impairment of respiratory burst and bacterial killing, natural killer cell activity, T lymphocyte proliferation and production of T helper 1 cytokines. T lymphocyte proliferation was lower by 50% to 60% in iron deficient than in iron-replete housebound older Canadian women [40]. Studies show that, excess of iron impairs the immune function [41-44], which causes damaging inflammation. This condition invites micro-organisms and favours the growth of the pathogen. Therefore several host immune mechanisms have developed for withholding iron from a pathogen [45-48].

Copper: Main sources of copper are shellfish, nuts, liver, some vegetables. Copper is a trace element that helps in the functioning of immune cells such as NK cells, macrophages, neutrophils, and monocytes. Its deficiency causes less effective immune responses against infections and increases virulence [49,50]. *In vitro* studies show that copper ions block a fundamental protein for SARS-CoV-1 replication [51]. It is found that copper has antiviral properties acting at two levels: enhancing the components of the immune system to fight against infections and by direct contact with virus [52].

Selenium: Main sources of selenium are fish, shellfish, meat, eggs and some nuts. Selenium is an important trace element useful in many processes of innate immune system such as differentiation, proliferation, and normal functioning . It has role as antioxidants and in attenuating free radicals released during immune response. Selenium helps in production and development of antibody for adaptive response [53]. Selenium deficiency in laboratory animals adversely affects several components of both innate and acquired immunity, antibody production and increases susceptibility to infections. Lower concentrations of selenium diminish natural killer cell activity and increased mycobacterial disease. Deficiency of selenium results in decreased cytotoxicity of NK cells, decrease antibody production. It's deficiency also impairs cellular immunity and decrease response to vaccination. While selenium supplementation improves cellular immunity and immune response against viruses [54]. The selenium salts have also been used as a therapy to reduce the risk of blood clot formation in SARS-CoC2 infected persons [55]. As blood clot is one of the important COVID-19 collateral death causes [56].

Long chain omega-3 fatty acids (EPA and DHA): Fatty acids are mainly found in oily fish DHA, docosahexaenoic acid; EPA and eicosapentaenoic acid etc. Polyunsaturated Fatty Acids (PUFA) are present in fish oils, algae, and other food sources [57]. Omega-3 PUFAs eicosapentaenoic acid (EPA) and

docosahexaenoic acid (DHA) have anti-inflammatory properties [58,59].

Probiotic bacteria and respiratory infections: It is found in a research that gut microbacteria are protective against respiratory infection. Absence of gut bacteria in mice leads to impaired immune responses and causes bacterial or viral respiratory infection [60]. Healthy microbiota can also benefit the immune system. Many plant foods, fibres and fermented foods maintain healthy gut microbiota and help to boost the immune system. The gut bacteria fight against bacteria and viruses if infected.

4.4 Daily Requirement of Nutrients

Daily requirement of Vit A as recommended is 900mcg and for Vit. B6 is 1.7mg for mature persons. Daily dose of 400 msg of Folate is recommended and for Vitamin C is 90mg. Approximately requirement of Vit. D has to be 20 mcg and 15mg for vit E. In the same way daily requirement of zinc is about 11mg , for selenium 55mcg and about 18 mg of iron and 0.9mg for copper has been recommended daily for mature persons (Table 1) [61]. The amounts of nutrients should not be taken in excess as these are required only in little amount .

Table 1. Daily requirement of vitamin and mineral

Vitamin/Mineral	Source	Quantity (Per day)	Immune Function
Vitamin A	Fruits, Green Vegetables spinach, kale, broccoli, Meat and Nuts etc.	900 mcg	Maturation of immune cells
Vitamin B6	Fruits other than citrus Potatoes and Salmon	1.7 mg	In activity of natural killer cells and CD8+ cytotoxic T lymphocytes,
Folate	Beans and peas , grain products e.g., bread, cereal, pasta, rice, Green leafy vegetables , Oranges and orange juice	400 msg	Folate supports the activity of natural killer cells and CD8+ cytotoxic T lymphocytes
Vitamin C	Citrus fruits, kiwifruit, and strawberries, Vegetables e.g., broccoli, sprouts, peppers, and tomatoes	90 mg	Vit C helps in proper functioning of T lymphocyte particularly of CD8+ cytotoxic T lymphocytes and antibody production.
Vitamin D	Eggs, Fish oil and cod liver oil, Fortified orange juice and Mushrooms	20 mcg	Vit D promotes antigen processing by dendritic cells, phagocytosis
Vitamin E	Fortified cereals ,Green vegetables Nuts , seeds peanut butter, Fish and Vegetable oils	15 mg	Vitamin E helps in cell-mediated immunity
Iron	Whole grain, cereals, Fruits, Green vegetables, Meat ,Nuts	18 mg	In T lymphocyte proliferation and production of T helper
Zinc	Poultry, Dairy products, Fortified cereals, Beans ,Nuts and Whole grains	11 mg	Zinc helps in proliferation of CD8+ cytotoxic T lymphocytes and in maintaining the numbers of T and B lymphocyte
Selenium	Eggs, Meat, Nuts and seeds and Whole grains	55 mcg	In innate immune system
Copper	Nuts and seeds , Organ meats e.g., liver and Whole grains	0.9 mg	In functioning of immune cells such as NK cells, macrophages, neutrophils, and monocytes.

5. CONCLUSION

Healthy lifestyle and balanced diet with micronutrients such as vitamins A,B,C, D and E, iron, zinc and selenium are required for being healthy. These all vitamins and minerals are known to support the immune system. The deficiency of these vitamins and trace elements impairs the immune system and causes many diseases. Therefore optimal intake of vitamins and minerals in the body is important for proper working of immune system to overcome infections like COVID-19. We can get protection against this virus by enhancing our immune system. Along with diet, physical activity and proper sleep also helps to boost the immune system.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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