**THE ROLE OF NUTRITION IN THE PREVENTION OF IMMUNITY RELATED COMPLICATIONS**

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**ABSTRACT**

The immune system is required for basic physiological activities such as development, reproduction, and wound healing. The immune system is constantly working and monitoring, but it is hampered if a person becomes infected. Nutrition serves as a backbone for the immune system, enhancing and supporting it through the manufacture of regulatory molecules, all of which are derived from an energy-balanced diet. The lack of understanding of virus biological mechanisms, as well as the lack of efficient disease treatments (COVID-19) and/or vaccinations, has brought variables that can limit the immune system's ability to combat infectious diseases into the spotlight. A number of vitamins (fat and water soluble) as well as traces of metals like copper, zinc, and iron have been shown to support the human immune system and reduce the risk of infection. Nonetheless, the European Food Safety Authority (EFSA) determined that six vitamins (D, A, C, Folate, B6, B12) and four minerals (zinc, iron, copper, and selenium) are required for optimal immune system function. Individuals should consume a sufficient amount of essential nutrients to support their immune systems. The immune system is enriched by eating habits and living a healthy lifestyle. The gut microbiome aids in immune system education and regulation. The value of each type of nutrient has been described in a nutritional recommendation. This review looks at immune considerations specific to rural and urban areas in India, malnourished children, a tool to help individuals and populations strengthen their immune systems and prepare for infectious diseases such as COVID-19, the risk of infection, micronutrient requirements and deficiencies exhibited over the life course, and the available evidence regarding the effects of micronutrient supplementation on immune function and infection, as well as the available evidence regarding the effects of micronutrient supplementation on immune function and infection.

**KEYWORDS**: Immune system, Nutrition Guidelines, Vitamins, Gut Microbiota, COVID-19, Malnourished children.

**I. INTRODUCTION**

Nutrition is a complex network that constantly works to maintain the body cells active and protect them from pathogens by boosting immunity power. 1 The SARS-COV-2 epidemic has had a profound impact on global health and triggered a global crisis. 2 The severity of COVID-19 and the degree of the physical, societal, and economic ramifications that have resulted from the presence of SARS-CoV-2 have brought attention to the destruction that infectious sickness may wreak, as well as the significance of having well-functioning immune systems. 3 Signs and symptoms of COVID-19 may appear 2 to 14 days after exposure. This time after exposure and before having symptoms is called the incubation period. 4 When the body does not receive adequate nutrients, malnutrition results. Poor diet, intestinal problems, or another disease are all possible causes. Fatigue, dizziness, and weight loss are common symptoms. 5 Malnutrition that goes untreated can lead to physical and mental disabilities. 6 Diet and nutrition have long been considered crucial to one's health. Dietetics did not advance significantly until the 19th century, when chemistry advanced. 7 Early study concentrated on vitamin deficient illnesses, whereas later researchers advocated daily protein, fat, and carbohydrate requirements. 8 Dietetics received a boost during World War II when the military acknowledged its importance. 9 In certain ways, nutrition and infectious diseases are interconnected. First, nutrition has an impact on the immune system development of humans. 10

Furthermore, food poisoning, intestinal disorders, and systemic viral diseases can all be influenced by nutrition. 11 A healthy diet is very much essential in the preventing of malnutrition in all forms, besides non-communicable diseases and disorders. However, owing to greater production of processed foods, urbanization, and lifestyles modifications, dietary habits have seen many changes and has also led to innumerable diseases. 12 People generally consume more foods higher in energy, fats, sugars, and salt, and don’t prefer eating fruits, vegetables, and other dietary fibre like whole grains which are enriched with healthy nutrients and energy. 13 A healthier diet is much needed in the prevention of malnutrition in all forms.The lessons from this study of nutrition and immunity helps to know that the good nutrient supply leads good nutrient stores. A healthy diet chart and natural food can make our immunity stronger and prevent the problem of malnutrition. 14 The aim is to have knowledge about malnutrition and nutrition insufficiency in disease progression and to promote a healthy lifestyle. In this review, we have discussed about most important nutrients and immune suppression mechanisms by B lymphocytes, T-cells to gain insights about the significance of nutrition and enhance Immunity.

**II. NUTRITION OVERVIEW**

To function, our bodies require a particular number of nutrients on a daily basis. A balanced diet is necessary to provide these nutrients to our bodies. Eating healthily allows us to attain and maintain body compositions that allow us to do demanding mental and physical tasks while being healthy. 15 While the body can synthesis many nutrients, others, particularly critical nutrients, cannot be synthesized and it needs to be taken individually. As a result, we must provide them through our diet - the foods and beverages we consume. Macronutrients and micronutrients are the two types of nutrients in general. 16 Fats, proteins, carbohydrates, water, and some minerals are all macronutrients mostly present in nuts, 17 and our bodies require vast amounts of them on a daily basis. 18, 19 They provide the majority of the energy and building blocks we require for growth, activity, and upkeep. Vitamins and trace minerals are micronutrients that our systems require to digest macronutrients. Micronutrients are only needed in trace levels, ranging from milligrams to micrograms. 20

**III. ROLE OF NUTRITION IN IMMUNE ENHANCEMENT**

Immune system is an intricate plot and pathway in human body that protect against harmful microbes. 21, 22 Immune system protects the mankind from pathogenic organism as we are constantly exposed to such pathogens. 23 The optimal status of particular nutrients is thought to be critical for keeping immune components functioning normally, assisting in the prevention and treatment of infections. 24, 25 According to scientific data, the European Food Safety Authority (EFSA) has determined that six vitamins (D, A, C, Folate, B6, B12) and four minerals (zinc, iron, copper, and selenium) are required for the normal functioning of the immune system. 26, 27 One of the causes for the increased risk of more severe consequences from infection with COVID-19 is the negative impact of low nutrition on the immune system. 28, 29 Immunity can be compromised in older persons who are overweight or malnourished. 30 The new coronavirus epidemic is spreading, producing more public health, social, and economic issues.

The large disparity in mortality rates between countries raises concerns about the impact of lifestyle habits and immune condition of mankind. 31 The key functions of the immune system are discussed in this article, as well as how macronutrients, micronutrients, and metabolites from the gut microbiota can aid digestion while also boosting the immune system. Certain dietary patterns may help the body to prepare better for microbial attacks, excess inflammation and also from SARS-COV. 32, 33 Vitamin C, Vitamin D, Zinc, Selenium, Iron, and proteins (including amino acids and glutamine) are examples of nutrients supporting immune cell growth and function. 34, 35 These nutrient plays the vital role for the enhancement of immune system. Diet should contain prebiotic and probiotic foods which are beneficial. Prebiotics includes Garlics, Onions, Bananas, Seaweed etc. Probiotic includes Yogurt, Kimchi, Tempeh, Miso etc. 36 The lesson from study of nutrition and immunity helps to know that the good nutrients supply leads good nutrient stores hence leads to good immune response and defense against pathogens.

**IV. NUTRITION AND INFECTION**

Infection and nutrition are complex interaction that influences human health. Malnutrition plays a crucial influence in the spread of infection, which is a worldwide health problem. Malnutrition is widespread in less developed regions and is one of the primary cause of immune deficiency. 37 Nutrition metabolism, which begins with the absorption of food, is a set of physical and chemical reactions that occur in the body to obtain energy and use it to synthesis, process, transform, and eliminate substances in order to maintain life. 38 Thus, the immunological capacity of the host is a defining property of defence against the genesis and progression of infectious disease. Nutritional inadequacy is the inadequate supply of essential nutrients (vitamins and minerals) in diet resulting the malnutrition and infection. Inadequacy of nutrition’s leads to many adverse effects including Inflammation and oxidative stress, weakened immunity, gut dysbiosis, loss of lean mass, functional decline, and infections. 39

The World Health Organization's publication of Interaction of Nutrition and Infection in 1968 revealed that infection and malnutrition had a synergistic relationship. Weight loss, reduced immunological function, mucosal injury, pathogen invasion, and slowed growth are all symptoms of insufficient nutritional intake in children. 40 It is widely known that diseases can have a negative impact on a person's nutritional health, resulting in a reduction in the body's ability to fight infections. 41 Many physiological systems are influenced by the gut bacteria, which is a metabolic powerhouse. It could play a role in the onset and progression of important diseases like cancer, metabolic disorders, and infectious diseases. 42 Innate and adaptive immunity, metabolism, and nutrition are all influenced by microbes in the gastrointestinal tract. Gut microorganisms are extremely likely to play a significant role in human nutrition-infection interactions, given their various activities. As a result of the direct link between nutrition and infections, diseases have a detrimental impact on dietary patterns and nutritional levels. 43 Malnutrition is one of the major contributors to diseases that are more serious and even lethal. The interaction between infections and malnutrition is complex, and increasing nutritional status has a lot of potential for preventing and treating infections.

**V. GUIDELINES FOR NUTRITIOUS FOOD**

Malnutrition in all kinds, as well as Non-Communicable Diseases (NCDs) such as Diabetes, Heart Disease, Stroke, and Cancer, can all be prevented by eating a healthy diet. 44 Health problems are caused by a poor diet and a lack of physical activity. Energy intake and expenditure should be balanced. Total fat should not exceed 30% of total daily calories to avoid unhealthy weight gain. 45 Healthy eating habits promote normal growth and development, as well as lowering the risk of becoming overweight or obese, as well as other chronic conditions. It is advisable to drink water, tea & coffee with low amount of sugar or no sugar. 46 Limited juices are also good. Eat variety of whole grains such as whole-grain pasta, brown rice, whole-wheat bread etc. Limited white rice and white bread. Eat fish, poultry, beans, nuts for getting high calories. 47 Avoid bacon, processed meats. Limited red meat and cheese. Use healthy canola oil or olive oil for cooking and in salad. Limited butter is good but avoid trans-fat. 48 More vegetables in variety means better health. keep all types of vegetables in dish. Avoid French fries. Choose all types of plenty fruits. Seasonal fruits are more preferable. Keep dark chocolate, higher cocoa in diet. Eat fish, shellfish, chicken, eggs, lean beef, pork for acquiring energy. 49 Intake of soy bean, canola, sunflower, corn, extra virgin olive oils, liquid plant oils (except tropical oils) can be increased. Choose plain yogurt, milk, fermented milk or cheese (with reduced fat) instead of highly processed cheese products. 50 In this review, we got a point that there is no magic diet for COVID-19 disease. Only a healthy and energetic diet works as a shield by developing your immune system stronger. 51 Follow these guidelines as heath tips and we hope we’ll defeat this pandemic very soon.

Table 1: Nutritious foods and guidelines according to age

|  |  |  |  |
| --- | --- | --- | --- |
| **Age** | **Medium** | **Nutrients required most** | **Calorie Intake** |
| 0-6 months | Liquid | Energy driven foods | 55-500 |
| 6 months – 1year | Mashed food | Energy driven foods | 500-800 |
| 1-2 year | Chopped table food | Iron rich foods | 800-1000 |
| 2-5 year | Medium Foods | Reduced fatty foods | 1000-1200 |
| 5-10 year | Regular Foods | Mild fat intake | 1200-1800 |
| More than 10 years | Regular Foods | Maintained balanced diet | 1800-2200 |

**VI. NUTRITION AND IMMUNE SUPPRESSION MECHANISM**

The availability of all essential nutrients in sufficient proportions to ensure appropriate growth and maintenance of physiological functions is known as nutrition. 52 It consists of a number of chemical processes (oxidation, reduction, hydrolysis, acetylation, methylation, and so on) as well as physiological operations that turn food into body tissues that grow and perform their functions on a regular basis. It entails digestion, food absorption, and nutrient delivery into cells. The SARS-COV-2 epidemic has had a profound impact on global health and triggered a global crisis. Despite high infection rates, India, as a densely populated country, has successfully combated the pandemic outbreak, with a significantly lower rate of fatality. 53 Nutrition is important for immunological function because it provides critical nutrients. 54 Some nutrients that assist a healthy immune system include protein, a macronutrient that is required for the production of antibodies and immune cells. Nut butters, oatmeal, Greek yoghurt, spinach, broccoli, beans, eggs, chicken, salmon, pork, prawns, and so on are all good sources. Zinc, aids in the formation of new immune cells and cell reproduction. Sweet potatoes, legumes, shellfish, spinach, mushrooms, nuts, crab, beef, oysters, and other foods are good sources. 55

Vitamin D maintains equilibrium and modulates the immune system. Egg yolk, tuna, salmon, mushrooms, fortified yoghurt are the important sources of Vitamin D. Vitamin C helps to maintain healthy skin by preventing germs and dangerous bacteria from entering. Lemons, oranges, tomatoes, papaya, strawberries, blackcurrants, and other citrus fruits. Vitamin E Protects the body from free radicals and reduces inflammation. Olives, almonds, hazelnuts, kale, turnip greens, trout, shrimp, and other sources 56 Prebiotic and Probiotic foods influence immune cell activity and inflammatory regulation. Onions, tomatoes, bananas, barley, oatmeal, legumes, and other sources of prebiotics Lassi, Natto, Coconut kefir, Non-dairy yoghurt, Miso, Chutneys, Pickles, and other probiotic-rich foods. Vitamin A supports skin and tissue health, which helps to control the immune system and fight infections. Carrots, Lettuce, Apricot, Beef Liver, Sweet Pepper, Sweet Potatoes, Mango, Cheese, Pumpkin, Egg, Fish, and so on are examples of food sources. The immune system defends the body against disease-causing microorganisms such as bacteria, viruses, parasites, and fungi. Immune system suppression after infection or inflammation is a critical step that controls immune-mediated pathogenesis.

Several immune suppression mechanisms have gotten a lot of attention in the last few decades. 57 These methods involved suppressive cytokines such as interleukin (IL)-10 and transforming growth factor (TGF)-beta, as well as apoptosis mediated by death ligands such as Fas ligand (FasL) and tumour necrosis factor-related apoptosis inducing ligand (TRAIL), which are expressed by cytotoxic cells. 58 Suppression mechanism generated from myeloid cells: MDSCs (myeloid-derived suppressor cells) are a diverse group of cells that grow in response to cancer, inflammation, and infection, and have a remarkable ability to block T-cell responses. These cells are a special type of immune cell that modulates immunological responses in healthy people and in the setting of various disorders. 59, 60 Mechanism of SARS COV-2 Suppression include Antiviral immune responses to be triggered in order for an infection to recover. The activation of cytotoxic follicular helper T-cells and the decrease of regulatory T-cells are both associated with a poor prognosis. 61, 62

**VII. COMPARISON BETWEEN ENHANCED IMMUNITY OF RURAL AND URBAN PEOPLE**

Greater prevalence of physical and mental problems has been linked to increased urbanization and environments with a limited range of microbial exposure. 63 As the second more severe wave of COVID-19 continues to spread, metropolitan regions appear to be suffering more than rural ones. 64 Although cases and deaths have been reported from rural areas, the numbers in cities are disproportionately greater. Better-off areas within cities appear to be more negatively affected than slums. 65 Slums, on the other hand, are more densely crowded, making it difficult for residents to maintain distance and making them negligent with masks. After all, half of India's population is malnourished and anaemic, with the majority of these people living in rural areas and slums. 66 In comparison to more affluent persons living protected lives, rural and urban impoverished communities appear to have inherently higher immunity to the SARS COV-2 virus. 67 The impoverished and rural people have a very different lifestyle from the middle and upper middle classes. They confined themselves to indoor pastimes and avoided physical labour. Rich people are likely to spend a lot of time in air-conditioned environments. 68 On the other hand, urban poor and rural folks are mostly engaged in physical labour and are out in the open. This is why, despite poor health indicators, the urban poor and rural populace have a strong immune system and can better withstand virus attacks. 67 There are few reports of coronavirus illnesses or deaths in tribal regions, 69 where people are attached to nature and breathe fresh air.

Tribals, on the other hand, are noted for dealing better with natural disasters due to their intrinsic instincts. An overactive immune system is associated with stress-related disorders and may potentially play a role in their aetiology, according to human and animal research. A healthy urban individual without pets had a higher number of peripheral blood mononuclear cells (PBMCs) and plasma interleukin-6 (IL-6) following acute psychosocial stress generated by the Trier Social Stress Test (TSST) than a rural area person with farm animals. 70 People with lower socioeconomic position and minority populations are more likely to live in cities and are less likely to have health insurance. As a result, these individuals experience barriers to care, receive lower-quality care, and do not make adequate use of emergency systems. On the other side, the huge number of people without health insurance or citizenship places a greater strain on the existing system. Reduced exposure to microorganisms with which mammals coevolved is thought to play a role in increased inflammation in urban areas. 71 Immune modulation was facilitated throughout human evolution by linkages between the ancient microbiota and the innate immune system. 72 Thus, regular contact with animals appears to be the most important element contributing to the decline in contact with elderly people in both urban and rural locations. Childhood asthma and other inflammatory illnesses can be reduced by interacting with pets and farm animals. 73 Rural environments are rich in biodiversity and beneficial bacteria, providing immune-protective habitat. 74 Due to changing microbial exposures, urban settings have little biodiversity and are not immune protective. 75 Malnutrition is a serious problem in our country, and we account for one-third of the global burden of malnutrition. A healthy diet plan that includes natural, fresh, unprocessed foods can boost our immunity and prevent malnutrition. To do this, we must all promote a healthy diet that excludes harmful, high-fat, trans-fat foods. A healthy, energy-balanced diet, as well as living close to nature and relying on traditional healing methods, can help to prevent more COVID-like diseases, teaching us to live more in harmony with nature.

**VIII NUTRITION IMPACT ON HUMAN HEALTH**

Increasing consumption of dry beans and other pulses may be a sustainable method to help address the present obesity epidemic and prevent many of the most prevalent chronic diseases, according to scientific research. Despite the many health advantages, intake of pulses is still low, especially in developed nations. 76 Polyphenols in the diet have been shown to have health-promoting qualities that reduce endothelium dysfunction, lower blood pressure and cholesterol, and modulate energy metabolism. Specifically, this is true of catechins, quercetin, hesperidin, anthocyanins, and phenolic acids, which have anti-oxidant, anti-retroviral, anti-hypertensive, anti-inflammatory, anti-aging, and insulin-sensitizing properties. Flavonoids on the other hand impact on enhanced immunity, anti-inflammatory, anti-cancer, and anti-diabetic property. 77 **Numerous studies on soy-based protein products have revealed that they include antioxidants (phytate, isoflavones), operate as tyrosine kinase protein inhibitors, regulate cell life and death, decrease lipid and bile acid absorption from the digestive system, and enhance anti-neoplastic enzyme action. 78** Functional foods have exerted their beneficial effects using metagenomics and metabolomics technologies and short chain fatty acids have been known to implement several immunomodulatory activities. Antioxidants present in foods are known to prevent cellular damage and inflammation in specific pathologies. 79,80 Anthocyanins (Phenolic compounds) from various sources were studied for its effect on hypertension, type 2 diabetes mellitus and showed beneficial effects with no positive effects seen in breast or gastric cancer. 81 Seaweed oil includes mono- and polyunsaturated fats and is utilised as a source of fatty acid nutritional supplements. It is also used to make biofuel, massage oil, soaps, and cosmetics. 82 The prebiotic effects of these polyphenolic chemicals, the decrease of oxidative stressors, interactions with cell receptors and enzymes, and other mechanisms all contribute to their protective benefits. 83 Various physicochemical properties of dietary rich fibres are known to influence their role in combating various diseases and their progression and it has been widely used as functional foods due to its advantage in health. 84 Resveratrol is a phenolic compound known to counteract with immune cells and its action on SIRT1 to modulate both inflammatory and non-inflammatory process and acts a possible adjuvant to pharmacological therapies. 85

**IX Complications with Nutrition Therapy**

Nutritional therapy is vital in maintenance of human health but in previously reported cases, membranoproliferative glomerulonephritis and glomerulonephritis is reported from chronic intake of home parenteral nutrition. This case study describes a 16-year-old woman who was treated with HPN for short bowel syndrome. She experienced acute kidney injury after being on HPN for 11 years, manifesting as macroscopic haematuria, nephrotic-range proteinuria, and a decreased glomerular filtration rate. 86 Another case scenario of o 68-year-old male with a history of peripheral vascular disease, coronary artery disease, atrial fibrillation, hypertension, hyperlipidemia, and atrial fibrillation developed nonocclusive mesenteric ischemia while receiving enteral nutrition. 87 A case of 4-year-old boy with neurological impairment and severe growth retardation, recurrent vomiting and gastric reflux, as well as symptoms of long-term malnutrition, hypotonia, and seizure disorders presented recurrent diarrhoea that was diagnosed as an intolerance to enteral feeding. 88 An instance of intestinal necrosis linked to a jejunostomy for enteral nutrition in a patient who underwent an oncologic gastrectomy was described in a study. 89 A retrospective study also found that Gastrointestinal complications develop frequently while patients are given enteral nutrition and the choice of nutrition and necessity should also be considered. 90

**CONCLUSION**

Nutrition is an important part of the immune response, and proper nutrition is required to keep the immune system functioning. Immunity enhancement is crucial. Immunity can be impaired in the elderly, particularly if they are fragile, fat, malnourished, or have insufficient mineral and vitamin intake. Malnutrition-induced immune dysfunction increases infection susceptibility and permits infections to become more severe, even fatal. By enabling dysregulated inflammation and oxidative damage, inadequate nutrition contributes to frailty and poor infection outcomes. The deleterious impact of poor nutrition on the immune system, particularly its inflammatory component, could be one of the explanations for the increased risk of more severe SARS-CoV-2 infection symptoms seen in the elderly and obese. There is a necessity of good nutrition in establishing a diverse gut microbiota, in order to improve the immune system. It is also worth noting that age and weight affect the gut microbiome. The importance of good nutrition in stimulating immune responses also applies to ensuring that vaccinations are effective. As a result, in order to appropriately support the immune response, attention should be directed on correcting the current dietary deficiencies in the population such as malnutrition and micronutrient insufficiency.

**Conflict of Interest**

The authors have no competing interests to declare that are relevant to the content of this article.

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