Let nutrition be your vaccine amid COVID-19- a narrative review

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Abstract

There has been a growing body of evidence highlighting the radical effect of nutrition on the immune system and disease susceptibility. The current COVID-19 crisis awakens an urgent calling for optimum nutrition which boosts immunity and prevents diseases, just like a vaccine. Though there have been several national guidelines regarding diet during COVID-19, there has been sparse research and literature available in this field. This review aims to summarise the existing evidence on various aspects of nutrition and immunity pertaining to the COVID-19 crisis.

Introduction:

Amid our battle with COVID-19, it is worth Napoleon Bonaparte’s most celebrated statement- “An Army marches on its stomach”. We are what we eat, and our current nutritional status will result in either prevention, decrease the severity of the disease or decrease the duration of the convalescence period. It is a known fact that co-morbidities increase the susceptibility as well as the severity of COVID-19. William Foege stated that vaccines are the tugboats of preventive health, and balanced nutrition can also play a similar role in human health. Appropriate and adequate nutrition is also essential to foster the function of immunological cells and to initiate rapid and effective responses against pathogens. This demand for energy and nutrients can be supplied by exogenous sources like a balanced diet. Thus, it is clear that nutrition plays a significant role in the functioning of the immune system, which needs to be strengthened during this pandemic. About 70% of total mortality in developing nations are due to diet associated NCD (Non-Communicable Diseases), which pose a major public health challenge. Though many public health strategies have been developed, the significance of immuno-nutrition has been mentioned little, leading to scarce data regarding the same. Current data will be resourceful in enhancing the knowledge and understanding of the role of

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nutrients as health protectants. Here, we review the existing evidence on various aspects of nutrition and immunity pertaining to the COVID-19 crisis.

**Literature review and search strategy**

Searches for appropriate literature were categorised by subtopics. Each subtopic was further investigated by a group of two to three authors. Literature and search strategy included PubMed and Google Scholar for articles on various aspects of nutrition in promoting immunity and its relation to COVID-19 using appropriate keywords. This was supported with a manual search of article reference lists. No systematic assessment of study quality was performed. The search included articles published within the last five years (2015).

**Concept of Immuno-nutrition:**

In view of the ongoing pandemic of COVID-19, it would be appropriate to mention that, a robust immune system is one of the significant defences, as there is still no curative or preventive medicine available. A significant aspect of nutrition and health is immuno-nutrition, which can be explained as the potential to modulate the activity of the immune system by interventions with specific nutrients. These nutrients are vital for the function of T cells, B cells, killer cells, macrophages, neutrophils/granulocytes that are involved in the killing and elimination of infectious microbes. Additionally, many other immune-related functions are performed by these nutrients and phytonutrients. An array of nutrients and dietary interventions, for example, probiotics and resistant starch, have illustrated the ability to optimise the functioning of the gut or to decrease gut inflammation.

**Nutrients in Focus**

Some nutrients play a major role in boosting immunity, therefore the recommendations for servings during the COVID-19 period are relatively higher than the usual WHO dietary recommendations, viz. fruits, vegetables and a combination of whole-grain cereals, a variety of meats and beans. Sufficient intake of iron, zinc, and vitamins A, D, E, B6, folate, and B12 is cardinal for the maintenance of immune function. Nutrients like n-3 PUFA (polyunsaturated fatty acids), EPA (eicosapentaenoic acid), DHA (docosahexaenoic acid) phytochemicals like Epicatechin, Resveratrol, Curcumin, EGCG (epigallocatechin gallate) have a potential preventive or therapeutic impact on risk factors associated with acute COVID-19. Also, an imbalance in the adequate proportion of macronutrients increases the chances of developing chronic diseases and may negatively impact the micronutrient profile.

**Protein:** Provision of sufficient protein intake, amino acids, and in particular glutamine, are essential energy substrates for immune cells such as lymphocytes. Power stores of the immune system like antibodies also rely on protein and deficiency of protein in the diet may lead to symptoms of weakness, fatigue, apathy and weakened immunity. Immunomodulatory properties to control various...
life-threatening diseases have been attributed to protein intake and specifically to some amino acids such as arginine, glutamine, taurine and sulphur-containing amino acids.12

Food sources: Seafood, lean meat, poultry, eggs, soya bean, beans, dha’s, peas, un-salted nuts and seeds. Milk and milk products like curd, cheese.

**Vitamin C:** Combined results from many prophylactic trials state that statistically significant (80% or greater) reduction in pneumonia incidence was observed in the vitamin C groups. Therefore, the therapeutic use of vitamin C supplementation could be economical for patients with pneumonia and low plasma vitamin C levels as it has low cost and health risks.5

Food Sources: Red peppers, oranges, strawberries, broccoli, mangoes, lemons, Indian gooseberry (Amla), dark green leafy vegetables (DGLV), capsicum, tomatoes, potatoes and cabbage.

**Vitamin A:** Vitamin A has a regulatory function in both cellular and humoral immune responses. It has the ability to enhance the antibody response after some vaccines, including measles and anti-rabies vaccination (2.1 times), on supplementation in infants.8 It also preserves the structure and function of the mucosal epithelial cells of the respiratory tract and boosts mucosal immunity (critical for the prevention of respiratory infection).5

Food Sources: Preformed Vitamin A in the liver, fortified milk and dairy products, carotene in dark green leafy vegetables, deep yellow fruits and vegetables like carrots, papaya, yellow bell peppers.

**Vitamin D:** Vitamin D has a crucial role in modulating both innate and adaptive immune responses. Epidemiological data have suggested that Vitamin D deficiency is linked to increased susceptibility to acute viral respiratory infections. Recent reviews analyzing possible mechanisms indicate that vitamin D plays a critical modulatory role in the innate immune responses to respiratory viral infections, such as Influenza A and B, parainfluenza 1 and 2, and Respiratory syncytial virus (RSV).3 Furthermore, quarantine results in less outdoor time, decreased exposure to sunlight, thus little production of Vitamin D leads to lower levels of 7-dehydrocholesterol in the skin.14

Food Sources: Fortified milk and dairy products, fish, liver, eggs. It is also synthesized in the skin under exposure to sunlight.

**Vitamin E:** Vitamin E deficiency impairs both humoral and cellular immunity in the treatment of chronic hepatitis B in a small pilot RCT. In a study, the healthy elderly population was administered with 800 mg 2-ambo-α-tocopherol or placebo/d for 30 days and it showed increased delayed-type hypersensitivity (DTH) levels which is an indicator of cell-mediated immunity. Also, it was found that Vitamin E is associated with increased plasma Vitamin E, DTH score and mitogenic response.15

Food Sources: Vegetable oils, cereal grains, nuts, dairy products.

**Zinc:** Zinc deficiency is manifested with depressed immune functions, lymphopenia and decreased numbers of circulating T and B lymphocytes, and impaired chemotactic responses of neutrophils, monocytes and macrophages. Evidence also suggests that zinc inhibited severe acute respiratory syndrome (SARS) coronavirus RNA-dependent RNA polymerase (RdRp) template binding.14

Food Sources: Oysters, red meat, milk, liver, poultry, seafood, green leafy vegetables, legumes, nuts, pumpkin seeds, sesame seeds, beans and lentils.

**Selenium:** Deficiency of selenium has been characterised for higher risk of diseases caused due to oxidative stress. Supplementation of selenium showed increased resistance to diseases and viral infections has been observed. Selenium influences both the components of the immune system – innate, the non-adaptive one and acquired the adaptive one.15 It also aids the anti-oxidant system and helps in antibody production with Vitamin E. Additionally, it helps in the synthesis of the active thyroid hormone.5

Food Sources: Organ meats, eggs, whole grains, beef, turkey, chicken, fish, shellfish.

**Iron:** From the data collected from NFHS-4 (2015–2016) and previous literature, it is confirmed
that nutritional status and anaemia influence respiratory diseases such as COVID-19. The iron homeostasis maintaining cytokines function via hepcidin or directly regulates iron metabolism in immune cells, e.g. pro-inflammatory cytokines like IFN–γ downregulate transferrin receptor (TfR1) expression in macrophages, leading to a reduction in intracellular iron in these immune cells. Since the 1970s, iron homeostasis on the immune function and susceptibility of infection is being studied. The iron availability in the serum influences the maturation and proliferation of immune cells such as lymphocytes.

Food Sources: Liver, meat, legumes, poultry, dark green leafy vegetables, broccoli, peas, dried fruits, potatoes, eggs, whole grain cereals, jaggery.

Spices and herbs: Few of the household spices are not only used for taste, flavour, palatability but also as medicines as per traditional Ayurveda therapeutic systems. Antioxidants and phytochemicals present in ginger (gingerol), garlic (allicin), tulsi (eugenol), turmeric (curcumin), lemongrass (triterpenoids) act as antivirals. These ingredients can be used in daily cooking or as tea/concoction to improve immunity gradually.

Essential Fatty acids: The essential fatty acids (EFA) have a key role in immune response as they possess regulating effects on immunity and inflammatory processes. EFA and related long-chain polyunsaturated fatty acids (PUFA) act as a substrate for oxylipins (OxL) and endocannabinoids (eCB) generated by immunocompetent cells assisting in immune functions and regulating inflammation. Therefore, a balanced diet must include adequate essential fatty acids and both n-6 and n-3 PUFA for OxL and eCB to restraint inflammation. Omega-3 and omega-6 PUFA accentuate anti-inflammatory and pro-inflammatory effects. As they are precursors of resolvins/protectins and prostaglandins/leukotrienes, respectively omega-3 including protecting D1, serving as a novel antiviral drug, could be considered as one of the potential interventions of the novel virus COVID-19.

Magnesium: Plays a role in innate and acquired immunity by boosting immunoglobulins.

Food sources: Ragi, jowar, pulses, legumes, GLV (green leafy vegetables), almonds, cashews, black sesame seeds, sunflower seeds, garden cress seeds.

Prebiotics and Probiotics: They help to reinforce the immune system, increase immune responses and promote specific immune signalling. Prebiotics forms the dietary fibres which trigger the growth of gut microbiota.

Food sources: Garlic, onion, banana, barley, oats, apples, flaxseeds, wheat bran.

Probiotics: They are a specific strain of live bacteria found in foods, help in maintaining a healthy community of gut microbes. Food sources: Fermented milk, yoghurt, fermented food products.

Hydration is equally important. 10 cups of water a day is recommended by the WHO.

Medical Nutritional Therapy for COVID-19 Patients

Nutritional status is believed to be of paramount importance in association to outcomes of patients with COVID-19. As per the nutritional indications suggested by Kaiying and Hanping, the five-step method, diet plus nutrition education, oral nutritional supplementation (ONS), tube feeding, supplementary parenteral nutrition (SPN), and total parenteral nutrition (TPN), are the cornerstone treatment for optimal recovery of the patients. However, the recommendations should be customised according to the condition of each patient.

Patients with mild symptoms of COVID-19:

Nutritional counselling is fundamental. Identification of risk and presence of malnutrition should be an early step in the general assessment of all patients, with regard to more at-risk categories including older adults and individuals suffering from chronic and acute disease conditions. Nutrition assessment using MUST (Malnutrition Universal Screening Tool) or NRS (Nutritional Risk Screening) - 2002 should be carried out. Depending upon the dietary problems, optimisation of nutritional status is carried out. Energy requirements are calculated at 27-30 kcal/kg body weight (BW)/day. Protein needs are kept at 1 g/kg/BW. Fat: CHO ratio is
maintained at 30:70. Supplementation with vitamins and minerals is done. The use of omega-3 fatty acids may be relevant because of their recognized anti-inflammatory properties. MCT oils can be added to increase calorie density and easy assimilation. Adequate hydration to balance fluid loss occurring due to sweating, coughing, breathing, vomiting and diarrhoea is recommended.

According to the IDA (Indian Dietetic Association) Nutrition guidelines for COVID-19 patients, good nutrition helps the body fight infections, so provide adequate but not excessive nutrients (avoid overfeeding) and maintenance of healthy body weight is important. Increase the frequency of meals to compensate for the increased caloric requirements of fever. A balanced diet including all the food groups is essential. Supplement with vitamin C, zinc, vitamin A, B6, D, E, iron, folate and fibre if not getting enough from the diet. The use of culinary herbs like kalonji (onion seeds) turmeric, ajwain, ginger, oregano, sage and cinnamon is beneficial. Increased consumption of fruits and vegetables is encouraged to improve antioxidant levels in the body. Enough sleep, reduced stress, exercise should be ensured to avoid intake of alcohol and tobacco products.

Oral nutritional supplements (ONS) should be used whenever possible to meet the patient’s needs when dietary counselling and food fortification are not sufficient to increase dietary intake and reach nutritional goals. ONS shall provide at least 400 kcal/day including 30 g or more of protein/day and shall be continued for at least one month.

For patients treated in the home-quarantined environment, a diet rich in protein, carbohydrates and micronutrients is recommended to be consumed orally and may be combined with ONS to meet nutritional targets for early recovery.

Critical patient in intensive care with respiratory insufficiency.

ICU stays, and particularly their longer duration, are well-documented causes of malnutrition, with loss of skeletal muscle mass and function which also lead to poor quality of life, disability, and morbidity long after ICU discharge.

In a cross-sectional study by Li et al., performed in hospitalized elderly patients with COVID-19 reported that 53% of patients were malnourished. For patients age above 65 years, along with the COVID-19 risk factor, another aspect coexists with markers of poor nutrition status such as sarcopenia irrespective of their body mass index. This encourages nutritional support guidelines to be incorporated in the global management of the COVID-19 patient. In cases where ICU stay lasts longer than 48 hours as expected, the medical nutritional therapy must be started with the following priority: a) early Enteral Nutrition (EN) must be started within 48 hours, if no contraindications are present; b) Parenteral Nutrition must be started within three to seven days and must be considered when all strategies for EN have failed to avoid severe malnutrition. A recent meta-analysis showed, in critically ill patients, compared to EN introduced later after insufficient oral refeeding, early EN, reduced the mortality rate and complications, particularly pneumonia. Continuous feeding is recommended compared to bolus feeding. Patients on invasive mechanical ventilation have to be handled cautiously as they may develop persistent inflammation-immuno-suppression and catabolism syndrome, often ensuing in secondary infections and/or viral reactivation associated with an elevated risk of morbidity and mortality.

Nutrient requirements: Energy: COVID-19 patients need more energy than normal. According to the IDA MNT expert recommendations report, it is recommended that the resting energy expenditure (REE) can be calculated from the VCO2 value measured by the ventilator. The calculation formula is:

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\text{REE (kcal)} = \text{VCO}_2 \times 8.19
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If it cannot be the VCO2 was measured, the estimated energy requirement according to body weight: For non-obese critically ill patients, the recommended amount of energy target of 25 ~ 30 kcal per day/kg (body weight over the calculation), ideal body weight (kg) = height (cm)-105 (suitable for adult males), ideal body weight (kg) = [height (cm)-100] \times 0.85 (suitable for adult females). For obese and critically ill patients, if the BMI is 30 ~ 50 kg/m2,
the recommended energy target is 11 ~ 14 kcal/kg per day (calculated by actual body mass). If BMI > 50 kg/m², the recommended energy target is 22 ~ 25 kcal/kg per day (calculated by ideal body mass).²⁶

Protein: It is indicated to increase protein supply as a top priority to reduce the catabolism due to the inflammatory mediators. It is recommended 1.3 g/kg/day increasing the supply of branched-chain amino acids to 50%, to prevent muscle loss, elevate the strength of respiratory muscles. Carbohydrates: Carbohydrate administration should be limited in the critically COVID-19 patient with respiratory failure. The carbohydrate requirement is 2 g/kg/day and must not exceed 150 g/day. Fat: the lipid requirement of the critically ill patient is 1.5 g/kg/day. Fluid volume: It is important to maintain neutral fluid balance in critically COVID-19 patients, with particular consideration to renal and prerenal failure. Micronutrients: among common supplements of multivitamins and minerals, a complex of vitamin B, zinc and selenium are added. Immunonutrients such as arginine, nucleotides, glutamine, ω-3 fatty acids can be used.²³

Social Aspects

COVID-19 pandemic which is now posing to be a prime public health threat has created a major disruption in our daily schedules with the invasion of quarantine and lockdown conditions. These situations lead to boredom and anxiety leading to over-eating and frequent snacking of comfort foods, respectively. In recent surveys, findings suggest, that snacking has increased in the group of middle-class population and patients with type 2 diabetes during this lockdown period.³¹ The increase in the consumption of some types of food is linked with their symbolic value and their tendency to carry on at home some external socialization habits.³² These deleterious nutritional habits along with physical inactivity could spike the risk of developing obesity which is not only a chronic state of inflammation, but also often complicated by heart disease, diabetes, and lung disease which have been indicated to increase the risk for more serious complications of COVID-19.¹¹ Recently, in a five-way model of emotions and diet, it was established that changes in food intake may be the “natural” response to stress and heightened emotional states through both psychological and physiological mechanisms.³⁰ As we fight anxiety due to pandemic, and desperately wait for solutions, we have shunned the basics of diet and lifestyle.

This outbreak has also led to the spread of fake messages of single foods/herbs assuring cure or prevention of the infection. Such baseless claims lead to effects ranging from giving a false sense of protection against the infection to toxicity.³⁰ Further, fear, anxiety related to the uncertainty of the surroundings, also impact psychological wellness, and that has a profound effect on individual physiology too.

Therefore, regular physical exercise or yoga asana, pranayama and meditation not only help to keep organs and muscles active but also balance the level of hormones.³⁵ Good food hygiene practices like clean surfaces, separating raw meat/fish from other food items while preparing food, avoiding consumption of undercooked meats should be practised.

Some sections of society have also witnessed catastrophic conditions like a lack of basic food items. Therefore, at the level of the community, there is an urgent need to identify these vulnerable groups and offer assistance in food access and availability through a structured and reliable support system, during COVID-19 constructing irrepressible food systems requires ingenious context-specific demand and supply-side strategies.³⁴ Optimizing public health during this pandemic requires not only knowledge from the medical and biological sciences, but also of all human sciences related to lifestyle, social and behavioural studies, including dietary habits and lifestyle.³³ Thus, National programs which lessen the diet insecurities and imbalances need to be fostered.² Vaccines prevent illness and save lives; nutrition also possesses the same potential. In conclusion, the interplay of various nutrients plays a monumental role in the functioning of the immune system. Highlighting this is crucial in the current crisis of pandemic, as nutritional guidelines can be preventive as well as therapeutic. Moreover, these will also reduce the burden on healthcare systems, leading to efficient use of available resources and manpower.
A balanced diet remains the cornerstone for good health. It would be wise to eat healthy, in order to suffer less.

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