SHORT COMMUNICATION

Immune System Enriching Micronutrients: Essential Ingredient for Wellbeing in COVID-19

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ABSTRACT

The World Health Organization (WHO) on March 11, 2020, has declared the novel coronavirus (COVID-19) onset a global pandemic. Consequently, there has been noticeable economic adversity globally and a significant loss of life. A strong functioning immune system is crucial for adequate defense against pathogenic organisms. The intricacy of the interplay between nutrition and immunology is wide ranging. In the context of novel corona virus disease, competent immune system requires adequate supply of essential nutrients including vitamin C, D, E, A, B_6, B_{12}, folate and trace elements, including zinc, iron, selenium, magnesium, copper to support innate and adaptive immune systems. Other nutrients such as omega-3 fatty acids also support immune system effectively, specifically by helping to resolve the inflammatory response. Deficiencies or suboptimal status in micronutrients negatively affects immune function and can decrease resistance to infections. Although much remains to be known about COVID-19, it is important that, to avert the likelihood of being infected with COVID-19, nutrition intake targeted towards boosting immune system is indispensable.

Key Words: *COVID-19, Infection, Immune system, Nutrition, Nutrients, Vitamin.*

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The disease, that is now called coronavirus disease-19 (COVID-19), is caused by a novel coronavirus, specified as severe acute respiratory syndrome corona virus -2 (SARS-CoV-2), which was discovered through whole-genome sequencing, polymerase chain reaction (PCR) of culture of bronchoalveolar lavage fluid obtained from affected patients.[1] This COVID-19 pandemic has engulfed the world, affecting more than 180 countries. The vulnerable as well as immunocompromised are more susceptible to severe complications. As of September14th 2020, there are more than twenty-nine million confirmed cases of COVID-19 and almost 926,000 deaths globally.[2]

The pulmonary and systemic inflammatory responses linked to COVID-19 are generated by the innate immune system when it identifies the viruses.[3] Primary goals include prevention of transmission and diminishing the rate of new infections.[4]

The innate immune response is responsible for restricting virus replication, enhances virus clearance, promotes tissue repair and triggers a prolonged adaptive immune response against the viruses SARS CoV-2 infection which can be practically divided into three stages including stage I, an asymptomatic incubation period with or without detectable virus, stage II, non-severe symptomatic period with the presence of virus, stage III, severe respiratory symptomatic stage with high viral load.[5] From the perspective of prevention, individuals at stage I, the stealth carriers, are manageable, the first asymptomatic transmission has been reported in Germany.[5]

Mast cells (MCs) which are contained in the submucosa of the respiratory tract as well as in the nasal cavity symbolize a barrier of protection against microorganisms.[2] Stimulating of MCs early releases inflammatory molecules, including histamine as well as proteases and late activates production of proinflammatory IL-1 family members, including IL-1, IL-6 as well as IL-3. Clinical evidence has shown that severe COVID-19 patients have elevated cytokine profile as previously observed in SARS-CoV-

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1 as well as the Middle East respiratory syndrome (MERS).[2] The levels of inflammatory factors in patients with COVID-19 are elevated , among which are IL-1RA, IL-1B, IL-7, IL-8, IL-9, IL-10, granulocyte-macrophage colony stimulating factor (GM-CSF), IFN-γ, fibroblast growth factor (FGF), granulocyte-colony stimulating factor (G-CSF), interferon-γ-inducible protein (IP10), macrophage inflammatory protein 1 alpha (MIP1A), platelet-derived growth factor (PDGF), monocyte chemoattractant protein (MCP1), vascular endothelial growth factor(VEGF) and tumor necrosis factor (TNF-α). Additionally, levels of IL-2, IL-6, IL-7, IL-10, IP10, G-CSF, MCP1, MIP1A and TNF-α were elevated in critically ill patients withCOVID-19 than those in mild groups. As established by Blanco-Melo et al, unique disproportionate inflammatory response of COVID-19 is as a result of the low levels of type I and II interferons in association with an increased expression of IL-6 and increased chemokines. They hypothesized that increased inflammatory response, in conjunction with diminished innate antiviral defense, can be defining and driving feature of COVID-19 infections.[2]

Immunity and Nutrition Interface

A strong functioning immune system is crucial for provision of adequate defense against pathogenic organisms as well as furnishing tolerance to non-threatening organisms. The immune system is functioning perpetually, but specific immunity, occurs in the presence of pathogens. This leads to elevation in the demand of the immune system for substrates as well as nutrients.[6]

This requirement can be met from exogenous sources. Cells of the immune system have the capacity to use glucose, amino acids and fatty acids as fuels for energy production, that involves electron carriers and range of coenzymes, which are usually derivatives of vitamins. Undernutrition diminishes immune defenses, making an individual additionally susceptible to infection. Micronutrient deficiencies weaken immune function.[6]

It is established that viral clearance as well as infection recovery needs activation of the host's immune response, consequently nutrition could be a means of attaining this outcome.[7] An individual's general nutrition status, state of nourishment, as well as pattern of food intake including foods,nutrients and non-nutritive bioactive compounds have brunt on the functioning of immune system at the level of physical barriers including skin, intestinal mucous membranes, the microbiome, the innate immune system macrophage function and polarization as well as the adaptive immune system including T- and B-cell function.[8] Undernutrition impairs the immune system, suppressing immune functions that are fundamental to host protection against pathogenic organisms.[9]

Micronutrients with Essential Role in enhancing Immunity

Maintaining nutritional status at this time is vital , It is evident that social isolation as well as mitigation measures including stay at home orders will persist for a protracted period for millions of people around the world.[2] Deficiencies or suboptimal status in micronutrients negatively affect immune function and can decrease resistance to infections.[10]

Vitamin C has an impact on various aspects of immunity. These include supporting epithelial barrier function, growth and function of both innate and adaptive immune cells, white blood cell migration to sites of infection, phagocytosis as well as microbial killing and antibody production.[10] Vitamin C increases the immune function response and reduces the duration and severity of common cold.[14] Considering the presence of lower respiratory tract infection in COVID-19, higher dietary intake of vitamin C sources such as citrus fruits and green leafy vegetables or supplements are recommended.[11]

Myriad immune cells contain vitamin D receptors which affect their function after ligand binding, accordingly vitamin D greatly has an impact on immunity.[10] Observational study have shown that there is a an association between low blood concentrations of 25-hydroxyvitamin D , the major vitamin D metabolite and susceptibility to acute respiratory tract infections.[10]

Vitamin A deficiency weakens barrier function, changes immune responses and increases susceptibility to a range of infections. Vitamin A regulates neutrophil maturation.[12] Natural killer cell activity is lowered by vitamin A deficiency. There is a linkage between plasma vitamin E and cell-mediated immune responses.[12]

Zinc (Zn) has a role in DNA synthesis, in cellular

growth as well as differentiation, also in antioxidant defense, all vital to immune cell function. Limited or mild Zn deficiency in human subjects causes lowering of natural killer cell activity, lymphocyte proliferation, IL-2 production as well as cell-mediated immune responses that can all be corrected by Zn repletion.[12] Iron deficiency leads to thymus atrophy and has various effects on immune function in humans.[12] Selenium is a cofactor for several enzymes. A few of these have a role in antioxidant defenses, like glutathione peroxidase. Selenium can protect against the immunosuppressive effects of oxidative stress and strengthens immune function.[12] Magnesium controls the activation of peripheral blood neutrophils as well as eosinophils.[13] Calcium signalling is of predominant relevance to immunity.[14] Laboratory studies with flavonoids have revealed proteolytic activity of the original SARS-CoV 3CLpro inhibited by apigenin, luteolin, quercetin, amentoflavon, daidzein, puerarin, epigallocatechin, epigallocatechin gallate, gallocatechin gallate as well as kaempferol.[15]

Trace elements have significant effects on immune responses. Natural compounds from medicinal plants have antioxidant as well as immune modulatory activities[16]. If the balance between free radical production and antioxidant defenses lowers, it has a detrimental effect on functions of body and leads to senescent corrosion essentially linked to oxygen stress.[16]

Indigenous bacteria create barrier against colonization by pathogenic bacteria.[8]This barrier can be preserved by provision of supplements incorporating live desirable bacteria, called probiotics. Fermented foods, including traditionally cultured dairy products and newer kinds of fermented milks containing probiotics. Insufficient levels of folic acid and B_{12} remarkably affect immune responses as they paly role in production of nucleic acid, protein synthesis, inhibition of immune cells as well as interfering with metabolic processes.[17]

Inflammation usually winds up quickly at climax of immune response, due to the omega-3 fatty acids, eicosapentaenoic acid (EPA) as well as docosahexaenoic acid (DHA) which are at the site of inflammation being enzymatically converted to particular pro-resolving mediators (SPMs) known as resolvins, protectins and maresins[10]. Strikingly, nutritional deficiencies in these essential fatty acids can cause impediments in resolution of inflammation. This is vital in relation to severe COVID-19 which is marked by uncontrolled inflammation, cytokine storm, related to acute respiratory distress syndrome (ARDS). The role of EPA and DHA in mitigating inflammation and lung injury has been established by a recent cochrane review of trials as culiminating in advancement in blood oxygenation as well as symbolic curtailing of ventilation requirement, organ failures, length of stay in the intensive care unit and mortality at 28 days.[10]

It is therefore recommended that intake of foods especially rich in immunomodulating nutrients should be enhanced. Furthermore few nutrient supplementations including vitamin C, vitamin D,omega-3 fatty acids, vitamin E, zinc and selenium have advantageous effects in patients with COVID-19.

REFERENCES

1. Arabi YM, Murthy S, Webb S. COVID-19: a novel coronavirus and a novel challenge for critical care. Intensive Care Med. 2020; 3 : 1–4.
2. Zabetakis I, Lordan R, Norton C, Tsoupras A. COVID-19: The Inflammation Link and the Role of Nutrition in Potential Mitigation. Nutrients 2020; 12: 1466.
3. Li G, Fan Y, Lai Y, Han T, Li Z, Zhou P, et al. Coronavirus infections and immune responses. J Med Virol. 2020; 92: 424-32.
4. Cucinotta D, Vanelli. WHO Declares COVID-19 a Pandemic.Acta Biomed. 2020; 91:157-60.
5. Shi y, Wang Y, Shao C, Huang J, Gan J, Huang X. COVID-19 infection: the perspectives on immune responses. Cell Death & Differentiation. 2020; 27: 1451–4.
6. Calder PC. Conference on 'Transforming the nutrition landscape in Africa' Plenary Session 1 Feeding the immune system. Proceedings of the Nutrition Society. 2013; 72: 299–309.
7. Derbyshire E, Delange J. COVID-19: is there a role for immunonutrition, particularly in the over 65s? . BMJ Nutrition, Prevention & Health. Epub ahead of print: [16.04.2020]. 2020; 0: 1–6.
8. Venter C, Eyerich S, Sarin T, Klatt KC. Nutrition and the Immune System: A Complicated Tango. Nutrients. 2020; 12: 818.
9. Calder PC, Kew S. The immune system: a target for functional foods?. Br J Nutr. 2002; 88 : S165-77.
10. Calder PC, Carr AC, Gombart AF, Eggersdorfer M. Optimal Nutritional Status for a Well-Functioning Immune System is an Important Factor to Protect Against Viral Infections. Nutrients. 2020;12: 1181.

11. Khayyatzadeh SS. Nutrition and Infection with COVID-19. Journal of Nutrition and Food Security (JNFS). 2020; 5: 93-6.
12. Calder PC. Feeding the immune system. Proceedings of the Nutrition Society. 2013; 72 : 299–309.
13. Gombart AF, Pierre A, Maggini S. A Review of Micronutrients and the Immune System–Working in Harmony to Reduce the Risk of Infection. Nutrients. 2020; 12: 236.
14. Trebak M, Kinet JP. Calcium signalling in T cells. Nature Reviews Immunology. 2019; 19: 154–69.
15. Peterson LE. COVID-19 and Flavonoids: In Silico Molecular Dynamics Docking to the Active Catalytic Site of SARS-CoV and SARS-CoV-2 Main Protease. 2020. (Preprint)
16. Hajian S. Positive effect of antioxidants on immune system. Immunopathol Persa. 2015; 1: e02.
17. Mikkelsen K, Apostolopoulos V. Vitamin B12, Folic Acid, and the Immune System. In: Mahmoud M, Rezaei N, eds. Nutrition and Immunity. Tehran: Springer. 2019; P: 103-14.