

REVIEW ARTICLE

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Research in Health Sciences**Journal homepage: www.ijfrhs.com**FAVOURAL IMPACT OF NUTRIENT SUPPLEMENT FOR COVID'19**Kalepu srinath¹, Anagha jammalamadka¹, Masilamani K², Senthilnathan B², Swarna priya B², Vigneshwar M*²

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Abstract

The CoVID'19 pandemic outbreak has been excruciating for all of us since it is rapidly spreading and there are no definite treatments available. The mortality rate is elevated and the reasons divulge is because of the shorter incubation period resulting in severe atypical pneumonia. In the early 2020 doctors and researchers have pin pointed that this corona virus infection are at a higher risk for the people having pre-existing conditions (i.e. diabetes, heart problems etc.) which can be relatable to the individual's lifestyle and diet. Despite the fact that all the researchers, doctors, paramedics and the government are taking several wide steps to revamp this situation, this article discuss the purpose and recommendation of nutritional treatments for CoVID'19. Thus we have framed this review in accordance with the specific nutrition supplements which can battle against this miserable life-chasing covid19 pandemic.

Keywords: COVID'19, mortality rate, pre-existing condition, nutrition, lifestyle.

Introduction

Covid'19 is an infectious disease caused by the newly discovered corona virus. In late December 2019, a zoonotic infection was identified in Wuhan city, China. Though initial investigations reported the spread of animal to human transmission, later investigations have declared the human-human transmissions as well through close contact with an infected person and even from coughing and sneezing since the virus generally spreads via airborne zoonotic droplets. The virus replicates in the ciliated epithelium causing cellular damage and infection. However, previous studies have found that eating certain foods can improve your health and strengthen your body's ability to fight other invasive viruses and maintaining a healthy diet to help boost your immune system may also give you an edge for other future infections [1]. In the 100th situation report released by WHO; as per the web-analysis, the data sets over journals and social media are more about

the illness i.e. symptoms and transmission (56%) compared to that of the cause i.e. immunity (11%) [2]. Saying that immune system is directly related to our lifestyle and diet, the population is more addicted with high fat and salt foods, these foods serve more calories ignoring the nutritional requirements of the body. In today's fast moving life, the lifestyles of people have undergone drastic changes which have brought about major impact on their dietary patterns. Increased consumption of processed meat and food items put the population on high risk of diseases. A higher prevalence of type 2 diabetes mellitus was found in urban population than in rural subjects [3]. Food consumption patterns have completely changed and people are now more inclined towards preserved and packed food; also because of work pressure and fast lifestyle people tend to have packed food for their convenience. Researchers have shown that supplementing our body with nutritious food, getting proper sleep and having exercise routine are the chief strategies to amplify your immune system

thereby improving the immune potential immune response against illness [4]. Every living organism demands for nourishment; the nourishment can be greatly acquired by a good nutrition which is crucial for health, particularly during this time when our immune system needs to fight back the infection. Immune system is a complex consisting of variety of cells, mechanisms, chemicals and properties which constantly help to fight against the illness thus immune system in other words is the defense system of the body. A double-blind study with 96 senior citizens with average age of 74 have been treated physiologically with micronutrients and have reported that subjects in the supplemented group had a higher number of T cells, NK cells, IL-2, enhanced proliferation response to mitogen, higher antibody response and less illness from infection [5]. Nutrient deficiency can have a direct impact in functioning of immune cells mostly when their concentrations are reduced in plasma. These can alter the cytotoxicity of the immune cells where they can get lessened (low iron concentrations can increase the cytotoxicity of macrophages) [6]. 'Proper well-balance diet and hydration is vital to fight against CoVID'19' says WHO [7]. The available literatures only provide information regarding effect of nutraceutical supplements on immune system and describing the risk of infection. Therefore, the present article was shaped to study the purpose of fundamental diet to enhance the immune system of the individual keeping in mind that a good immune system can fight any pathogenic infection especially COVID'19.

1.2 PREFACE: IMMUNE SYSTEM

An immune system is a multiplex network which is made up of various organs, tissues, cells and molecules to fight against pathogens like virus, bacteria and toxins. In simple words the main functions of immune system include, identifying the threat, generating immune response, mount the attack, eliminate the pathogen and remember the distinctiveness of the pathogen which it has already assassinated. The immune system has broadly been branched namely innate immunity and Adaptive immunity. The innate immunity can be characterized by the presence of non-specific cells, rapid immune response (within minutes of aggression) and has no immunological memory. On the other hand, adaptive immunity is quite opposite which possess specific cells, capacity of memory and rapid immune response only when the host is exposed to antigen. The innate immunity and adaptive immunity mutually can upshot in synergic response which can cause harm to host (autoimmune diseases,

hypersensitivity etc.). Other largely classified types are cell-mediated immunity and antibody-mediated immunity. Where the antibody-mediated immunity relies on antibodies produced by B cells (Immunoglobins) which has varied functions of neutralization and response, cell-mediated immunity doesn't involve antibodies but rather induces the effect and response of T cells, NK cells, Macrophages and cytokines [8]. This type of cell-mediated immunity is effective against organisms which survive the phagocytosis and in eliminating virus-infected cells.

1.2.1 Innate immunity

Other than the three main characteristics mentioned above, there is other vital uniqueness incorporate are chemical barriers (low pH in stomach, lysozymes in tears) and physical barriers (epithelium in skin and gut, cilia in airway lining) which are for a purpose of immunity itself. The components of innate immunity include neutrophil, eosinophil, basophil, mast cells, dendritic cells, natural killer cells, macrophage and monocyte. The response in innate immunity takes place in 2 types namely: Phagocytosis and Apoptosis. The phagocytosis is regulated by phagocytes (macrophages and neutrophils) and the process of apoptosis is regulated by NK cells [9]. The apoptosis is initiated by the release of perforins and granzymes which induce apoptosis during which caspases triggers the cell death by cleavage of specific proteins of nucleus and cytoplasm producing apoptotic bodies. This apoptotic bodies containing foreign particles enter into phagocytic phase where the phagocytosis is initiated by engulfing of the microbes and killing them through lysosome and oxidative burst.

1.2.2 Adaptive immunity

Adaptive immunity usually comes into action when innate immunity is ineffective in eliminating infectious agents. The primary function of adaptive immunity starts with recognition of non-self-antigens in the presence of self-antigens and secondarily generation pathogen-specific immunological effectors pathways to eliminate the pathogen-infected cells. Not to forget that the key function of adaptive immunity is the development of the immunological memory that can rapidly eliminate or kill the pathogens on subsequent infections [10]. The components of adaptive immunity include T cells, B cells and APC (antigen-presenting cells) which include dendritic cells, macrophage, monocyte, epithelial cells and fibroblast. The T cells originate from hematopoietic stem cells in bone marrow

and mature in the Thymus while B cells also originate from bone marrow and mature in same. T cells differentiates into cytotoxic T cells (T helper cells – Th1 and Th2) which co-ordinate macrophages, natural killer cells and regulatory T cell whereas B cells produce 5 types of antibodies namely IgA, IgD, IgE, IgG and IgM (Immunoglobins) which recognizes specific antigens and aiding their destruction[11]. After the demolition of the pathogen, all the produced T cells and B cells die leaving one from each behind. These T cell and B cell turn out to be the memory cells which are long lived survivors of past infection and continue to express antigen-binding receptors, these can be called upon to respond immediately and eliminate the antigen upon re-exposure.

The amalgamation of innate and adaptive immunity is significantly sufficient to fight against any genre of invading pathogen but all it needs is the proper supplement to intensify and boost the production of immune cells by providing essential nutrition.

1.3 NUTRITIONAL SUPPLEMENT

The checklist of essential nutrients requisite to support and nourish immune system are discussed below.

1.3.1.1 VITAMIN C

Vitamin C otherwise known as Ascorbic acid is highly essential for growth, development and repair of body tissues. It plays an imperative role in many body functions such as formation of collagen, absorption of iron, the immune system, wound healing and the maintenance of bones, cartilages and teeth. Vitamin C has a number of activities that could satisfyingly contribute to immune-modulating effects. The unique properties of vitamin C comprises of the ability to donate electron (protecting important biomolecules from damage during normal cell metabolism) and cofactor a family of biosynthetic (stabilization of tertiary structure of collagen for generation of metabolic energy) and gene regulatory enzymes [12]. Vitamin C supports the cells of innate immunity as well as adaptive immunity by supporting the epithelial barrier cells thereby promoting oxidative scavenging activity of the skin to fight against pathogen and accumulate in phagocytic and enhance chemotaxis, phagocytosis, and generation of reactive oxygen which ultimately leads to microbial killing. This is also crucial for apoptosis and clearance of necrosis thereby decreasing the potential tissue damage. It has also shown to advance the proliferation and maturation of T

cells. Vitamin C deficiency results in impaired immunity and higher susceptibility to infections. In early clinical studies it has been reported that vitamin C can help to eliminate alveolar fluid and reducing the alveolar epithelial water channel damage, also it has been shown to produce protective effects against common cold and influenza [13]. In a controlled yet randomized trail it was found that 85% of 252 patients experienced reduce symptoms when treated with vitamin C [14]. Still studies have been continuously developed by various institutions in this regard and there are strictly no evidence that vitamin C could cure COVID'19 rather can just boost the immune system and can help in preventing and reducing the incidence and susceptibility of corona virus infection. The Daily Value for vitamin C is studied to be 90mg per day for normal adult and 30mg extra for breast feeding women and 35mg extra for people who smoke. Examples of foods containing vitamin C are: citrus fruits, papaya, tomatoes, guavas, lime, cabbage, pine apple, red bell peppers, strawberry, broccoli etc.

1.3.2 VITAMIN D

Vitamin D is a fat- soluble vitamin which is produced endogenously when the ultra-violet rays from the sunlight strikes our skin to induce vitamin D synthesis. This vitamin D from sunlight, foods and supplements are biologically inert and these need to undergo two hydroxylations. First is when liver metabolises vitamin D to convert into calcidiol and second is when kidney forms calcitriol. The core functions of vitamin D are enhancing the calcium absorption in gut for maintaining adequate serum calcium and phosphate concentrations to prevent hypocalcemic tetany, osteomalacia and osteoporosis [15]. Above all this, vitamin D is said to have immune properties which acts as autocrine manner in local immunological milieu. Vitamin D can modulate innate and adaptive immunity and its deficiency was found to be associated with increased autoimmune response as well as increased susceptibility to infections. It was also used (unknowingly) to treat tuberculosis before the evidence of antibiotics and this treatment has also been employed for general increased protection from infections [16]. A multiple cross sectional study conducted from 1988-1994 with a sample size of 19,000 subjects reported that individuals with vitamin D deficiency (>30ng/ml) were more likely to have upper-respiratory tract infections when compared to sufficient vitamin D level individuals [17]. It is identified that macrophages recognize lipopolysaccharides (LPS) who are surrogates for bacterial infections; through toll like receptors (TLR)

and engagement of TLRs leads to events that produce peptides with potent bactericidal properties. These peptides colocalize within phagosomes with ingested bacteria where they disrupt the bacterial cell membranes thereby producing anti-microbial properties [18]. The other finer functions of vitamin D in immune system is inhibiting B cell proliferation, suppress T cell proliferation and results in the shift of Th1 to Th2 phenotype. This results in the decreased production of inflammatory cytokines and decreased production of anti-inflammatory cytokines. It also inhibits monocyte production and DC differentiation thereby decrease expression to MHCII molecules. The Recommended Dietary Allowance (RDA) for vitamin D intake ranges from 15mcg-20mcg for all the group of people. Sources: yogurt, egg yolk, prawns, beef liver, butter, cod liver oil, mushrooms, oat-milk, almonds, and carrots etc.

1.3.3 VITAMIN A

Vitamin A is a fat soluble vitamin with properties such as immune system, reproduction, vision and cellular communication. The forms of vitamin A available in the diet are preformed vitamin A and provitamin A carotenoids. Vitamin A role in immune system is helps to maintain structural and functional integrity of mucosal cells in innate barriers and is also important in functioning of NK cells, macrophages and neutrophils [19]. It is also known to be necessary for normal functioning of T and B lymphocytes and for the generation of antibody responses to antigen and involved in development of differentiation in Th1 and Th2 cells to support anti-inflammatory response.

Vitamin A supplement is said to reduce all-cause mortality and incidence of diarrhea, measles and other infectious diseases [20]. A sufficient vitamin A intake is proved to produce early lung development, alveolar formation, tissue maintenance and regeneration; In fact chronic vitamin A Deficiency (VAD) has been associated with histopathological changes in pulmonary epithelial lining and disrupt the normal lung physiology makes the lung prone to tissue dysfunction and respiratory diseases [21]. In addition there are alterations of the structure and composition of ECM with the thickening of alveolar membrane and ectopic deposition of collagen I. The RDA for vitamin A 700-900mcg and for lactating women 1,300mcg. Sources: sweet potato, lettuce, peas, turnip, spinach, pumpkin, milk, pepper, mangoes etc.

1.3.4 VITAMIN E

Vitamin E is a fat-soluble vitamin with distinctive antioxidant properties which protects the cells from damaging effects of free radicals containing unshared electrons. Studies have reported increased lymphocyte proliferation in response to mitogenic stimulation, enhanced delayed type hypersensitivity reaction with increased IL-2 and decreased IL-6. Vitamin E especially alpha-tocopherol decreased PGE2, COX2, NO, IL-12, migration, IL-4 and activation of induced cell death, Increase in proliferation, synapse formation, IL-2, antibody response and NK cells [22]. Animal and human studies have demonstrated that vitamin E deficiency can impair both cell-mediated and humoral mediated immunity [23]. It was also demonstrated that vitamin E supplementation was effective in reducing neutrophil migration and production of inflammatory cytokines thereby decreased the susceptibility and risk of pneumonia, influenza, asthma in mice [24]. A prospective cohort study has examined decreased risk and susceptibility of infants associated with maternal vitamin E intake during pregnancy, these infants had relatively low risk. RDA for vitamin E is 15mg and 19mg for lactating women. Sources: Wheat, avocado, fish, sunflower oil, vegetable oil, peanuts, almonds, mango, kiwi, tomato and spinach etc.

1.3.5 ZINC

Zinc is a very essential nutrient which helps almost all the metabolisms of the body. Zinc is mandatory for every cells of immune system to function effectively. Zinc has antioxidant, anti-inflammatory properties and also been proved to have anti-cancer properties. Zinc affects multiple aspects of immune system. It is crucial for normal development of neutrophils, NK cells, macrophages on the other hand, phagocytosis, intercellular killing are mostly affected by zinc deficiency. Zinc deficiency adversely affects the growth and function of T cells and B cells [25]. The ability of zinc is to stabilize membranes and has a role in the prevention of radical-induced injury during inflammatory processes. Zinc also enhances the expression of IL-1 and IL-2 and decrease oxidative stress and inflammatory cytokines. A double-blind controlled study suggests reducing the incidence of acute lower respiratory infections in infants and preschool, 609 children's were treated with 10mg of elemental zinc daily and were monitored for 6 months. Within 120 days there was decrease in rate of infection per year in zinc-supplemented group (0.19) compared to

the control group (0.35) [26]. A data also suggested that zinc is an essential trace element for the activation of great number of enzymes, transcription factors as well as immune and anti-oxidant response, apoptosis and mental health. Although, optimal immunostimulatory dose of zinc has not yet determined, this supplement can restore the immune response and can lower the risk of infection. Sources: whole grains, meat, cereals, brown rice, kidney beans, flax seeds, garlic, sesame seeds, nuts, dairy, eggs and etc.

1.3.6 IRON

Iron is a mineral which is naturally present in foods as well as is available in supplements. Iron is an essential component in almost all the part of the body and has numerous functions such as physical growth, neurological development, cellular functioning and synthesis of several hormones. Iron has two main forms: heme and nonheme; plants and iron-fortified foods contain non-heme whereas foods such as meat, sea food and poultry contain both heme and non-heme [27]. Most of the iron is used up by hemoglobin whereas the remaining iron is stored in liver, spleen, bone marrow or as myoglobin in muscle tissues. Other than the functions listed above there is one another main function to regulate the immune system. It is proved that iron regulates cytokine production and action, forms highly-toxic radicals for killing of bacteria by neutrophils, generation of ROS that kill pathogens, differentiation and proliferation of T lymphocytes and growth and functioning of immune cells [28]. A study has also shown that iron supplementation through mechanisms related to anti-oxidant and cellular immune responses that defers malarial infection and expands cellular innate defenses [29]. The RDA of iron is 8mg in male, 18mg in female, 27mg in pregnancy and 9mg for lactating women. Sources: millets, beans, cereals, spinach, olives, beef and potato etc.

1.3.7 PROTEIN

Proteins are large complex macromolecules having structural units called as amino acids. Proteins play a major part in building and repairing tissues and also used to synthesize hormones, enzymes and other body chemicals. Proteins are the building bricks of muscles, bones, cartilages, skin and blood. It is proven that protein calorie malnutrition impairs host immune system thereby paving ways for greater opportunistic infections with increased morbidity and mortality [30]. A study has also proven that arginine supplementation enhances T-lymphocyte and T-helper cells with a rapid

return to T cell function in post-operative patients. Proteins regulate immune cells such as T cells, B cells, NK cells, macrophages, antibodies, cellular redox state, cytokines and gene expressions [31]. Emerging evidence shows that albumin can directly influence the outcomes of covid-19. Arginine, glutamine and cysteine precursors are best prototypes. A study deals with oral attenuation of rota-virus in pig resulted that protein-deficient pigs had lower protection rates compared to protein-sufficient counterparts [32]. Sources of proteins include chia seeds, oats, Chana dal, meat (WHO: 1-2 times a week), fish, eggs, poultry items (WHO: 2-3 times a week) and whole grain etc.

1.3.8 SELENIUM

Selenium is a trace element and plays a crucial role in reproduction, thyroid hormone metabolism, DNA synthesis and prevention from oxidative damage and infection. The unique functions of selenium include anti-oxidant properties, T cell proliferation and modulation of humoral immunity. Selenium contains many proteins having varied functions. The anti-oxidant properties of selenium are very essential against asthma and asthma related allergies and it decreases the airway hyper-activity, mucous secretion and broncho-constriction and a study involving small group of individuals (sample size-33) were treated with se-supplement or placebo showed a relative increase in cytotoxic T lymphocyte, mitogen-induced proliferation of T lymphocytes, NK cells and mixed lymphocyte reaction and particularly it was concluded that for viral infections Se-deficiency leads to increased susceptibility to host and high Se-levels can be beneficial to host especially in cases of HIV-1 [33]. A double blind study containing 22 adults received se-supplements showed positive results of augmented cellular immune response, increased production of interferon gamma, increase in T-helper cells and other cytokines [34]. Recent studies have also reported that mild strain of influenza virus and polio strain showed increased virulence in selenium deficient mice and its virulence is related to several modifications in the viral genome [35]. RDA for selenium is 55mcg, 60mcg for pregnancy, 70mcg for lactating women. Sources: fish, grains, liver, garlic, cheese, mushrooms, banana, nuts, chicken, egg and bread etc.

1.4 CONCLUSION

The raising disconsolate situation of global threat for corona virus with no definite treatment coming soon; individual protective and preventive measures can at

most alter the personal risk of acquiring the disease. The body's defense system undergoes many changes during our lifespan and this is extremely crucial period when our immune system together with us has to fight back against global pandemic of COVID-19. The above data supports the evidence that these nutrient supplements can enhance the function of immune system which plays a significant role in abating COVID'19. But at the same time we should also acknowledge that no nutrient supplement can cure or treat COVID'19 rather can only reduce the risk and susceptibility of COVID-19 and other subsequent opportunistic infection. Demographic factors such as nutritional status, age, sex, lifestyle and medical conditions are the keys which govern the individual's risk towards clinical severity. We can make this wrestling easy by providing tailored supplementation on adequate basis for optimal immune function. It is always preferable to take a giant step towards self-care techniques rather to panic along the statistics.

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