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Nutrition as a Key Weapon in Strengthening Immune System Relative to Pandemic Novel Coronavirus Disease (COVID-19): A Review

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ABSTRACT

The Lethal novel coronavirus, COVID-19, caused by specific Coronavirus (SARS-CoV 2) began in Wuhan, Hubei, China in December 2019. The emerging infectious viral diseases with pathogenic properties present a major public health issue worldwide. It has been spreading expeditiously across the globe and recognized as a pandemic by the World Health Organization (WHO). The review focused on strengthening the immune system with plant-based food of all age groups to counter novel coronavirus. The immune system is involved in the detection of the host against a variety of agents from viruses to parasitic worms, thereby protecting the integrity of the body. Even though no vaccine has been developed yet, healthy dietary patterns will improve immunometabolism. A well-balanced diet should be maintained for the normal functioning of the immune system with adequate intakes of micronutrient and macronutrient. Diet with a variety of fruits, vegetables, pulses and unprocessed foods is a key component, which provides vitamins, minerals, dietary fiber, protein, and antioxidants and plays a vital role in preserving the immune system against infection and other diseases. Nonetheless, there is a need for preparedness of global health security by optimizing the nutritional status that is crucial for a healthy immune system to prevent COVID-19 by staying physically active, good hygiene practice, and staying home.

Keywords: Novel coronavirus – pandemic, nutrition, immune system, micronutrient, macronutrient.

INTRODUCTION

The outbreak of the novel coronavirus noted in Wuhan, China in the late December 2019, and become the public health emergency worldwide (Weston, S et al 2020; Enserink M 2020). The World Health Organization (WHO) on January 30, 2020, declared it to be a "public health emergency of international concern" (PHEIC) and on February 2020, the disease named as COVID-19 by WHO in Geneva, Switzerland (Log S 2020; Zhou P et al 2020). The 82 percent of genome structure of COVID-19 is uniform to SARS- CoV genome, hence the virus will be referred to as CoV-2, or SARS-CoV-2 (Gorbalenya AE et al, 2020; Zhang N et al, 2020). The zoonotic diseases emerged as a different strain of the species in the third instance, succeeding severe acute respiratory syndrome (SARS) in 2003 and Middle East respiratory syndrome coronavirus (MERS-CoV) in 2012 (Zhong NS et al 2003; Ramadan N et al 2019). As per the report of World Health Organization (WHO) released on March 11, 2020, stated that coronavirus is still on rise and labelled it as a pandemic as it affected 216 countries, areas and territories all over the world. The total number of COVID-19 case globally reported by WHO prior to July 13, 2020 are 12,880,565 including 568,573 deaths (Figure 1).

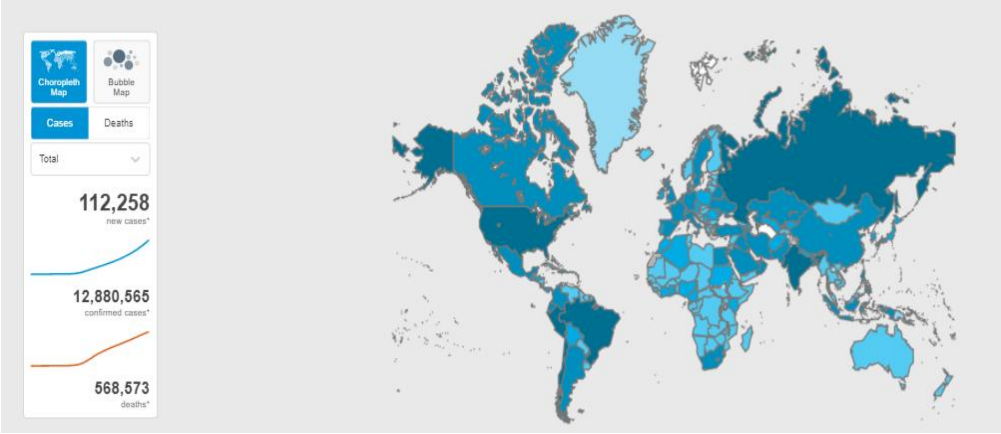

Figure 1: ***Globally, total number of confirmed cases of COVID-19 are 12,880,565 including 568,573 deaths (Source: World Health Organisation, 13 July 2020).***

India has witnessed a rapidly exploding pandemic of COVID-19 with first confirmed case was reported in the state of Kerala on 30 January 2020 followed by new cases in New Delhi, Mumbai, Bengaluru, Hyderabad, and Patna. According to the press report by the Indian Council of Medical Research (ICMR) on July 13, 2020, over 1.1 crore samples has been tested for COVID-19 in collaboration with the facilities of government and private laboratories. The current scenario of coronavirus among all state of India is depicted in figure 2 which show the distribution of positive cases along with recovery rate until May 27, 2020 and the cases until May 8, 2020 have been shown on an geographical map of India in figure 3 (Kumar SU et al, 2020). COVID-19 affecting the population in different ways some shows symptomatic whereas other have asymptomatic behaviour. The symptoms of COVID-19 include fever, cough, respiratory symptoms, shortness of breath, breathing difficulties, fatigue and a sore throat. According to WHO, older people and those suffering with chronic diseases such as hypertension, diabetes, cancer are prone to develop coronavirus with severe symptoms and therefore need medical intensive care.

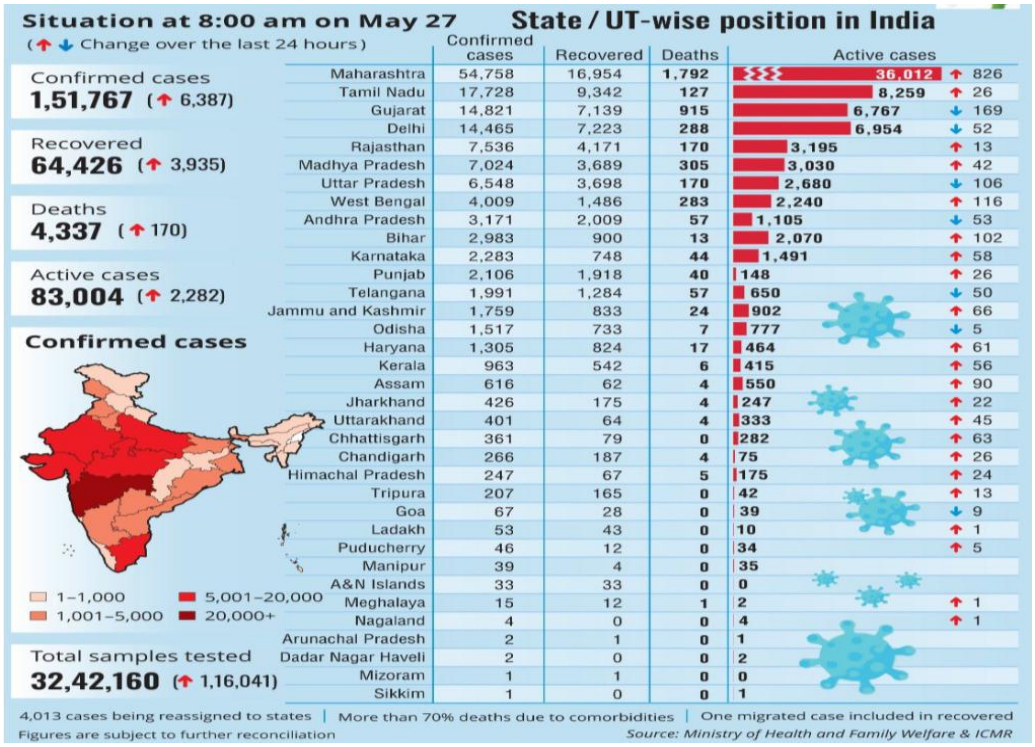

Figure 2: ***Current status of confirmed cases, recovery rate and death rate of COVID-19 in India (Source: Ministry of health and family welfare & ICMR, 27 May 2020).***

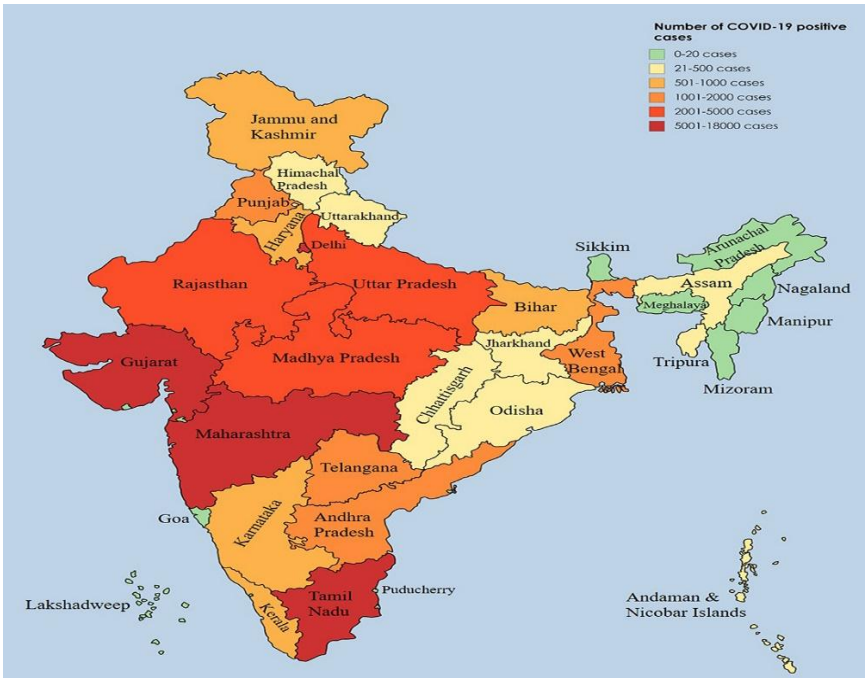

Figure 3: ***State-wise distribution of coronavirus cases in India (Source: Kumar SU et al; 2020)***

One of the crucial shelter in contrast to Covid-19 is immunity. People with good immune systems are able to fight the infection better. Immune system is a biological structure composed of cell, tissue, protein which defend our body against the foreign bodies by identifying and killing the pathogens and tumor cells. It detects variety of agents from viruses to parasitic worms that need to be distinguish from the organism to function properly. According to Calder PC et al 2020, the factor affecting the immune response include genetics, stress, time of day, gut microbiome, physical fitness, smoking, alcohol, age and obesity. Adequate and appropriate nutritional status is a key component to a strong immune system, which defeat invading pathogen and provide protection from illness. A well-balanced healthy diet is recommended diet with a variety of fresh fruits, vegetables, pulses, milk and milk products and unprocessed foods is followed regularly, to provide the body with the essential elements such as vitamins, minerals, dietary fibre, protein, and antioxidants (WHO, 2020). No one food can be considered as a super food but they have contain bioactive component which may help to support immune system by including whole range of nutrients in the eating plan on a daily basis. Staying hydrated helps to eliminate toxins and bacteria that cause illness. Drinking water works to carry oxygen to different cells of the body, which in turn guard the body against any foreign bodies and helps in maintaining the proper functioning of the body. According to a report of Centre for Disease Control and Preventative (CDC), hydration plays a major role in regulation of body temperature. Hydration also enables in the transmission of nutrients to all parts of the body and support organs functioning efficiently to keep the risk of infections at bay.

Researcher have shown the effects of nutritional elements on immune system and reported a significant impact on supporting immune system and in deficiency, it suppresses the immune system leading to malnutrition (Coico R et al 2009; Chandra RK 2003). The dietary components which cause harm to immunity functions are either deficient intake of macro-nutrient elements (fat, carbohydrate, protein) or deficiency in some specific micronutrient elements (vitamin, mineral, water) (Table 1). Balanced nutrition, especially in terms of adequate vitamin, mineral and protein

intake, enhances the resistance against infections (Chandra RK 1997). In this view, there is a need to understand the role of nutrition to boost immune system against novel coronavirus.

Table 1. ***Selected vitamins and trace elements support immune function by strengthening epithelial barriers and cellular and humoral immune system.***

Epithelial barriers	Cellular immunity	Antibody production
Vitamin A	Vitamin A	Vitamin A
Vitamin C	Vitamin B6	Vitamin B6
Vitamin E	Vitamin B12	Vitamin B12
Zinc	Vitamin C	Vitamin D
	Vitamin D	Vitamin E
	Vitamin E	Folic acid
	Folic acid	Zinc
	Iron	Copper
	Zinc	Selenium
	Copper	
	Selenium	

Role of macronutrient in supporting the immune system

Imbalance in the adequate proportion of macronutrients increases the risk of developing chronic diseases and may adversely affect the micronutrient profile. *Macronutrient* is define as chemical element or substance required in large quantities that provide the energy needed to maintain body functions and carry out the daily activities of life. Carbohydrate, protein, and fat are the three essential macronutrient for health maintenance, growth, reproduction, immunity, and healing. Deficits or excesses of any of these nutrients may compromise these processes, resulting in poor health outcomes, which vary depending on the life stage of the affected person. Macronutrients, also called energy providing nutrients, produce 4 kcal of protein, 9 kcal of lipid, 4 kcal of carbohydrate per gram.

Carbohydrate **(CHO)** is an important fuel cell to support immune system, typically providing 50% to 60% of total calories (ICMR). Carbohydrates found in food containing carbon, hydrogen and oxygen molecules. They are classified as simple carbohydrates like those found in fruits and processed sugars break down very rapidly in the body, making them a good source of quick energy. On the other hand, complex carbohydrates like those present in rice, potatoes, and pasta, take longer to break down in the body, and provide a more even distribution of energy over a longer period. Once ingested carbohydrates converted into glucose, which circulates in the bloodstream being readily available, and into glycogen, which is stored in the liver and muscle cells. However, hyperglycaemia reduces immunity by reducing the functioning of immune cells and being a stress factor, it increases cortisol secretion. Neutrophil activity can be reduced by 50 per cent by excess sweet and sugar intake (Xiu F et al, 2014). Adequate intake of CHO reduces severity of infection as it the most important fuel and its ability of prevention decrease of number of cells conjoint to apoptosis, makes it a key component in immunity (Brian A. Cobb et al 2005).

Protein is crucial to regulate immune system, especially for building and repairing body tissue and fighting viral and bacterial infections. Immune system powerhouses such as antibodies rely on protein and impairment of protein in the diet may lead to symptoms of weakness, fatigue, apathy, and poor immunity. Foods rich in protein should be included such as seafood, lean meat, poultry, eggs, beans and peas, soy products, unsalted nuts and seeds. It also help to keep the GI tract and immune system healthy. According to Li P et al 2007, immunomodulatory properties to control various life-threatening diseases have been attributed to protein intake and notably to some amino acids such as arginine, glutamine, taurine and sulfur-containing amino acids. Declines in both adaptive (specific) and innate (non-specific) immunity have been reported in association with under-nutrition and protein deficiency.

Polyunsaturated **fats** will lower your blood cholesterol level. It can be found in foods such as: almonds, pecans, sunflower oil, corn oil, fish, mayonnaise, safflower oil, soybean oil, walnuts and in most margarines. Furthermore, polyunsaturated fatty acids (PUFA), as well as their metabolic derivate, contribute to maintain cell functions such as omega-3

fatty acids (EPA and DHA) that influence immune cell functions (Gleeson M 2013).

Depending on the severity of diseases, it is recommended to provide 20 ~ 30 kcal/kg/day and protein requirement is suitable in the range of 1.2 to 2.0 g/day. Protein lack causes atrophy of lymph organs with reduction in T lymphocyte production and supplementing protein intake can reduce mortality (Nicolo M et al 2016, Weijs PJ et al 2019, Li XY et al 2020). Omega-3 and omega-6 PUFAs predominantly promote anti-inflammatory and pro-inflammatory effects. Being precursors of resolvins /protectins and prostaglandins/leukotrienes, respectively, omega-3 including protecting D1, serving as a novel antiviral drug, could be considered for one of the potential interventions of the novel virus COVID-19 (Zhang, L et al 2020).

Role of micronutrient to boost immune system

Micronutrient deficiencies probably have few direct effects on the functioning of immune cells. The main function have shown a reduction in cell mass that may indirectly affect immune cell function, where T helper cell numbers are reduced (Thurnham DI 1997). Integrated immune system play vital synergistic roles at every phase of the immune response and needs multiple specific micronutrients, including vitamins A, D, C, E, B6, and B12, folate, zinc, iron, copper, and selenium (Gombart et al, 2020). Adequate amounts are essential to ensure the proper function of physical barriers and immune cells; however, daily micronutrient intakes necessary to support optimum immune function and marginal deficiencies in certain nutrients have been shown to impair the immune system (Figure 4).

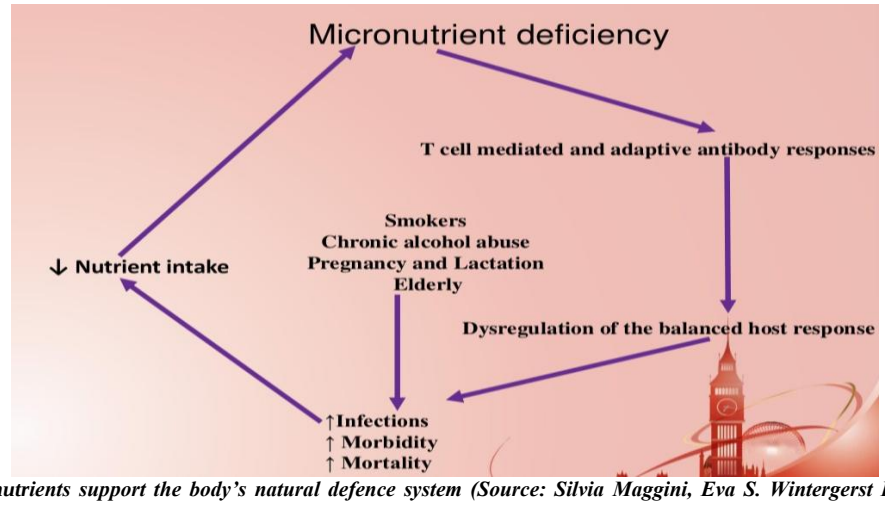

Figure 4: ***Micronutrients support the body's natural defence system (Source: Silvia Maggini, Eva S. Wintergerst British Journal of Nutrition, 2007)***

Vitamin A is referred to as "anti-inflammation vitamin" as it aids to support the immune system and protect against infections by keeping stomach, intestines and respiratory system healthy. Source includes animal products i.e. Pre-formed vitamin A (liver, egg yolk, butter, whole milk, cheese) and fruit and vegesil products i.e. Pro-vitamin A (orange flesh fruit, green leafy vegetables, carrots, pumpkin, red palm oil). It has a central role in the regulation of cellular and humoral immune response (Huang et al 2018). Vitamin A is important for epithelial cell integrity and immune function of the mucosa. The WHO recommends the vitamin A supplementation for children with measles at risk of vitamin A deficiency (D'Souza RM and D'Souza R 2002).

Vitamins B is required for maintenance of normal blood homocysteine levels comprises of thiamine, riboflavin, niacin, folate, vitamin B6, vitamin B12, biotin and pantothenic acid. Deficiencies of

vitamins B have been linked to impaired immune response such as T and B-lymphocytes or macrophages and impair the ability to adhere to microorganisms (Kjer-Nielsen L et al 2012; Mazur-Bialy A. L. et al 2013). A variety of different foods affluent in vitamin-B found in diet ranging from whole grains, dairy products, green leafy vegetables, meats and alternatives. Inadequacy of folic acid can also weaken the immune system by impeding the production of antibodies or new immune cells (Dhur A 1991). People with symptoms of COVID-19 should be supplemented to enhance their immune system. Therefore, B vitamins involved in the production of antibodies and in cellular immune defense (Folkers K. et al 1993; Jee J et al 2013).

Vitamin C has an important role in wound healing and as an antioxidant, potentially protecting cells from oxidative damage caused by free radicals. Vitamin C helps in the protection of against infections and inflammation by supporting various cellular function of both innate and adaptive immune system. It boosts antibodies as well as white blood cell (leukocytes, lymphocytes, T cells) and macrophages, prolonging their function, and can stimulate the release of the signaling molecule interferon, which is involved in the defense against viruses. It may function as a weak anti-histamine agent to provide relief from flu-like symptoms such as sneezing, a runny or stuffy nose, and swollen sinuses (Field CJ et al 2002). Fruits like oranges, papaya, kiwi, and some vegetables like eggplant, bell peppers, beetroots, spinach, and cauliflower are known to be quite rich in vitamin C and are good for immunity. Green vegetables like broccoli, mushrooms, and even kale are a few immunity boosters that one can include in the diet (Hill, 2018). They improve the immune system of older people quite rapidly. Berries can also be included in the diet along with foods rich in omega-3 fatty acids- beans, flax seeds, and even some nuts. Elderly people should consume Spirulina and Curcumin, as they are extremely rich in vitamin C and minerals. These super foods help in building and strengthening immunity at great level. Other ways vitamin C aids the body are as a pro-oxidant for immune cells, antioxidant for lung epithelial cells, and immunosuppressive effects (Erol, 2020).

Vitamin D works with T cells, the body's natural killer cells, to fight off infection. According to Zdrenghea MT et al 2017, it has shown a significant correlation with mild protective effect against respiratory tract infections. It stimulates the maturation of cells, including immune cells and thereby, immune cells convert $25(OH)D_3$ into $1,25(OH)_2D_3$, its active form (Sassi F et al 2018). Study conducted by Nonnecke BJ et al 2017 in animal shown that decrease in Vitamin D status reported in calves had been reported to cause the infection of bovine coronavirus. Some of the food sources include milk, fortified rice or soy beverage, and canned tuna and salmon and exposure of sunlight being the major source of vitamin D.

Vitamin E acts as a powerful antioxidant by protecting cell membranes against attack by free radicals. The free radicals occur in the body as a result of metabolic processes like immunological reactions and the effect of environmental influences. Mocchegiani E. et al 2014, findings reveals that vitamin E can stimulate the immune system by acting on the mast cells (mastocytes), which belong to the leukocyte (white blood cell) group thus play a role in wound healing and avert pathogens. A study by Lee and Hang 2018, reported the protective role against infectious diseases. Include vitamin E in the diet with fortified cereals, sunflower seeds, almonds, vegetable oils (such as sunflower or safflower oil), hazelnuts and peanut butter.

Zinc, regarded as a 'guard' of immune function as ions play a role in the regulation of intracellular signalling pathways in adaptive and innate immune cells. Zinc is also involved in inflammation, its deficiency results in dysfunction of both humoral and cell-mediated immunity and

increases risk of mortality and morbidity cause due to infection (Tuerk MJ et al 2009). The replication of RNA viruses can be impaired efficiently with the increase in the concentration of intracellular zinc with zinc-ionophores like pyrithione. Composite of zinc and pyrithione in at low concentrations inhibits the replication of SARS coronavirus (SARS-CoV) (te Velthuis AJW et al 2010). It is commonly present in lean meat, poultry, seafood, milk, whole grain products, beans, seeds and nuts.

Covid-19 and lifestyle risk factors

Sleep, is detrimental to the immune system as lesser sleep will prevent the body from resting and this will impair the bodily function that have a direct impact on immunity (Kamdar BB et al 2012). Complex feedback loops involving cytokines, such as interleukin-1 and tumor necrosis factor influence and are influenced by sleep. Better sleep improves B-cell function, and inflammation, by itself can reduce sleep. Furthermore, lack of sleep adversely affects the action of the flu vaccine (Besedovsky L et al 2012).

Stress, releases the hormone known as cortisol, which negatively alter the immune system and makes body susceptible to infections. The best way to relieve stress is through meditation and keeping away from the television is important to calm the nerves (Sallehs MR, 2008).

Exercising, known to have a profound impact on the normal functioning of the immune system and lower the infection risk. It helps to raise the levels of white blood cells and antibodies that protect against the infections (Join & Calendar, 2020). Exercise is important after a critical illness to improve muscle mass, strength, and resiliency. Exercise can also help with the prevention of blood clots, which have been a symptom for some people who contracted COVID-19 (Richard J 2020).

Staying hydrated also keeps infection at bay, by drinking at least 8 - 10 cups of water daily. Water is essential as it transports nutrients and compounds in blood, regulates body temperature, gets rid of waste and lubricates and cushions joints. Water is the best choice, other drinks can also be consumed such as lemon juice (diluted in water and unsweetened), tea and coffee. Avoid consuming too much caffeine, sweetened fruit juices, fizzy drinks and drinks high in sugar

Regular consumption of fermented dairy products such as yoghurt or kefir may enhance the immune defences in the gut. Recent research results suggest that yoghurts made with certain bacteria (probiotics) may have a beneficial effect on the immune system. Consume unsaturated fats rather than saturated fats. Avoid processed meats as it is high in salt and fat and industrially produced trans fat - fast food, fried food, etc.

CONCLUSION AND PERSPECTIVE

With the rapid transmission of COVID-19 globally, scientists across the world are working "around-the-clock" to ensure the smooth testing of samples and finding out the cure with the existing which could halt the spread of deadly coronavirus. Evidence gives an insight to indicates that global burden of infection is high and vulnerable populations (infant, elderly, pregnant and lactating women) are undoubtedly more 'at risk' from the harmful ramifications of such infections. Nevertheless, the greatest risk of COVID-19 infection is exposure. It is paramount that additional measure are required to adopt healthy dietary pattern with limited option of exercise along with maintaining social distancing and proper hygiene. Immune system serves to remove foreign bodies or pathologically altered cells. However, if the immune reaction is not appropriate it increases vulnerability to infections. The adequate availability of micronutrients is needed for protective and signaling functions of the body. Potential deficiencies can affect both unspecific (innate) and specific (acquired) immunity.

General recommendations to support the immune system includes fresh fruits and

vegetable which will provide vitamins A, B_6, B_{12}, C, D, E, and folate; trace elements, including zinc, iron, selenium, magnesium, and copper; and the omega-3 fatty acids eicosapentaenoic acid and docosahexaenoic acid . Also, restrict the intake of foods which low in saturated fats and trans fats, animal-derived proteins, and added/refined sugars. During the magnitude of crisis, Government of India (GoI) has announced the relief fund and free ration per person per month for all eligible households to ease the distress. There is a need to promote awareness regarding supplementation of the above micronutrient and low-cost food strategy for the mass. Moreover, to manage future epidemic outbreaks, ongoing research need to be carried out which will focus on the immunonutrition benefiting vulnerable, at risk.

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