International Journal of Food Science and Nutrition
ISSN: 2455-4898; Impact Factor: RJIF 5.14
Received: 10-05-2020; Accepted: 27-05-2020; Published: 13-06-2020
www.foodsciencejournal.com
Volume 5; Issue 3; 2020; Page No. 112-119

The efficacy of vitamins and minerals in strengthening immune system, pre and post hospitalisation in COVID-19 and other coronavirus pandemic patients

Sana Afreen[1], Virginia Paul[2]
[1] Phd Research Scholar, Department of Food Nutrition and Public Health, Ethelind College of Home Science, Sam Higginbottom University of Agriculture, Technology, Prayagraj, Uttar Pradesh, India
[2] Professor, Department of Food Nutrition and Public Health, Ethelind College of Home Science Sam Higginbottom University of Agriculture, Technology, Prayagraj, Uttar Pradesh, India

Abstract
The world is dealing with a contagious disease caused by newly identified virus named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Coronavirus mainly targets the human respiratory system. Hence attacking the immunity system of a person. While data regarding nutrition in coronavirus infection (COVID-19) is on its way, in this review we aimed to explore the various vitamins and minerals which have been proven effective in previously occurred viral infections and epidemics (with special emphasis on respiratory infections), and also summarising the conclusion of results gained in the past 4 months from COVID-19 patients. Clinical trials conducted on COVID-19 patients using vitamins and minerals have also been summarised. The review also aims at changing the perspective towards benefits of taking vitamins and minerals on daily basis in daily diet. The study concludes that intake of a balanced diet with recommended amount of fruits and vegetables on a daily basis which provides all the essential vitamins and minerals keeps the immune system strong. Infection fighting abilities are better in subject taking a balanced diet. While in case of weakened immune system and susceptibility to life threatening diseases, including COVID-19, it has been found that large and or intravenous doses of certain vitamins and minerals have shown improvement in the patient's condition. Hence nutritional therapy can also be used in treatment of COVID-19.

Keywords: strengthening immune system, Hospitalisation, COVID-19

1. Introduction
The world is dealing with a contagious disease caused by newly identified virus named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). (WHO, 2019) This infection started in Wuhan, China in December 2019. (Hui *et al*., 2020) [29]. As per the World Health Organization (WHO), COVID-19 has so far affected 213 countries or territories or areas and has infected over 2 million people globally. The continuously growing list of globally spread corona virus-19 disease (COVID19) patients has demonstrated the high transmission rate among human population. (WHO, 20th April 2020)
The lethality of coronaviruses was demonstrated when the outbreak of severe acute respiratory syndrome (SARS) in 2002 and Middle East respiratory syndrome (MERS) in 2012 occurred and they crossed the species barrier and infected humans. SARS-CoV and MERS-CoV all belong to the β-coronavirus family. Recently found novel flu-like coronavirus (COVID-19) is related to the MERS and SARS coronaviruses and an evidence of human-to-human transmission has been confirmed among close contacts. (Zhang *et al*., 2020) [75, 76, 13]. Coronavirus is one of the major pathogens that mainly target the human respiratory system. (Bogoch *et al*., 2020) [6]. Hence attacking the immunity system of a person.
No diet or food has been proven to cure COVID. The BDA explained simply that one cannot "boost" his or her immune system through diet, and no specific food or supplement can prevent one from catching COVID-19. (British Dietetic Association, 30th April 2020). Although 12 new drugs are being tried for management of COVID19, currently there are no FDA approved drugs or vaccines to prevent and treat the infection of the SARS-CoV-2. Considering the current state of affairs, there is an urgent unmet medical need to identify novel and effective approaches for prevention and treatment of COVID-19. (Maurya *et al*., 2020) [50].
Largest study done in China by Center for Disease Control and Prevention's on 44,000 covid-19 patients confirmed that older age, cardiovascular disease, diabetes, chronic respiratory disease, hypertension, and cancer were all associated with an increased risk of death. (Wu *et al*., 2020) A healthy immune system is the most important weapon against the viral infections. Hence one can always aim at maintaining and or improving his state of health by maintaining a balanced diet.

Vitamins
"A vitamin is a substance that makes you ill if you don't eat it." (Albert Szent-Gyorgyi, 1937). Vitamins are vital organic nutrients in our meal that are utilized by the cells of our body for proper growth, development, disease prevention like deficiency disorders, and to improve immune system efficacy. Vitamins are required in proper trace amounts so that all the barriers of the immune system such as skin, cell-mediated and humoral immune response etc. could be sustained. The immune system protects from the agents that lead to diseases. (Ibrahim *et al*., 2015) [33]. Vitamins have innate and adaptive immune responses. Although vitamin C and E and members of the B complex, can act in a relatively nonspecific manner in the immune system (for example, as

antioxidants) (Pleiner *et al*., 2008) [35]. Healthy tissues of the body are protected from disease promoting factors in presence of a healthy immune system. Major aspects of immune system are highly affected by the availability of nutrients in the body. Similarly, deficiency of a variety of nutrients will lead to impaired immune responses, and replenishment of those specific components will typically restore the affected responses vitamins. Vitamin A and D are certain vitamins which can influence the immune response in highly specific ways. (Fernandes *et al*., 2006) [21].

Available substantiation indicates that supplementation with numerous micronutrients with immune supporting characters may modify immune function and lessen the risk of infection. Micronutrients with the strongest evidence for immune support are vitamins C and D and zinc. (Gombart *et al*., 2020 [22]; Case HS, 2017) [11]. Most of the vitamins like, B6, B9, B12, A and D are furthermore functional in our body to boost-up the cell-mediated immune response with the production of cytokines and T-lymphocytes. Overall, inadequate intake and depressed nutritional status of these vitamins and trace elements may lead to suppressed immunity, which predisposes to infections and aggravates malnutrition. Therefore, it has been proven that cognitive power of the body can be supported by the intake of suitable amounts of all such essential vitamins in regular diet, and can also help in wellbeing of health. (Comerford KB, 2013) [12].

In times like these where the population is under lockdown and are staying at a distance from each other one can function well at the individual level. The common denominator that drives most of the nutrition and dietary recommendations to combat viral infections, including COVID-19, lies within the link between diet and immunity. Existing suggestion highlights that diet has intense effect on people's immune system and disease proneness. It has been demonstrated that specific nutrients or nutrient combinations may affect the immune system through the activation of cells, modification in the production of signaling molecules, and gene expression. (Valdés *et al*., 2010) [68].

Vitamins and immunity

Vitamin C

Vitamin C boosts up human immunity towards infections and cold illnesses by increasing phagocytosis, lymphocyte proliferation and neutrophil chemotaxis against exogenous pathogens. An essential role of killing foreign invaders is done by antioxidants like vitamin C. vitamin C neutralizes reactive oxygen species (ROS) formed in immune cells. In the absence of optimum level of vitamin C, reactive oxygen species will not be eliminated from immune cells which would lead to the destruction of immune cells. (Maggini *et al*., 2007) [32].

Vitamin C is found in higher concentrations within the leukocytes. Hume *et al*., found that during any kind of infection, vitamin C concentrations in the immune cells (e.g., leukocytes) falls rapidly to lower concentrations due to its utilization and then after eradicating the cause of infection it again restores back to normal, this proves that vitamin C actively takes part in warding off the infectious agents during an infection (Hume *et al*., 1973) [30]. Vitamin C fights all types of viruses. Hunt *et al*., suggested that a high dose or even a low supplemental amount of vitamin C saves lives. This works well in low income populations who have few treatment options. Hunt *et al*., conducted a one well-controlled, randomized study where 200 mg/day vitamin C was given to the elderly. It resulted in improvement in respiratory symptoms in the most severely ill, hospitalized patients. Overall 80% fewer deaths in the vitamin C group was seen. (Hunt *et al*., 1994) [31].

Early in March of 2020 the government of Shanghai, China, announced its official recommendation that COVID-19 should be treated with high amounts of intravenous vitamin C. (OMNS Mar 3, 2020)

The coronavirus, in acute infections, may be expected to be just as susceptible to vitamin C as all of the other viruses against which it has been proven to be extremely effective. There has never been a documented situation in which sufficiently high dosing with vitamin C has been unable to neutralize or kill any virus against which it has been tested. (OMNS Jan 30, 2020). Physicians have demonstrated the powerful antiviral action of vitamin C for decades. (Saul AW, 2020). The Japanese College of Intravenous Therapy (JCIT) recommends intravenous vitamin C (IVC) 12.5/25g (12,500 - 25,000 mg) for acute viral infections (influenza, herpes zoster, common cold, rubella, mumps, etc.) and virus mimetic infections (idiopathic sudden hearing loss, Bell's palsy). In adults, IVC 12.5g is given for early stage illness with mild symptoms, and IVC 25g for moderate to severe symptoms. IVC is usually administered once or twice a day for 2-5 continuous days, along with or without general treatments for viral infections. (Saul *et al*., Feb 2, 2020)

Hence it can be said that regular consumption of vitamin C in daily diet will maintain the immune system and ward off the free radicals present in body. It has been seen that old age brings an increase in the production of free radicals and increased oxidative stress hence to avoid infection and rapid ageing one should consume a diet rich in Vitamin C.

Citrus fruits like oranges, tangerines, lemons, sweet lime, goose berries, and red bell pepper are good source of Vitamin C. Papaya, guava, apple, grapes, mango and many other fruits and Green leafy vegetables are also rich in Vitamin C. (ICMR-NIN, 2020)

Vitamin D

Vitamin D_3 (VD_3), the most physiologically relevant form of vitamin D. It is synthesized in the skin from 7-dehydrocholesterol. This process depends on sunlight, specifically ultraviolet B radiation. Alternatively, diet and/or vitamin supplements are its other sources, (Holick, 2007) [58].

Clinical data from COVID-19 patients suggests a higher risk for the development of severe COVID-19 in patients with prior hypertension or diabetes (C. Huang *et al*., 2020 [8]; C. Wu *et al*., 2020; F. Zhou *et al*., 2020) [9, 19]. Patients with these conditions are treated with ACE inhibitors and angiotensin II type-I receptor blockers (ARBs) which increase the expression of angiotensin-converting enzyme 2 (ACE2) which can lead to severe infection with COVID-19 (Lancet Respir. Med, 2020). Variation in ACE2 expression may play an important role in growth rate and severity of COVID-19. (NEJM, 2020)

Daneshkhah *et al*., examined that subjects with a severe deficiency of Vit D have 1.4 times higher risk for production of high CRP. It is hypothesized that Vit D deficiency increases the risk for Cytokine storm in COVID-19 patients and increases the concentration of CRP in a

similar fashion as it is reported in healthy controls. It is also hypothesized that a high CRP increases the chance of severe COVID-19. Sufficient supplementation of Vit D might have inhibited damage to the body, leading to less frequent production of a high concentration of CRP. The risk of high CRP in patients with normal Vit D levels is 0. 45 and reaches 0.63 in patients with severe deficiency of Vit D. (Daneshkhah *et al*., 2020) [14, 15].

Various studies suggest that Coronaviruses cause pneumonia and influenza both. Case-fatality rate study in the United States from the 1918-1919 influenza pandemic showed that most deaths were due to pneumonia. The SARS-coronavirus and the current SARS-Cov-19 were both most common in winter, when vitamin D status was at its lowest. (Cannell, 2006 [10]; Grant, 2009 [23]; Martineau, 2017; Yin, 2018 [74]; Zhu, 2020) [13, 76]. Hence, after the outbreaks of H1N1 influenza in 2009, Edlich *et al*. strongly recommended to g*et al*l health care workers and patients tested and treated for vitamin D deficiency to prevent exacerbation of respiratory infections. Vitamin D also reduces the production of proinflammatory cytokines, which may reduce the risk of cytokine storm in H1N1 infection. (Edlich *et al*., 2009) [18].

Daneshkhah *et al*. studied COVID-19 patients from all over the world and realised that Italy, Spain (countries with severe VitD deficiency) have a notably higher ratio of confirmed elderly patients (age ≥ 70 yo) and also a higher CFR among the elderly population (age ≥ 70 yo) than other countries such as Germany, China, and South Korea. A sensitivity analysis among the countries with similar screening methods (US, France, Iran, Switzerland, UK, and Italy) shows France (a country with the more severe Vit D deficiency) has reported a notably higher adjusted (a fixed confirmed/tested ratio) mortality rate which fits into the hypothesis. Analysis suggested a 15% reduction in the number of severe COVID-19 cases given a normal Vit D status within a population. (Daneshkhah *et al*., 2020) [14, 15].

Wayse found out that in Indian children younger than 5 years, subclinical vitamin D deficiency was a significant risk factor for severe acute lower respiratory tract infections. (Wayse, 2004) Hence in a study when 94 children received vitamin D supplementations it was noted that there was a lower incidence of respiratory tract infections. (Linday, 2004) [44]. It has been established that Vitamin D decreases the inflammatory response to Respiratory syncytial virus (RSV) infections in airway epithelium without jeopardizing viral clearance. (Hansdottir, 2010) [26].

The immunomodulatory properties of vitamin D has shown influence on acute lower respiratory tract disease severity (McNally, 2009) [51]. and may thus protect against asthma. A recent randomized controlled trial involving Japanese students found a reduced incidence of asthma in those taking vitamin D. (Urashima *et al*., 2010) [67]. Moreover, in children with asthma, decreased vitamin D status is associated with increased use of corticosteroids. (Searing *et al*., 2010) [61].

Hence it can suggested that maintaining optimum levels of vitamin D aids in good respiratory health and keeps the immune system strong and healthy and maintains factors like CRF and CRP. Since Vitamin D is a fat soluble vitamin and is mostly taken by sunlight its deficiency not easily and rapidly shown hence one should aim at including vitamin D rich foods on a regular basis in his/her diet.

Main food sources of vitamin D include, fish liver oils, eggs of hen but the common source of vitamin D present in nature is the sunlight (Kraemer K, 2012) [40].

B vitamins

B vitamins are water-soluble vitamins and work as part of coenzymes. Each B vitamin has its special functions.

Vitamin B2 (riboflavin) plays a role in the energy metabolism of all cells. Vitamin B2 deficiency had been suspected to occur among US elderly. (Powers *et al*., 2003) [55]. Keil *et al*. [39]. had reported that vitamin B2 and UV light effectively reduced the titre of MERS-CoV in human plasma products. (Keil *et al*., 2016) [39].

Vitamin B3, also called nicotinamide, could enhance the killing of Staphylococcus aureus through a myeloid-specific transcription factor and vitamin B3 was efficacious in both prophylactic and therapeutic settings. Moreover, vitamin B3 treatment significantly inhibited neutrophil infiltration into the lungs with a strong anti-inflammatory effect during ventilator- induced lung injury. However, it also paradoxically led to the development of significant hypoxemia.

Vitamin B6 is also needed in protein metabolism and it participates in over 100 reactions in body tissues. In addition, it also plays important role in body immune function as well. As shortage of B vitamins may weaken host immune response, they should be supplemented to the virus-infected patients to enhance their immune system. Therefore, B vitamins could be chosen as a basic option for the treatment of COVID-19. (Zhang *et al*., 2020) [75, 76, 13].

Vitamin B6 helps to improve immune response to the increase in production of antibodies and also helps in communicative interactions between cytokines and chemokines. (Kunisawa, 2013) [41]. Vitamin B6 deficiency reduces the lymphocyte growth and proliferation, antibody formation and T-cell activity. (Rail, 1993) [56].

Vitamin B9 or Folic acid (folate) also plays a role in immunity enhancement. It is commonly a key role player in the biosynthesis of nucleic acids, proteins blood cells and nervous tissues (Huskisson *et al*., 2007) [32]. Rich sources of folic acid include, poultry, shellfish, salmon, tuna, dark leafy vegetables, whole grains, beans, orange juice, citrus fruits, cantaloupes, asparagus, milk etc.

Vitamin B12

It ministers mechanism of metabolism in every cell of the human body, particularly abjecting DNA synthesis, fatty acid, and amino acid metabolism.It is also implicated in B-cell synthesis and T-cell multiplication (Sakane *et al*., 1982) [59]. According to Vellema in animal models, Deficiency of vitamin B12 in the diets of animal models caused immune response reduction all through viral and bacterial infections. This experimentation of Vellema proved the importance of vitamin B12 in body's immunity boosting. Natural synthesis of vitamin B12 cannot be done in humans and plants.The enzymes needed for B12 synthesis is solely possessed by bacteria.Vitamin B12 sources are mainly animal products which include meat, fish, poultry and dairy products. (Vellema, 1996) [69].

B vitamins are mostly found in animal products but can also be obtained from plant sources provided it is taken along with absorption enhancers. Having an alkaline medium in body is also crucial to avoid destruction of B vitamins in the gut.

Papaya, guava, apple, grapes, mango and many other fruits

are rich in B vitamins. Milk and dairy products, Eggs, Animal liver and kidneys, Beef are the non-vegetarian sources of B vitamins (ICMR-NIN, 2020)

Vitamin E

When the diet is supplemented with vitamin E, it out turns in the mitogen stimulated augmented T-lymphocyte multiplication, increased cytotoxic cell activity and make the most of the action of macrophages against the intruders thereby providing a rigid and strong base of action against infections (Pae *et al*., 2014). A boost in vitamin E is also known for inhibiting the activation of protein kinase C (PKC) enzyme which in turn leads to the reduced platelets, nitric oxide and also shows reduced superoxide accumulation in macrophage cells and neutrophils (Azzi*et al*., 2002) thus provided that the strong basis of action against infections (Pae *et al*., 2014). A boost in vitamin E is also known for inhibiting the activation of protein kinase C (PKC) enzyme which in turn leads to the reduced platelets, nitric oxide and also the shows reduced superoxide accumulation in macrophage cells and neutrophils (Azzi*et al*., 2002)

Table 1

Options		Virus targeted and functions related
Nutrients		
1.	Vitamin A	Measles virus, human immunodeficiency virus, avian coronavirus
2.	B vitamins	MERS-CoV; ventilator-induced lung injury
3.	Vitamin C	Avian coronavirus; lower respiratory tract infections
4.	Vitamin D	Bovine coronavirus
5.	Vitamin E	Coxsackievirus, bovine coronavirus
6.	Omega-3 polyunsaturated fatty acids	Influenza virus, human immunodeficiency virus
7.	Selenium	Influenza virus, avian coronavirus; viral mutations
8.	Zinc	Measles virus, SARS-CoV
9.	Iron	Viral mutations

(Zhang *et al*., 2020) [75, 76, 13].

Vitamin A

Vitamin A is the first fat-soluble vitamin to be recognized and β-carotene is its plant-derived precursor.There are three active forms of vitamin A in the body, retinol, retinal, and retinoic acid. Vitamin A is also called "anti-infective" vitamin and many of the body's defenses against infection depend on an adequate supply (Guillin *et al*., 2019) [24, 25]. Vitamin A deficiency is highly involved in measles and diarrhea (Kantoch *et al*., 2002) [38]. and measles can become rigorous in vitamin A-deficient children.

Vitamin A deficiency is highly involved in measles and diarrhea. (Kantoch *et al*., 2002) [38]. and measles can become severe in vitamin A-deficient children. Adding up, Semba *et al*., 1999 had reported that vitamin A supplementation reduced morbidity and mortality in various infectious diseases, such as measles, diarrheal disease, measles-linked pneumonia, human immunodeficiency virus (HIV) infection, and malaria. Vitamin A supplementation also offers some defence against the complications of other life-threatening infections, together with malaria, lung diseases, and HIV. (Villamor *et al*., 2002) [70]. The mechanism by which vitamin A and retinoids hold back measles replication is up regulating elements of the instinctive immune response in uninfected bystander cells, making them obstinate to productive infection during subsequent rounds of viral replication. (Trottier *et al*., 2009) [64].

Hence, vitamin A could be a more promising and potential alternative for the treatment of this novel coronavirus and the deterrence and prevention of lung infection. Therefore, vitamin A could be a promising option for the treatment of this novel coronavirus and the prevention of lung infection. (Zhang *et al*., 2020) [75, 76, 13].

Fish, Carrots, Spinach, Sweet Potatoes, and Papaya are rich sources of Vitamin A. Since it is a fat soluble vitamin it is stored in the body and it deficiency is rare but till the time its deficiency symptoms show up the body has lost all its reserves and bringing the levels back to normal takes a long time. Hence it can be suggested that Vitamin A rich foods should be taken in daily diet.

Minerals and immunity

Magnesium

Body's cellular energy (ATP) currency is made by magnesium. Neither detox nor cell building and repair can take place exclusive of energy and magnesium is at the core of the energy production. Magnesium: 400 mg daily (in citrate, malate, chelate, or chloride form). The key to resilience in health is a fine metabolism. Most people are deficient in magnesium, as contemporary agriculture does not frequently supply adequate magnesium in the soil, and food processing removes magnesium. A blood test for magnesium cannot correctly diagnose a deficiency. A prolonged deficiency of magnesium is capable of building up in the body that may take 6 months to a year of higher than usual doses to replete. An extremely economical and thoroughly beneficial add-on for any acute infection, chiefly viral, is oral magnesium chloride. Levy TE and Dean C implied that remarkably, similarly as vitamin C has been shown to cure polio, an oral magnesium chloride regimen has shown corresponding results, as or even more efficiently than the vitamin C. (Levy TE 2019 [42]; Dean C 2017) [17].

Supplementation with magnesium can reverse this oxidative and inflammatory effect. De and his co researchers in a study with high magnesium with mice showcased an significant improvement in anemia, increased serum and erythrocyte magnesium, increased erythrocyte magnesium, increased erythrocyte potassium, reduced potassium chloride cotransport, and diminished cell dehydration. (De *et al*., 1997). Elderly populations have a propensity to have declining levels of magnesium, which associate with the onset of disease and a high rise of pro inflammatory cytokines (IL-6, THF-x), according to a number of studies. This means they have a tendency to experience additional

oxidation, free radical damage and inflammatory responses. Older people also get effortlessly dehydrated because cells require the right electrolyte charge to take up sufficient water. Magnesium can also rest the muscles of the lungs and facilitate to open airways via its command of calcium channels. Calcium contracts and magnesium relaxes. Fawcett stated that "The magnesium ion has an inhibitory action on smooth muscle contraction, on histamine release from mast cells and on acetylcholine release from cholinergic nerve terminals." (Fawcett *et al*., 1999) [20].

Whilst people comprise other co-morbid health conditions and a weakened immune system, These instigating coronaviruses are capable of directing secondary infections, leading to complications and acceleration to pneumonia. these initiating coronaviruses can lead to secondary infections, leading to complications and escalation to pneumonia. Sandy suggested that, "The escalation involves a lot of inflammation, which causes blockage of tubules, pain and lack of oxygen." (Sandy, 2020) [34].

Selenium

Dietary selenium deficiency that causes oxidative stress in the host can alter a viral genome so that a normally benign or mildly pathogenic virus can become highly virulent in the deficient host under oxidative stress. (Guillin *et al*., 2019) [24, 25]. Deficiency in selenium also induces not only impairment of host immune system, but also rapid mutation of benign variants of RNA viruses to virulence. It is because that selenium could assist a group of enzymes that, in concert with vitamin E, work to prevent the formation of free radicals and prevent oxidative damage to cells and tissues. (Harthill *et al*., 2011) [27]. It was reported that synergistic effect of selenium with ginseng stem-leaf saponins could induce immune response to a live bivalent infectious bronchitis coronavirus vaccine in chickens. (Ma *et al*., 2019) Therefore, selenium supplementation could be an effective choice for the treatment of this novel virus of COVID-19. (Zhang *et al*., 2020) [75, 76, 13].

Zinc

Zinc is a dietary trace mineral and is important for the maintenance and development of immune cells of both the innate and adaptive immune system. (Maares *et al*., 2016) [46]. Zinc deficiency results in dysfunction of both humoral and cell-mediated immunity and increases susceptibility to infectious diseases. (Tuerk *et al*., 2009) [65]. Zinc supplement given to zinc-deficient children could reduce measles-related morbidity and mortality caused by lower respiratory tract infections. (Awotiwon *et al*., 2017) [4]. Increasing the concentration of intracellular zinc with zinc-ionophores like pyrithione can efficiently impair the replication of a variety of RNA viruses. In addition, the combination of zinc and pyrithione at low concentrations inhibits the replication of SARS coronavirus (SARS-CoV). (te Velthuis *et al*., 2010) [63]. Therefore, zinc supplement may have effect not only on COVID-19-related symptom like diarrhoea and lower respiratory tract infection, but also on COVID-19 itself. (Zhang *et al*., 2020) [75, 36, 13].

Hence foods rich in zinc should be included in diet on a daily basis in order to maintain proper reserves in body. Legumes like chickpea, green gram, black gram, lentils, and beans provide many nutrients including iron and Zinc and can be consumed as lunch or dinner. (ICMR-NIN, 2020)

Iron

Iron is required for both host and pathogen and iron deficiency can impair host immunity, while iron overload can cause oxidative stress to propagate harmful viral mutations. (Wessling, 2018) [72]. Iron deficiency has been reported as a risk factor for the development of recurrent acute respiratory tract infections. (Jayaweera *et al*., 2019) [37]. Hence a balance of iron status in the body is necessary. One should avoid consumption of iron absorption inhibitors along with iron rich foods and combine it with foods which enhance the absorption of Iron. Hence optimum iron intake might result in less chances of occurrence of recurrent acute respiratory tract infections.

Hence food rich in iron should be consumed on a daily basis and recommended daily allowances should be met.

Copper

Copper plays a crucial role in immunity by participating in the development and differentiation of immune cells [Li C *et al*., 2019]. Turnlund *et al*. conducted a study to determine the effect of long-term high copper intake on indices of copper status, oxidant damage, and immune function. Their results showed that plasma ceruloplasmin activity, benzylamine oxidase, and superoxide dismutase were significantly higher when copper intake was 7.8 mg/day, in comparison to 1.6 mg/day, indicating an improvement in antioxidant status. However, the higher copper intake (7.8 mg/day) significantly reduced the percentage of circulating neutrophils, serum IL-2R and the antibody titer against the Beijing strain of influenza [Turnlund *et al*., 2004 [66]; Jayawardena, 2020) [36]. Since it has been established above that SARS-COV-19 is a similar strain to that of influenza, it can be concluded that Copper might prove helpful in treating and/or preventing COVID-19.

Hence copper rich foods should be included in ones diet in order maintain optimal levels and aid in strong immune system.

Conclusion

From the above mentioned studies it can be concluded that consuming recommended dietary allowances of fruits and vegetables which provide the optimum level of phytonutrients, vitamins and minerals works best in maintaining the immune system of a human body. Infection fighting abilities are better in subjects taking a balanced diet as it is able to fight free radicals and reduce oxidative stress. While in case of already weakened immune system and susceptibility to life threatening diseases, including COVID-19, it has been found that large and or intravenous doses of certain vitamins and minerals have shown improvement in the patient's condition. Hence nutritional therapy can also be used in treatment of COVID-19.

References

1. Andrew W Saul, Atsuo Yanagisawa. Hospital-based Intravenous Vitamin C Treatment for Coronavirus and Related Illnesses; Orthomolecular Medicine News Service, 2020.
2. Andrew W Saul. Shanghai Government Officially Recommends Vitamin C for COVID-19 by Orthomolecular Medicine News Service. (OMNS, 2020), 2020.
3. Are patients with hypertension and diabetes mellitus at increased risk for COVID19 infection?, Lancet Respir.

Med, 2020. https://doi. org/10.1016/S2213-2600(20)30116-8.
4. Awotiwon AA, Oduwole O, Sinha A, Okwundu CI. Zinc supplementation for the treatment of measles in children. Cochrane Database Syst Rev. 2017; 2017(6):CD011177. https://doi.org/10. 1002/ 14651858.CD011177.pub3
5. Azzi A, Ricciarelli R, Zingg JM. Nonantioxidant molecular functions of αtocopherol (vitamin E). FEBS letters. 2002; 519:8-10.
6. Bogoch II, Watts A, Thomas-Bachli A, Huber C, Kraemer MU, Khan K, *et al*. Pneumonia of unknown etiology in Wuhan, China potential for international spread via commercial air travel. J Travel Med. 2020; 272:1-3.
7. British Dietetic Association, 30th april 2020 https://www.bda.uk.com/resource/there-is-no-diet-to-prevent-coronavirus.html There is no diet to prevent Coronavirus)
8. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, *et al*. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China, The Lancet. 395 (2020) 497–506. https://doi.org/10.1016/S0140-6736(20)30183-5.
9. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S,*et al*. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China, JAMA Intern. Med, 2020. https://doi.org/10.1001/jamainternmed.2020.0994.
10. Cannell JJ, Vieth R, Umhau JC, Holick MF. Epidemic influenza and vitamin D. Epidemiol Infect. 2006; 134:1129-1140. https://www. ncbi.nlm.nih.gov/pubmed/16959053.
11. Case HS. Orthomolecular Nutrition for Everyone: Megavitamins and Your Best Health Ever. Basic Health Pubs. ISBN. 2017; 13:978-1681626581
12. Comerford KB. Recent developments in multivitamin/mineral research. Advances in Nutrition: An International Review Journal. 2013; 4:644-656.
13. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, *et al*. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China, JAMA. 2020; 323:1061-1069. https://doi. org/10.1001/jama.2020.1585.
14. Daneshkhah Ali. "The Role of Vitamin D in Suppressing Cytokine Storm in COVID-19 Patients and Associated Mortality." *medRxiv*, 2020.
15. Daneshkhah Ali. "The Role of Vitamin D in Suppressing Cytokine Storm in COVID-19 Patients and Associated Mortality." *medRxiv*, 2020.
16. De Franceschi, Brugnara LC, Beuzard Y. *Dietary magnesium supplementation ameliorates anemia in a mouse model of beta-thalassemia*. Blood. 1997; **90**(3):1283-90.
17. Dean C Magnesium, 2017. http://www.Ortho molecular.org/resources/omns/v13n22.shtml. The Magnesium Miracle. 2nd Ed., Ballantine Books. ISBN-13: 978-0399594441
18. Edlich RF, Mason SS, Dahlstrom JJ, Swainston E, Long WB 3rd, Gubler K. Pandemic preparedness for swine flu influenza in the United States. J Environ Pathol Toxicol Oncol. 2009; 28:261-264
19. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, *et al*. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study, The Lancet, 2020. https://doi.org/10.1016/S0140-6736 (20)30 566-3.
20. Fawcett WJ, Haxby EJ, Male DA, Magnesium: physiology and pharmacology. BJA: British Journal of Anaesthesia. 1999; 83(2):302-320
21. Fernandes G, Jolly CA, Lawrence RA. Nutrition and the immune system. In: Shils M.E., Shike M., Ross, A.C., Caballero, B. and Cousins, R.J. eds. Modern Nutrition in Health and Disease. 10th ed. Philadelphia: Lippincott Williams & Wilkins, 2006, 670-684
22. 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(1):E236. https://www.mdpi. com/2072-6643/12/1/236.
23. Grant WB, Giovannucci E. The possible roles of solar ultraviolet-B radiation and vitamin D in reducing case-fatality rates from the 1918-1919 influenza pandemic in the United States. Dermatoendocrinol. 2009; 1:215-219. https://www. ncbi. nlm.nih.gov/pubmed/20592793.
24. Guillin OM, Vindry C, Ohlmann T, Chavatte L. Selenium, selenoproteins and viral infection. Nutrients. 2019; 11:2101. https://doi.org/ 10.3390/ nu11092101
25. Guillin OM, Vindry C, Ohlmann T, Chavatte L. Selenium, selenoproteins and viral infection. Nutrients. 2019; 11:2101. https://doi.org/ 10.3390/ nu11092101
26. Hansdottir S, Monick MM, Lovan N, Powers L, Gerke A, Hunninghake GW, *et al*. Vitamin D decreases respiratory syncytial virus induction of NFkappaB-linked chemokines and cytokines in airway epithelium while maintaining the antiviral state. J Immunol. 2010; 184:965-974
27. Harthill M. Review: micronutrient selenium deficiency influences evolution of some viral infectious diseases. Biol Trace Elem Res. 2011; 143:1325-1336. https://doi.org/10.1007/s12011-011-8977-1
28. Hemalatha R. Nutrition, Lifestyle & Immunity, ICMR-National Institute of Nutrition, 2020.
29. Hui DS, Azhar E, Madani TA. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health—The latest 2019 novel coronavirus outbreak in Wuhan, China. Int J Infect Dis. 2020; 91:264-66.
30. Hume R, Weyers E. Changes in leucocyte ascorbic acid during the common cold. Scottish Medical Journal. 1973; 18:3-7.
31. Hunt C, Chakravorty NK, Annan G, Habibzadeh N, Schorah CJ. The clinical effects of vitamin C supplementation in elderly hospitalized patients with acute respiratory infections. Int J Vitamin Nutr Res. 1994; 64:212-219. https://www.ncbi. nlm.nih.gov/pubmed/7814237.
32. Huskisson E, Maggini S, Ruf M. He influence of micronutrients on cognitive function and performance. Journal of International Medical Research. 2007; 35:1-19
33. Ibrahim KS, El-Sayed EM. Potential role of nutrients on immunity. International Food Research Journal. 2015; 23:464-474
34. Immune System Defence with Vitamin C and Magnesium By Sandy Sanderson / Updated on March 31, 2020 Elektra Magnesium
35. Intra-arterial vitamin C prevents endothelial

dysfunction caused by ischemia-reperfusion. Pleiner J, Schaller G, Mittermayer F, Marsik C, MacAllister RJ, Kapiotis S, Ziegler S, Ferlitsch A, Wolzt M Atherosclerosis. 2008; 197(1):383-91.
36. Jayawardena R, Sooriyaarachchi P, Chourdakis M, Jeewandara C, Ranasinghe P, Enhancing immunity in viral infections, with special emphasis on COVID-19: A review, Diabetes & Metabolic Syndrome: Clinical Research & Reviews, 2020. doi: https://doi.org/10.1016/ j.dsx.2020.04.015.
37. Jayaweera J, Reyes M, Joseph A. Childhood iron deficiency anemia leads to recurrent respiratory tract infections and gastroenteritis. Sci Rep. 2019; 9:12637. https://doi.org/10.1038/s41598-019- 49122-z
38. Kantoch M, Litwinska B, Szkoda M, Siennicka J. Importance of vitamin A deficiency in pathology and immunology of viral infections. Rocz Panstw Zakl Hig. 2002; 53:385-392.
39. Keil SD, Bowen R, Marschner S. Inactivation of Middle East respiratory syndrome coronavirus (MERS-CoV) in plasma products using a riboflavin-based and ultraviolet light-based photochemical treatment. Transfusion. 2016; 56:2948-2952. https://doi.org/10.1111/trf.13860
40. Kraemer K. Introduction: He diverse and essential biological functions of vitamins. Annals of Nutrition and Metabolism. 2012; 61:185-191.
41. Kunisawa J, Kiyono H. Vitamin-mediated regulation of intestinal immunity. Frontiers in immunology. 2013; 4:189.
42. Levy TE. Magnesium: Reversing Disease. Medfox Pub. ISBN. 2019; 13:978-0998312408
43. Li C, Li Y, Ding C. The role of copper homeostasis at the host-pathogen Axis: from bacteria to fungi. Int J Mol Sci. 2019; 20(1):175.
44. Linday LA, Shindledecker RD, Tapia-Mendoza J, Dolitsky JN. Effect of daily cod liver oil and a multi-vitamin-mineral supplement with selenium on upper respiratory tract pediatric visits by young, inner-city, Latino children: randomized pediatric sites. Ann Otol Rhinol Laryngol. 2004; 113:891- 901
45. Ma X, Bi S, Wang Y, Chi X, Hu S. Combined adjuvant effect of ginseng stem-leaf saponins and selenium on immune responses to a live bivalent vaccine of Newcastle disease virus and infectious bronchitis virus in chickens. Poult Sci. 2019; 98:3548-3556. https://doi.org/10. 3382/ps/pez207
46. Maares M, Haase H. Zinc and immunity: an essential interrelation. Arch Biochem Biophys. 2016; 611:58-65. https://doi.org/10.1016/j. abb. 2016.03.022
47. Maggini Silvia, *et al*. "Selected vitamins and trace elements support immune function by strengthening epithelial barriers and cellular and humoral immune responses." *British Journal of Nutrition*. 2007; 98(1):S29-S35.
48. Martineau AR, Jolliffe DA, Hooper RL. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. BMJ. 2017; 356:i6583. https://www.ncbi.nlm.nih.gov/ pubmed/28202713.
49. Maslova E, Hansen S, Strøm M, Halldorsson TI, Olsen SF. Maternal intake of vitamins A, E and K in pregnancy and child allergic disease: a longitudinal study from the Danish National Birth Cohort. British Journal of Nutrition. 2014; 111:1096-1108.
50. Maurya Dharmendra, Deepak Sharma. "Evaluation of traditional ayurvedic preparation for prevention and management of the novel Coronavirus (SARS-CoV-2) using molecular docking approach, 2020.
51. McNally JD, Leis K, Matheson LA, Karuananyake C, Sankaran K, Rosenberg AM, *et al*. Vitamin D deficiency in young children with severe acute lower respiratory infection. Pediatr Pulmonol. 2009; 44:981-988
52. Naming the coronavirus disease (COVID-19) and the virus that causes it, 2019. https://www.who. int/emergencies/diseases/novel-coronavirus-2019/ technical guidance/
53. Orthomolecular Medicine News Service, Nutritional Treatment of Coronavirus by Andrew W. Saul, Editor, 2020.
54. Pae M, Meydani SN, Wu D. He role of nutrition in enhancing immunity in aging. Aging and disease. 2014; 3:91-129
55. Powers HJ. Riboflavin (vitamin B-2) and health. Am J Clin Nutr. 2003; 77:1352-1360. https://doi.org/10.1093/ajcn/77.6.1352
56. Rail LC, Meydani SN. Vitamin B6 and immune competence. Nutrition reviews. 1993; 51:217-225
57. Renin–Angiotensin–Aldosterone System Inhibitors in Patients with Covid-19 | NEJM, (n.d.). https://www.nejm.org/doi/full/10.1056/NEJMsr2005760?url_ver=Z39.882003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dpubmed.
58. Review Vitamin D deficiency. Holick MF N Engl J Med. 2007; 357(3):266-81
59. Sakane T, Takada S, Kotani H, Tsunematsu T. Effects of methyl-b12 on the *in vitro* immune functions of human T lymphocytes. Journal of clinical immunology. 1982; 2:101-109
60. Saul AW. (Vitamin C Protects Against Coronavirus, 2020. http://orthomolecular.org/ resources/ omns/v16n04.shtml
61. Searing DA, Zhang Y, Murphy JR, Hauk PJ, Goleva E, Leung DY, *et al*. Decreased serum vitamin D levels in children with asthma are associated with increased corticosteroid use. J Allergy Clin Immunol. 2010; 125:995-1000
62. Semba RD. Vitamin A and immunity to viral, bacterial and protozoan infections. Proc Nutr Soc. 1999; 58:719-727. https://doi.org/10.1017/ s00296 65199000944
63. te Velthuis AJW, van den Worm SHE, Sims AC, Baric RS, Snijder EJ, van Hemert MJ, *et al*. Zn(2+) inhibits coronavirus and arterivirus RNA polymerase activity *in vitro* and zinc ionophores block the replication of these viruses in cell culture. PLOS Pathog. 2010; 6:e1001176. https://doi.org/ 10.1371/journal.ppat.1001176
64. Trottier C, Colombo M, Mann KK, Miller WH Jr., Ward BJ, *et al*. Retinoids inhibit measles virus through a type I IFN-dependent bystander effect. FASEB J. 2009; 23:3203-3212. https://doi.org/ 10.1096/fj. 09-129288
65. Tuerk MJ, Fazel N. Zinc deficiency. Curr Opin Gastroenterol. 2009; 25:136-143. https://doi.org/ 10.1097/MOG.0b013e328321b395

66. Turnlund JR. Long-term high copper intake: effects on indexes of copper status, antioxidant status, and immune function in young men. Am J Clin Nutr. 2004; 79(6):1037-1044.
67. Urashima M, Segawa T, Okazaki M, Kurihara M, Wada Y, Ida H, *et al*. Randomized trial of vitamin D supplementation to prevent seasonal influenza A in schoolchildren. Am J Clin Nutr. 2010; 91:1255-1260.
68. Valdés-Ramos R, Martínez-Carrillo BE, Aranda-González II, Guadarrama AL, Pardo-Morales RV, Tlatempa P, *et al*. Diet, exercise and gut mucosal immunity. Proc Nutr Soc. 2010; 69:644-50.
69. Vellema P. He effect of cobalt supplementation on the immune response in vitamin B12 deficient Texel lambs. Veterinary immunology and immunopathology. 1996; 55:151-161.
70. Villamor E, Mbise R, Spiegelman D. Vitamin A supplements ameliorate the adverse effect of HIV-1, malaria, and diarrheal infections on child growth. Pediatrics. 2002; 109:e6. https://doi.org/10.1542/peds.109.1.e6
71. Wayse V, Yousafzai A, Mogale K, Filteau S. Association of subclinical vitamin D deficiency with severe acute lower respiratory infection in Indian children under 5 y. Eur J Clin Nutr. 2004; 58:563-567
72. Wessling-Resnick M. Crossing the iron gate: why and how transferrin receptors mediate viral entry. Annu Rev Nutr. 2018; 38:431-458. https://doi.org/10.1146/annurev-nutr-082117-051749
73. Wu Z, McGoogan JM Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. JAMA, 2020. doi:10.1001/jama.2020.2648 pmid:32091533
74. Yin Y, Wunderink RG. (Yin) MERS, SARS and other coronaviruses as causes of pneumonia. Respirology. 2018; 23(2):130-137. https://www.ncbi.nlm.nih.gov/pubmed/29052924.
75. Zhang Lei, Yunhui Liu. "Potential interventions for novel coronavirus in China: a systemic review." Journal of medical virology. 2020; 92:479-490. https://doi.org/10.1002/jmv. 25707
76. Zhu N, Zhang D, Wang W. China Novel Coronavirus Investigating and Research Team. (2020) A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med. 2020 Jan 24. doi: 10.1056/NEJMoa2001017. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/31978945