Health and Nutritional Implications of COVID-19: A Mini Review

Tasmia Tasnim[1], Kazi Muhammad Rezaul Karim[2]*

[1]Department of Nutrition and Food Engineering, Daffodil International University, Bangladesh
[2] Institute of Nutrition and Food Science, University of Dhaka, Bangladesh

Abstract

The COVID-19 outbreak is a worldwide hazard and a pandemic. It affects primarily the respiratory system of the infected persons. The severity of infection depends on various factors such as individual health, age, lifestyle, gender, dietary habits, environment, and medications. COVID-19's catastrophic results are exacerbated by a high BMI and chronic conditions. The study's goal was to look at the effects of antioxidant foods on immune function and their possible involvement in the treatment of COVID-19 infection. The human immune cell is always active, and the activity of the immune system is improved when there is an infection requiring energy sources and substrates taken from the food. A range of vitamins and trace minerals has been found to have crucial functions in enhancing immune function and decreasing the chance of infection. The gut microbiota strives to empower and regulate the immune system. Dietary methods for achieving a healthy microbiome can also improve the immune system. According to worldwide standards, the best way to maintain the immune system is to consume a healthy balanced diet rich in plant and animal foods, as well as appropriate prebiotic and probiotic prophylactic supplements.

Keywords: Covid-19, Nutrition, Immunity, Vitamins, Antioxidants, Health

Introduction

COVID-19, a new coronavirus outbreak, has become a global human hazard and a pandemic. A group of patients with initial pneumonia diagnosis with uncertain etiology was admitted into hospitals by late December 2019 (Bogoch et al., 2020). Early warnings foresaw the beginning of a potential SARS-CoV-2 coronavirus epidemic, leading to COVID-19 illness. COVID-19 Coronavirus is one of the principal pathogenic agents that attack the respiratory system in humans, in some cases, the gastrointestinal tract as well (Laviano et al., 2020). Coronavirus-induced respiratory symptoms can vary from cough and cold to severe pneumonia. In severe cases, ventilator support may be required. The WHO has declared the current outbreak a worldwide major disaster (Zhu et al., 2020). The Covid-19 outbreak has raised medical and social awareness about the significance of food and health, especially immune support. Since the immune system works to deter viruses from entering the body and killing them and generating an immune memory, viral infections like COVID-19 increase the metabolic activity of immune cell groups. This increased activity comes with requirements of higher energy and nutrients from the diet, in order to satisfy the needs of the immune cells (Gombart et al., 2020). The food eventually provides these energy sources, substrates, and regulatory chemicals. As a result, an appropriate intake of a variety of nutrients is required to maintain the immune system's optimal function (Gombart et al., 2020; Calder 2013). Chronic illness such as obesity, cardiovascular diseases (CVD), hypertension, and type 2 diabetes (T2D) appears to be associated with poor outcomes in COVID-19 infection, such as the requirement of intensive care, ventilation support, mortality, etc. (de Frel et al., 2020). In order to prevent it, a proper lifestyle approach may be required to improve cardiometabolic conditions, with nutrition at the forefront (Kushner & Sorensen, 2013). The goal of this literature review is to consolidate existing research on the links between health, lifestyle, obesity, dietary consumption pattern, and increased vulnerability to viral infections. It also intends to provide the most recent knowledge on the impact of various nutrients in immune system support, notably for viral infections such as COVID-19.

**Corresponding Author, Email: rkarim98@gmail.com, rezaul.infs@du.ac.bd*

Effect of health and nutritional status on COVID-19 infection outcomes

People's dietary and health states are utilized to assess their potential to withstand the COVID-19 pandemic (Bogoch et al., 2020). Nutritional status is important for optimum prognosis in people afflicted with SARS-CoV-2 and can measure COVID-19's clinical gravity (Laviano et al., 2020). Nutrition and nutrient absorption have an impact on the immune system via the expression of genes, cell activation, and signal molecule alteration. A person's nutritional status is influenced by a variety of factors such as lifestyle, age, health condition, gender, and medicines. Under present conditions, the only long-term method to live is to enhance one's immune system (Aslam et al., 2017). Immunosenescence, a condition linked with aging that results in a loss of immunological competence, such as decreased generation of immune cells from the bone marrow, might incline older persons to far more serious infections. Ageing too is associated with a rise in blood concentrations of certain inflammatory mediators, which contributes to an elevated risk of chronic age-related disorders such as multiple metabolic diseases.

Obesity is another factor that can cause a loss in immune capacity. It is associated with elevated blood levels of multiple inflammatory mediators along with a loss in the operation of various cells of the immune system and decreased production of antibodies (Honce et al., 2019; Calder et al., 2011). In a recent study, it was observed that obese people have a roughly threefold elevated chance of extreme COVID-19 (Gao et al., 2020) and are consequently in greater need of intrusive mechanical ventilation (Petrakis et al., 2020). Furthermore, obesity increases the risk for hospitalization and the need for emergency treatment in those under the age of 60, who are often assumed to be at a lower risk of serious disease. As a result, obesity is one of the most likely causes of serious cases of COVID-19 (Lighter et al., 2020).

The Chinese Center for Disease Control reports that individuals having comorbidities had a greater COVID-19 mortality rate than those without comorbidities (Wu & McGoogan 2020). American and European research indicates that individuals with comorbidities are more prone to suffer or develop serious illnesses and that obesity is an additional risk factor (Garg et al., 2020). The involvement of Type 2 Diabetes worsens the prognosis in COVID-19 patients (Yan et al., 2020; Targher et al., 2020). A recent study revealed that Type 2 Diabetes is related to a nearly two-fold increase in the severity of COVID-19 infection after adjusting for age, gender, smoking, hypertension, and obesity (Targher et al., 2020). Furthermore, individuals with diabetes and COVID-19 had greater rates of ICU hospitalization and death risk (Roncon et al., 2020).

COVID-19 has a high prevalence of CVD as comorbidity (Garg et al., 2020). There has been no direct investigation into the relationship between CVD and the ability to respond to viral threats. Furthermore, hypertension is frequently reported as prevalent comorbidity in critically sick patients with COVID-19 (Garg et al., 2020). According to studies, patients with COVID-19 who have hypertension have a higher ICU admittance rate and a higher death rate (Cook, 2020). However, such data should be interpreted with care because age and CVD might be important confounders (Li et al., 2020).

Link with nutrition and immunity

The immune system is the combination of tissues and cells which defend the body against harmful infections. To support normal immune function, adequate energy and nutrition are needed. There is a lack of experimental proof of the impact of diet on COVID-19. The immune system is a complex network of cells and tissues that defend the body against harmful infections. A range of vitamins, amino acids, trace minerals, and fatty acids, on the other hand, have been demonstrated to play vital roles in boosting the host immune response and decreasing the infection risk (Childs et al., 2019). Among them, Vitamin D, selenium, and zinc appear to be especially important for antiviral immunity (MCI, 2016; Haryanto et al., 2015; Maggini et al., 2008).

Activation of the innate immune system in the presence of a pathogen necessitates the availability of energy-producing substrates (glucose, fatty acids, and amino acids) for increasing the production of lymphocytes, DNA, RNA, and a variety of proteins such as immunoglobulin, chemokine, cytokine, acute-phase proteins, etc. (Calder, 2020). Several micronutrients (for example zinc, folate, magnesium, and iron) are likewise engaged in the making of building blocks of DNA (Calder, 2020).

The systemic assessments and meta-analyses of vitamin A studies in children have demonstrated a lower incidence of measles and diarrhoea, decreased morbidity and mortality, and improved symptoms of acute pneumonia (Imdad et al., 2017). People who do not get enough vitamin C are more likely to have severe respiratory problems like pneumonia. A meta-analysis has shown that vitamin C supplements significantly reduced the risk of pneumonia, particularly among those who have poor dietary consumption (Hemilä & Louhiala, 2013). Vitamin C supplementation has also been shown to slow the progression and severity of upper respiratory infections, such as the common cold, particularly in people who are under physical stress (Hemilä, 2017; Hemilä & Chalker, 2013). Studies on vitamin D have discovered an unambiguous inverse connection between serum 25(OH)-vitamin D and infection in the upper side of the respiratory tract (Ginde et al., 2009). According to several studies, people with low vitamin D levels are more likely to get viral respiratory tract infections (Sabetta et al., 2010). Vitamin D supplementation of Japanese kids for 4 months mostly during the winters reduced the influenza incidence by roughly 40%. According to a systematic analysis of previous data, vitamin D intake can lower the incidence of acute respiratory infections (Martineau et al., 2017; Pham et al. 2019; Zhou et al., 2019). Similarly, while one research found that vitamin E intake reduced the likelihood of respiratory illness in the elderly (Meydani et al., 2004), another study found that it had no effect on the severity of respiratory infections (Graat et al., 2020). Zinc is also crucial since its shortage is linked to the increased risk of infection, especially lower respiratory and gastrointestinal infections. Recent reviews and meta-analyses have shown that zinc decreases the duration of common cold in adults, reduces pneumonia incidents and prevalence in children, and reduces death in those with severe pneumonia. Some observations suggest that supplementation of selenium (100-300 μg per day depending on the research) enhances certain elements of human immunological function (Roy et al., 1994).

Thus, Nutrients play numerous and diverse roles in immune system development, and they are needed for an adequate immune response. The specific roles of each micronutrient in immunity and infection are summarized in table 1.

Role of the gut microbiome and pro/pre-biotics in immunity against COVID-19

The large intestine of the human body has the highest number and variety of bacterial species, and the gut microbiota is heavily regulated by nutrition. Obesity and chronic age-related illnesses are associated with an aberrant gut flora, known as dysbiosis. It's worth noting that Xu and his co-authors mention that some Chinese patients with COVID-19 had dysbacteriosis, with low quantities of lactobacilli and bifidobacteria (Xu et al., 2020). The intestinal microbiota should considerably affect the development of the innate and adaptive immune system (Negi et al., 2019). Bacteria in the gut can aid enhance intestinal barrier integrity and prevent potential pathogen binding (Myles, 2014). Intestinal commensals also release antimicrobial peptides and thereby promote the condition of homeostasis by competing for nutrients and the environment. Nonpathogenic bacteria in the digestive system are considered to help the host's immunological protection. Disease and antibiotic use can weaken this barrier, creating an environment that encourages the growth of dangerous microorganisms. Consuming external, living, 'good' bacteria, known as probiotics, has been shown to help preserve the host's intestinal barriers (Bron et al., 2017).

The composition of the balanced gut microbiota has a significant impact on the effectiveness of lung immunity. The "gut-lung axis," a crucial bridge between the gut microbiota and the lungs, has been shown to influence pulmonary health (Bingula et al., 2017). The intestinal axis must be bidirectional, which means that the micronutrients can have an influence on the lungs through the blood and can change the gut microbiota if inflammation occurs in the lungs. This gives rise to an exciting chance that new SARS-Cov2 might affect the intestinal microbiome too. In fact, several studies have shown a change in the composition of the gut microbiota as a result of respiratory infections. One of Covid-19's serious clinical manifestations is pneumonia and advancement to AAC, in particular in the elderly. It is recently shown that exogenous, living, 'desirable' bacteria called probiotics can help maintain the gastrointestinal barrier of the host (Bron et al., 2017). Lactobacilli and Bifidobacteria are the most common commercial organisms. Probiotic organisms can be found in fermented foods such as traditionally produced milk and milk-based products.

Prebiotics has been studied in the context of altering the human gut microbiota. Prebiotics like polydextrose, maize roughage, and inulin have been shown to improve immunity, intestinal biodiversity, metabolism, and other processes in people, particularly the elderly (Kleessen et al., 1997). In addition to changing the makeup of the microbiota, prebiotics causes significant changes in immunological and metabolic indicators. Consumption of whole-grain fibre has been related to decreased levels

Table 1. Immune functions, the impact of deficiency and important dietary sources of micronutrients

Micronutrient	Role in immunity function	Effect of deficiency	Food sources
Vitamin A	Needed for normal epithelial tissue differentiation as well as immune cell maturation and function (Biesalski, 2016). There are also reduced functioning of the barrier, modified immune reactions, and enhanced vulnerability to a variety of infections in vitamin A deficiencies (Sirisinha, 2015).	Impairment of the barrier function, altered immunological responses including impairment of macrophages' intake and killing of germs, and increased susceptibility to various infections are connected with deficiency (Calder, 2020).	Liver, cheese, eggs, dark green leafy vegetables (e.g. spinach), and orange-coloured fruits and vegetables (Calder, 2020).
Vitamin D	Help to modulate the intestinal microbiota to make it healthy, to strengthen the intestinal obstacle, and to protect the lungs against infection (Clark & Mach, 2016). Promotes antigen treatment (Maggini et al., 2008), Role of MHC-II downregulation (Saeed et al., 2016).	Lower vitamin D levels are linked to a weaker immune response and an increased risk of virus-related respiratory area infections (Cannell et al., 2006). The immune capability of macrophages (including antimicrobial activity) is impaired; lymphocyte number is reduced (Cannell et al., 2006).	Fish oil, eggs, some nutrient-fortified breakfast cereals, spreads dairy products as well as dairy replacements (Calder, 2020).
Vitamin E	Safeguards cell membranes from oxidative stress and promotes the stability of epithelial barriers (MCI, 2016); Maintains or improves the cytotoxic function of NK cells; suppresses macrophage PGE2 synthesis;	Vitamin E insufficiency can result in decreased humoral and cell-mediated elements of adaptive immunity, such as B and T cell function (MCI, 2016), as well as reduced T cell maturation (Saeed et al., 2016).	Assortment of vegetable oils, nuts and seeds, and wheat kernel (in cereals) (Calder, 2020).
Vitamin C	Involved in neutrophil, monocyte, and phagocyte proliferation, function, and movement; maintains or amplifies NK cell activity and chemotaxis (Maggini et al., 2018). High amounts can increase antibacterial activities (MCI, 2016); controls cytokine production and lowers histamine levels; and regenerates other antioxidants (Carr & Maggini, 2017). Increases the production of lymphocytes and antibodies (Carr & Maggini, 2017).	Vitamin C deficiency is linked to impaired immune responses by T-lymphocytes to recall antigens (Calder, 2020) as well as susceptibility to severe respiratory infections like pneumonia (Prentice, 2017).	Citrus fruits, green vegetables cauliflower, and tomatoes (Calder, 2020).

Table 1. (Continued)

Micronutrient	Role in immunity function	Effect of deficiency	Food sources
Vitamin B12	It is vital for the single carbon metabolism (folate interactions) and promotes the growth of T-cells, for example, cytotoxic T-cells.	The ratio CD4+/CD8+ is always very high, and the activity of the natural killer cell (corrected with vitamin B12 therapy) substantially diminished (Lockyer,2020).	Animal sources such as fish, shellfish, milk and cheese, meat, eggs, and other dairy and yeast extract (Calder, 2020).
Folate	Supports the mediated immune response of Th 1, Important to antibody synthesis and metabolism; Maintains or increases NK cell cytotoxic function (Maggini et al., 2018).	Folate deficiency reduces the proportion of circulating T-cells (Caplan et al., 2007) and their proliferation in response to mitogen activation (Lockyer,2020).	Green vegetables, peas, lettuce, pulses, oranges, nuts and seeds, cheeses, wholemeal bread, and fortified breakfast cereals (Calder, 2020).
Iron	Engaged in the control of cytokine synthesis and function (Haryanto et al., 2015); essential for neutrophils to generate pathogen-killing ROS during an oxidative burst (MCI, 2016); important in T cell differentiation and proliferation (MCI, 2016); helps to control the ratio of T helper cells to cytotoxic T cells (Haryanto et al., 2015).	Iron deficiency causes thymus contraction, which reduces the production of naïve T cells and has a number of other impacts on immunological function in humans (MCI, 2016).	Mostly animal source foods e.g. Meat and liver. Plant sources include beans, nuts, dried fruit (e.g., apricots), whole grains (, fortified cereals, most dark green leafy vegetables (spinach, kale) (Calder, 2020)
Selenium	Selenoproteins that are vital to the internal antioxidant system that affects leukocyte and NK cell activity (Saeed et al., 2016); Essential for selenoprotein activity as redox and cellular antioxidants, which can neutralize ROS created during oxidative stress (Maggini et al., 2018); Helps sustain levels of antibodies (Saeed et al., 2016).	Selenium deficiency is associated with suppression of immune function, diminished NK-cell cytotoxicity (Maggini et al., 2008), impaired humoral and cell-mediated immunity, decreased immunoglobulin titers, impaired cell-mediated immunity, and decreased response to vaccination (MCI, 2016).	Fish, meat, nuts, and eggs (Calder, 2020).
Zinc	Helps preserve skin and mucosal membrane integrity (for example the metalloenzyme cofactor needed to repair the cell membrane) (Lin et al., 2017). Improve NK cytotoxic activity, a key function in cell proliferation and cell differentiation (Maggini et al., 2018); Antimicrobial agent (Jarosz et al., 2017).	Zinc deficiency leads to deteriorating antibody response, altered cytokine production, increased oxidative stress, and reduced lymphocyte production and antibody response (MCI, 2016; Maggini et al., 2008).	Meat, dairy, nuts (Calder, 2020).

of inflammation-inducing cytokine IL-6 and insulin resistance (Keim & Martin, 2014).

Since intestinal microbiota is changeable and diet regulated, customized dietary interventions must be used as a complement to present routine therapy. Assessing the particular patients' gut microbiota and proposing an efficient diet that includes specific pre/probiotics and various strains of lactobacilli to prevent gut dysbiosis and hence increase their overall immune response may achieve this. This can help and speed up recovery in individuals with the SARS-Cov2 infection, particularly the elderly and the immune-compromised patients.

Healthy diet pattern

With the advent of COVID-19 infection, the role of optimum nutritional status for stronger immunity through intake of balanced meals has become apparent. A high-energy diet with low nutrient content, namely the ultra-processed ones containing a high amount of sugar and fats, has an increased risk of non-communicable illnesses and a lower immunity (Myles, 2014). Several international organizations have generated COVID-19 related dietary guidelines that placed special emphasis on micronutrients such as zinc and vitamins C, A, and D for optimizing the immune system (EFIC, 2020; de Faria Coelho-Ravagnani et al., 2021; WHO,2020; FAO, 2020). A daily diet that includes meat, fish, lentils and beans, dairy foods, nuts, seeds, eggs, citrus fruits (e.g., orange, lemon, grapefruit), and vegetables such as cauliflower, pumpkin, spinach, sweet potato, and carrots can provide adequate intakes of these micronutrients. This description correlates to a healthy whole-food diet, such as a vegetarian or Mediterranean diet, which has been associated with a lower risk of chronic non-communicable disease and improved immune function (McCartney & Byrne, 2020). Overall, the FAO and the WHO guidelines endorse the consumption of a healthy and diversified diet with the inclusion of whole grains, fruits, vegetables, healthy fats and exclusion of excess fat, sugar, salt, and processed foods (WHO, 2020; FAO, 2020).

Conclusion

The body's immune system is indeed active, conducting surveillance, but its actions are increased when a person becomes infected. This activity will be completed if the individual maintains a healthy lifestyle and consumes a well-balanced and diverse diet. This review highlighted the health and lifestyle factors that modulate immune function and consequently disease severity such as in COVID-19 infection. It also examined the different evidence pertaining to the effect of nutrition and gut microbiota in aiding immune response. Vitamins (A, B complex, C, D, and E) and minerals (iron, copper, zinc, and selenium) help the body's immunological response and prevent infection. As a result of the diversification and existence of helpful bacteria in the gut, the immune system is supported. It is best to eat a variety of foods from both animal and plant sources, as well as plenty of fruits and vegetables, and to adhere to the national dietary guidelines. To summarize, it is preferable to strengthen the immune system by eating a diversified and varied diet of plant-based and animal-based foods that adheres to current healthy eating standards. Besides, the provision of specific prebiotic and probiotic prophylactic supplements can assist in improving gut-regulated immune response in COVID-19 infected people

References

Aslam, M. F., Majeed, S., Aslam, S., Irfan, J. A. (2017). Vitamins: Key role players in boosting up immune response- A mini review. *Vitamins & Minerals,* 6:153.

Biesalski H. K. (2016). Nutrition meets the microbiome: micronutrients and the microbiota. *Annals of the New York Academy of Sciences*, *1372*(1), 53–64.

Bingula, R., Filaire, M., Radosevic-Robin, N., et al. (2017). Desired turbulence? Gut-lung Axis, immunity, and lung cancer. Journal of Oncology, 2017.

Bogoch, I. I., Watts, A., Thomas-Bachli, A., Huber, C., Kraemer, M., & Khan, K. (2020). Pneumonia of unknown aetiology in Wuhan, China: potential for international spread via commercial air travel. *Journal of travel medicine*, *27*(2), taaa008.

Bron, P. A., Kleerebezem, M., Brummer, R. J., Cani, P. D., Mercenier, A., MacDonald, T. T., Garcia-Ródenas, C. L., & Wells, J. M. (2017). Can probiotics modulate human disease by impacting intestinal barrier function? *The British journal of nutrition*, *117*(1), 93–107.

Calder P. (2020). Nutrition, immunity and COVID-19. *BMJ Nutrition, Prevention & Health*, *3*(1), 74-92.

Calder P. C. (2013). Feeding the immune system. *The Proceedings of the Nutrition Society*, *72*(3), 299–309.

Calder, P. C., Ahluwalia, N., Brouns, F., Buetler, T., Clement, K., Cunningham, K., et al. (2011). Dietary factors and low-grade inflammation in relation to overweight and obesity. *The British journal of nutrition*, *106 Suppl 3*, S5–S78.

Cannell, J. J., Vieth, R., Umhau, J. C., Holick, M. F., Grant, W. B., Madronich, S., Garland, C. F., & Giovannucci, E. (2006). Epidemic influenza and vitamin D. *Epidemiology and Infection*, *134*(6), 1129–1140.

Caplan, M., Calder, P., and Prescott, S. (eds.) (2007). Scientific Review: The Role of Nutrients in Immune Function of Infants and Young Children Emerging Evidence for Long-chain Polyunsaturated Fatty Acids Glenview, US. Mead Johnson & Compan: Glenview, IL, USA

Carr, A. C., & Maggini, S. (2017). Vitamin C and Immune Function. *Nutrients*, *9*(11), 1211.

Childs, C. E., Calder, P. C., & Miles, E. A. (2019). Diet and Immune Function. *Nutrients*, *11*(8), 1933.

Clark, A., & Mach, N. (2016). Role of Vitamin D in the Hygiene Hypothesis: The Interplay between Vitamin D, Vitamin D Receptors, Gut Microbiota, and Immune Response. *Frontiers in immunology*, *7*, 627.

Cook T. M. (2020). The importance of hypertension as a risk factor for severe illness and mortality in COVID-19. *Anaesthesia*, *75*(7), 976–977.

de Faria Coelho-Ravagnani, C., Corgosinho, F. C., Sanches, F., Prado, C., Laviano, A., & Mota, J. F. (2021). Dietary recommendations during the COVID-19 pandemic. *Nutrition reviews*, *79*(4), 382–393.

De Filippis, F., Pellegrini, N., Vannini, L., et al. (2016). High-level adherence to a Mediterranean diet beneficially impacts the gut microbiota and associated metabolome. *Gut*, *65*(11), 1812–1821.

de Frel, D. L., Atsma, D. E., Pijl, H., Seidell, J. C., Leenen, P., Dik, W. A., & van Rossum, E. (2020). The Impact of Obesity and Lifestyle on the Immune System and Susceptibility to Infections Such as COVID-19. *Frontiers in nutrition*, *7*, 597600.

European Food Information Council (EFIC). (2020). Food and coronavirus (COVID-19): what you need to know. https://www.eufic.org/en/food-safety/article/food-and-coronavirus-covid-19-what-you-need-to-know. Updated March 26, 2020. Accessed April 12, 2020.

Food and Agriculture Organization of the United Nations (FAO). (2020). Maintaining a healthy diet during the COVID-19 pandemic. http://www.fao.org/3/ca8380en/CA8380EN. pdf. Published March 27, 2020. Accessed April 12, 2020.

Gao, F., Zheng, K. I., Wang, X. B., Sun, Q. F., Pan, K. H., Wang, T. Y., Chen, Y. P., Targher, G., Byrne, C. D., George, J., & Zheng, M. H. (2020). Obesity Is a Risk Factor for Greater COVID-19 Severity. *Diabetes care*, *43*(7), e72–e74.

Garg, S., Kim, L., Whitaker, M., O'Halloran, A., Cummings, C., Holstein, R., et al. (2020). Hospitalization rates and characteristics of patients hospitalized with laboratory-confirmed coronavirus disease 2019. COVID-NET, 14 states. *Morb Mortal Wkly Rep.* 69:458–64.

Ginde, A. A., Mansbach, J. M., Camargo, C.A. (2009). Association between serum 25-hydroxyvitamin D level and upper respiratory tract infection in the Third National Health and Nutrition Examination Survey. *Arch Intern Med*,169:384–90.

Gombart, A. F., Pierre, A., & Maggini, S. (2020). A Review of Micronutrients and the Immune System-Working in Harmony to Reduce the Risk of Infection. *Nutrients*, *12*(1), 236.

Graat, J. M., Schouten, E. G., & Kok, F. J. (2002). Effect of daily vitamin E and multivitamin-mineral supplementation on acute respiratory tract infections in elderly persons: a randomized controlled trial. *JAMA*, *288*(6), 715–721.

Haryanto, B., Suksmasari, T., Wintergerst, E., Maggini, S. (2015). Multivitamin Supplementation Supports Immune Function and Ameliorates Conditions Triggered By Reduced Air Quality. *Vitamins & Minerals,* 3: 128.

Hemilä H. (2017). Vitamin C and Infections. *Nutrients*, *9*(4), 339.

Hemilä H. (2017). Zinc lozenges and the common cold: a meta-analysis comparing zinc acetate and zinc gluconate, and the role of zinc dosage. *JRSM open*, *8*(5), 2054270417694291.

Hemilä, H., & Chalker, E. (2013). Vitamin C for preventing and treating the common cold. *The Cochrane database of systematic reviews*, *2013*(1), CD000980.

Hemilä, H., & Louhiala, P. (2013). Vitamin C for preventing and treating pneumonia. *The Cochrane database of systematic reviews*, (8), CD005532.

Hill, C., Guarner, F., Reid, G., et al. (2014). Expert consensus document. The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic. *Nature reviews. Gastroenterology & hepatology*, *11*(8), 506–514.

Honce, R. and Schultz-Cherry, S. (2019). Impact of Obesity on Influenza A Virus Pathogenesis, Immune Response, and Evolution. *Frontiers in Immunology*, 10:1071.

Imdad, A., Mayo-Wilson, E., Herzer, K., & Bhutta, Z. A. (2017). Vitamin A supplementation for preventing morbidity and mortality in children from six months to five years of age. *The Cochrane database of systematic reviews*, *3*(3), CD008524.

Jarosz, M., Olbert, M., Wyszogrodzka, G., Młyniec, K., & Librowski, T. (2017). Antioxidant and anti-inflammatory effects of zinc. Zinc-dependent NF-κB signaling. *Inflammopharmacology*, *25*(1), 11–24.

Keim, N. L., & Martin, R. J. (2014). Dietary whole grain–microbiota interactions: insights into mechanisms for human health. *Advances in nutrition (Bethesda, Md.)*, *5*(5), 556–557.

Kleessen, B., Sykura, B., Zunft, H. J., & Blaut, M. (1997). Effects of inulin and lactose on fecal microflora, microbial activity, and bowel habit in elderly constipated persons. *The American journal of clinical nutrition*, *65*(5), 1397–1402.

Kushner, R. F., & Sorensen, K. W. (2013). Lifestyle medicine: the future of chronic disease management. *Current opinion in endocrinology, diabetes, and obesity*, *20*(5), 389–395.

Laviano, A., Koverech, A., Zanetti, M. (2020). Nutrition support in the time of SARS-CoV-2 (COVID-19). Nutrition, 74:110834.

Li, G., Li, H., Lu, J. (2020). No adequate evidence indicating hypertension as an independent risk factor for COVID-19 severity. *Clin Res Cardiol*, 109:1–2.

Lighter, J., Phillips, M., Hochman, S., Sterling, S., Johnson, D., Francois, F., & Stachel, A. (2020). Obesity in Patients Younger Than 60 Years Is a Risk Factor for COVID-19 Hospital Admission. *Clinical infectious diseases: an official publication of the Infectious Diseases Society of America*, *71*(15), 896–897.

Lin, P. H., Sermersheim, M., Li, H., Lee, P., Steinberg, S. M., & Ma, J. (2017). Zinc in Wound Healing Modulation. *Nutrients*, *10*(1), 16.

Lockyer S. (2020). Effects of diets, foods and nutrients on immunity: Implications for Covid-19? *Nutrition Bulletin*, 45(4):456-473

Maggini, S., Beveridge, S., Sorbara, P.J., & Senatore, G. (2008). Feeding the immune system: the role of micronutrients in restoring resistance to infections. Cab Reviews: Perspectives in Agriculture, Veterinary Science, Nutrition and Natural Resources, 3, 1-21.

Maggini, S., Pierre, A., Calder, P.C. (2018). Immune function and micronutrient requirements change over the life course. *Nutrients,* 10, 1531.

Martineau, A. R., Jolliffe, D. A., Hooper, R. L., *et al*. (2017). Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. *BMJ*, 356:i6583.

McCartney, D. M., & Byrne, D. G. (2020). Optimisation of Vitamin D Status for Enhanced Immuno-protection Against Covid-19. *Irish medical journal*, *113*(4), 58.

Meydani, S. N., Leka, L. S., Fine, B. C., Dallal, G. E., Keusch, G. T., Singh, M. F., & Hamer, D. H. (2004). Vitamin E and respiratory tract infections in elderly nursing home residents: a randomized controlled trial. *JAMA*, *292*(7), 828–836.

Micronutrient Information Center (MCI). Immunity in Depth. Linus Pauling Institute. 2016. Available online:http://lpi.oregonstate.edu/mic/health-disease/immunity (accessed on 10 May 2019).

Myles I. A. (2014). Fast food fever: reviewing the impacts of the Western diet on immunity. *Nutrition Journal*, *13*, 61.

Negi, S., Das, D.K., et al. (2019). Potential role of gut microbiota in induction and regulation of innate immune memory. Frontiers in Immunology, 10 (October), 1–12. https://doi. org/10.3389/fimmu.2019.02441

Petrakis, D., Margină, D., Tsarouhas, K., Tekos, F., Stan, M., Nikitovic, D., Kouretas, D., Spandidos, D. A., & Tsatsakis, A. (2020). Obesity a risk factor for increased COVID19 prevalence, severity and lethality (Review). *Molecular medicine reports*, *22*(1), 9–19.

Pham, H., Rahman, A., Majidi, A., Waterhouse, M., & Neale, R. E. (2019). Acute Respiratory Tract Infection and 25-Hydroxyvitamin D Concentration: A Systematic Review and Meta-Analysis. *International journal of environmental research and public health*, *16*(17), 3020.

Prentice S. (2017). They Are What You Eat: Can Nutritional Factors during Gestation and Early Infancy Modulate the Neonatal Immune Response?. *Frontiers in immunology*, *8*, 1641.

Roncon, L., Zuin, M., Rigatelli, G., & Zuliani, G. (2020). Diabetic patients with COVID-19 infection are at higher risk of ICU admission and poor short-term outcome. *Journal of clinical virology: the official publication of the Pan American Society for Clinical Virology*, *127*, 104354.

Roy, M., Kiremidjian-Schumacher, L., Wishe, H. I., Cohen, M. W., & Stotzky, G. (1994). Supplementation with selenium and human immune cell functions. I. Effect on lymphocyte proliferation and interleukin 2 receptor expression. *Biological trace element research*, *41*(1-2), 103–114.

Sabetta, J. R., DePetrillo, P., Cipriani, R.J., *et al*. (2010). Serum 25-hydroxyvitamin D and the incidence of acute viral respiratory tract infections in healthy adults. *PLoS One,* 5:e11088.

Saeed, F., Nadeem, M., Ahmed, R., Nadeem, M., Arshad, M., Ullah, A. (2016). Studying the impact of nut`ritional immunology underlying the modulation of immune responses by nutritional compounds—A review. *Food and Agricultural Immunology*, 27(2): 205-229.

Sirisinha S. (2015). The pleiotropic role of vitamin A in regulating mucosal immunity. *Asian Pacific Journal of allergy and immunology*, *33*(2), 71–89.

Targher, G., Mantovani, A., Wang, X. B., Yan, H. D., Sun, Q. F., Pan, K. H., Byrne, C. D., Zheng, K. I., Chen, Y. P., Eslam, M., George, J., & Zheng, M. H. (2020). Patients with diabetes are at higher risk for severe illness from COVID-19. *Diabetes & metabolism*, *46*(4), 335–337.

World Health Organization Regional Office for the Eastern Mediterranean (WHO). (2020). Nutrition advise for adults during the COVID-19 outbreak. http://www. emro.who.int/nutrition/nutrition-infocus/nutrition-advice-for-adults-during-the- covid-19-outbreak.html. Published March 27, 2020. Accessed April 12, 2020.

Wu, Z., & McGoogan, J. M. (2020). Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. *JAMA*, *323*(13), 1239–1242.

Xu, K., Cai, H., Shen, Y., *et al*. (2020). Management of corona virus disease-19 (COVID-19): the Zhejiang experience. *Journal of Zhejiang University Medical sciences*, *49*(1), 147–157.

Yan, Y., Yang, Y., Wang, F., Ren, H., Zhang, S., Shi, X., et al. (2020). Clinical characteristics and outcomes of patients with severe COVID-19 with diabetes. *BMJ Open Diabetes Res Care*, 8:e001343

Zhou, Y. F., Luo, B. A., Qin, L.L. (2019). The association between vitamin D deficiency and community-acquired pneumonia: a meta-analysis of observational studies. *Medicine,* 98:17252.

Zhu, N., Zhang, D., Wang, W., Li, X., Yang, B., Song, J., et al. (2020). A novel coronavirus from patients with pneumonia in China, 2019. The New England Journal of Medicine, 382:727–33.