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# IMPACT OF NUTRITIONAL INTERVENTIONS ON CORONA VIRUS INFECTION – REVIEW ARTICLE

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**ABSTRACT**

Protection of host against environmental agents such as pathogenic micro-organisms (bacteria, fungi, and viruses) and chemicals, has been controlled by immune system, thereby preserving the integrity of the body. Adequate nutritional status should be maintained with appropriate intakes of calories, vitamins, minerals to preserve organism defense mechanisms and water that should be continuously provided by a healthy diet. The emergence of new infectious diseases with new pathogenic properties constitutes a serious health issue worldwide. Severe acute respiratory syndrome (SARS) represents one of the most recent emerging infectious diseases, caused by a novel coronavirus member called (SARS-CoV-2), identified in Wuhan, Hubei, China in December 2019, and recognized as pandemic by the World Health Organization (WHO). The nutritional status of each COVID-19-infected patient should be assessed prior undertaking treatments. Nutritional support should be the basis of management of any infected individual. Therefore, preventive measures remain the first priority and strategy to develop throughout proper hygiene, healthy diet and staying home.

**KEYWORDS:** Nutrition, vitamins, minerals, Immune system, Viral diseases, SARS-CoV-2.

## 1.0. INTRODUCTION

Coronaviruses are a group of related RNA viruses that cause diseases in mammals and birds. In humans, these viruses cause respiratory tract infections that can range from mild to lethal. Mild illnesses include some cases of the common cold (which is caused also by certain other viruses, predominantly rhinoviruses), while more lethal varieties can cause SARS, MERS, and COVID-19. Symptoms in other species vary: in chickens, they cause an upper respiratory tract disease, while in cows and pigs they cause diarrhea. There are as yet no vaccines or antiviral drugs to prevent or treat human coronavirus infections.[1]

Coronaviruses constitute the subfamily *Orthocoronavirinae*, in the family *Coronaviridae*, order *Nidovirales*, and realm *Riboviria*. They are enveloped viruses with a positive-sense single-stranded RNA genome and a nucleocapsid of helical symmetry. The genome size of coronaviruses ranges from approximately 26 to 32 kilobases, one of the largest among RNA viruses. They have characteristic club-shaped spikes that project from their surface, which in electron micrographs create an image reminiscent of the solar corona, from which their name derives.[2,3]

### 1.1. Etymology

The name "coronavirus" is derived from Latin *corona*, meaning "crown" or "wreath", itself a borrowing from Greek.[4] The name was coined by June Almeida and David Tyrrell who first observed and studied human coronaviruses. The word was first used in print in 1968 by an informal group of virologists in the journal *Nature* to designate the new family of viruses.[5] The name refers to the characteristic appearance of virions (the infective form of the virus) by electron microscopy, which have a fringe of large, bulbous surface projections creating an image reminiscent of the solar corona or halo. This morphology is created by the viral spike peplomers, which are proteins on the surface of the virus.[6]

### 1.2. History

Coronaviruses were first discovered in the 1930s when an acute respiratory infection of domesticated chickens was shown to be caused by infectious bronchitis virus (IBV).[7] Arthur Schalk and M.C. Hawn described in 1931 a new respiratory infection of chickens in North Dakota. The infection of new-born chicks was characterized by gasping and listlessness. The mortality rate of the chicks was 40–90%. Fred Beaudette and Charles Hudson six years later successfully isolated and cultivated the infectious bronchitis virus which caused the disease.[8]

Human coronaviruses were discovered in the 1960s.[9] They were isolated using two different methods in the United Kingdom and the United States.[10] E.C. Kendall, Malcom Byone, and David Tyrrell working at the Common Cold Unit of the British Medical Research Council in 1960 isolated from a boy a novel common cold virus B814.[11] The virus was not able to be cultivated using standard techniques which had successfully cultivated rhinoviruses, adenoviruses and other known common cold viruses. In 1965, Tyrrell and Byone successfully cultivated the novel virus by serially passing it through organ culture of human embryonic trachea. The new cultivating method was introduced to the lab by Bertil Hoorn.[12] The isolated virus when intranasally inoculated into volunteers caused a cold and was inactivated by ether which indicated it had a lipid envelope. Around the same time, Dorothy Hamre and John Procknow at the University of Chicago isolated a novel cold virus 229E from medical students, which they grew in kidney tissue culture. The novel virus 229E, like the virus strain B814, when inoculated into volunteers caused a cold and was inactivated by ether.[13]

**1.4. Microbiology**

Coronaviruses are large mostly spherical, sometimes pleomorphic, particles with bulbous surface projections. The average diameter of the virus particles is around 125 nm (.125 μm). The diameter of the envelope is 85 nm and the spikes are 20 nm long. The envelope of the virus in electron micrographs appears as a distinct pair of electron dense shells.[14,15] (fig .1)

The viral envelope consists of a lipid bilayer where the membrane (M), envelope (E) and spike (S) structural proteins are anchored. The ratio of E:S:M in the lipid bilayer is approximately 1:20:300. On average a coronavirus particle has 74 surface spikes. A subset of coronaviruses (specifically the members of betacoronavirus subgroup A) also have a shorter spike-like surface protein called hemagglutinin esterase (HE).[16,17] (Fig. 2 & 3).

The coronavirus surface spikes are homotrimers of the S protein, which is composed of an S1 and S2 subunit. The homotrimeric S protein is a class I fusion protein which mediates the receptor binding and membrane fusion between the virus and host cell. The S1 subunit forms the head of the spike and has the receptor binding domain (RBD). The S2 subunit forms the stem which anchors the spike in the viral envelope and on protease activation enables fusion. The E and M protein are important in forming the viral envelope and maintaining its structural shape.[17]

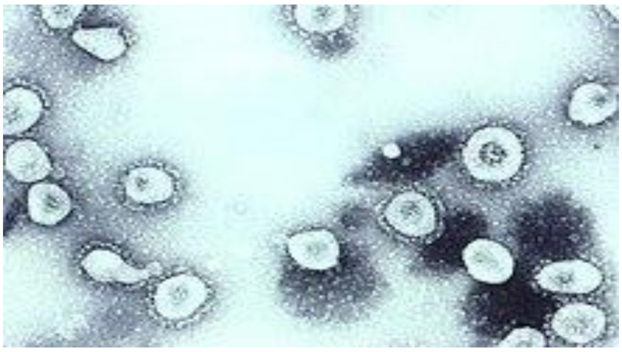

**Fig. 1: Transmission electron micrograph of organ cultured coronavirus.**

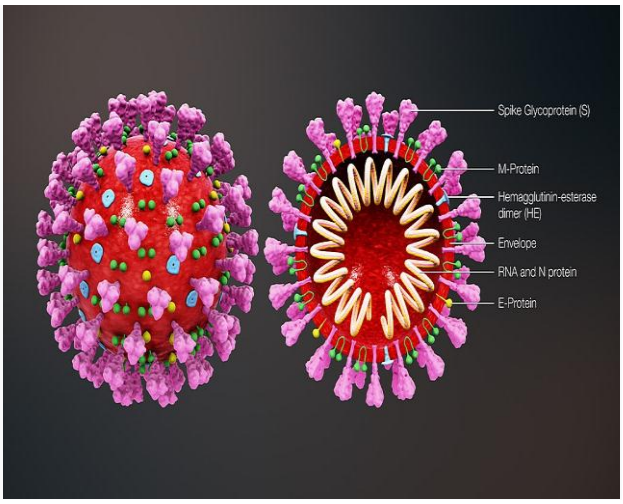


**Fig. 2: Cross-Sectiional model of corona virus.**

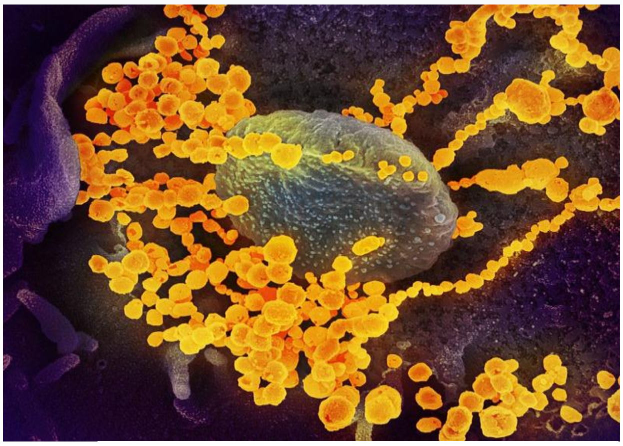

**Fig. 3: Scanning electron microscope image of the virus emerging from the surface of cells.**

**2.0. General Treatment For Viral Infection**

**2.1. Vitamin A**

Vitamin A is the first fat-soluble vitamin to be recognized and β-carotene is its plant-derived precursor (Table 1). 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. Researchers have believed that an impaired immune response is due to the deficiency of a particular nutritional element.[18] Vitamin A deficiency is strongly involved in measles and diarrhea,[19] and measles can become severe in vitamin A-deficient children. In addition, Semba et al,[20] had reported that vitamin A supplementation reduced morbidity and mortality in different infectious diseases, such as measles, diarrheal disease,measles-related pneumonia, human immunodeficiency virus (HIV) infection, and malaria. Vitamin A supplementation also offers some protection against the complications of other life-threatening infections, includingmalaria, lung diseases, and HIV.13 Jee et al,[21] had reported that low vitamin A diets might compromise the effectiveness of inactivated bovine coronavirus vaccines and render calves more susceptible to infectious disease. The effect of infection with infectious bronchitis virus (IBV), a kind of coronaviruses, was more pronounced in chickens fed a diet marginally deficient in vitamin A than in those fed a diet adequate in vitamin A. The mechanism by which vitamin A and retinoids inhibit measles replication is upregulating elements of the innate immune response in uninfected bystander cells, making them refractory to productive infection during subsequent rounds of viral replication.[22] Therefore, vitamin A could be a promising option for the treatment of this novel coronavirus and the prevention of lung infection.

### 2.2 Vitamins B

B vitamins are water-soluble vitamins and work as part of coenzymes. Each B vitamin has its special functions. For example,vitamin B2 (riboflavin) plays a role in the energymetabolismof all cells. 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.[23] Moreover, vitamin B3 treatment significantly inhibited neutrophil infiltration into the lungs with a strong anti-inflammatory effect during ventilatorinduced 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.

### 2.3 Vitamin C

Vitamin C is another water-soluble vitamin and it is also called ascorbic acid, which means “no-scurvy acid.” Vitamin C is best known for its role in the synthesis of collagen in connective tissues and acts as an antioxidant. Vitamin C also supports immune functions and protects against infection caused by a coronavirus.[24] Vitamin C may also function as a weak antihistamine agent to provide relief from flu-like symptoms such as sneezing, a running or stuffy nose, and swollen sinuses. Three human controlled trials had reported that there was significantly lower incidence of pneumonia in vitamin C-supplemented groups, suggesting that vitamin C might prevent the susceptibility to lower respiratory tract infections under certain conditions.[25] The COVID-19 had been reported to cause lower respiratory tract infection, so vitamin C could be one of the effective choices for the treatment of COVID-19.

### 2.4 Vitamin D

Vitamin D is not only a nutrient but also a hormone, which can be synthesized in our body with the help of sunlight. In addition to its role in maintaining bone integrity, it also stimulates the maturation of many cells including immune cells. A high number of healthy adults have been reported to be with low levels of vitamin D, mostly at the end of the Winter season.[25] In addition, people who are housebound,or institutionalized and those who work at night may have vitamin D deficiency, as do many elderly people, who have limited exposure to sunlight. The COVID-19 was first identified in Winter of 2019 and mostly affected middle-aged to elderly people. The virus-infected people might have insufficient vitamin D. In addition, the decreased vitamin D status in calves had been reported to cause the infection of bovine coronavirus.[26] Therefore, vitamin D could work as another therapeutic option for the treatment of this novel virus

### 2.5. Vitamin E

Vitamin E is a lipid-soluble vitamin and it includes both tocopherols and tocotrienols. Vitamin E plays an important role in reducing oxidative stress through binding to free radicals as an antioxidant.[27] Vitamin E deficiency had been reported to intensify the myocardial injury of coxsackievirus B3 (a kind of RNA viruses) infection in mice and increased the virulence of coxsackievirus B3 in mice due to vitamin E or selenium deficiency. In addition, the decreased vitamin E and D status in calves also caused the infection of bovine coronavirus.[28]

### 2.6. Selenium

Selenium is an essential trace element for mammalian redox biology. The nutritional status of the host plays a very important role in the defense against infectious diseases. Nutritional deficiency impacts not only the immune response but also the viral pathogen itself. 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. Deficiency in selenium also induces not only impairment of host immune system, but also rapid mutation of benign variants of RNA viruses to virulence.[29] 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.[30] Therefore, selenium supplementation could be an effective choice for the treatment of this novel virus of COVID-19.

### 2.7. 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.[31] Zinc deficiency results in dysfunction of both humoral and cell-mediated immunity and increases susceptibility to infectious diseases.Zinc supplement given to zinc-deficient children could reduce measles-related morbidity and mortality caused by lower respiratory tract infections.32 Increasing the concentration of intracellular zinc with zinc-ionophores like pyrithione can efficiently impair the replication of a variety of RNA viruses.[33] In addition, the combination of zinc and pyrithione at low concentration inhibits the replication of SARS coronavirus (SARS-CoV). Therefore, zinc supplement may have effect not only on COVID-19-related symptom like diarrhea and lower respiratory tract infection, but also on COVID-19 itself.

### 2.8. 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. Iron deficiency has been reported as a risk factor for the development of recurrent acute respiratory tract nfections.[34]

**Table 1: General supportive treatments.**

| Options | Virus targeted and functions related |
|---|---|
| Vitamin A | Measles virus, human immunodeficiency virus, avian coronavirus |
| B vitamins | MERS-CoV; ventilator-induced lung injury |
| Vitamin C | Avian coronavirus; lower respiratory tract infections |
| Vitamin D | Bovine coronavirus |
| Vitamin E | Coxsackievirus, bovine coronavirus |
| Selenium | Influenza virus, avian coronavirus; viral mutations |
| Zinc | Measles virus, SARS-CoV |
| Iron | Viral mutations |

**Abbreviations:** MERS-CoV, Middle East respiratory syndrome coronavirus; SARS-CoV, severe acute respiratory syndrome coronavirus.

## 3.0. CONCLUSION

In this review we summarize all the nutritional interventions for viral and COVID-19 infection. Nutrition constitutes a fundamental element in the development and the decline of immune status by maintaining immune homeostasis throughout life and reinforce immunity mechanisms especially among vulnerable individuals (elderly, pregnant, and infant groups). Nutritional upport remains the basis of the treatment and no specific food or supplement will prevent OVID-19/Coronavirus affection. However, the nutritional status of the host, until recently, has not been considered as a contributing factor to the emergence of viral infectious diseases. Therefore, we suggest to assess the nutritional status of COVID-19 infected patients prior undertaking general treatments. Due to the increasing propagation of COVID-19, it is vital that infection control and safety precautions must be strictly adhered to minimize contamination. Home stay is a fundamental safety step that can limit infections from spreading widely. Regular physical activity and routinely exercising in a safe home environment should be maintained to avoid anxiety and depression and that constitutes a strategy for healthy living during the coronavirus crisis. However, appropriate and continuous hygiene practice and limit contact with people remains the best means of avoiding infection.

## CONFLICT OF INTERESTS

The authors declare that there are no conflict of interest

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