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The Role of Vitamin D and Zinc In Facing COVID-19 Injury

Yazi Abdullah Jassim^{a*}

^a Biology Department, College of Science, University of Babylon – Iraq

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ABSTRACT

There is no universal cure in treating patients with COVID-19. Although many countries have announced findings of extrapolation on the COVID-19 vaccine trial, it will be difficult to determine the urgent need for an urgent issue that will likely require several months, including vaccination. At the same time, a strategic, preventive, immune-enhancing approach should be considered to commit to strengthening the immune system to enhance host resistance to infection. Aim: This review article aims to review the current literature to explore scientifically discussed updates that stimulate the immune system as a prevention and treatment for COVID-19, based on its antiviral properties.

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1. Introduction

Global health has been experiencing its third coronavirus crisis in less than twenty years. SARS-CoV emerged in 2002 as 8422 people were reportedly infected and 916 killed worldwide. Following MERS-CoV in 2012 1401 were infected and 543 killed (Li, et al., 2020) and now nCoV (Wuhan), on December 31, 2019, the Wuhan Health Commission reported the outbreak of a mysterious new pneumonia in Wuhan City, which is progressing at a significant rate. As a result of research, it was concluded that Coronavirus is China (Kelvin & Rubino, 2020). Virus was linked to a wholesale seafood and animal market in Wuhan, China (Zhu, et al., 2020). This prevalence of infections and epidemics over the past 20 years indicates that coronaviruses, the situation is a threat to humanity, and it also affects the entire world economy (Li, et al., 2020). Coronaviruses were first identified in 1960 (Vahdat, et al., 2014). Therefore, the cooperation of health workers, governments and all people is needed to prevent the spread of new coronavirus. The first sequence of the 2019- nCoV genome was published online one day after approval by Zhang and other scientists at Fudan Shanghai University. Subsequently, on January 11, five more

genomic sequences of the virus were placed on the GSAID database by various institutes across China, and allowing researchers around the world to begin research on the new coronavirus (Zhu, et al., 2020). Isolation and sequencing of the successful genomic sequence of Coronavirus 2019- nCoV have been instrumental in understanding the origin of the virus and its infectious properties. However, there is still a lot of ambiguity and scientists are doing extensive research on this new virus. Following the outbreak of the virus, on January 30, 2020, the World Health Organization (WHO) issued a statement declaring the outbreak of new coronavirus to be the sixth leading cause of public health emergency worldwide, threatening not only China but all countries. On February 11, 2020, the WHO changed the name of the new coronavirus to COVID 19 (Lai, et al., 2020). On the same day, the International Committee on Taxonomy of Viruses (Coronaviridae Study Group) named it SARS-CoV-2 (Gorbalenya, et al., 2020; Liming, 2020). On March 11, the WHO upgraded the status of the COVID-19 outbreak from epidemic to pandemic.

The leading global challenge of COVID-19 pandemic crisis made the universe to remind ourselves to preserve and regulate better nutritional status to battle this virus

* **Corresponding author:** Yazi Abdullah Jassima, Biology Department, College of Science, University of Babylon – Iraq
 E-mail addresses: yaziabdalla2014@gmail.com

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It is evident that balanced nutrition impact the immunity; therefore, it has a substantial way to develop and strengthen the human system of immunity (Lai, et al., 2020; Gorbalyena, et al., 2020). While collecting pieces of evidence on our battle against COVID-19, we might have witnessed plenty of scientific and clinical reports that demonstrated the only compelling sustainable way to improve our fighting mechanism is to boost the immune system (Jayawardena, et al., 2020). In the perspective synthesis of immunity, this paper discusses the benefits of vitamin D, zinc supplementation, and the necessity of a healthy lifestyle (Tayyib, et al., 2020) by regular practices of yoga.

In the last months since the outbreak of COVID-19, the role of vitamin D in preventing COVID-19 infection has been the core debate on the topic. The statement issued by the "Joint Guidance on Vitamin D in the Era of COVID-19" issued by the American Society for Bone and Mineral Research, the Endocrine Society, and the American Society of Clinical Endocrinologists as of July 10, 2020, states that vitamin D is safe in a reasonable dosage which is required Vital for muscle and bone health. The main reason for the low level of vitamin D during this pandemic is due to individuals reducing their outdoor activities (Mc Call, 2020).

2. Materials & Methods

Zinc (Zn) is a dietary trace mineral and is essential for maintaining and developing immune cells of both innate and adaptive immune systems. Zinc deficiency results in dysfunction of both humoral and cell-mediated immunity and increases susceptibility to infectious diseases (Zhang & Liu, 2020). Besides, COVID-19 stress made every human to undergo stress and unprecedented consequences that necessitate the importance of regular exercises, relaxation strategies, self-care, and social connection that would facilitate with better sleep (Intermountain Healthcare, 2020). This paper tries to reveal the disrupted homeostasis that affects the immune system and also discusses the combination of vitamins and minerals (Vitamin D and Zinc). The comprehensive approach of healthy lifestyles added to the discussion to keep our body fit to battle against these coronaviruses.

2.1. Immunity and Vitamin D

It is now clear that vitamin D has important roles in addition to its classic effects on calcium and bone homeostasis. As the vitamin D receptor is expressed on immune cells (B cells, T cells and antigen presenting cells) and these immunologic cells are all are capable of synthesizing the active vitamin D metabolite, vitamin D has the capability of acting in an autocrine manner in a local immunologic milieu. Vitamin D can modulate the innate and adaptive immune responses. Deficiency in vitamin D is associated with increased autoimmunity as well as an increased susceptibility to infection. As immune cells in autoimmune diseases are responsive to the ameliorative effects of vitamin D, the beneficial effects of supplementing vitamin D deficient individuals with autoimmune disease may extend beyond the effects on bone and calcium homeostasis (Gombart, et al., 2020).

A large body of data from scientific communities and mainstream media showed the association between vitamin D and COVID-19. It linked the low-level vitamin D with respiratory infections, which suggested

hypovitaminosis is more likely one among the causative factors in Covid-19 infection and risk factors. The essential role of vitamin D that interplays with the cells of the immune system, such as B and T lymphocytes, macrophages, neutrophils, and dendritic cells, tends to decrease the secretion of cytokines (Pro-inflammatory), and enhances the release of cytokines (anti-inflammatory) (Di Rosa, et al., 2011). Worldwide, Spain, Italy, and India have a high prevalence of vitamin D deficiency, where age-specific highest fatality rate exist (Martineau & Forouhi, 2020; Lau, et al., 2020). Hypovitaminosis D is also prevalent in these nations, as compared to other nations. Shortage of B cell memory and divergent innate immunity are more likely to create a cytokine storm that is also observed among COVID-19 patients (Biesalski, 2020). A similar study emphasized the importance of the supportive therapy of vitamin C, and D, along with zinc supplementation to battle coronaviruses (Das, 2020).

There are retrospective studies that demonstrated the association between vitamin D and COVID-19, while others did not find the association though variables are adjusted. However, the correlation of vitamin D and the risk of acute viral respiratory infection (ARTI) and pneumonia has shown positive, including findings showed an inhibitory effect of viral replication or immunomodulatory impact. Safe and adequate vitamin D supplementation against ARTI has been discussed in a meta-analysis. Thus, vitamin D deficiency needs to be considered during this pandemic crisis to maintain circulating 25(OH)D at an optimum level (Ali, 2020).

Most importantly, patients admitted in the Intensive care unit significantly have an increased serum level of granulocyte colony-stimulating factor (GSCF), IP 10, and TN, which indicate a cytokine storm, an underlying reason for the disease severity (Harapan, et al., 2020). A study by Daneshkhah et al. showed the possible correlation of high C-reactive protein with severe Covid-19. Researchers associated the link to explore the crucial role of vitamin D in lowering the risk exposed to cytokine production and chronic inflammatory conditions of daily admitted, recovery, and deceased patients data with COVID-19. Daneshkhah also documented that cytokine storm can seriously damage lungs, which would lead to ARDS as an end-stage complication, that might kill, that might kill most of the COVID-19 patients. Destruction of the lungs is the complication, not the virus (Daneshkhah, et al., 2020). Several studies validated the pathogenesis of cytokine peak in order to modulate the immunity of the COVID-19 infected patients.

Backman believes that the significant role of vitamin D not only improves our immune system but also protects the immune system from becoming dangerously overactive. Hence it is understood that the appropriate level of vitamin D will protect all human beings against getting severe illnesses, including fatality from COVID-19. In vitro study by Dancer et al. hypothesized vitamin D deficiency in an experimental model with ARDS, resulted in profused epithelial damage, including exaggerated inflammation of alveolar cells and found that vitamin D has a tremendous trophic impact also affect >600 genes. They concluded that low-level vitamin D is one of the causative factors for developing ARDS (Dancer, et al., 2015; Nesburg, 2020).

Currently, COVID-19 represents the robust global humanitarian crisis where little is known about the

protective strategies of this infection. WHO committee on an emergency basis declared COVID-19 outbreak is an anticipated lengthy duration and insisting on the importance of national, regional, and global level efforts. Therefore, we need a platform towards preventive measures that can minimize the risk of infection, transmission, progression, and risk that are desperately required (UK Health Security Agency, 2021; NC for Immunization, 2021).

2.2. The Role Of Zinc In Immune Activity

Zinc plays a vital for a healthy immune system, correctly synthesizing DNA, promoting healthy growth during childhood, and healing wounds. As of the European Journal of Immunology, Zinc regulates immune function, and the human body needs Zinc to activate T lymphocytes (T cells), which help the body in two ways first controlling and regulating immune responses and second attacking infected or cancerous cells (WHO, 2020). Despite its benefits, deficiency can severely impair immune system function, and excessive zinc intake can be harmful and has severe adverse effects such, nausea, vomiting, loss of appetite, stomach pains, headaches, and diarrhea (Smith, et al., 2006; Simonet, et al., 2018).

Dietary sources of Zinc are absorbed in the small intestine and then distributed to peripheral tissues that account for 60% of Zinc, which is stored in skeletal muscle, 30% in bones, and 5% is stored in the liver and skin (Backhed, et al., 2015). The remaining percentage is distributed to other tissues such as the brain, kidney, and pancreas. Excess Zinc is excreted through gastrointestinal secretion, sloughing mucosal cells (Ishida, 2019; Razzaque, 2020).

In developing countries, according to the WHO, zinc deficiency is currently the fifth leading cause of mortality and morbidity that affects approximately one-third of the population globally. Zinc deficiency contributes to 16% lower respiratory tract infections, 18% malaria, and 10% diarrheal diseases. Nevertheless, globally severe Zc deficiency is rare; mild to moderate deficiency is prevalent worldwide (Gammoh & Rink, 2017). Zinc element is an essential micronutrient for human health. Zinc controls the enzymes that operate and renew the body cells, in which zinc play in the regulation of immune functions including cellular and humoral immunity and changes in the intracellular concentration of zinc ions control immune cell signal transduction by regulating the activity of major signaling molecules including kinases, phosphatases, and transcription factors. Zinc establishes an essential immune system, which zinc flux and zinc homeostasis control the adequate function of innate as well as adaptive immunity (Skalny, et al., 2020).

Zc deficiency, affects primarily the immune system, which is markedly susceptible to changes in levels of Zc (Vahdat, et al., 2014). Dietary Zn may influence the immune system that, at low concentrations of Zinc, it serves as an essential nutrient and functions as a metal cofactor for several enzymes, and high concentrations are relatively nontoxic. These concentrations have proven useful as an alternative dietary approach for molt induction. Moreover, Zinc deficiency, as well as zinc excess, results in severe disturbances in immunity, which can result in increased pathogenesis owing to susceptibility to infections and the development of

inflammatory diseases. Zinc can be recognized as a potential therapeutic for clinical use to contribute beneficially to the stability of patients suffering from immune and inflammatory diseases (Ishida, 2019).

2.3. The Role Of Zinc As An Antiviral

Zinc having the nature of anti-viral properties it is one of the micronutrients that could be taken to reduce the intensity of COVID-19 infection and perhaps lessen the respiratory tract infection for its anti-viral properties. Supplementation of Zc against rhinovirus infection, or "common cold" viruses, including the influenza virus, has shown promising anti-viral effects with reduced disease burden. Evidences mounted on Zc supplementation on reducing the in vitro replication of influenza causing viruses, the likely impact of nanoparticles Zc oxide, and inhibition of replication of syncytial virus (Bhardwaj, et al., 2020). During a pandemic crisis, a robust attempt to use Zinc to decrease disease burden is worth trying to. More significantly, consuming around 25-50 mg zinc in a day is affordable, and less likely to impact human toxicity, as >200 to 400 mg in a day of zinc consumption has shown to enhance adverse effects, including nausea, vomiting, epigastric pain, lethargy, and fatigue.

This opinion-based mechanistic discussion of the existing published information by Velthuis AJ et al. focused on the benefits of maintaining adequate Zinc to reduce COVID-19 associated illnesses load Of clinical significance, severe acute respiratory syndrome (SARS). COVID-19 virus replication has shown to be inhibited by Zinc. Furthermore, zinc supplementation in developing countries among children significantly reduced the prevalence of pneumonia. Despite How Zinc exerts its anti-viral effects are not yet apparent, scientific papers have raced its endeavors in revealing the inhibitory role of viral-binding mucosa in prohibiting subsequent replications. In vitro studies have shown that Zinc could induce the generation of anti-viral interferon (IFN)- and IFN- to exert anti-viral effects. Besides, Zinc could also suppress inflammatory events (Te Velthuis, et al., 2010).

Zinc induced anti-virus activity may be enhanced for Tcell division, maturation and differentiation, lymphocyte response to mitogens, programmed cell death of lymphoid and myeloid origins, gene transcription, and biomembrane function. Zinc-binding activity of human metapneumovirus (M21) protein was found to incorporate zinc ions, although the specific roles of the zinc-binding activity in viral replication and pathogenesis remain unclear. The pathogenic process or viral pathogenesis is the process by which an infection leads to disease that pathogenic mechanisms of viral disease include viral entry, local replication, and spread to organs and shedding of disease site (Haase & Rink, 2014).

Accordingly, the Zinc induced Zn²⁺ ion coordinated activity results in regulation of viral growth and may lead to virus death in host cell-virus interaction during the pathogenesis process. So viral prevention is a significant objective in human health. One attractive approach to prevention is the inhibition of virus replication [44]. In a recent study by Nahla et al. described the global prevalence of zinc deficiency using a conditional statement between zinc supplementation and the impact on treating COVID-19 patients. It was also mentioned that micronutrient supplementation at an optimal level would not create an adverse effect (Lai, et al., 2020).

3. Conclusion

Although the leading health authorities of national and international health institutions, the Centers for Disease Control and Prevention, and the World Health Organization consistently providing standard guidelines focusing on treatment, prevention, and promotion perspectives, this article mechanistically discussed the host immunity about Zinc, Vitamin D, and a comprehensive approach towards COVID-19

Competing Interests

The authors have declared that no competing interests exist.

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