A review of the effect of COVID-19 on immune responses of the body

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ABSTRACT

After the world faced the epidemic of COVID-19 caused by the novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), novel clinical evidence and genetics related to this virus are emerging. This virus presents a broad range of clinical manifestations that mainly include various asymptomatic infections and severe pneumonia that are followed by multiple organ failures which could lead to death. The immune system has a critical role in the protection of the body against viruses and diseases and the production of antibodies against pathogens. The present study aimed to investigate the effect of COVID-19 on immune responses of the body. A comprehensive collection of related clinical trials and reviews on the issue of COVID-19 were searched. The main focus of the reviewed studies was on immune response in COVID-19. In this regard, various databases of PubMed, EMBASE, Scopus, CINAHL Plus, Cochrane Library, and Google Scholar were reviewed and all related articles from 2010 to 2021 were investigated. All records were searched in the English language and finally records with the highest thematic relevance were included in the main criteria of the study. It is well-known that the immune system’s response to the SARS-CoV-2 virus involves all the components of the immune system that are responsible for viral elimination and recovery of the body. However, these immune system responses are involved in the progression of COVID-19 to a severe and lethal process. When the period of COVID-19 in the body increases, the regulation between protective and altered responses will be lost because of exacerbation of the inflammatory components. Therefore, all the responsible factors which affect immunity should be investigated just like that performed in this study.

Keywords: Coronavirus, COVID-19, immune system response, inflammation

Introduction

Nearly all around the world, the expansion of COVID-19 has had destructive effects on human lives. This disease is highly contagious and rapidly will be spread among humans that causes severe infections which lead to death. Such patients need specialized medical care under the supervision of specialists in intensive care units (ICU). Consequently, on January 30, 2020, the World Health Organization (WHO) declared this situation as a Global Sanitary Emergency. Coronavirus comprises four genera named alpha, beta, gamma, and delta coronaviruses. The novel coronavirus which causes severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) belongs to the beta genus. SARS-CoV is its most similar relative to this virus among human coronaviruses with about 80% genetic similarity. Anyway, with nearly 95% similarity, the most similarity of SARS-CoV-2 is with bat coronavirus RaTG13.

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The receptor-binding domain of the SARS-COV-2 spike protein (S protein) has six amino acids that are correlated with the Angiotensin-converting enzyme 2 (ACE2) receptor. Additionally, the polybasic cleavage site of S proteins is not the same as previous ones that make SARS-CoV-2 more aggressive to cause cellular infections among humans. One of the most important aspects of the COVID-19 crisis is the speed of development of related research studies which provides the possibility of comprehension of risk factors, transmission dynamics, epidemiology, and clinical manifestations. Moreover, the etiological agents such as molecules, morphological structure, and its genome should be identified as well as their relationship with other coronaviruses. Other important aspects that should be highlighted include the entrance of the virus into the host cells through binding the Angiotensin II Converting Enzyme (ACE2), the responses of the immune system in infected patients, and intracellular replication during this disease.

In this regard, various clinical trials and review studies should be conducted for the development of effective medical tests, appropriate strategies for clinical management, development of beneficial antiviral agents, and finally, introducing ways to improve the function of the immune system. The present review study is aimed to investigate the effect of COVID-19 on immune responses of the body. Consequently, all the inflammatory and protective responses following the clinical spectrum of COVID-19 ranging from presentations without and symptoms to severe disease should be investigated.

**Method**

A comprehensive collection of related clinical trials and reviews on the issue of COVID-19 were searched. Special keywords of Coronavirus, SARS-CoV-2, COVID-19, Inflammation, and Immune system response were used for exploring various medical databases of PubMed, EMBASE, Scopus, CINAHL Plus, Cochrane Library, and Google Scholar. Among all searched, those which were in the time period of 2010 to 2021 were selected. Due to the diversity of available articles in various languages, just articles that were in English were selected to be studied. On the basis of the steps mentioned in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) method the process of selection of articles was carried out in four main steps of Identification, Screening, Eligibility, and Included. At first 238 articles were searched which were deleted because of similarity and in some cases being duplicated. After that, and records were deleted due to thematic dissimilarity and some specific reasons respectively. Finally, extra related records found from other available resources and added to inclusion criteria of the study.

**Initial characteristics**

Wuhan in China was the first place that the emergence of pneumonia of unknown causes was reported in December 2019. Nearly all the initially detected cases were epidemiologically linked to the Wuhan South China Seafood Wholesale Market named Huanan. After that, it was found that the appeared pneumonia was due to beta coronavirus that was discovered from the samples collected from the lower respiratory tract of affected patients. In this regard, for separating the 2019–novel Coronavirus (2019–nCoV), epithelial cells of the human airway were used.

Using an electron microscope it was observed that the diameter of this virus is nearly similar to those of the Coronaviridae family from 60 to 140 nm with particular spikes of 9 to 12 nm. From a phylogenetic point of view, it was revealed that the novel coronavirus exactly looks like bat-derived coronavirus strains with a similarity rate of 90%. While its similarity to humans SARS virus and MERS is less, with similarity rates of 80% and 50% respectively. On February 11, 2020, the Coronaviridae Study Group of the International Committee on Taxonomy of Viruses named the novel coronavirus based on phylogeny and taxonomy as SARS–CoV2. The resultant disease caused by this virus was named Coronavirus disease (COVID-19) by the WHO. After the identification of the situation of this disease across the globe by WHO, COVID-19 was declared as a pandemic on March 11, 2020 [Figure 1].

**Epidemiology**

Due to the rapid spread of COVID-19, there should be a wide range of information on the epidemiology of this disease to provide adequate data for the development of suitable strategies for controlling COVID-19 disease. After the outbreak of COVID-19 because of SARS-CoV-2 in December 2019 from Wuhan, China, it rapidly spread throughout China and all around the world and becomes a massive threat to public health. On the basis of the data presented by WHO, up to now more than 126M cases of COVID-19 have been reported worldwide, of which nearly one-fourth were in the USA and the rest in other countries. Reports also indicate that there have been 2.77M
deaths in the world and fortunately 71.5M have been recovered. However, SARS–CoV2 quickly crosses the borders of many countries, and unfortunately, every day more individuals from different countries have been involved in COVID-19.[19]

Some countries such as South Korea, Taiwan, Singapore, Thailand, and Japan due to their proximity to China, were among the first countries affected by SARS–CoV2. Among them, Japan was the most affected country by COVID-19 that initially was transferred to there by cruise ship passengers. Uncontrolled direct air communication of other countries with China was the main reason for the spread of COVID-19 into the borders of other countries in the world.[20]

Despite all these facts, having an accurate comprehension of the transmission risk is incomplete. The initial epidemiological studies at the beginning of the outbreak revealed that there is a close association between the seafood market in Wuhan and COVID-19. Anyway, after the progression of the outbreak, the main mode of transmission was introduced to be person-to-person spread.[21]

The primary way of transmission of SARS-CoV-2 is the direct person-to-person respiratory transmission.[22] When individuals are in close contact, respiratory particles could be transferred easily between them. In affected individuals, the virus could be transmitted through their respiratory secretions when talking, sneezing, and coughing and infect other individuals especially if it sticks into the mucous membranes. Another way that infection could be transferred to other individuals is when the nose, mouth, or/and eyes be touched by contaminated hands.[23]

In a population susceptible to serious Illness from COVID-19, the basic reproduction number is the expected number of secondary cases that are expected to arise from the affected case. The main essence of the epidemiology of infectious disease is the basic reproduction number that indicates the risk of an epidemic spread. On the basis of the relevant studies, the basic reproduction number for SARS–CoV2 is estimated to be in a range of 2.0 to 3.0.[24] The secondary attack rate is another parameter that determines infectivity. The secondary attack rate is defined as the possibility of occurrence of infection in a particular group of susceptible populations who are exposed to a primary case. To understand the fact that how social behaviors affect transmissibility, the rate of secondary attack should be investigated. A study by Burke et al.[25] revealed that the rate of secondary attack among household contacts from the United States and South Korea were nearly similar with the percentages of 10.5% and 7.5% respectively.[25]

All around the world, the implementation of strategies of community mitigation, and differences in timing could be beneficial to the decrement of the prevalence of COVID-19 among various geographic regions.[26] Various mitigation practices could be applied for the reduction of viral transmission, which includes contact tracing, mask policies, shelter in place orders, and gathering limitations that have been implemented on local, state, and national levels. Mitigation strategies that are timed effectively are capable of decreasing the rate of infection, hospitalizations, and mortality.[27]

In spite of the effectiveness of these strategies in some countries, the inability to implement and poor timing was the main limitation to these strategies. Other limiting factors including lack of awareness about COVID-19, opposition to face coverings, and laissez-faire policies have led to a disturbing rise in the rate of COVID-19 worldwide.[28]

**Process of the immune system**

All the organs of the body’s immune system protect you against diseases and have a significant role in maintaining the body’s healthy and pathogenesis. Moreover, it protects the body from cell changes, germs, and harmful substances.[29,30] Various organs of the immune system are demonstrated in [Figure 2]. White blood cells have the most significant role in the immune system of which travels throughout the body inside the blood vessels. The body exchanges fluids and cells between lymphatics and blood that gives the possibility of monitoring invading microbes to the lymphatic

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**Figure 2:** Illustration showing the various organs of the immune system

**Figure 3:** Adaptive and Innate immune system
### Table 1: Effect of COVID-19 on various organs of the body

| Diseases                                      | Mechanism of action                                                                 | Further syndromes and consequences                                                                 | More details                                                                 | Treatments                                      |
|-----------------------------------------------|--------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|-----------------------------------------------|
| **Inflammation and endothelins**<sup>[35,36]</sup> | It infects the endothelial cells in multiple organs It could cause an increment in cytokines by white blood cells Increment of catecholamines called cytokine release syndrome or hypercytokinemia | Systemic inflammatory response syndrome (SIRS) Acute respiratory distress syndrome (ARDS) Multi-organ injury Shock Death | This leads to vasoconstriction and diffuse lymphocytic endothelitis Causes hyperperfusion that leads to organ ischemia | Anti-cytokine biologics Immunomodulatory therapies |
| **Effect on coagulation**<sup>[37‑40]</sup>       | Impair fibrinolysis and hypercoagulability due to inflammation and fever It increases antiphospholipid antibodies that cause thrombosis Increment of procoagulant substances in the liver | Deep vein thrombosis (DVT) Cor pulmonale Pulmonary embolism (PE) Venous thromboembolism (VTE) Myocardial infarction (MI) Ischemic stroke | DVT and PE could lead to death Could cause platelet activation, Hypercoagulability, Endothelial dysfunction, Constriction of blood vessels Disseminated intravascular coagulation (DIC) | Direct oral anticoagulant such as rivaroxaban and/or apixaban Heparins (downregulates Interleukin 6 (IL-6) and decreases immune activation) Systemic anticoagulation Extended-duration venous thromboembolism (VTE) prophylaxis High-flow nasal cannula (HFNC) oxygen therapy Prone positioning for improving oxygenation |
| **Pulmonary effects**<sup>[41‑43]</sup>          | Disruption of alveolar and endothelial cells Cellular and fluid exudation Formation of hyaline membrane Vascular angio genesis | Could cause classic diffuse alveolar damage Organizing pneumonia Acute fibrinous Airway inflammation Alveolar and interstitial edema | CT findings show ground-glass opacity and consolidation on chest | Anticoagulation therapy (for acute coronary syndrome) Fibrinolytic therapy Percutaneous Coronary Intervention (PCI) Angiotensin II receptor blockers (ARBs) Angiotensin II receptor blockers (ARBs) Angiotensin-converting enzyme (ACE) inhibitors Peritoneal dialysis (Due to the shortage of continuous renal replacement therapy) Placing the catheter on the side of the abdomen could be effective Sedative (Such as dexmedetomidine and propofol) Benzodiazepine |
| **Cardiac effects**<sup>[44,45]</sup>            | Plaque rupture and thrombosis Inadequate oxygen supply | Ischemic cardiac injury Myocarditis (Due to a systemic inflammatory response) Heart failure and arrhythmias Brain-type natriuretic peptide (BNP) elevation (Leads to death) | Invasion of the virus to muscle cells may happen Diabetes, obesity, age, and hypertension (risk factors leading to death) Myocarditis more likely to happen in younger patients | | |
| **Renal effects**<sup>[46,47]</sup>              | SARS-CoV-2 virus infects the cells through the angiotensin-converting enzyme 2 (ACE2) receptor Cytokine storms | Acute kidney injury (Due to hyperventilation antivirals such as redeliver) | Patients may experience fever and diarrhea | Anticoagulation therapy (for acute coronary syndrome) Fibrinolytic therapy Percutaneous Coronary Intervention (PCI) Angiotensin II receptor blockers (ARBs) Angiotensin-converting enzyme (ACE) inhibitors Peritoneal dialysis (Due to the shortage of continuous renal replacement therapy) Placing the catheter on the side of the abdomen could be effective Sedative (Such as dexmedetomidine and propofol) Benzodiazepine |
| **Effect on brain**<sup>[48,49]</sup>            | In the brain stem and cerebral cortex, the ACE2 receptors are present SARS-CoV-2 virus causes oxygen starvation in brain stem Brain inflammation and edema due to cytokine storms Elevated serum creatine kinase | Neurological manifestations Stroke Cerebral hemorrhage Seizure Araxia Encephalitis Headache Impaired consciousness Meningitis Delirium Inability to rouse Acute disseminated encephalomyelitis (ADEM) | Hypoxic changes are available in the brains of dead patients Cranial nerves may be involved The impaired sense of taste, dysgeusia, and anosmia are reported | | |
| **Effect on eyes**<sup>[50,51]</sup>             | Availability of both transmembrane serine protease 2 (TMPRSS2) and ACE2 receptors in ocular surface cells, in the white of the eye, inside the eyelid, and in the cornea superficial cells of the eye are reservoirs and portals of entry of the virus | Ocular abnormalities (conjunctivitis) | Primary Ocular involvement eye viral infection could remain in the eye for about three weeks | | |

*Contd...*
Table 1: Contd...

| Diseases                        | Mechanism of action                                                                 | Further syndromes and consequences                                      | More details                                                                 | Treatments |
|---------------------------------|--------------------------------------------------------------------------------------|---------------------------------------------------------------------------|------------------------------------------------------------------------------|------------|
| Gastrointestinal effect[52,53]  | Overactive immune response mainly to drugs that damage the liver                     | Abdominal discomfort or pain                                              | Cough, myalgia, fever are further possible symptoms                          | -          |
|                                 | Availability of ACE2 receptors in the lower GI tract                                 | Diarrhea                                                                  | Availability of intact infectious virus in some patients’ stool               |            |
|                                 |                                                                                        | Vomiting                                                                  |                                                                              |            |
|                                 |                                                                                        | Nausea                                                                    |                                                                              |            |
|                                 |                                                                                        | Loss of appetite                                                          |                                                                              |            |
|                                 |                                                                                        | Injury to the bile ducts or liver                                         |                                                                              |            |
| Effect on skin[54]              | Abnormalities of blood clotting                                                      | Petechiae                                                                  | Mainly the trunk is affected                                                 | Lesions will be healed Spontaneously in a few days. |
|                                 |                                                                                        | Rosacea                                                                   |                                                                              |            |
|                                 |                                                                                        | Psoriasis                                                                 |                                                                              |            |
|                                 |                                                                                        | Eczema                                                                    |                                                                              |            |
|                                 |                                                                                        | Acne                                                                      |                                                                              |            |
|                                 |                                                                                        | Neurogenic problems                                                       |                                                                              |            |
|                                 |                                                                                        | Microthrombotic Complications                                             |                                                                              |            |
|                                 |                                                                                        | Immune complex-mediated problem                                            |                                                                              |            |
|                                 |                                                                                        | Chickenpox-like fluid-filled vesicles                                     |                                                                              |            |
|                                 |                                                                                        | Livedo reticularis (LR)                                                   |                                                                              |            |
| Psychological effects[55]       | Social isolation and financial difficulties                                           | Deaths of despair                                                         | Individuals with autism, mental illness, and dementia face greater risks     | Meeting friends or/and support professionals could be effective             |
|                                 |                                                                                        | Suicide                                                                   | Alzheimer’s or Parkinson’s disease (As long-term effects)                   |            |
|                                 |                                                                                        | Substance abuse                                                           |                                                                              |            |
|                                 |                                                                                        | Dysexecutive syndrome                                                     |                                                                              |            |
|                                 |                                                                                        | Anxiety                                                                   |                                                                              |            |
|                                 |                                                                                        | Depression,                                                              |                                                                              |            |
|                                 |                                                                                        | Post-traumatic stress disorder (PTSD)                                     |                                                                              |            |

Table 2: Different factors that could affect the immune system of the body

| Factors                        | Effectiveness                                                                 | Recommendation                                                                 | Borderline                                                                 | More Details                                                                 |
|---------------------------------|-------------------------------------------------------------------------------|--------------------------------------------------------------------------------|----------------------------------------------------------------------------|-------------------------------------------------------------------------------|
| Diet[64]                        | The diet affects the overall health and immunity                             | Diets with low-carb (Controlling blood pressure and sugar)                    | Follow the correct dosage of supplements                                  | Some herbs improve your immunity: Black cumin, Basel leaves, Garlic Melon seeds, pumpkin seeds, Flaxseed, and sunflower seeds are full of vitamin E. |
|                                 | Controlling diabetes                                                         | A diet full of:                                                              | Sleep lower than 7 h impairs your brain activity and leave you tired       | The lack of sleep impairs body function and prevent the body from resting     |
|                                 | Protein enrichment                                                           | Bell pepper                                                                  | Drink more than 8 glasses of water                                        | For beating the heat, some alternatives could be used such as coconut water, citrus fruits juices |
|                                 | Eat fruits and vegetables a lot                                              | Tomato                                                                      |                                                                              |                                                                                |
|                                 | Supplying Ascorbic acid, Beta carotene, and essential vitamins                | Mushrooms                                                                   |                                                                              |                                                                                |
|                                 |                                                                                | Spinach                                                                      |                                                                              |                                                                                |
|                                 |                                                                                | Broccoli                                                                     |                                                                              |                                                                                |
|                                 |                                                                                | Omega 3 & 6 fatty acids                                                     |                                                                              |                                                                                |
|                                 |                                                                                | Consumption of vitamin E boosting immunity                                  |                                                                              |                                                                                |
| Sleeping[66]                    | Well sleeping increases the immunity of your body                             | Sleep well for about 7-8 h a day                                            | Sleep lower than 7 h impairs your brain activity and leave you tired       | The lack of sleep impairs body function and prevent the body from resting     |
| Water consumption[67]           | Staying hydrated is critical for staying healthy and improving the function of the heart, brain, and muscles | Drink 8-10 glasses of water daily                                           | Drink more than 8 glasses of water                                        | For beating the heat, some alternatives could be used such as coconut water, citrus fruits juices |
| Exercise[68]                    | Improves your body metabolism                                                | Following an appropriate diet, have an exercise routine                      | Exercise at least for half an hour (based on your stamina)                 | The metabolism of your body is directly correlated with body immunity         |
|                                 | Exercise releases the toxins from your body                                  |                                                                              |                                                                              |                                                                                |
| Stress[69]                      | Stress decreases immunity                                                    | Practice mindfulness                                                        | Quarantine and staying home long decreases your mental wellbeing          | Take your health seriously and schedule telehealth appointments              |
|                                 |                                                                                | Prioritize exercise                                                         |                                                                              |                                                                                |
|                                 |                                                                                | Keep the virtual connection with your friends                               |                                                                              |                                                                                |

system. Each lymph gland contains specialized sections that provide the potential of encountering antigens. The immune cells and foreign particles enter the lymph gland through the incoming lymphatic vessels and after entering the bloodstream, are transported to tissues all over the body. Immune cells continue the cycle all over the body to find any foreign antigens and then go back to the lymphatic system. The main role of immune cells is to confront antigens in the spleen’s compartments and lymph glands.[31,32]
**Effect of COVID‑19 on the organs**

The respiratory system is the most common biological system that SARS-CoV-2 is developed in easily. Anyway, this virus is capable of affecting any other organs in the body, and patients with severe disease, multiple organs are affected. SARS-CoV-2 binds to angiotensin-converting enzyme 2 (ACE2) receptors in various organs on the body such as kidneys, brain, heart, liver, intestine, lungs, pharynx, and any other tissues with vascular endothelial cells. COVID‑19 directly injures all the organs in the body. Additionally, systemic disease caused by SARS-CoV-2 leads to organ dysfunction. So, during the management of COVID‑19 patients, evaluation of all their multiple organs of the body for any possible injuries is essential. The vascular endothelium and coagulation disorders are the most common disturbances with a lower possibility of leading to symptoms in the early stages. Anyway, they cause injuries in multiple organs. Among patients who die, renal and cardiac dysfunction are the most common ones. One of the main challenges in this disease is that injured organs might be detected a long time after the subsidence of the acute infection. In this regard, various organs of the body may be affected altered and then chronic injury may happen while their rehabilitation would be difficult and take long time.

COVID‑19 disease could cause a variety of diseases due to the effect of the SARS–CoV2 virus on various organs of the body that all are summarized in [Table 1].

**The responses of the immune system to COVID‑19**

Due to the lack of adequate therapies for controlling and treatment of COVID‑19, the immune system is the best defense option supporting the body’s natural ability to defend against resists infections and pathogens. If the immune system functions normally itself, the infectious diseases such as COVID‑19 could not be noticed. As could be seen from [Figure 3] two main types of immunity are innate immunity (rapid response), adaptive immunity (slow response). Just like in COVID‑19 disease, the first time when the body encounters viruses or germs, the function of immune system will be disrupted and illness could occur. Educating the immune cells provides the possibility of improving their functional efficiency by migrating them and from sites of injury via blood and recirculating between central and peripheral lymphoid organs.

**Improving the performance of immune system**

When there is not any remedial option or vaccines for controlling or treatment of COVID‑19, the efficiency and functionality of the immune system response has the most critical role in defending the body against viral infections. Several microelements, vitamins, and nutrients are available that have a critical role in the enhancement of immune system responses to function normally. In addition, providing these nutrients using dietary supplementation could have a lot of advantages to the immune responses to viral infections. Various clinical investigations have demonstrated that the supplementation of vitamins D and A improves the humoral immunity of pediatric patients after influenza vaccination. In patients with transfusion-transmitted infection (TTI), dietary supplementation enriched with zinc could improve immunity. Moreover, high doses of selenium improve the immune response after administration of influenza vaccination.

Some relevant studies have demonstrated that probiotics, herbal therapeutics, and several micronutrients could improve the function of the immune system in the prevention and treatment of viral infections. However, some special nutraceuticals have shown to have immunomodulatory effects. One of the main causes of increment of illness and mortality is malnutrition, which remarkably influences the healthcare system and economic situations of each country. Immune homeostasis could be regulated by providing essential nutrition. Any deficiencies of micronutrients will disturb the immune response. Some of the main consequences of malnutrition are delayed recovery and increment of infection rates. When the body is infected, the body will need various nutrients more. In a recent study Calder et al revealed that providing balanced nutrition is critical for improving the immune responses against viral infection. Another study by Alagawany et al also showed that the availability of some probiotics and nutraceuticals could be beneficial in the prevention and management of COVID‑19 disease.

Aiming to boost the immune system of the body against coronavirus and decrease the infection risk, several strategies are available that are summarized in [Table 2].

**Conclusion**

Having knowledge about the main mechanism and process of the immune system function could be considered as an acceptable source of knowledge for the development of immune system responses. In this regard, it is recommended that further investigations carried out on the clinical observations regarding COVID‑19 treatment. The most fundamental achievement is when all the available challenges being solved. Improvement of immunity function against pathogens is not a simple process and normally will be happening over a period of 2 weeks. In the absence of an appropriate medicine for the prevention or treatment of COVID‑19 patients, the body immediately responds to the viral infection in which accessory cells, neutrophils, and macrophages slow down the progress rate of the virus and also are capable of preventing it from causing subsequent symptoms.

Keeping healthy styles of living decreases the possibility of being affected with COVID‑19. In this regard, developing healthy lifestyle habits boosts immunity and decreases the rate of inflammation among COVID‑19 patients. Keeping some healthy habits such as breathing exercises, walking, and maintaining a healthy eating lifestyle improves the capacity of the lung as well as the immunity of the body. Consumption of anti-inflammatory herbal foods such as cinnamon and ginger is proven to improve immunity and decrement of COVID‑19 severity. Finally, investigating around sufficient nutrition to improve the immune system function should be considered as a critical choice in line
with the administration of other clinically approved medicines for the prevention and treatment of COVID-19.

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Conflicts of interest
There are no conflicts of interest.

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