Delta University Scientific Journal
Journal home page: https://dusj.journals.ekb.eg

Review article

COVID-19 infection: an overview on Coronavirus Characteristics, Post Covid Syndrome, Treatment and Role of Nutrition and Supplementation

Rasha M. El-Morsi[1], Faris M. Abdel Hai[2], Ahmed S. Al-Shahat[2], Iman E. El Sheikh [2], Asma D. Othman[2], Reem M. Al Shafei[2], Mahmoud M. Al-Alfi[2], Seif El-Din R. Ismail[2], Aya E. El-Metwally[2], Maha A. Zahran[2], Nadi A. Shawqi[2], Heba A. Ramadan[1]

[1]*Department of Microbiology & Immunology, College of Pharmacy, Delta University For science and Technology, Gamsa, Egypt.*

[2]*Department of Microbiology & Immunology, member of graduation project in Delta University For science and Technology, Gamsa, Egypt.*

*Corresponding author: Rasha Medhat, Department of Microbiology & Immunology, Delta University For science and Technology, Gamsa, Egypt, Email: rashamedhat07@gmail.com

ABSTRACT

COVID-19 is primarily a viral respiratory illness caused by SARS-CoV-2, that has posed a serious threat to world health. Most patients who contract this virus typically develop pneumonia. Based on the broad clinical manifestations associated with multi-organ involvement, COVID-19 is now considered as a systemic disease. It typically affects the respiratory, cardiovascular, and hematopoietic systems. In addition, to a lesser extent, the neuropsychiatric, renal and endocrine systems are also involved. The immediate complications of COVID-19 are well defined and often associated with increased mortality. However, long-term complications of COVID-19 are increasingly associated with morbidity.
This work aimed to describe the etiology, epidemiology, clinical features and complications of COVID-19. In addition; it summarized the latest available treatments for COVID-19 infection.

Key words: *COVID-19, viruses, vaccine,* complications.

Introduction

1. What is coronavirus?

Coronavirus disease of 2019 (commonly referred to as COVID-19) is caused by a virus from the Coronaviridae family that causes severe acute respiratory syndrome. Coronavirus (CoVs) can infect patients of all ages, mainly through airborne droplets and aerosols. The 2019 coronavirus disease was first identified in the city of Wuhan in China in 2019, causing the worst global pandemic in recent history in a very short period of time (Tamimi et al., 2022). Based on the WHO epidemiological data, five SARS-CoV-2 VOCs have been identified since the start of the pandemic, includes; Alpha: first worrying variant described in the United Kingdom at the end of december 2020, then, Beta: first reported in december 2020 in South Africa, followed by Gamma: first reported in Brazil in early January 2021, Delta: first reported in December 2020 in India and finally, Omicron: first reported november 2021 in South Africa (Cascella et al., 2022).

Genomic characterization has shown that bats and rodents are the likely genetic sources of Alpha-CoV and Beta-CoV. On the contrary, bird species seem to represent the genetic sources of Delta-CoVs and Gamma-CoVs. Coronavirus have become the main causative agents of respiratory disease epidemics. Members of this large family of viruses can cause respiratory, intestinal, liver and neurological diseases in various animal species, including camels, cattle, cats and bats (Cascella et al., 2022). These viruses can cross species barriers and can cause diseases in humans ranging from the common cold to more serious illnesses like MERS and SARS. Seven human CoVs have been identified that can infect humans. Overall, estimates suggest that 2% of the population are healthy carriers of CoVs and that these viruses are responsible for approximately 5-10% of acute respiratory infections. (Tamimi et al., 2022).

2. Signs and symptoms of covid-19

The most important signs and symptoms include the following; cough, fever or chills, fatigue, shortness or difficulty breathing, headache, muscle pain, new loss of taste or smell, runny nose, nausea, vomiting and diarrhea (Elliott et al., 2021). Patients with severe COVID-19 infection from SARS-CoV infection may develop an acute respiratory distress syndrome (ARDS). It has been discovered that cytokine storm is an immune reaction to viral infection. Therefore, severe COVID-19 patients exhibited a significant rise in cytokines like IL-2, IL-7, IL-10, monocyte chemoattractant protein-1 (MCP1), granulocyte colony-stimulating factor (GSCF), macrophage inflammatory protein 1A (MIP1A), IFN-g-induced protein-10 (IP10), and tumour necrosis factor-a (TNF-a), which may have extremely harmful effects. As a result, an essential treatment method to preserve the lives of patients, is the administration of potent anti-inflammatory medications (Elebeedy et al., 2021).

3. Complications and post covid syndrome

3.1. Complications of the Immune System:

The chain of immunological events associated with SARS-CoV-2 is characterized by the evolution of adaptive immunity (mediated by T and B lymphocytes) to the virus. Guillain-Barré syndrome (GBS) has been linked to COVID-19. This disease is characterized by an abrupt evolution, with an inflammatory cascade of the peripheral nerves and loss of the myelin sheath (polyneuropathy). GBS has been reported in clinical trials in adult, young and child patients during or after coronavirus infection. Symptoms ranged from severe respiratory complications to motor paralysis (Silva Andrade et al., 2021).

Rheumatoid arthritis (RA) associated with COVID-19 has been widely described in case reports and observational studies. The study identified 456 rheumatic patients with an average age of 63 and showed the highest risk factor for severe COVID-19 (28.1%) in positive patients who were continuously taking immunosuppressants. These results were consistent with other studies by Haberman et al. (2020). Additionally, a cross-sectional study of the effects of COVID-19 on rheumatic patients found that patients presented with arthralgia, myalgia, and weakness, with manifestations that preceded respiratory symptoms of COVID-19. Autoinflammatory diseases, including Kawasaki disease (KD), have been reported in children. This disease mainly affects children under five years old and is characterized by an acute inflammatory process in small and medium caliber vessels, showing greater cardiac involvement and greater inflammatory response with activation of macrophages. (Silva A Andrade et al., 2021).

3.2. Complications of the Hematological System:

The hematological system and hemostasis are significantly impacted by the systemic infection COVID-19. Lymphopenia is a significant laboratory result that has the ability to predict outcome. Peak platelet/lymphocyte ratio and neutrophil/lymphocyte ratio may also be prognostic indicators for serious cases. In order to identify instances with a poor prognosis and initiate treatment as soon as possible in order to improve outcomes, longitudinal analysis of lymphocyte count dynamics and inflammatory markers, such as LDH, CRP, and IL6, may be useful along the course of the disease. High blood procalcitonin and ferritin levels are two biomarkers that have been identified as poor prognostic indicators. Furthermore, hospitalised COVID-19 patients frequently have blood hypercoagulability. Although elevated D-Dimer levels are frequently observed, their progressive rise over the course of an illness is particularly linked to the deterioration of that condition. PT and other coagulation anomalies (Terpos etal., 2020).

3.3 Complications of the Pulmonary System:

Pulmonary complications accompanying the ongoing-COVID-19 phase are mainly secondary infections, lung function impairment, pulmonary thromboembolic disease (pulmonary embolism, stroke), pulmonary hypertension, pulmonary fibrosis, cavitary lesions and small airway diseas. In the post-COVID-19 period, lung function impairment, in particular reduced diffusing capacity, ILD including pulmonary fibrosis, bronchiectasis, tracheomalacia and small airway disease are most frequently observed (Jakubec etal., 2022).

3.3. Complications of the Cardiovascular System:

Pathophysiological findings in patients with SARS-CoV and MERS-CoV have shown that both are associated with myocardial damage, myocarditis and heart failure. In contrast, the main mechanisms of myocardial injury are heterogeneous and primarily involve the cardiopulmonary and vascular systems. In these cases, the cardiovascular system is affected in several ways by a severe acute respiratory tract infection with SARS-Cov-2. Myocardial injury is identified in 25% of hospitalized patients with COVID-19 and is associated with an increased risk of mortality. The occurrence of major cardiovascular events such as type I and II acute myocardial infarction associated with SARS-Cov-2 infection significantly increases the risk of cardiac injury. Growing clinical evidence and epidemiological findings have shown that patients with cardiovascular comorbidities may be associated with an increased risk of death from COVID-19. Additionally, gross histopathological findings at autopsy of COVID-19 patients showed signs of chronic heart disease, including myocardial hypertrophy (92.9%), mild to severe coronary artery atherosclerosis (100%), and focal myocardial fibrosis (21.4%). Acute myocardial infarction was an additional cause of death in 21.4% of patients (Silva Andrade et al., 2021).

3.4. Complications of Nervous System:

Although severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) is regarded as a respiratory infection, acute COVID-19 is accompanied with a wide range of neurologic consequences, including disorientation, stroke, and neuromuscular abnormalities. As part of a group of symptoms now known as Long Covid, illnesses like poor attention, headaches, sensory abnormalities, depression, and even psychosis may last for months after infection. Acute COVID-19 and Long COVID neuropsychiatric disorders can manifest in even young people with minimal initial illness. Although evidence generally points to immunological dysfunction, including generalized neuroinflammation and antineutral autoimmune dysregulation, the pathophysiological processes are not well understood (Spudich and Nath, 2022).

3.5. Complications and Impacts on Mental Health:

In addition to physical illnesses, the COVID-19 pandemic has taken a heavy toll on the mental health of the world's population. Quarantine and self-isolation were the main measures taken to prevent the spread of the disease, resulting in an abrupt change in people's lifestyles, causing panic and fear in a significant number of people. Studies have shown that stress was identified as the most common mental health consequence (48.1%) of the COVID-19 pandemic, followed by depression (26.9%) and anxiety (21.8%). Healthcare professionals working to combat COVID-19 have been more severely affected by psychiatric disorders related to depression, anxiety, insomnia, stress and indirect trauma than other professions (Silva Andrade et al., 2021).

4- Treatments of covid-19:

4.1 Old treatment for covid-19

There are some potential therapeutic agents for treating COVID-19, such as antivirals, chloroquine / hydroxychloroquine as an antimalarial drug, dexamethasone (anti-inflammatory), and restorative plasma transfusion, but most still show inconsistent results. Various antiviral drugs are being researched as a treatment for COVID-19. Remdesivir is one of the antivirals used for COVID-19 and is known as an adenosine analog that can be assembled into viral RNA chains resulting in its premature termination, but the remdesivir clinical trial was terminated early due to severe side effects in the treatment and control groups (Gautret et al., 2020).

Lopinavir/ritonavir is a fixed-dose antiviral combination used to treat HIV infection. Lopinavir/ritonavir use reduced intubation rate, steroid requirements and mortality in patients with SARS. This study reported that the use of lopinavir/ritonavir in COVID-19 could reduce mortality (Verdugo et al., 2020).

4.2 New treatments for covid-19

New treatments are needed to reduce the risk of progression of coronavirus disease 2019. An example is Paxlovid (oral antiviral drug from Pfizer), which is a combination of two antiviral drugs, namely; nirmaltrelvir and ritonavir.
Nirmatrelvir is an orally bioavailable protease inhibitor that is in clinical trials. Which is responsible for the cleavage of polyproteins 1a and 1ab of SARS-CoV-2. Without protease enzyme activity, non-structural proteins cannot be released to perform their functions, thereby inhibiting viral replication. Ritonavir is an HIV protease inhibitor that interferes with the reproductive cycle of HIV. Although originally developed as an antiviral agent in its own right, it has been shown to have beneficial properties in combination therapies with low dose ritonavir and other protease inhibitors. Paxlovid significantly reduces hospitalizations and deaths in people with COVID-19 who are at high risk of severe disease compared to placebo (Mahase, 2021 and Hammond et al., 2022).

Another new antiviral agent is molnupiravir, a small molecule N-hydroxycytidine (NHC) ribonucleoside prodrug that is active against SARS-CoV-2 and other RNA viruses and exhibits a high barrier to resistance development. After oral administration of molnupiravir, NHC circulates systemically and is phosphorylated intracellularly to NHC triphosphate. NHC triphosphate is incorporated into viral RNA by viral RNA polymerase and then hijacks the viral polymerase to incorporate either guanosine or adenosine during viral replication. This leads to an accumulation of errors throughout the viral genome which ultimately renders the virus non-infectious and unable to replicate. (Jayk et al., 2022).

Among the 202 treated participants, virus isolation was significantly lower in participants who received 800 mg of molnupiravir (1.9%) compared to placebo (16.7%), the virus was not isolated from any participant who received 400 or 800 mg of molnupiravir, compared with 11.1% of those who received placebo. Time to viral RNA clearance was shortened and a higher percentage achieved overall clearance in participants given molnupiravir 800 mg compared to placebo. Molnupiravir was generally well tolerated, with a similar number of adverse events in all groups (Fischer et al., 2021).

5. The role of nutrition:

Currently, the COVID-19 pandemic is a major challenge worldwide. Achieving and maintaining good nutritional status is mandatory to fight the virus. A person's nutritional status is influenced by various factors, such as age, gender, health, lifestyle, and medications. A quality diet is important for building an adequate immune response, which in turn can affect susceptibility to infection, severity, and recovery from treatment (Rishi et al., 2020).

Malnutrition, overweight and obesity have been widely shown to negatively affect the immune system, leading to viral infections, and several studies have shown that dietary interventions can act as immune boosters and help prevent viral infections (Mitra et al., 2020).

5.1. Cytokine, gut microbiota and COVID-19:

COVID-19 infection associated with significant mortality, especially in the high-risk group like healthcare providers and the elderly. Recently, it has been suggested that people with underlying chronic intestinal inflammation are more susceptible to an elevated cytokine storm when infected with this virus. Cytokine storm has been defined as the overproduction of high levels of cytokines in the early response that do not decrease over time, leading to an increased risk of vascular hyperpermeability, multiple organ failure, and eventual death (Maslowski et al., 2011).

Many people have been forced to fast during the COVID-19 pandemic; this could have affected their microbiota. COVID-19 suppresses the immune system by triggering a systemic inflammatory response, leaving COVID-19 patients with elevated levels of pro-inflammatory cytokines and chemokines (Filosa et al., 2018).

5.2. Role of anti-inflammatory diet:

Chronic intestinal inflammation results from a specific constitution of the intestinal microbiome, which is regulated by diet. For example, plant-based foods are likely to support a gut microbiome capable of eliciting an appropriate level of anti-inflammatory response in the host, foods such as wheat, red meat and alcohol, resulting in chronic intestinal inflammation (Filosa et al., 2018).

There is evidence that a high-fiber, home-cooked, plant-based diet may have led to the formation of a symbiotic microflora, thereby inducing anti-inflammatory responses. They are fermented in the colon after escaping digestion in the small intestine, leading to the production of short-chain fatty acids (SCFAs), which serve as an energy source for colonocytes, lower colon pH and alter blood lipids, thereby influencing an immune response beyond the gut. At the same time, it has been reported that switching from an animal diet to a plant-based high-fiber diet is associated with a change in the microbiota (which changes within days or weeks). This could regulate pre-existing chronic inflammation by reducing the occurrence of a cytokine storm (Filosa et al., 2018).

5.3. Role of Dietary Nutrients:

The amount of nutrients in the diet, including micronutrients (polyphenols and vitamins), macronutrients (carbohydrates, fats and proteins), as well as trace minerals and metals (magnesium, iron, selenium, zinc) would have a significant effect on the intestinal microbiota by inhibiting the growth of potentially pathogenic bacterial species (Sood et al., 2020).

Vitamins C (lemon, spinach, broccoli), D (eggs, fish) and E (almonds, spinach, broccoli, olive oil) have been shown to supplement the health-promoting microbiota. However, the modulation of the intestinal microbial profile depends on the levels of vitamins in the host. Therefore, clinical trials addressing concerns about excessive vitamin supplementation are needed to address these issues (Sood et al., 2020).

Vitamin D plays an important role in maintaining immune homeostasis. Low vitamin D status is associated with many noncommunicable diseases. Several studies have shown that the active metabolite of vitamin D involved in the development of various immune-related diseases can inhibit inflammatory responses and inhibit storms of inflammatory factors. A recent meta-analysis shows that vitamin D supplementation has a protective effect on acute respiratory infections (Jain et al., 2018).

Low vitamin D levels are also associated with increased susceptibility to infectious diseases. As a regulator of innate immunity, it could regulate virus resistance, including induction of antimicrobial peptides and autophagy. It is also used as an adaptive immune regulator (Jain et al., 2018).

A recent retrospective cohort study of 489 patients found an association between low vitamin D status (one year before the COVID-19 test) and a positive COVID-19 test result. For patients with vitamin D deficiency status, the relative risk of testing positive for COVID-19 is 1.77 times greater than for patients with adequate vitamin D status testing (Leeming et al., 2019).

Conclusion

COVID-19 causes multi-system disruption. Many systems of the human body affected by the long and post-COVID-19 symptom including; immune system, pulmonary system, hematological system, cardiovascular system . Oral antivirals are urgently needed to treat coronavirus disease. It prevents the progression of severe disease. Understanding how the immune system works to prevent and eliminate viral infections is essential for anyone working to develop a new strategy that involves not only drugs but also nutrition and supplements that can protect against these diseases. Although a lot of research has been published in this area, we still need more to fully understand and save humanity from this pandemic.

Disclosure

The author reports no conflicts of interest in this work.

References

Cascella M, Rajnik M, Aleem A, et al. Features, Evaluation, and Treatment of Coronavirus (COVID-19) (Updated 2022 Jun 30). In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan- . Available from: https://www.ncbi.nlm.nih.gov/books/NBK554776/.

Elebeedy D, Elkhatib WF, Kandeil A, Ghanem A, Kutkat O, Alnajjar R, Saleh MA, Abd El Maksoud AI, Badawy I & Al-Karmalawy AA. Anti-SARS-CoV-2 activities of tanshinone IIA, carnosic acid, rosmarinic acid, salvianolic acid, baicalein, and glycyrrhetinic acid between computational and in vitro insights. *RSC Adv*. 2021;11(47):29267-29286. doi: 10.1039/d1ra05268c. PMID: 35492070; PMCID: PMC9040650.

Fischer, W., Eron J., Holman, W. et al: Molnupiravir, an Oral Antiviral Treatment for COVID-19. *National Center for Biotechnology Information (NCBI)*, 2021: Version 1.

Filosa S, Di Meo F, Crispi S. Polyphenols-gut microbiota interplay and brain neuromodulation. *Neural Regen Res*; 2018. **13**:2055–2059.

Gautret, P., Lagier, J. C.& Parola, P. Hydroxychloroquine and azithromycin as a treatment of COVID-19: result of an open label non-randomized clinical trial, *Journal of Antimicrobial Agents*. 2020; **56** (1).

Hammond, J. ,Heidi Leister-Tebbe, B.S.N. and Gardner A. Oral Nirmatrelvir for High-Risk, Non-hospitalized Adults with Covid-19, *the new England journal of medicine*; 2022: **386**:1397-1408

Haberman R, Axelrad J, Chen A, Castillo R, Yan D, Izmirly P, Neimann A, Adhikari S, Hudesman D and Scher JU. Covid-19 in Immune-Mediated Inflammatory Diseases - Case Series from New York. *N Engl J Med*. 2020; **383**(1):85-88. doi: 10.1056/NEJMc2009567. Epub 2020 Apr 29. PMID: 32348641; PMCID: PMC7204427.

Jakubec P, Fišerová K, Genzor S, Kolář M. Pulmonary Complications after COVID-19. Life (Basel). 2022 Feb 28;12(3):357. doi: 10.3390/life12030357. PMID: 35330108; PMCID: PMC8955291.

Jain, A., Li, X.H. & Chen, W.N. (): Similarities and differences in gut microbiome composition correlate with dietary patterns of Indian and Chinese adults. AMB Expr; 2018, **8**, 104.

Jayk Bernal, A. and Monica M. Gomes da Silva, et al. : Molnupiravir for Oral Treatment of Covid-19 in Non-hospitalized Patients. *the new England journal of medicine*. 2022; **386**:509-520.

Leeming, E.R.; Johnson, A.J.; Spector, T.D.; Le Roy, C.I. Effect of Diet on the Gut Microbiota: Rethinking Intervention Duration. Nutrients; **2019**, 11, 2862.

Mahase, E (2021): Covid-19: UK becomes first country to authorise antiviral molnupiravir, BMJ. 2021; 4; 375: n2697.

Maslowski, K., Mackay, C (): Diet, gut microbiota and immune responses. *Nat Immunol* ; 2011.**12**: 5–9.

Mitra, P., Misra, S. and Sharma, P.: COVID-19 pandemic in India: what lies ahead. *Ind J Clin Biochem;* 2020: **35**(3):257–259.

Rishi, P., Thakur, K., Vij, S. et al.: Diet, Gut Microbiota and COVID-19. *Indian J Microbiol*; 2020: **60**, 420–429.

Silva Andrade B, Siqueira S, de Assis Soares WR, de Souza Rangel F, Santos NO, Dos Santos Freitas A, Ribeiro da Silveira P, Tiwari S, Alzahrani KJ, Góes-Neto A, Azevedo V, Ghosh P, Barh D. Long-COVID and Post-COVID Health Complications: An Up-to-Date Review on Clinical Conditions and Their Possible Molecular Mechanisms. Viruses. 2021;13(4):700. doi: 10.3390/v13040700. PMID: 33919537; PMCID: PMC8072585.

Sood, N., Zheng, J., Hoffman, K., Chen, J., Shivappa, A., Browman, G. and Daniel, C., Dietary inflammatory potential in relation to the gut microbiome: Results from a cross-sectional study, *British Journal of Nutrition*, 2020, **124**(9), 931-942.

Spudich S, Nath A. Nervous system consequences of COVID-19. Science. 2022; **375**(6578):267-269. doi: 10.1126/science.abm2052. Epub 2022 Jan 20. PMID: 35050660.

Tamimi F, Altigani S, Sanz M. Periodontitis and coronavirus disease 2019. Periodontol 2000. 2022 ;89(1):207-214. doi: 10.1111/prd.12434. Epub 2022 Mar 4. PMID: 35244975; PMCID: PMC9115349.

Terpos E, Ntanasis-Stathopoulos I, Elalamy I, Kastritis E, Sergentanis TN, Politou M, Psaltopoulou T, Gerotziafas G, Dimopoulos MA. Hematological findings and complications of COVID-19. Am J Hematol. 2020 Jul;95(7):834-847. doi: 10.1002/ajh.25829. Epub 2020 May 23. PMID: 32282949; PMCID: PMC7262337.

Verdugo-Paiva, F., Izcovich, A., Ragusa, M. and Rada, G. Lopinavir/ritonavir for the treatment of COVID-19: A living systematic review protocol. medRxiv 2020.04.11.20062109; doi: https://doi.org/10.1101/2020.04.11.20062109. Now published in Medwave doi: 10.5867/medwave.2020.06.7966.