

Original Article**Oxidative Stress, Covid-19 and Nursing Care****Tuba Karabey, BSc, MSc, PhD, RN****Gaziosmanpasa University Faculty of Health Science, Division of Nursing, Department of Fundamentals of Nursing, Tokat, Turkey****Sumeyya Deniz Aybek, BSc, MSc, PhD****Gaziosmanpasa University, Medical Faculty, Department of Medical Biology, 60100, Tokat, Turkey****Correspondence:** Sumeyya Deniz Aybek Address: Gaziosmanpasa University, Medical Faculty, Department of Medical Biology, 60100, Tokat, Turkey, e-mail: sumeyyadenizcelik@gmail.com**Abstract**

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2, previously 2019-nCoV) taxonomically belongs to the Coronaviridae family and genus Betacoronavirus that contain other several species are the cause of severe human diseases. Coronavirus disease 2019 (COVID-19) pandemic registered in Wuhan, China for the first time in December 2019, and it has rapidly spread worldwide via close human relationships. While, the coronavirus pandemic was brought under control in China, the COVID-19 has quickly spread across the globe, causing important mortality and morbidity in the whole world. Currently, SARS-CoV-2 outbreak has led to more than 100 million people infected, more than 2 million virus-related deaths. Clinical experiences are show that symptoms of COVID-19 are highly heterogeneous, ranging from being asymptomatic and infection to severe pneumonia and causing death. COVID-19 patients often develop oxidative stress compensated by oxygen therapy. Oxidative stress makes a major contribution to pathogenesis of the severe COVID-19 infection. Nursing care is of great importance in preventing these destructive effects of oxidative stress. Nurses, who were at the forefront of the covid 19 pandemic process, the role of nurses, who consider human beings biologically, psychologically and socially, and who believe that human beings are critical and valuable, goes beyond just providing care to the sick individual.

Keywords: oxidative stress, Covid-19, nursing care**Introduction**

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2, previously 2019-nCoV) taxonomically belongs to the Coronaviridae family, Orthocoronavirinae subfamily, Sarbecovirus subgenus, and genus Betacoronavirus that contain other several species are the cause of severe human diseases (Pal et al., 2020; Verma et al., 2020). Studies have shown that genome sequencing of SARSCoV-2 is 96.2% similarity to the bat coronavirus (BCoV) and 79.6% similarity to SARS-CoV, and 50% identical to Middle. Eastern Respiratory Syndrome (MERS-CoV).

(Verma et al., 2020). Ecologically, there are several types of CoVs, and bats may be natural reservoirs for a lot of these viruses (Pal et al., 2020). SARS-

CoV-2 has nearly 29.9 kb nucleotides and helically symmetrical nucleocapsid, which is a positive-sense single-stranded RNA (+ssRNA) virus (Verma et al., 2020). Structural, accent, and enzymatic proteins of SARS-CoV-2 play important roles in the pathogenesis of the coronavirus disease 2019 (COVID-19). The virus is usually transmitted via direct contact or indirect contact of mucous membranes with the spilled respirational materials of the infected individual. Previously study showed that angiotensin-converting enzyme 2 (ACE 2) is the receptor used by SARS-CoV-2 to enter into the human cells and the virus is a highly infectious respiratory pathogen that is the cause of the COVID-19 (Pal et al., 2020).

Epidemiology of COVID-19: COVID-19 pandemic registered in Wuhan, China for the first time in December 2019, and it has rapidly spread worldwide via close human relationships. In the whole World, the COVID-19 pandemic causes serious health and socioeconomic problems and unfortunately the effects of the pandemic will last for a long time (Chen et al., 2021; Yüce et al., 2021). Initially, quarantine measures such as social distancing, staying at home, hand washing, wearing mask and gloves, and a complete lock-down were implemented in Wuhan. While, the coronavirus pandemic was brought under control in China quite quickly, the COVID-19 has quickly spread across the globe, causing important mortality and morbidity in Italy, then other European countries, Brazil, United States, and the other countries of the world. The World Health Organization (WHO) declared COVID-19 a serious global outbreak, on March 11, 2020 (Chen et al., 2021). Currently, SARS-CoV-2 outbreak has led to more than 100 million people infected, more than 2 million virus-related deaths (Pohl et al., 2021).

Clinical Progression and Laboratory diagnosis of COVID-19: The incubation period of SARS-CoV-2 virus may average between 2 to 7 days. The COVID-19 is characterized by distinct medical symptoms and signs that include high fever, difficulty in breathing, chills, and cough. The patients may also present with other some symptoms such as fatigue, diarrhea, expectorations, myalgia, and hemoptysis (Pal et al., 2020). Nearly 80% of the COVID-19 patients had a mild illness, 14% of patients developed severe illness, and 5% of patients showed critical illness requiring mechanical ventilation or intensive care. People with comorbidities such as diabetes, chronic obstructive pulmonary disease, heart disease, and hypertension and elderly people have an increased risk of severe illness (Wang et al., 2021). In the disease, most important problem is respiratory failure; at least half of the COVID 19 patients need supplemental oxygen therapy during the intense phase, while around 20% of the patients requiring mechanical ventilation due to they develop to acute respiratory distress syndrome (ARDS). Immunoglobulin G (IgG) antibodies had been measured 10-15 days after the onset of illness symptoms, and the remission of the disease correlated with the decrease of the viral load (Pal et al., 2020). The severity of

the COVID 19 was found to associate with increasing age. According to age, the highest mortality rate was observed in COVID 19 patients aged 80 years and older. In mortality risk, largest increase was observed in the 60–69 years age group compared with 50-59 years age group (Bananad et al., 2020). For the disease, other host risk factors include male sex and smoking. Clinical experiences are show that symptoms of COVID-19 are highly heterogeneous, ranging from being asymptomatic and infection to severe pneumonia and causing death (Chen et al., 2021). Some individuals may not have any clinical symptom at after SARS-CoV-2 infection that asymptomatic individuals play a significant role in the ongoing outbreak. Asymptomatic individuals seem to account for almost 40% to 45% of all COVID-19 cases, and they can spread the virus to other persons for a prolonged period that lasts 14 days or more (Oron & Topol, 2020).

Currently, the diagnosis of the SARS-CoV-2 is done using quantitative reverse transcriptase PCR (RT-qPCR) in various human clinical specimens (Sputum, nasal secretions, throat swab, feces), viral culture techniques for the isolation of SARS-CoV-2 from clinical specimens, immunological tests for the detection of SARS-CoV-2-specific antibodies and antigens such as indirect fluorescent antibody technique, rapid immunochromatographic tests, enzyme-linked immunosorbent assay, and immunofluorescence techniques. Immunological tests for SARS-CoV-2-specific IgM and IgG plays a key role in understanding and controlling the outbreak. Immunological screening may also allow the identification of plasma donors for use as a potential therapy for COVID-19 treatment (Renard et al., 2021). A recent study reported that individuals with COVID-19 had at about 1 in 5 chance of getting a false negative result during their COVID-19 infection, even if they had actually a positive result. According to the researchers, the false negative RT-PCR test rate for SARS-CoV-2 is extremely high, even at its lowest on 3 days after symptom onset or 8 day after virus exposure (Kucirka et al., 2020). The false negative results could be obtained both in the initial phase of the COVID-19 and at the ‘tail end’ of COVID-19 infection due to epidemiologic characteristics of the virus, such as viral shedding and low viral load, below analytical sensitivity of RT-qPCR (Torretta et al., 2020). Other laboratory

tests include complete blood count, D-dimer, C-reactive protein (CRP), clotting tests, ferritin, and procalcitonin identify risk of COVID-19 with greater severity, lactic dehydrogenase (LDH), myocardial damage, thromboembolic complications, and/or worse prognosis. Chest radiography tests may be useful for COVID-19 diagnosis, particularly when negative result was found in other laboratory tests and there was a compatible clinical picture (Goudouris, 2021).

Treatment and New Variants of Covid-19: There were study of many numbers of known drugs that reported some antiviral activity against COVID-19, including Lopinavir/ritonavir (Antiretroviral protease inhibitors), Remdesivir (Antiviral drug), Favipiravir (Guanine analogue), Chloroquine and hydroxychloroquine (Aminoquinolines), Interferon- α and beta (Antiviral agent), Ribavirin (Guanosine analogue), and Tocilizumab (Recombinant humanized monoclonal antibody/IL-6 receptor antagonist). However, there is still discussing for clinical benefits and substantial side effects of the potential treatment agents for COVID-19 (Lu et al., 2020). Many countries have started large scale vaccination programmes for COVID-19 pandemic. The Coronaviridae family have four major structural proteins of consists of the spike surface glycoprotein (S), matrix protein (M), a small envelope protein (E), and nucleocapsid protein (N) (Verma et al., 2020). The vaccines express virus spike protein, which has great importance for entry into the host, the main target of neutralising antibodies in SARS-CoV-2 infection (Darby and Hiscox 2021). Currently, vaccines derived from inactivated virus, mRNA, and recombinant adenoviral vectors have already gained approvals in certain governments. The first mRNA vaccine (Pfizer-BioNTech, Fosun Pharm) was received by FDA EUA on 10 December 2020, giving a COVID-19 efficacy of 95% while the second mRNA vaccine (Moderna, NIAID) was approved by FDA EUA a week later on 18 December 2020. Many institutions and companies in China, UK, Russia, and USA developed recombinant adenoviral vector that can express SARS-CoV-2 genes as vaccines. For inactivated vaccines based on traditional vaccine, outcomes of a phase 1/2 trial on BBIBP-CorV (Sinopharm, Beijing Institute of Biological Products Co. Ltd) were reported on 1 January 2021. These vaccines are effective in protecting against the

COVID-19 but not against the infection, in this case vaccinated people can still be infected and cause spread the virus around. Social distancing, home staying, and use of facemask will still be required to control and prevention of COVID-19 pandemic. SARS-CoV-2 is an RNA virus, which can easily and rapidly mutate to “escape” the body's immune response (Wang et al., 2021).

In the SARS-CoV-2 genome, some specific mutations are being identified during COVID-19 pandemic (Chen et al., 2021). New SARS-CoV-2 strains emerged in South Africa (known as B.1.351 variant) and in UK (known as B.1.1.7 variant) and in Brazil (known as P.1) and this mutations in the spike protein that may change virus-host cell interactions (Wang et al., 2021; Hoffmann et al., 2021). The spike proteins of the SARS-CoV-2 variants mediate potent entry into host cell. P.1 and B.1.351 variants can escape inhibition by neutralizing antibodies. The B.1.351 and P.1 variants were also less efficiently inhibited by sera and convalescent plasma from peoples vaccinated with mRNA vaccine (Pfizer-BioNTech, Fosun Pharm) (Hoffmann et al., 2021). The variants might be correlated with changes in both morbidity and mortality of the COVID-19 disease (Darby and Hiscox 2021). The strains have now been detected to over 50 countries, around the world and this variant may be more virulent (Wang et al., 2021).

Pathogenesis of COVID-19: Oxidative Stress and COVID-19: The immune system is strongly modulated by inflammatory processes and oxidative stress, which contribute to the biological processes of the human body (Iddir et al., 2020). Oxidative stress is the result of an imbalance between reactive oxygen species (ROS) and reactive nitrogen species (RNS) and antioxidant mechanisms, which play important physiological roles in regulating various biological processes including autophagy, differentiation, immune cell activation, and metabolic adaptation (Laforge et al., 2020; Schonrich et al., 2020). In long-lasting viral infections, high production of free ROS by immune cells at the site of infection triggers oxidative stress and there is a close relationship between oxidative stress and inflammation exists (Iddir et al., 2020). Moderate and severe COVID-19 patients often develop acute respiratory distress compensated by oxygen therapy that could cause ARDS and oxidative stress. Hypoxia-induced ROS generation

in mitochondria inhibits oxidative phosphorylation (Chernyak et al., 2020). In oxidative stress, excessive production of ROS is an important cause of tissue damage, which makes a major contribution to pathogenesis of the severe COVID-19 infection. During SARS-CoV-2 infection, ROS levels in elder patients may increase and it triggers inflammatory tissue damage and overactivation of NF- κ B (Schonrich et al., 2020). Furthermore, expression level of the antioxidant enzyme superoxide dismutase 3 (SOD3) decreased in the lungs of elderly patients with COVID-19 and there is relation between COVID-19 and disease severity (Laforge et al., 2020). In addition to, men, who have higher susceptibility to oxidative stress, are more prone to severe COVID-19 than women. Insufficient and delayed IFN-I response to SARS-CoV-2 causes prolonged virus replication and increased oxidative stress, which led to a NF- κ B-driven cytokine storm resulting in uncontrolled systemic excessive inflammation (Schonrich et al., 2020). Interestingly, the formation of severe COVID-19 is less among children than adult due to children's neutrophils are less adherent and reactive. In SARS-CoV-2 infection, the oxidative stress state undoubtedly led to the severity of disease and needs to be further research in field (Laforge et al., 2020).

Nursing Roles and Challenges in Pandemics :

Florence Nightingale was one of the first nurses and pioneers in history to deal with epidemics and principles of hygiene and sanitation. Nightingale showed the relationship between infection control and hand washing for effective nursing care practices (World Economic Forum, 2020). Lessons learned from Florence Nightingale's nursing practice during the Crimean War are applied during the COVID-19 pandemic, which we can still call war today, during basic hand washing, maintaining cleanliness standards, learning from data and more (Bonnie et al., 2020). The World Health Organization develops strategies, initiatives and mechanisms to address emerging and recurring epidemics to reduce the impact on affected populations and to prevent and prevent international spread. As this is a new virus outbreak, it is expected that all COVID-19 protocols will be used and implemented mainly by nurses and healthcare professionals. In addition, nursing leaders should formulate more practical solutions that are easy to apply and solution-oriented (Corless et al., 2018).

Nurses, who were at the forefront of the covid 19 pandemic process, took on a consultancy role in the proper and regular nutrition of the patient. The role of nurses in the Covid 19 process goes beyond patient care. Nurses, who play a key role in reducing the risk of the coronavirus global pandemic, undertake a safe and highly important mission that integrates all interprofessional teams and communities in different professions or sectors to ensure effective communication. The emerging global pandemics pose high risks for individuals and communities. Nurses play a large and highly important role in the provision of healthcare services to control the spread of infectious diseases such as COVID-19, which is considered the third leading cause of death worldwide, and to take care of individuals (WHO, 2020).

One of the difficulties faced in the process of COVID-19 is the delay in early identification of infections due to the long incubation period, which can last up to fourteen days. It poses a serious threat to those who will first come into contact with infected people, especially nurses. (Corless et al., 2018). Nurses play a crucial role in providing public education, not only in the role of practitioners in the prevention of infectious diseases and in reducing the spread of false and incomplete information regarding covid 19 (Wen et al., 2020; Choi, Jeffers, & Logsdon, 2020).

During a worldwide response to a novel coronavirus such as COVID-19, nurses' known primary role was to assist and provide support to people infected with covid 19. However, nurses are expected to play an even more pivotal role in preparation for and management of- the pandemic. The nurses' role in a pandemic begins even before a disease has an opportunity to cause widespread devastation (American Nurses Association, 2020)

It is presented within the scope of nursing knowledge and skills in practices and regulations regarding screening, disease identification, rapid intervention, community participation, inter-institutional and internal communication, government reporting and coordination (Corless et al., 2018). The role of nurses, who consider human beings biologically, psychologically and socially, and who believe that human beings are critical and valuable, goes beyond just providing care to the sick individual (American Nurses Association, 2020). It

is the brainchild of the team that integrates all interprofessional teams and communities in different professions or sectors to ensure effective communication to reduce the risk of the latest coronavirus global pandemic. In the Covid 19 pandemic war, it was once again revealed that the value of health professionals, especially nurses who actively use their heart and brain and show great courage, are indispensable (Molina-Mula & Gallo-Estrada, 2020).

Nurses, who were at the forefront of the covid 19 pandemic process, took on a consultancy role in the proper and regular nutrition of the patients. In this context, they should provide individuals with accurate and up-to-date information on proteins, fats, carbohydrates, dietary fiber, intake, vitamin D and A vitamin. The impact of nutrition on recovery from various illnesses is well recognised. Malnutrition can affect duration of hospitalisation and impede recovery, and therefore it is important to monitor this condition, especially in at-risk groups, such as older adults and those with chronic disease. Underlying malnutrition impairs the immune system, potentially making people more vulnerable to infections such as COVID-19 and impacting recovery (Holdoway, 2020).

It is very important to diagnose malnutrition risk and implement appropriate care plans with an effective multidisciplinary team understanding in the care environments of nurses. High quality proteins are an essential component of an anti-inflammatory diet the consumption of a certain amount of proteins of high biological value is known to be crucial for optimal production of antibodies (Li et al., 2007). Some amino acids modulate the metabolism and immune functions (Cruzat et al., 2018; Kim et al., 2018). For instance, arginine supplementation increased the response of T-lymphocytes and T-helper cell numbers, and rapidly returned to normal T-cell function after operations, compared to control subjects (Kim et al., 2018). In this context, nurses should provide appropriate training and care for protein intake. Low protein status, characterized by low albumin or pre-albumin levels, but also low iron and vitamin E correlated with lower responses to influenza vaccination in the elderly, thereby highlighting the interrelation between various nutrients and the immune response (Iddir et al., 2020). Fatty acids (FAs) may significantly alter immune responses, including changes in the

organization of cellular lipids and interactions with nuclear receptors (Harbige et al., 2003). An imbalance of FA, such as saturated/unsaturated FAs, and omega-6/omega-3 FAs has important implications for immune system homeostasis, which can foster the onset of allergic, autoimmune, and metabolic conditions (Radzikowska et al., 2019; Scaioli et al., 2017; Van Elten et al., 2015)

Carbohydrates and Dietary Fiber High glycemic index-induced acute hyperglycemia and acute insulin response, due to high consumption of processed carbohydrates (white flour, refined sugar), lead to an overload of the mitochondrial capacity and an increase of the production of free radicals (O'Keefe et al., 2008). Even a single high glycemic index meal has been associated with an immediate increase of inflammatory cytokines and C-reactive protein (Monnier et al., 2006). Increased levels of TNF- and IL-6 have also been correlated with a higher glycemic index/glycemic load GI/GL (Bullo et al., 2013). Even if isocaloric, choosing higher-quality carbohydrates can improve postprandial glycemia and lower inflammatory responses (Iddir et al., 2020). In contrast, less processed, low-GL foods, such as vegetables, fruit, nuts, seeds, and whole grains, do not trigger such adverse post-prandial inflammatory (Egger & Dixon, 2009). Increased whole-grain intake (again with amounts of fiber even below 5 g/d) has been associated with decreased hs-CRP, IL-6, and TNF- and increased SCFA, markedly decreasing inflammation-mediated disease risk (Pol et al., 2013). Interestingly, dietary fiber consumption in adult Americans has been inversely linked to the risk of death from respiratory and infectious diseases (Park et al., 2011). In this study, for each 10 g increase in dietary fiber per day, the mortality-relative risk from infectious and respiratory diseases decreased by 34% and 18% in men and 39% and 34% in women, respectively.

Also vitamin A deficiency has traditionally been associated with increased risk of infection (Huang et al., 2018). In fact, it is among the most abundant micronutrient deficiencies worldwide, especially in countries with low protein and meat intake (Ross et al., 2010). Furthermore, individuals with low vitamin A status exhibit histopathological alterations to the pulmonary epithelial lignin and lung parenchyma, resulting in increased risk of lung dysfunction and respiratory disease (Timoneda et

al., 2018). This is particularly relevant considering the effects that COVID-19 has on lung function (Siddiqi, 2020).

Vitamin D can be taken up from the diet via fish, eggs, fortified milk, and mushrooms, but it can also be synthesized under the skin in the presence of UV-light from cholesterol. The active form of vitamin D, calcitriol (1,25 dihydroxyvitamin D), formed following kidney and liver hydroxylations, is most renowned for its regulating role in calcium homeostasis and thus bone health, but it has also been shown to regulate the immune system. Nursing education is extremely important for adequate vitamin intake in the Covid 19 process.

Conclusions: The COVID-19 outbreak causes serious health and socioeconomic problems in the whole world and new many viral variants are emerging and unfortunately the effects of the pandemic will last for a long time. As malnutrition left undetected and untreated can increase length of hospital stay, result in readmissions and impede recovery, nutritional screening and appropriate nutritional care should be an integral component of holistic care for people who have or have had COVID-19 illness. In this context, nursing practices are of great importance. In this review, we highlight the importance of an optimal status of relevant nutrients to effectively reduce inflammation and oxidative stress, thereby strengthening the immune system during the COVID-19 crisis. Increased global human mobility and urbanization are shape the conditions for future epidemics and pandemics such as COVID-19 outbreak. In all fields scientific studies will provide new insights to humanity and open new paradigms in pandemic control and prevention.

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