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Effects of COVID-19 on Homeostatic Balance

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Abstract

Coronavirus disease 2019 (Covid-19) has become a global epidemic affecting millions of people around the world. It has been declared a pandemic by the World Health Organization as of March 2020. The symptoms of Covid-19 were variable, and even though the course was not the same in all patients, it often resulted in asymptomatic infection, acute lung injury, severe respiratory distress syndrome (ARDS), and death. Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) uses ACE-2 receptors to enter the cell, similar to SARS-CoV. ACE-2 is wide in the lung and small intestinal epithelium of humans. This clearly makes respiratory and gastrointestinal system elements the target tissue. The ample expression of ACE-2 on the surface of bronchial epithelial cells results in local inflammation, coagulation, and leakage from capillaries in case of infection. Disrupted endothelial structure initiates unregulated cytokine release. It is clear that the overproduction and release of pro-inflammatory cytokines is the crux of the cytokine storm. In this situation; The need for mechanical ventilation can lead to sepsis, septic shock, acute respiratory distress syndrome (ARDS), and multiple organ dysfunction syndromes. Alterations in the intestinal microbiota may induce negative effects on the brain and lung tissues through various mechanisms. Abnormal levels of liver enzymes have been noted in patients infected with SARS-CoV-2. Most liver damage is mild and temporary, but serious liver damage can also happen. People with severe diseases have a higher rate of liver damage. Covid-19 leads to the deterioration of iron metabolism in patients. Common findings of patients with anemia include advanced age, impaired renal function, and elevated inflammation markers. Apart from these, monitoring different hematological, immunological, and biochemical markers can give us information about the disease.

Keywords: SARS-CoV-2, homeostasis, pandemic, ACE-2, Covid-19 mechanism

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Introduction

The human body has the ability to regulate the physiological conditions of its internal environment within variable external conditions. This review is planned to reveal how homeostasis is affected in various systems and components of the human body when faced with coronavirus disease-2019 (Covid-19).

In late 2019, an increase in pneumonia cases was observed in Wuhan, China (1). After a while, it was determined that this new and rapidly spreading disease, called coronavirus disease-2019 (Covid-19), was induced by severe acute respiratory syndrome coronavirus-2, that is, SARS-CoV-2 (2). coronaviruses; They have enveloped RNA viruses with pointed protrusions on the surface, ranging in diameter from 60 nm to 140 nm. They get their name from the crown-like appearance they give under the electron microscope. In the past 20 years, there have been two other diseases that have emerged as a result of cross-contamination of animal beta-coronaviruses with humans. Covid-19 spreads faster than SARS and MERS but has a lower mortality rate (3).

The genome sequence shows up to 82% sequence similarity to SARS-CoV of the gene region of SARS-CoV-2 that encodes and expresses pointed (S) glycoproteins that can bind to angiotensin-converting enzyme 2 (ACE-2) to enter human cells. (4;5). In other words, as in SARS-CoV, in SARS-CoV-2, ACE-2 is the receptor that facilitates the entry of the virus into the cell. However, the affinity of SARS-CoV-2 for ACE-2 was found to be approximately 10-20 times higher than SARS-CoV (5,6). This explains why SARS-CoV-2 spreads faster than SARS-CoV.

Effect of Covid-19 on Pulmonary System

The main place where Covid-19 induced by SARS-CoV-2 manifests itself is the respiratory tract and organs. The direct contact of the respiratory system with the external environment makes it the primary host site for airborne pathogens.

Chest radiography (CXR) is routinely used in the standard and initial clinical evaluation of lung infections (7). Ground glass image on chest radiograph (CXR) was commonly seen in Covid-19 patients. However, CXR results were negative in 25% of cases (8).

Symptoms of Covid-19 can range from mild respiratory problems to life-threatening severe acute respiratory distress syndrome (ARDS). It is clear that overproduction and release of pro-inflammatory cytokines is the crux of the cytokine storm in patients with Covid-19, whose disease is severe and whose health is deteriorating day by day. This may lead to the need for mechanical ventilation, sepsis, septic shock, acute respiratory distress syndrome (ARDS), and multiple organ dysfunction syndromes (9;10; 8). Menter et al. Research conducted by Kovid-19 show us that severe bronchopneumonia may develop in patients with Covid-19 (11). When SARS-CoV-2 infects cells expressing the ACE-2 and TMPRSS2 surface receptors, active replication and release of the virus induce damage to the host cell. Damage is recognized by

adjacent epithelial cells, endothelial cells, and alveolar macrophages and initiates the release of proinflammatory cytokines and chemokines (12). These proteins attract monocytes, macrophages, and cytotoxic T cells to the site of infection as a result of adaptive immune activation, promoting further inflammation in the infected lung. This creates a proinflammatory positive feedback loop (13; 8). The resulting cytokine storm can lead to multiple organ damage. In a healthy immune response, the initial inflammation that occurs attracts virus-specific T cells to the site of infection, where they can sift infected cells before the virus spreads. In these patients, neutralizing antibodies can block viral infection and alveolar macrophages recognize and eliminate neutralizing viruses and apoptotic cells by phagocytosis. Consequently, this process helps to clear SARS-CoV-2 from the tissue and to ensure healing by causing minimal lung damage (14; 13).

ACE-2 is also abundantly expressed on the surface of type I and II alveolar epithelial cells and bronchial epithelial cells. ACE-2 expression levels are not much variation in patients with asthma and chronic obstructive pulmonary disease (COPD) than in healthy individuals. Similarly, no significant differences are observed depending on gender and age. However, an increase in ACE-2 expression has been detected in people with chronic smoking. In addition, the presence of viral bodies in the endothelial cells and the accumulation of inflammatory cells that can induce endothelial damage have been detected in Covid-19 patients. Various studies have revealed that capillary endothelial cell damage may be interrelated with systemic arterial events (15;16;17;18;19). endothelial dysfunction; It strengthens platelet activation, alterations homeostasis between vasoconstrictors/vasodilators and increases oxidative stress in vascular cells.

It is thought that Covid-19 patients who need intensive care unit are at high thrombotic risk as a result of prolonged immobility, mechanical ventilation, vascular injury or surgery(20). Even though the studies are heterogeneous, the incidence rates of pulmonary embolism (PE) and deep vein thrombosis in patients with Covid-19 are 16.5% and 14.8%, respectively, according to the weighted average (21). D-dimer levels play an important role in the diagnosis of PE (22). Elevated D-dimer levels in Covid-19 patients may result from prothrombotic coagulopathy or pulmonary microvascular thrombosis. D-dimer levels were found to be higher in patients with PE than in patients without PE (23; 21; 24), but D-dimer levels were found in Covid-19 patients without PE. even tends to be high. Consequently, patients with severe Covid-19 have higher D-dimer levels than those without severe disease, and D-dimer levels greater than 0.5 μg/ml are interrelated with a severe infection in Covid-19 patients.

Effect of Covid-19 on Gastrointestinal System

Nausea and vomiting symptoms are also significantly lower in Covid-19 patients compared to SARS and MERS (4). Liver damage is up to 17.57% in Covid-19 patients with gastrointestinal (GIS) symptoms compared to 8.84% without gastrointestinal symptoms (5). Patients with GI symptoms are more likely to have a severe course of the disease. In addition, the decline in serum sodium levels and electrolyte disturbances may occur in patients due to diarrhea. Fort

his reason, gastrointestinal symptoms of patients should also be evaluated during the diagnosis and treatment of Covid-19.

Mechanisms that induce gastrointestinal damage

Direct infection of gastrointestinal cells

Since ACE-2 expression was found to be high in organs on the gastrointestinal tract (GIS) (25;5), it was found that coronavirus can infect the GIS, and GIS symptoms that can be seen in some of their patients are induced by SARS-CoV-2. proven. It is observed that angiotensin II (Ang-II) accumulation is significantly increased in Covid-19 patients. The reason for this increase is that SARS-CoV-2 binds to the ACE-2 receptor, causing a decline in the number and activity of the receptor (26). A decline in ACE-2 activity also significantly reduces serum tryptophan levels (5). Tryptophan is mainly absorbed by the B0AT1/ACE2 pathway on the luminal surface of intestinal epithelial cells, activating mTOR. Thus, the expression of antimicrobial peptides is regulated and the intestinal flora is affected.

Gastrointestinal effects stand out as common side effects in almost all of the drugs used in the treatment of Covid-19 or thought to have the potential to be effective (27). In summary, it should be considered that the symptoms that occur may be due to Covid-19 infection or may result from a drug side effect.

Effect of Covid-19 on gut microbiota

The most common pathway of SARS-Cov-2 is that it binds to ACE-2 receptors on alveolar epithelial cells and enters the cell and induces infection in the region. However, studies have shown that the virus can also be detected in the stool of a patient infected with SARS-Cov-2 (28). It is reported that more than 60% of Covid-19 patients are confirmed to have gastrointestinal symptoms such as nausea, vomiting, and diarrhea (29). ACE-2 receptors in the intestine fulfill their function by regulating the homeostasis of intestinal amino acids, the expression of antimicrobial peptides, and directly the intestinal microbiota (5). The diversity in the gut microbiota declines with increasing age (30). Older individuals, whose microbiota diversity and quality decline, become more susceptible to Covid-19 due to weakened immune systems. Regular use of prebiotic/probiotic supplements may be one of the prophylactic ways in these individuals.

Intestinal microbiota and lung axis

Alterations in the gut microbiota, called intestinal dysbiosis, are interrelated with various diseases and disorders such as inflammatory bowel disease (IBD), type 2 diabetes, cardiovascular diseases, and depression. It has been shown that the communication pathway, called the gut-lung axis, and the gut microbiota can also affect lung health (28). However, new therapeutic strategies aimed at altering the gut microbiome with prebiotics, probiotics, antibiotics, phytotherapeutics and diet have been tried in clinical and laboratory studies of

variation ocurlung diseases. Similarly, it is thought that the infection occurring in the lungs may also affect the intestinal microbiota. In many studies, it has been observed that lung-related diseases such as COPD, asthma, cystic fibrosis, allergies and lung cancer are interrelated with disorders in the intestinal microbiota (29).

Gut microbiota and brain relationship

Autopsy studies performed on patients during the SARS epidemic that happened in 2002-2003 revealed SARS-CoV-1-related tissue inflammation in the neuron cytoplasm on brain tissue samples (31). The pathway of SARS-CoV-1 penetration into the brain is likely to be mediated by the olfactory pathway and the ACE-2 receptor. This hypothesis has also been demonstrated in experimental models on transgenic mice (32). The way in which SARS-CoV-2 reaches the central nervous system has not yet been clarified. It is likely that many of the mechanisms applicable to SARS-CoV-1 also apply to SARS-CoV-2, as it has structural and clinical features similar to SARS in many ways (33).

Effect of Covid-19 on Liver

Bacterial imbalance in the gut microbiota can also affect the gut-liver axis. In the gut-liver axis, SARS-CoV-2 binds with ACE-2 to enter the gut, inhibits the B0AT1/ACE2 pathway, and affects mTOR activation to reduce the expression of antimicrobial peptides. Intestinal flora is transferred to the liver via the portal vein, where it binds to receptors and induces hepatitis. In addition, the liver can transport metabolites to the intestine by releasing them into the systemic circulation through the bile. This suggests that the portal vein has a bidirectional axis relationship between the intestine and the liver. People with severe diseases have a higher rate of liver damage. According to biochemical analyzes, liver function-related aspartate aminotransferase (AST), alanine aminotransferase (ALT), and serum bilirubin levels are higher in those with gastrointestinal symptoms (34;4;5).

One of the potential reasons put forward to explain liver damage in Covid-19 patients is that SARS-CoV-2 directly attacks hepatocytes and leads to abnormal liver enzyme levels. However, it has been shown that it does not express a significant number of ACE-2 receptors on the surface of hepatocytes. This does not make the liver a possible target in case of infection. Another reason is that abnormal liver function test results are induced by drug side effects. Even though this theory seems possible given that the significant side effect of high doses of acetaminophen is the development of hepatotoxicity, the recommended doses for controlling headache and fever symptoms in Covid-19 infections are unlikely to induce liver damage. It is also possible that the cytokine storm induced by systemic inflammatory response syndrome and multi-organ dysfunction may contribute to liver damage. This may explain the abnormal liver enzyme values in patients with severe Covid-19 infection.

Renal Effects of Covid-19

Impaired kidney function is a common complication in up to 46% of hospitalized patients with Covid-19. It has been suggested that the main reason for the lack of homogeneity in the

appearance of complications is racial differences (35;36). Various glomerular and tubular disorders happen in patients infected with SARS-CoV-2. According to the postmortem study conducted by Menter et al., 12-18% of patients were found to have hypertensive nephropathy and diabetic nephropathy (11). The most common glomerular disorder was recorded as collapsing glomerulopathy (36). According to the results of a large-scale study prepared on the basis of data from 17,391 Covid-19 patients, the most frequently reported renal complications during the 2-28 days hospitalization of hospitalized patients were electrolyte disturbance (12.5%), acute kidney injury (11.0%), respectively. kidney replacement therapy (6.8%) (RRT). Acidosis and alkalosis were also reported following these complications, but it could not be distinguished whether this situation was of kidney origin or lung origin (37). Acute renal failure requiring RRT has been interrelated with increased mortality (35).

Direct damage due to viral uptake and replication

SARS-CoV-2 enters the tissues through the ACE-2 receptor. ACE-2 is particularly highly expressed in the proximal tubules. In fact, ACE-2 expression in the kidneys is about 100 times higher than in the lungs. It is predicted that SARS-CoV-2, which enters cells by targeting ACE-2, may induce kidney damage. The onset of proteinuria and/or increase in serum creatinine in one-third of the patients showed that SARS-CoV-2 can induce direct damage to the renal tissue. Acute tubular damage was clearly seen in light microscopy, and viral particles were detected in renal tubular epithelial cells and podocytes by electron microscopy. The presence of apolipoprotein 1 (APOL1) genotypes in individuals play an important role in the pathogenesis of the disease and creates a genetic predisposition in individuals of African descent (36).

Effect of systemic inflammatory response and cytokine storm

When metabolized by enzymes in the blood, the lipopolysaccharide expressed in the membrane of gram-negative bacteria becomes endotoxin, which can induce septic shock. Thus, septic acute kidney injury may happen. Rhabdomyolysis, metabolic acidosis, and hyperkalemia can also happen in Covid-19 patients and are almost always interrelated with hemodynamic instability. This results in tubular toxicity.

Cytokine formation happens with extracorporeal membrane oxygenation, invasive mechanical ventilation, and continuous renal replacement therapy. Direct cytokine lesions may happen through hemophagocytic syndrome, which is characterized by a clinical picture of fever, hepatosplenomegaly, and cytopenia as a result of impaired functions of cytotoxic T-lymphocytes and natural killer (NK) cells, activation of macrophages and T-lymphocytes, overproduction of proinflammatory cytokines, and hemophagocytosis. cytokine storm; may contribute to cardiomyopathy, acute viral myocarditis, renal vein occlusion, hypotension, and renal hypoperfusion, leading to a decline in glomerular filtration rate (38).

Deterioration in oxygen saturation

The increased serum concentration of IL-6 in acute kidney injury is interrelated with higher alveolar-capillary permeability and pulmonary hemorrhage. Damage to alveoli leads to renal

medullary hypoxia; high airway pressure and intra-abdominal hypertension can induce damage to the renal compartments (38). At the same time, hypoxia can easily induce rhabdomyolysis (36).

Anemia and Iron Metabolism

Iron is an essential element for all organisms (39). It has been reported that acute respiratory distress syndrome (ARDS) induces a decline in serum iron levels. It may take more than a month for post-infection ferritin values to return to normal after the initial rise. So, it is observed that Covid-19 patients remain elevated during their stay in the intensive care unit (40). Most viruses require iron to replicate their genome on the host and to produce mRNA for active protein translation. For this reason, cellular iron supplementation can increase viral replication and spread, while iron deficiency may negatively impact the viral life cycle (39).

Anemia is identified as a decline in the proportion of red blood cells. Erythropoietin (EPO), produced in the kidney, is the main stimulator of red blood cell (RBC) production. Tissue hypoxia is the main stimulator of EPO production, and EPO levels are generally inversely proportional to hemoglobin concentration (41). Anemia that develops despite tissue hypoxia may be the result of restricted erythropoiesis resulting from alterations in iron metabolism. Studies have reported that anemia is interrelated with a 2.6-fold increased risk of mortality in chronic obstructive pulmonary diseases (10).

Retrospective analyzes of hospitalized Covid-19 patients (42) and prospective studies conducted in patients proven to have Covid-19 by laboratory tests have shown that an average of one-third of patients are anemic (43). Anemia is interrelated with high mortality rates, but not the need for intubation and length of stay in ICU.

Three potential pathways are thought to be involved in iron metabolism in the pathophysiology of Covid-19. The first of these ways; The pathological effects of SARS-CoV-2 on the respiratory system directly, causing hypoxia and observing the inflammatory response leading to anemia. Latter; This is beinduce the innate immune system aims to reduce the bioavailability of iron in order to prevent the expanding viral load in the acute phase of the infection. This leads to hepcidin activation, retention of iron within cells, increased ferritin levels and declined hemoglobin level resulting in hypoxia. The third potential route is; SARS-CoV-2 acts by mimicking hepcidin, the main regulator of iron metabolism.

The hemoglobin concentration is one of the most important determinants of the oxygen carrying capacity of the blood. The study by Fan et al. showed that patients hospitalized in intensive care units had significantly lower hemoglobin levels than patients who did not need an intensive care unit (44). Pathological level of ferritin is a more prominent finding in elderly, hypertensive and male individuals. Both anemia and hyperferritinemia are strong predictors of mortality, regardless of the underlying pathology.

Optimal iron levels in host cells are required for viral replication. For this reason, alterations in hepcidin levels occur in the acute phase of infection to limit virus replication and maintain iron homeostasis; With the activity of ferroportin, iron sequestration begins from cells, especially in hepatocytes, enterocytes and macrophages, and the amount of iron absorbed in the diet declines. The increase in intracellular iron secretion also induces an increase in the cytosolic ferritin level. The decline in the amount of iron required for erythropoiesis leads to worsening of the anemia. Hepcidin promotes iron entry into cells and induces the blockade of ferroportin, the most important extracellular transporter of iron. SARS-CoV-2 mimics hepcidin with the hepcidin-mimetic effect of the spike proteins on it. It can induce serum iron deficiency and hemoglobin deficiency while significantly increasing circulating and tissue ferritin. This may accelerate cell apoptosis (9).

Biomarkers

Hematological markers

While lymphopenia has been reported as 80% in severe cases (45), it has been reported as 25% in mild cases (46;47). In severe patients, lymphocytopenia affecting both CD4+ and CD8+ cells (46), a decline in eosinophils and monocytes, and a clear increase in neutrophils and NLR were observed. These parameters have been interrelated with disease severity and mortality (48;49) and can be used for diagnosis and early diagnosis in patients (22).

Naive CD4 T cells are the main producers of cytokines. Among the functions of lymphocyte CD4 cells are the creation of an immunological response, the regulation of B and cytotoxic T cell (CD8+) activities (50). A decline in the number of T cells was found in severe cases. It was observed that the number of helper T cells (CD4+) declined more than suppressor and regulatory T cells. An increase in the number of naive helper T cells was also observed. The declined amount of lymphocytes confirms these values (51; 48). Significant reductions in the number of natural killer cells, T cells, and B cells were seen in patients with SARS-CoV-2 infection. Declined CD8 and T cell complex is a hallmark of Covid-19 infection (48;52). The decline in T cells and their subsets increases the severity and mortality of the disease. Data interrelated with an increased risk of death are shown in Table 1.1 (53).

Table 1.1: T lymphocyte subset values interrelated with increased risk of death from Covid-19 in hospital

Subsets	Values
Lymphocyte	< 500 uL
CD3+T cell	< 200 uL
CD4+T cell	< 100 uL
CD8+T cell	< 100 uL
B cell	< 50 uL

Platelet count measurement is an important marker in the follow-up of severely hospitalized patients, as it is an easy-to-measure and inexpensive method. While the platelet count was higher in uninfected patients with SARS-CoV-2, it was found to be lower in patients who died, and higher in patients who survived the disease than in patients who died. Based on these data, it can be concluded that low platelet count can be used as an indicator of aggravation of the disease. Another research group found that patients with severe pneumonia induced by SARS-CoV-2 had higher platelet counts than those without (54).

Biochemical markers

Myocardial damage, D-dimer and cardiac markers are important in Covid-19 patient follow-up. Significant elevations in liver enzymes (alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are observed, possibly due to cardiac injury resulting from both viral myocarditis and multi-organ failure in the progression of the disease (22).

In a cohort of 799 patients (55), AST, ALT, creatinine, creatine kinase, lactate dehydrogenase, cardiac troponin I, N-terminal forebrain natriuretic peptide, and D-dimer concentrations were significantly higher in deceased patients than in convalescent patients. was observed to be higher. Cardiac troponin I≥ 0.05 ng/mL was identified among the risk factors predicting mortality.

Discussion

Entry and infection of SARS-CoV-2 into host cells happen via proteolytic cleavage by angiotensin-converting enzyme-2 (ACE-2) and transmembrane protease serine 2 (TMPRSS2) via spike (S) protein (12; 56; 57). It is argued that TMPRSS2 inhibitors and ACE-2 inhibitors can prevent cell entry of SARS-CoV-2 by blocking ACE-2, the host cell receptor for the S protein of SARS-CoV-2, and inhibiting TMPRSS2, which is necessary for S protein preparation. Even though theses (58) have been put forward, the number of studies pointing to the contrary is quite high. In individuals with cardiovascular disease, discontinuation of ACE-inhibitor/ARB therapy or evaluation of alternative treatment options is not recommended as it will increase the risk of mortality, especially in critically ill Covid-19 patients.

The distribution of ACE-2 in tissues is informative to elucidate probable infected tissues and damage mechanisms. ACE-2 has been shown to be widely expressed in many tissues and organs such as the lungs, small intestine, brain, kidneys, and cardiovascular system (59; 4). However, infection was detected in cells lacking ACE-2 (60). During the entry of SARS-CoV-2 into the cell, the tumor necrosis factor-α converting enzyme may be activated, causing the ACE-2 protein to cleave and shed its extracellular domain (59). McMillan et al. This event “Soluble ACE-2, also called serum or plasma ACE-2, corresponds to the ACE-2 enzyme ectodomain that leaves the cell surface, this process is called shedding. The purpose of the spill is unclear but appears to happen more frequently in patients with hypertension and heart disease.” expresses as. Soluble ACE-2 functionally moves away from the outer region of the membrane

and can efficiently bind to the spike protein of SARS-COV-2. Whether an increased concentration of soluble ACE-2 adversely affects blood pressure in patients is unknown, but downregulation of ACE-2 may stimulate TNF-α expression. This situation also explains the exacerbation of inflammatory damage in cardiovascular tissues (59;61;13). The fact that SARS-CoV-2 binds to the ACE-2 receptor and induces a decline in the number and activity of the receptor (26) also significantly reduces serum tryptophan levels (5). Tryptophan is mainly absorbed by the B0AT1/ACE2 pathway on the luminal surface of intestinal epithelial cells, activating mTOR. So, the expression of antimicrobial peptides is regulated and the intestinal flora is affected. Older individuals, whose microbiota diversity and quality decline, become more susceptible to Covid-19 due to weakened immune systems. Alterations in the gut microbiota can affect the lung and brain (28;31) and this can be affected by alterations in the tissues it affects (29).

High ferritin levels appear as an important risk factor interrelated to mortality in Covid-19 patients (9,39). In cases where this hyperferritinemia progresses much worse than typical liver function abnormalities; It is thought that the factor that induces cellular damage may not be the elevated ferritin alone or directly, and this may be due to the presence of immunological response (61).

IL-6; It is a proinflammatory cytokine that can be secreted by many cells such as monocytes, lymphocytes, fibroblasts, and endothelial cells (62;63). IL-1β, TNF-α, viral infections and Ang-II; It can induce IL-6 (64, 65). IL-6 activates endothelial cells at the onset of inflammation, increasing vascular permeability. It also plays an important role in the secretion of proinflammatory cytokines and chemokines by endothelial cells. In Covid-19 patients, IL-6 levels appear to be directly related to disease severity. Elevated proinflammatory cytokines in Covid-19 patients, especially IL-1β, IL-6 and TNF-α, and induce loss of normal antithrombotic and anti-inflammatory functions of endothelial cells, leading to disruption of the coagulation mechanism (66;67). The disorder in coagulation functions, which develops with an immunological response, is very important for Covid-19 patients.

Covid-19 contributes to the high risk of hypoxemia in patients (59; 9). Tissue hypoxia is the main stimulator of EPO production, and EPO levels are generally inversely proportional to hemoglobin concentration (41). Despite the resulting tissue hypoxia, anemia may develop. This may be a result of restricted erythropoiesis resulting from alterations in iron metabolism (10).

Conclusion

The ongoing Covid-19 pandemic continues to threaten the entire world. Based on the studies published so far, we can conclude that there are hematological (lymphocyte count, neutrophil count, and NLR), inflammatory (especially IL-6 and IL-10) and biochemical (D-dimer, cardiac troponin, AST, ALT) parameters. These and other probable parameters should be carefully studied to monitor disease progression and prepare treatment protocols. Determining the guiding parameters and understanding the mechanisms of involvement in SARS-CoV-2 infection will contribute to the development of treatment strategies.

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