

## CHAPTER III

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### A UNIQUE PANDEMIC: COVID-19

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#### **1.Introduction**

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a global public health problem that is causing a worldwide epidemic, currently unable to be effectively treated because there is no specific antiviral drug, and early detection of medical isolation is extremely important. It was named Coronavirus Disease 2019 (COVID-19) by the World Health Organization (WHO) and declared a pandemic on March 11, 2020 (1, 2). COVID-19 ranges from asymptomatic or cold-like symptoms such as dry cough, fever and fatigue to severe dyspnea and respiratory failure. It has been reported that COVID-19 disease has a more serious clinical course risk in patients with comorbidities such as hypertension, diabetes, and cardiovascular disease (3). Since the first reported COVID-19 case in Wuhan, China at the end of 2019, COVID-19 has rapidly spread throughout China and then to all countries of the world. As of January 01, 2021, more than 84 million cases have been confirmed worldwide and over 1,800,000 deaths (4).

#### **2.Etiology**

Coronaviruses (CoVs) belong to the subfamily Orthocoronavirinae in the family of Coronaviridae in the order Nidovirales, and this subfamily including  $\alpha$ -coronavirus,  $\beta$ -coronavirus,  $\gamma$ -coronavirus, and delta-coronavirus (5). Coronaviruses are generally not very resistant to the external environment. The durability period in the outdoor environment varies depending on factors such as the humidity and temperature of the environment, the amount of organic matter expelled, the texture of the contaminated surface. (2, 3). Coronaviruses primarily cause infections in birds and mammals. It has been seen to infect humans in recent years. The severe acute respiratory syndrome (SARS) outbreak in 2002 and the Middle East respiratory syndrome (MERS) outbreak in 2012 showed that coronaviruses are fatal when they infect humans (6). SARS CoV-2, which causes COVID-19 disease detected at the end of 2019, has also been shown

to have a typical coronavirus genome structure and belong to the  $\beta$  - coronavirus cluster, including SARS - CoV and MERS - CoV (7).

### **3. Transmission**

Most research conducted in Wuhan at the beginning of the outbreak has shown that the first patients worked or visited a market selling seafood in Wuhan. As the outbreak progresses, it has been shown that this viral infection is transmitted from person to person through droplets and through infected surfaces or contaminated hands (8). The virus can be found in the respiratory secretions of patients 1-2 days before the onset of clinical symptoms and two weeks after the symptoms of the disease (9, 10).

### **4. Clinical and epidemiological features**

Some of the COVID-19 patients may be asymptomatic, while others may have a wide variety of symptoms such as fever, cough, shortness of breath, myalgia, fatigue, headache, diarrhea, nausea, vomiting, loss of smell and taste (9, 11-14). The most common symptoms of infection are fever, fatigue and dry cough (12). Clinical symptoms differ according to age and gender (12, 13). All ages of the population are susceptible to SARS-CoV-2 infection and the average age of infection is approximately 50 years (12). In general, males over 60 years of age with comorbidities are more likely to develop severe respiratory disease requiring hospitalization and even death (12). However, most young people and children have only mild diseases or are asymptomatic (12, 14).

In a study by Chen et al, examining 99 patients hospitalized with the diagnosis of COVID-19 in the same hospital, they showed that the possibility of being infected is higher in elderly men and that they rapidly enter acute respiratory distress syndrome (ARDS), which creates a life-threatening situation (15). In a study where comorbidities were analyzed, it was shown that approximately 17% of the patients had hypertension, 8% had diabetes, 5% had cardiovascular diseases and 2% had respiratory system diseases (16). It has been reported that mild cases recover within 1 week and progressive respiratory failure resulting in death in severe cases may develop (14). It has been determined that most deaths from COVID-19 include cardiovascular disease, diabetes, chronic respiratory disease, hypertension, and cancer (10). In a study in which 72,314 cases were examined, it was reported that 81% of mild cases, 14% of severe cases requiring intensive care support, and 5% of critical cases with respiratory failure, septic shock and / or multi-organ dysfunction (17).

COVID-19 is a prothrombotic condition that causes both microvascular and macrovascular thromboembolic events and particularly pulmonary embolism in pulmonary and extrapulmonary organs (18). Thrombosis in COVID-19 patients is thought to be mainly due to

angiotensin converting enzyme-2 receptor-mediated endothelial damage. Endothelial damage causes macrophage activation syndrome, which leads to cytokine storm, intussusceptive angiogenesis and activation of the coagulation cascade (18-20).

The fact that WHO evaluated the  $R_0$  value between 1.4 and 2.5 and affected approximately 84 million people by the last day of 2020 indicates the difficulty of controlling the epidemic (4, 21, 22). The high transferability of SARS-CoV-2 can be attributed to the unique virological properties of SARS-CoV-2, its ability to stay on non-living surfaces for days, and the presence of high viral load in upper respiratory tract samples during the initial phase of the disease (23, 24). The COVID-19 patient spreads the viruses in liquid droplets during conversation. However, smaller and much larger numbers of particles known as aerosol particles can also stay in the air for a long time and then penetrate deep into the lungs when inhaled by someone else (25, 26). This explains the rapid geographic spread of COVID-19. Strict compliance with infection control measures in both the community and hospitals and the introduction of COVID-19 vaccines into clinical use seems to be the only way to control the disease.

## **5. Diagnosis**

Early diagnosis is very important to prevent COVID-19 disease (27). The gold standard in diagnosis is the rRT-PCR test positivity. However, COVID-19 cannot be excluded with a negative result of the RT-PCR test for SARS-CoV-2 in patients with clinical and epidemiological features compatible with COVID-19 infection. Poor sample quality, too early or too late sample collection time, incorrect storage and handling of samples, and virus mutations have been reported to cause false negative results (28). Since false negative results play an important role in the spread of the infection, alternative diagnostic methods are needed. At the onset of the COVID-19 outbreak, diagnosis was based on clinical features and thoracic imaging (29). Normal chest radiography does not exclude the disease, since the sensitivity of conventional chest radiography in thoracic imaging is 30-60% (30). Computed tomography (CT), another method used in thoracic imaging, has a higher sensitivity than lung radiography. Therefore, it has been reported that CT can be used as the first imaging technique in patients with high clinical suspicion for COVID-19 (31). Kant et al. showed that in patients with positive rtRT-PCR test, CT was positively correlated with the age and symptom duration of the patients (32). They reported that patients over 60 years of age with clinical and epidemiological findings consistent with COVID-19 were 7.17 times more likely to have CT findings (32). Typical imaging features of patients with COVID-19 are reported to have different features at different stages of the disease (31). While ground-glass opacity is seen in the initial stage of the

disease, other patterns such as pulmonary consolidation and paving stone appearance can be seen in the later stages (33, 34). In the studies of Kant et al., the CT positivity rate was 85.1% in patients with symptom duration longer than two days. In the examination of this parameter with ROC analysis, the area under the curve was reported as 0.869, sensitivity as 90.5% and specificity as 76.2% (32). Bernheim et al. showed that the CT finding was not sufficient for diagnosis in the first two days of the disease, but it had a diagnostic value in the following days (35). In the study of Kostakoğlu et al., they stated that rtRT-PCR positivity was associated with clinical findings (36). In this study, it was reported that age (<60), symptom duration less than 5 days, presence of headache and absence of shortness of breath correlated with rtRT-PCR positivity (36). In the studies of Guo et al., it was reported that the PCR positivity rate after the onset of symptoms was more than 90% in 1-3 days, less than 80% in the 6th day and less than 50% after 14 days. In this study, the PCR detection rate was higher than IgM ELISA before 5.5 days after the symptom onset, and the positivity rate of IgM ELISA was higher than the PCR method after 5.5 days (37). All these studies revealed that rtRT-PCR is not a reliable and independent test for COVID-19 screening. CT was found to be positively correlated with patients' age, symptom duration, comorbid disease, shortness of breath, and fever. It should be kept in mind that the negativity of the rtRT-PCR test does not rule out the diagnosis of COVID-19 in patients with symptom duration > 5 days, elderly, with comorbid disease and especially fever and shortness of breath. Typical CT findings for COVID-19 in these patients are diagnostic. If the first rtRT-PCR test is negative or the test is not performed, it is important for public health to diagnose patients according to CT imaging in order to prevent the spread of infection. Similarly, in patients with new onset symptoms, normal chest CT should not cause disruption of isolation measures until the PCR test is available.

## **6.Treatment**

There is no specific treatment for COVID-19. Symptomatic treatment is recommended for mild cases that progress as uncomplicated respiratory tract infections and do not require hospitalization (38, 39). In addition to supportive treatments such as oxygen therapy, intensive care, mechanical ventilation, treatments such as antivirals, antibiotics and steroids are also used in Covid 19 patients (38-40). Unfortunately, standard treatment against COVID-19 is currently lacking. Supportive care is important since there is no standard treatment regimen for COVID 19 treatment. In addition to conventional oxygen therapy, case series have been published dealing with prone positioning in awake and spontaneously breathing patients. It is unclear whether this measure will permanently improve oxygenation or prevent a possible intubation. However, it is stated

that the prone position reduces the need for intubation. Oxygen therapies applied with high-flow nasal cannulas (HFNC) can also be effective in clinically stable patients (41). Although the evidence for the benefit of using HFNC and non-invasive ventilation (NIV) is poor, these treatment modalities appear to be important in terms of avoiding intubation and prognosis. However, the treatment of these patients in the intensive care unit presents great difficulties for the entire treatment team (41).

Scientists around the world continue to simultaneously investigate the effectiveness of existing drugs against SARS-CoV-2, as well as developing new treatment options. And these drugs are used in the treatment of patients. The mechanisms of action of the drugs recommended for use in the guidelines are to prevent the entry of the virus into the cell, to reduce or inhibit its replication, and to suppress the increased and uncontrollable inflammatory response caused by the disease. It is aimed to neutralize the virus with immune plasma treatments that contain antibodies against the virus obtained from healed patients (42). For this purpose; convalescent plasma, immunomodulatory drugs (Chloroquine and Hydroxychloroquine, Azithromycin), RNA dependent RNA polymerase inhibitors (Favipiravir, Remdesivir, Ribavirin), protease inhibitor (Lopinavir / Ritonavir, darnunavir), Interleukin (IL) -6 inhibitor (Tocilizumab), Interleukiline -1 (IL-1) receptor antagonist (Anakinra) and other drugs (dexamethasone, prednisolone, Ivermectin, Teicoplanin and lipoglycopeptides, Oseltamivir and Baloxavir) are used (43, 44). There is insufficient evidence regarding the safety and efficacy of these treatments. In addition, there are non-virus-specific (such as low molecular weight heparin) treatment regimens used to prevent disease-related complications (45).

**As a result**, there is no specific drug or vaccine treatment yet for the new coronavirus. Given the spread of this virus and the increasing number of infected people, the COVID-19 pandemic will continue to be a major problem around the world. In pandemic control, the most important points are the prevention of transmission routes with the measures taken in the society, determination of patients and contacts, treatment and follow-up, isolation, hospital facilities and adequate treatment services. This pandemic should be managed by all countries, in line with epidemiological data and by using a suppression method, with an approach focused on preventing cases and deaths.

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