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Abstract
In the last days of 2019, the World Health Organization (WHO) Country Office reported cases of pneumonia of unknown etiology in Wuhan City, Hubei Province, China. The causative agent was isolated on January 7, 2020 and identified as a new type of coronavirus. A novel coronavirus outbreak known as SARS-CoV-2 was announced by the WHO as an urgent public health problem of international concern on January 31, 2020. The recent pandemic caused by a novel coronavirus, which occurs in humans in the form of severe acute respiratory syndrome and called SARS-CoV-2, has not only had a great impact on the health system and economy in all countries, but also has led to changes in habits and lifestyles. In this review, attention was drawn to the relationship between SARS-CoV-2, which is the cause of the current pandemic, and coronaviruses observed in animals, and its effect on humans. The new coronavirus and what we have learned about the pandemic, the situation in Turkey and current approaches in diagnosis and treatment were discussed.

Keywords
COVID-19; Virus; Laboratory Findings
Introduction

In the last 20 years, the swine flu, SARS, MERS, Zika, Ebola pandemics, and finally COVID-19 that emerged in Wuhan, China in December 2019 affected the entire world in a short time, are seen to be effective at a global level. In a review published in 2005, which was about the viruses that affect the lower and upper respiratory tract and cause clinical symptoms such as severe acute respiratory syndrome in children were described and many members of the coronavirus family were identified. Furthermore, the people are likely to be exposed to the other viruses belonging to this family, but have not been yet specified [1]. Therefore, it has been known for a long time that coronavirus family act on the respiratory tract and causes serious clinical features. Even so far, it is clearly known that viruses, which are members of this family can cause serious epidemics on a global scale, as the examples of SARS (Severe Acute Respiratory Syndrome) identified in February 2003, and Middle East Respiratory Syndrome (MERS) identified in September 2012 [2], (available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019).

The relationship between human health and animals was first pointed out by Rudolf Virchow, a pathologist of German origin, and the term "zoonosis" was introduced by this researcher in 1880 [3, 4]. It is noteworthy that in the last two decades, newly emerging and fatal zoonotic viruses, including the coronavirus infections mentioned above, are expected to originate from bats. Many studies have revealed that bats are exceptional mammals in their ability to be a natural reservoir of viruses and accommodate a wide variety of viruses to other animal species [5-8]. Though many studies have been conducted in recent years on the biological mechanisms underlying these determinations, it is considered certain that in the coming years the world will witness epidemics caused by bat-borne viruses [9, 10].

In 1937, Beaudette and Hudson identified the first coronavirus that cause respiratory infection in chickens [11]. The first case of human coronavirus (HCoV) infection was reported in 1960 in a patient suffering from the common cold [12]. These coronaviruses are divided into two different antigenic classes: HCoV 229E and HCoV OC43 [13]. HCoV NL-63 was defined in 2004 and HCoV HKU1 in 2005. In many studies, it has been determined that especially HCoV NL-63 causes respiratory system infections in children [14-17].

Started on December 31, 2019, a case of pneumonia that could not be determined with the existing tests in Wuhan city in China's Hubei province, revealed on January 7, 2020 that the agent was a new coronavirus, causing infections in humans (available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019), (available at: https://www.ecdc.europa. Eu/en/covid-19/latest-evidence/coronaviruses), (available at: https://hsgrm.saglik.Gov.tr/tr/covid19 ), [18-20]. It has been named as SARS-CoV-2 (severe acute respiratory syndrome-coronavirus-2) by the International Committee for Taxonomy of Viruses. It has been identified as the seventh CoV that causes disease in humans, and the third CoV that has passed from animals to humans since 2005 and has been associated with severe respiratory diseases [21]. The causative agent virus has been defined as 2019-nCoV (2019-novel coronavirus) and the disease was defined as COVID-19 (coronavirus disease-2019) by WHO (available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019).
RNA to the cytoplasm. Initially, two viral replicase polyproteins are synthesized. These two large polyproteases result in 16 non-structural proteins (nsp). These 16 nsp form double-membrane vesicles (DMV) and replication and transcription complex (RTC). These newly formed structural proteins and genomic RNA are combined in the ERGIC to create new virions. The formed virions exit the cell via exosomes [28]. Serological tests are usually designed against S proteins, as receptor binding constitutes the initiation process of infection [29,30].

**Epidemiology**

Although the source of the agent has not yet been precisely defined, the first cases were reported epidemiologically associated with the Huanan Seafood Wholesale Market, a livestock and seafood market in Wuhan. As there are predictions that the disease is transmitted from bats to humans, it has also been suggested that there is an intermediate host between bat and humans, and this intermediate host is an anteater (pangolin), and the new coronavirus may have originated from the recombination of bats and pangolin coronaviruses [31,32]. Although the disease is considered to be of zoonotic origin, human-to-human transmission has also been identified and has become the main route of transmission. In a short time, there was a significant increase in the number of cases, and the disease spread globally [18,33,34]. Although incubation begins 1-2 days before the symptomatic period and ends with the disappearance of symptoms, there are also opinions that viral spread may take longer depending on the severity of the disease (available at: https://hsgm.saglik.gov.tr/tr/covid19), (available at: https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19-epidemiology-virology-clinical-features-diagnosis-and-prevention-clinical-features-diagnosis-and-prevention). While the highest rates of infected people and deaths were reported from China in the first two months, the number of cases and deaths in China has decreased since the first week of March 2020, but the number of infected people and deaths has gradually increased in all regions where human life is located, except for Antarctica.

**Epidemic**

There are three zones on the epidemic curve: Increasing, plateau, and decreasing phases.

The period of increasing phase is affected by the country's demography, age distribution, the health system's preparedness, implementing some preventive measures, the reaction time of the country to the pandemic, and the reaction of the society to the new implementation rules. This period is usually 3 or 4 weeks for COVID-19 [35].

Plateau phase: The incidence of the disease is stable at this stage. For COVID-19, this phase lasts 2 or 3 weeks, depending on the daily data of the country [35].

Decreasing stage: Today, only China is at this stage, and disease activity can be detected at very low levels 2 or 3 weeks later [35].

The basic reproduction number (R0) is the estimated value expressed as the average number of individuals infected in a susceptible population during the period when an infected person was contagious (number of secondary cases) [31,36].

If R0<1, the infection will decrease and disappear over time and if R0>1, a pandemic is expected [36]. With the initial data, the basic reproduction number for COVID-19 caused by SARS-CoV-2 was estimated to be between 2.24 and 3.58, and a higher pandemic potential was predicted compared to SARS [18,31,37].

**Characteristics of clinical features**

As the pandemic continues, the distribution of clinical features commonly detected in patients with infection may change over time. In a recently published review, approximately 83-98% of cases complained of fever, cough in 76-82%, muscle pains, weakness, fatigue in 11-44%, headache, and it has been reported that sore throat, abdominal pain and diarrhea may accompany the clinical picture [38]. Furthermore, pneumonia is the most common serious state in the infection. Definitions regarding the severity of the disease are not yet clear and different classifications can be made [2], (available at: https://hsgm.saglik.gov.tr/tr/covid19), (available at: http://www.uptodate.com/contents/coronavirus-disease-2019-covid-19-epidemiology-virology-clinical-features-diagnosis-and-prevention-clinical-features-diagnosis-and-prevention).

**Laboratory findings**

Whole blood count findings may vary in COVID-19 cases. While lymphopenia is detected in most of the cases, varying degrees of leukopenia or leukocytosis can be seen. In the biochemical analysis, it is generally stated that lactate dehydrogenase (LDH) and ferritin levels are high, and as well as aminotransferase levels can be detected to a high degree. It has been reported that serum procalcitonin levels were within normal limits in most cases with pneumonia at the beginning, but these levels could be found to be increased if intensive care is needed. High D-dimer levels and the presence of lymphopenia have been associated with mortality (Tables 1 and 2) [31,39-41] (available at: http://www.uptodate.com/contents/coronavirus-disease-2019-covid-19-epidemiology-virology-clinical-features-diagnosis-and-prevention-clinical-features-diagnosis-and-prevention). In some cases of COVID-19, persistent fever progresses with high levels of inflammatory markers such as D-dimer, ferritin and proinflammatory cytokines. It has been reported in studies that an excessive or uncontrolled inflammatory response, similar to the situation defined as cytokine release syndrome or cytokine storm, and the presence of these laboratory findings is associated with the severity of the disease (available at: http://www.Uptodate.com/contents/coronavirus-disease-2019-covid-19-epidemiology-virology-clinical-features-diagnosis-and-prevention-clinical-features-diagnosis-and-prevent-ion), [42]

Increased levels of interleukin-6 (IL-6) were found to correlate with increased fibrinogen levels in a study by Ranucci et al. [43]. Tang et al. also found a significant correlation between disease severity and mortality risk with some hemostasis tests such as increased D-dimer level, fibrin degradation products, and prolonged prothrombin time (PT), and reported a significant difference between laboratory results in death patients and survived. Also, deceased patients showed a statistically significant increase in their D-dimer, PT prolongation, and a
COVID-19 epidemiology and laboratory findings

In a retrospective study conducted by Seyit et al. with patients with COVID-19, PT prolongation, and low fibrinogen were found to be significant in predicting severe disease [45]. In another study involving ninety-four patients, decrease in fibrinogen and antithrombin levels at the findings of 10-14 days [44]. In another study involving ninety-four patients with COVID-19, PT prolongation, and low fibrinogen were calculated to be significantly higher in COVID-19 negative patients. Laboratory results are presented in Table 3. Among 110 COVID-19 positive patients, 75 were hospitalized in different clinics, whereas 35 were monitored with self-isolation at home [47].

In a retrospective study conducted by Gormez et al. with 247 adult patients (154 males, 93 females; mean age: 51.3±14.2 years) hospitalized due to COVID-19, 48 of this patients were treated in the intensive care unit. The median length of stay in intensive care was 13 days, 4 patients died [48]. Shao et al. indicated that 18 patients of 155 individuals died; 80% of deaths occurred within the first three weeks. The deceased are reported to suffer from other underlying chronic diseases such as hepatitis, HIV, diabetes, and hypertension, and are elderly (73.5 years) accompanying COVID-19 [40]. In a retrospective study by Masetti et al., 229 individuals with a mild form of the disease out of 370 COVID-19 positive patients were included in the study; 196 of these individuals were discharged from the hospital within 9 days on average, 33 people (14%) died from respiratory failure [41]. Liu et al. determined that the total mortality rate was 13.47% [49].

Altıntaş et al. in a retrospective study conducted on the data of 56 patients (30 men, 26 women) who were positive for COVID-19, the most common laboratory findings were determined as lymphopenia (30.3%) and high CRP (62.5%). The findings of 23 patients were normal, and 25 patients were reported to have chronic diseases [50].

Ok et al. examined retrospectively 139 patients who were positive for COVID-19 by categorizing them into three groups according to the severity of the disease (medium: 85, severe: 34 and critical: 20). A total of 13 individuals from the severe group died (9.4%) [46]. The severity of COVID-19 can vary from patient to patient. According to the results of a retrospective study, advanced age, the presence of an underlying disease and the immune system can be considered as the main risk factors affecting the severity and survival time of the disease.

Table 1. China; Retrospective study: Clinical and biochemical characteristics of COVID-19 positive patients [40]. (Zhongnan Hospital of Wuhan University)

Table 2. Italy; Retrospective study: clinical and biochemical properties of COVID-19 positive patients [43]. (Single Center Emergency Service in Milan from 28 February to 10 April 2020)

Table 3. Turkey; Retrospective study: Clinical and biochemical properties of COVID-19 positive patients. Siirt State Hospital and Emergency Department of Pamukkale University between April and May 2020 [46,47].
**Diagnostic tests and screening**

People who need to be screened for SARS-CoV-2 and the decision on which people apply to diagnostic tests may vary according to national and local health policies. In addition, decisions on this issue are updated according to the changes in the distribution of incidence and mortality in the country. Currently, there are 2 currently valid test methods for the diagnosis of COVID-19 [51].

1. Tests to detect viral antigens/viral RNA
2. Serological tests

1. **Viral RNA tests**

The first method of choice for diagnosing COVID-19 is the detection of viral nucleic acid using reverse transcription-polymerase chain reaction (RT-PCR) [52]. Its sensitivity has been reported to be moderate, within the range of 63–78% on average [53].

2. **Serology**

Another broad category of tests in the diagnosis of COVID-19 is serological blood tests that detect IgM, IgA, IgG, and total antibodies. The development of an antibody response to infection depends on host immunity and requires a period [54].

**Treatment**

There is currently a certain treatment for COVID-19. Treatment is supportive and symptomatic. The first step is to provide adequate isolation to prevent contamination of other contacts, patients, and healthcare workers. General principles are to maintain hydration and nutrition and to control fever and cough [55]. Numerous clinical trials are ongoing to define new agents and drugs that will be more effective in treatment [31].

Antiviral drugs used in the early stages of COVID-19 constitute the basis of the treatments. Among these antivirals, two drugs have shown their efficacy in inhibition of SARS-CoV-2 replication in cell culture: "Remdesivir (GS-5734)", an experimental drug developed for the treatment of Ebola virus infection; and "Chloroquine (CQ)" which is used in the treatment of malaria and autoimmune diseases. A summary of candidate antivirals and their mechanisms, according to the highlight of the current publications, is given below [56].

- Mechanism to prevent cell entry by inhibiting TMPRSS2: "Camostat mesylate"
- By inhibiting membrane fusion via targeting to the S protein/AE: "Arbidol"
- Preventing the entry of the virus into the cell by endocytosis: "Hydroxychloroquine"
- By the action of a protease inhibitor: "Lopinavir, darunavir"
- With RNA-dependent RNA polymerase inhibition: "Ribavirin, remdesivir, favipiravir" [56].

SARS-CoV-2 is an RNA virus, and when it enters a cell, it performs protein synthesis with its RNA polymerase. Since it has a large RNA genome and has many repetitive parts, blocking the virus is one of the most limiting aspects of treatment. In addition, it is thought that different species use different receptors and use different pathways to enter the cell, therefore this state reduces the effect of antivirals [56].

Some drugs interact with antiplatelet or anticoagulant drugs, and a few can cause thrombotic events or thrombocytopenia. For example, dose adjustment of vitamin K antagonists, apixaban, and betrixaban may be required while using lopinavir/ritonavir. Lopinavir/ritonavir should not be used in combination with edoxaban or rivaroxaban. Among parenteral anticoagulants and research drugs, a major drug interaction has not been detected. Further studies are needed on this subject as well [57,58].

One of the other drug active substances discussed for patients with COVID-19 is the non-steroidal anti-inflammatory group drug, Ibuprofen. Ibuprofen has analgesic, anti-inflammatory, and antipyretic effects. The hypothetical information about Ibuprofen can increase the expression of ACE-2 [59], as well as the statements of the French Minister of Health, about the anti-inflammatory drugs such as ibuprofen and corticosteroids may worsen the infection by suppressing the immune system in COVID-19 patients have been the source of aforementioned debate [60,61].

It was pointed out that prostaglandins such as PGE2, PGD2, PGJ2 are factors that both support and restrain inflammation, and the use of ibuprofen and other non-steroidal anti-inflammatory drugs, which inhibit the synthesis of prostaglandins through cyclooxygenase (COX) inhibition, may increase the severity of the disease in COVID-19 cases. Therefore, it has been stated that it may be contradictory [62,63]. Furthermore, it was shown in 2003 that SARS-CoV viruses, causing the SARS outbreak, lead to an increase in COX-2 expression by direct binding to the COX-2 promoter [64]. It has been reported that the COX inhibitor, Indomethacin, exerts a potent antiviral effect by inhibiting the RNA synthesis of the SARS-CoV virus. It has been stated that antiviral activity of indomethacin occurs independently from COX inhibition [65]. In this context, it has been suggested that Indomethacin can be useful in the treatment of SARS infections with both its anti-inflammatory activity mediated by COX-2 inhibition and its antiviral activity independent of COX-2 [65].

Remdesivir is not recommended in patients with an alanine aminotransferase (ALT) values greater than or equal to ten times the upper limit of normal, and it is stated that it should be discontinued if ALT reaches the specified values during treatment or in the presence of any evidence of liver damage (available at: https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19-management-in-hospitalized-adults),WHO has initiated a multinational study to evaluate the efficacy of remdesivir, chloroquine, and hydroxychloroquine, and lopinavir/ritonavir with or without interferon-beta (available at: https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19-management-in-hospitalized-adults), (available at: https://www.sciencemag.org/news/2020/03/who-launches-global-megatrial-four-most-promising-coronavirus-treatments). The RNA polymerase inhibitor favipiravir, which is used in the treatment of influenza in Japan, has also been approved in China to be used in the experimental treatment of COVID-19 and has been used in treatment protocols in Turkey (available at: https://www.uptodate.com/contents/ coronavirus-disease-2019-covid-19-management-in-hospitalized-adults), (available at: https://hsrm.saglik.gov.tr/tr/covid19). Among the cytokines that are reported to be increased during...
hypercytokemia, the most important one is IL-6. In COVID-19-associated Macrophage activation syndrome (MAS), inflammation appears to be more lung-centered than multi-organ, so the argument for the involvement of IL-6 comes from changes in biochemical parameters, including ferritin, and reports of anti-IL6R efficacy. The timing of anti-IL-6R, if too early, may adversely affect viral clearance, which should be evaluated in trials. If blocking IL-6R early in COVID pneumonia MAS-like disease appears to have a detrimental effect on type-2 pneumocyte antiviral immunity, then local enhancement of IL-6 may be considered. There are concerns that its early use may be harmful due to Antibody-dependent enhancement (ADE) [66].

Recent studies have focused on the importance of viral load in COVID-19 pneumonia. Therefore, it is very important to find an effective antiviral drug and include it in the early treatment plan [66]. Other recommended drugs for treatment are arbidol (an antiviral drug available in Russia and China), intravenous immunoglobulin, interferons, anticoagulants, and plasma treatment [67].

Vaccines are the most effective strategy for preventing infectious disease because they are less costly than treatment protocols and reduce morbidity and mortality without long-term effects. In the last two decades, three human coronaviruses (SARS-CoV, MERS-CoV, and SARS-CoV-2) have emerged worldwide and pose a significant threat to global health. However, there are still no approved vaccines for human coronaviruses [18,68,69].

Conclusion

SARS-CoV-2, from the coronavirus family, is an RNA virus thought to originate from bats and started in China, affected the whole world and brought social and economic life to a stop. The frequent occurrence of zoonotic viruses such as Sars, Mers and finally SARS-CoV-2 from animals to humans reveals that issues such as the investigation, control and prevention of outbreaks are important issues that need to be carefully considered. Although it is thought that protease inhibitors may affect viral S proteins and viral RNA polymerases, there is no effective drug therapy developed and approved against coronavirus infections. Many drug or vaccination studies are being carried out intensively. Until a solution is reached, measures to prevent the spread of the epidemic should be strictly complied with, and a stable attitude should be shown in compliance with these measures taken by the health authorities of the society in combating the pandemic.

Laboratory findings have become much more important in combating this newly defined disease as its effects on the lockdown of health systems are observed. The main role of clinical laboratories in this pandemic has gone beyond the etiological diagnosis of COVID-19. In COVID-19 positive patients, especially hypoalbuminemia, lymphopenia and thrombocytopenia, and increases in aminotransferases, total bilirubin, D-dimer, CRP, erythrocyte sedimentation rate, cardiac troponins, creatinine, prothrombin time and procalcitonin levels should be monitored as markers for both the severity of the infection and the prognosis. It is critical to monitor the levels of these parameters in the process leading to multiple organ failure and death. In addition laboratory parameters still used in the clinical practice of COVID-19, researches continue searching for potentially useful and practical new biochemical parameters in screening, clinical management of COVID-19, as well as many studies on drugs or vaccines continues intensively. It is considered that in cases, laboratory tests (D-Dimer, CRP, AST, ALT, Ferritin, Fibrinogen, Neutrophil, Lymphocyte), which can help clinicians to identify and monitor patients with high risk of COVID-19, also guide the pathophysiology of the disease.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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Conflict of interest

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