

# European Archives of Medical Research

Formerly Okmeydanı Medical Journal

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## Healthcare Service Management in Prof. Dr. Cemil Taşçıoğlu City Hospital During COVID-19 Pandemic



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
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
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
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
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
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
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# Management Format in Turkey in the Pandemic; How was the Pandemic Managed in Our Hospital?

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**Keywords:** Pandemic, COVID-19, management, hospital

Dear Editor,

Coronavirus Disease-2019 (COVID-19) disease was first reported in Wuhan, China's Hubei region, and spread all over the world today. It was declared as a pandemic by the World Health Organization on March 11, 2020 (1). Studies on COVID-19 in our country started on January 10 and the first meeting of the Scientific Advisory Board of the Ministry of Health was held on January 22 (2). The Ministry of Health, Provincial Health Directorate, Public Hospitals Services Presidency and District Health Directorates have provided a very serious infrastructure support by providing all logistical support, medicine and material supply for our hospital. Secondly, everyone, from healthcare personnel, cleaning worker, warehouse manager to driver in our hospital have worked in unity and solidarity with the extraordinary efforts which has provided the greatest ease in managing the pandemic process. Thirdly, the great support of our nation has ensured the smooth progress of the process. The aid campaigns organized by our people have once again revealed the unity of the Turkish nation.

To talk about the pandemic process management in our hospital, pandemic preparations started on March 4, 2020 with planning and some changes in physical conditions. We can list the changes we have made as follows:

## Training/Protective Measures

Our main goal during the pandemic has been to protect our healthcare professionals. Clinical microbiology and infection diseases specialists, infection control committee nurses and training nurses gave trainings on COVID-19 precautions, the use of personal protective equipment, and hand washing to all nurses, doctors, clinical support personnel, technicians, cleaning staff and civil servants working in our hospital. Training on cleaning and disinfection control was also planned for cleaning staff. In addition to the training on COVID-19 precautions for our new staff members; orientation trainings were given by our training nurses. Three hundred and fifty people attended these trainings. None of the personnel who did not complete these trainings took an active role in the field.

## Pandemic Board

In order to organize the activities in the clinic, to plan the diagnosis, treatment and follow-up of the patients with scientific methods and with a multidisciplinary perspective, the "Pandemic Board" consisting of various branches, especially the Infectious diseases and clinical microbiology clinic, was formed by the experts of our hospital, who closely followed the national and international algorithms. In addition to the infectious diseases



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and clinical microbiology, faculty members from internal medicine, anesthesia and reanimation, emergency medicine, family medicine, pediatrics, and clinical microbiology clinics took part in the pandemic board. Daily meetings were planned with the pandemic board. The meetings started every morning at 9:00 am and lasted about an hour and a half. The follow-up of our current patients with suspected COVID-19 was carried out by our infectious diseases and clinical microbiology clinic. With the joint decision of our pandemic board, it was decided to complete the operations planned in the first week of the pandemic and then put the surgery programs on hold, except for emergency, urgency and malignancy. In each meeting, criticisms were made about the previous days and the next was planned accordingly. It was deemed appropriate to continue Central Physician Appointment System appointments in outpatient clinics and not to see patients without an appointment throughout March. With the recommendation of the pandemic board, temperature measurement practice was initiated for patients at all outpatient clinic entrances. Except for emergency conditions, endoscopic procedures were canceled. In the first stage, those who had suspicious contact or a history of traveling abroad were accepted as patients with suspected COVID-19. As the number of patients in our country increased, every patient who came into contact with patients with suspected COVID-19, as well as who had a history of overseas travel, was considered as patient with suspected COVID-19. The pandemic board dynamically followed the process and informed all clinics about the changes. One of the most important decisions of the pandemic board was to classify and evaluate patients according to the severity of infection. Providing high-flow oxygen therapies to patients with moderate infection in the early period enabled our patients to recover faster. They facilitated the operations in our hospital with many decisions they took like this.

## Physical Changes

The first physical change in our hospital, in line with COVID-19 measures, was initiated in the emergency room, where the patients with suspected COVID-19 were first admitted. Our emergency service was divided into two areas. A dirty area where patients with COVID-19 were treated and a clean area where other patients were examined, were created. The patients were guided according to whether they had COVID-19 by applying triage before being sent to these areas. Second, infectious diseases and clinical microbiology clinic was evacuated for the isolation and treatment of patients with COVID-19. As the number of our patients increased in the following days, other

clinics of our hospital started to be reserved for these patients. With the increasing number of patients in the process, evacuation continued on the other floors starting from the second floor of our hospital. Likewise, necessary arrangements were initiated in our intensive care units. Anesthesia intensive care units were separated into COVID-19 intensive care units and non-covid intensive care units. At first, 8-bed anesthesia and reanimation intensive care unit, then 6-bed cardiovascular surgery intensive care unit and 17-bed anesthesia and reanimation intensive care unit were reserved for patients with COVID-19. COVID-19 intensive care units served our patients with a bed capacity of 33 in the main building of our hospital. With our 48-bed anesthesia and reanimation intensive care unit opened in our new building, our adult intensive care bed capacity reserved for patients with COVID-19 has reached 81.

With the opening of our new hospital, 10 blocks in total were put into service for our patients with COVID-19, starting from the first block of the 7<sup>th</sup> floor to the last block of the 6<sup>th</sup> floor. The 6<sup>th</sup> and 8<sup>th</sup> floors of the main building, which were determined as clean areas, were used for all patients without COVID-19 disease who were still hospitalized and followed up in our hospital. The treatment of these patients who were hospitalized from the emergency department was carried out on these floors.

Our polymerase chain reaction (PCR) laboratory established for the COVID-19 diagnostic center on behalf of Presidency of Turkish Institutes of Health within our hospital has also facilitated the diagnosis and accelerated the treatment process.

## Changes in the Work Plan

For clinics that serve patients with COVID-19, a 3-group study schedule was created until the beginning of April. One full day work and three full days rest were adopted as the basic understanding to minimize contamination with patients. Personnel planning was made in the form of a resident serving in each ward and a specialist physician on each floor. Upon the increase in patients, floor duty plans were prepared again and it was decided that one specialist physician and 3 residents for each COVID-19 ward would work under the management of Infectious diseases and clinical microbiology clinic on these floors. All our physicians, from residents to senior faculty members, worked at COVID-19 wards.

In order to strengthen the communication in the field, on-duty experts and supervisor nurses were held every morning at the COVID-19 ward, and the problems in the field were monitored instantly. The Gülbahar District Outpatient Clinic, which served

as an additional building of our hospital, was closed with the start of the pandemic process. Our hospital's health board started a special process for our personnel with chronic health problems. Our healthcare professionals with chronic diseases were evaluated by the health board and revisions were made in the work programs of those deemed appropriate.

In order to reduce the concerns of relatives of our patients hospitalized in the COVID-19 wards during the pandemic, they were called by our residents by phone and given information.

With the increase in our intensive care bed capacity, residents and specialists from different branches were trained for anesthesia and reanimation intensive care and started to be assigned to COVID-19 intensive care units.

## Support Services

One of the important actions of our hospital was the provision of personal protective equipment. Pulse oximetry and stethoscope purchases were made rapidly for the increasing needs. Rapid antibody tests were obtained and used before distributed to hospitals. PCR sampling booths and stretchers with isolation were built with institutional facilities. The dining hall arrangement was adjusted to prevent contamination. Our prediction was that we would not reach, as many countries experienced difficulties in accessing personal protective equipment such as masks for healthcare workers. For this reason, masks designed by us started to be produced from American cloth fabric, and all kinds of materials based on scientific reason were provided to protect our employees at every stage of the process. The measures regarding the visitor ban in the hospital were kept at the highest

level and the field was informed on this issue. Visits of patients in intensive care units by their relatives were completely stopped when the pandemic began. Before the curfew, the discharges from the hospital were planned to be made until 12:00 in order to prevent the patients from suffering victimization, and the transfers of patients and employees were organized.

The pandemic has shown us that this is a state of mobilization. We have seen that with the support of the state organization and the nation, we can overcome any challenge. We think it will be beneficial for each hospital to develop its own strategies according to its own internal dynamics in disasters such as pandemics.

## Ethics

**Peer-review:** Externally and internally peer-reviewed.

## Authorship Contributions

Concept: P.İ. H.G., Design: P.İ. H.G., Analysis or Interpretation: H.G., Literature Search: P.İ. H.G., Writing: P.İ. H.G.

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# The Pandemic of COVID-19 and its Impact on Turkey

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## Abstract

The world and our country go through a pandemic period called Coronavirus Disease-2019 (COVID-19), which affects the health of billions of people both physically and psychologically, and their social life and economy. On December 31, 2019, the World Health Organization (WHO) reported cases of pneumonia of unknown etiology in Wuhan, China, Hubei province. Findings compatible with fever, dispnea and pneumonic infiltration in the lung were detected in the cases. On January 7, 2020, this was identified as a new coronavirus that has not previously been detected in humans. The name of the disease was accepted as COVID-19, the virus was named as Severe Acute Respiratory syndrome-coronavirus (SARS-CoV)-2 due to its similarity to SARS-CoV-2. The WHO classified the COVID-19 epidemic as the “public health emergency on an International scale” on January 30 and defined it as a global epidemic (pandemic) on March 10 due to the spread and severity of the virus to other countries. Studies on COVID-19 started on 10<sup>th</sup> of January in our country and on January 22, the Scientific Advisory Board of the Ministry of Health of the Republic of Turkey held its first meeting and measures were taken. The first COVID-19 case occurred on March 11, after neighboring countries such as Europe and Iran. After this date, local measures have been taken across the country to gradually prevent and reduce the spread of the virus in the community. It is the responsibility of the whole community to pay attention to the measures taken. The most important rules in preventing infection are the use of masks, maintaining social distance and paying attention to all measures. Healthcare professionals worked intensely and devotedly during this period, fulfilling their duties and will still continue till this period ends.

**Keywords:** COVID-19, pandemic, Turkey

## INTRODUCTION

### Coronavirus Disease-2019 (COVID-19) Pandemic

Pandemic is the general name given to outbreaks that spread and affect a wide area in more than one country or continent in the world. According to the definition of the World Health Organization (WHO), three criteria are sought in general terms for a disease to be a pandemic: emergence of a new virus or a mutated agent, its easy transmission to humans, and its easy and continuous transmission from person to person (1). Pandemic is announced by WHO when certain criteria are met. The reason for this announcement is that the disease poses a threat to all countries, in other words, the emerging new virus spreads quickly from person to person (1).

The degree of impact of the pandemic on the society varies depending on the infectivity and virulence of the virus, the immune status of the individuals in the society, the life habits and socio-economic status of the individuals, the risk factors, the quality of health services in their country and the climate (1,2). It is possible to reduce the spread of infection in the community and thus the number of people who will be infected in the early stages of the pandemic and the number of patients that will occur due to the pandemic.

Severe Acute Respiratory syndrome-coronavirus-2 (SARS-CoV-2) emerged as a previously unknown virus in 2003 as the first international health emergency of the 21<sup>st</sup> century, causing hundreds of people to die. In September 2012, Middle East Respiratory syndrome (MERS)-CoV-2, which was also a member



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of the CoV family, was not shown in humans or animals before, was first described in Saudi Arabia in humans (2,3).

On December 31, 2019, the WHO China Country Office reported patients with pneumonia of unknown etiology in Wuhan, China's Hubei province. It was stated that there was a cluster in Wuhan South China Seafood City Market employees in the south of Wuhan. Fever, shortness of breath and radiological findings compatible with pneumonic infiltration in the lung were detected in the patients. On January 7, 2020, the agent was identified as a new CoV that was not previously detected in humans. Later, the name of the disease was accepted as COVID-19, and the virus was named as SARS-CoV-2 due to its close similarity to SARS-CoV-2 (1,2).

The first imported patient was a 61-year-old Chinese woman reported from Thailand on January 13, 2020. In the following days, the number of countries reporting patients gradually increased, and there was an increase in patients with COVID-19 and deaths due to this infection in Iran, South Korea and Italy. The WHO classified the COVID-19 outbreak as an "international public health emergency" on January 30, and defined it as a global outbreak (pandemic) on March 11 due to the spread and severity of the virus in countries other than China, where

the pandemic started first. In the ongoing process, significant increases in the number of patients were observed in Europe, then in North and South America and all over the world. As of the beginning of June 2020, the pandemic continues and patients are reported from almost all countries in the world (1,3).

The first patient with COVID-19 in our country was observed on March 11 after neighboring countries such as Europe and Iran (1). Tables 1 and 2 show the number of patients and deaths in the continents and the top 10 countries with the highest number of patients on 15 June 2020 (4).

### General Information About COVID-19

CoV-2 are enveloped RNA viruses with rod-like extensions on their surface. Because of these protrusions, these viruses are named as CoV (crowned virus). These viruses can cause self-limiting mild infections, such as common cold in the population, and more severe infections such as MERS and SARS (2,3).

There are several subtypes of CoVs (HCoV-229E, HCoV-OC43, HCoV-NL63 and HKU1-CoV) found in humans that can be easily transmitted from person to person. These subspecies circulating among humans are mostly viruses that cause colds. However,

**Table 1. Status of patients with COVID-19 by continents (Worldometer 15 June 2020) (4)**

Continent	Total number of patients	Number of new patients (in the last 24 hours)	Total number of deaths
World	8,108,667	124,600	438,596
Africa	254,214	9,636	6,793
America	3,970,574	64,180	207,291
Europe	2,220,090	13,612	183,215
Asia	1,654,119	37,157	41,158
Australia	8,946	15	102

COVID-19: Coronavirus Disease-2019

**Table 2. Top 10 Countries in the world by total number of pases (Worldometer 15 June 2020) (4)**

Countries	Total number of patients	Number of new patients	Total number of deaths
USA	2,182,950	20,722	118,283
Brazil	891,556	23,674	44,118
Russia	537,210	8,246	7,091
India	343,026	10,243	9,915
UK	296,857	968	41,736
Spain	291,189	181	27,136
Italy	237,290	301	34,371
Peru	232,992	3,256	6,860
Iran	189,876	2,449	8,950
Germany	188,044	373	8,885

USA: United States of America, UK: United Kingdom



there are many CoV subspecies detected in animals, and it is known that these viruses can cause severe illness in humans by transmitting from animals to humans. As a result of detailed studies, it has been revealed that SARS-CoV-2 is transmitted to humans from musk cats and MERS-CoV-2 from dromedary camels (2,3).

The reservoir of SARS-CoV-2 is still under investigation. All available evidence for COVID-19 suggests that SARS-CoV-2 is a zoonotic source (2,3).

The disease is mainly transmitted by droplets. In addition, the droplets emitted by sick individuals through coughing and sneezing are transmitted by touching the mouth, nose or eye mucosa after contact with other people's hands (2,3).

Since viruses can be detected in respiratory tract secretions of asymptomatic people, these people can be contagious.

The entire population is sensitive to COVID-19. Healthcare professionals are the most risky occupational group in terms of encountering the agent. Men, people over the age of 50, people with comorbidities (hypertension, heart disease, diabetes, malignancy, chronic obstructive pulmonary disease, kidney disease, etc), seasonal agricultural workers and those living in care and rehabilitation centers, schools, barracks, detention houses and immigration camps are vulnerable groups in terms of COVID-19 (2,3).

Generally, the incubation period varies between 2-14 days. The contagious period of COVID-19 is not known exactly. Common symptoms of infection are respiratory symptoms, fever, cough, and dyspnoea. Symptoms such as headache, sore throat, runny nose, muscle and joint pain, extreme weakness, loss of sense of smell and taste, diarrhea can also be seen. Although patients can be asymptomatic, pneumonia, severe acute respiratory tract infection, kidney failure, and even death may develop in severe patients (2,3).

Contagiousness begins 1-2 days before the onset of symptoms, and the viral load increases during the onset of symptoms, decreasing rapidly in the first seven days, but may extend beyond the second week.

Management of patients with possible or definite COVID-19 is carried out according to "Patient Follow up Algorithm" (2).

Diagnosis is based on the determination of specific sequences of virus RNA using the polymerase chain reaction test and sequence analysis method in the sample taken from the throat and nose.

Antibody response [immunoglobulin (Ig)M, IgA and IgG] generally develops after a certain period of time in those who

have had COVID-19. Therefore, serological tests cannot be used for diagnosis in the early period of the disease. Although the first antibody response (IgM) starts after 6-7 days, antibody positivity develops 10 days after the onset of symptoms in most patients. Whether the detected antibodies provide immunity and how long it can be detected (IgG) are not clear today. Rapid antibody tests that detect IgM/IgG are currently used (2).

While the fatality rate was between 11% in the SARS and 35-50% in MERS-CoV-2, the fatality rate was reported as 3.8% according to the COVID-19 report of the Republic of China. This rate is 2.6% (2,3) in our country as of 02 May 2020.

COVID-19 does not have a definitive treatment yet. Anti-viral, anti-cytokine/anti-inflammatory drugs are used and coagulopathy management is performed. Vaccine studies are ongoing (1).

### **Situation in Turkey**

Studies on COVID-19 in our country started on January 10, 2020, and the first meeting of the Scientific Advisory Board of the Ministry of Health was held on January 22. The Ministry of Health published the "2019-nCoV Disease Healthcare Professionals Guide" on January 24 (2).

Thermal cameras were placed at airports. Citizens of the Republic of Turkey in Wuhan was brought to Turkey on January 31. The proposal to close Chinese flights was put into effect on February 3 (1,5,6).

The Iran border was closed on February 23, and the Iraq border was closed on February 29, flights to South Korea and Italy were stopped. On the same date, it was announced by the Ministry of Health that field hospitals would be opened on the borders of Iran and Iraq (5,6).

On March 10, the first patient with COVID-19 was reported from our country (2,3).

On March 15, citizens returning from Umrah were quarantined in state dormitories in Ankara and Konya (5,6).

The pandemic caused in taking radical decisions that led to important impacts and results in social, economic, political, economic, administrative, legal, military, religious and cultural fields in Turkey (6).

Education was suspended in schools and universities on March 16, sports competitions were decided to be played without spectators, and mass prayers were suspended in mosques (5,6).

All restaurants, cafes, museums, classrooms, courses, shopping malls, hotels; barbers, hairdressers and beauty centers; cafes, sports halls, concert venues, night clubs, and wedding/

engagement halls were temporarily closed; all citizens were prohibited from picnics and barbecues in forests, parks and gardens (5,6).

In order to reduce the rate of spread of the pandemic and to maintain social distance between people, curfews were initiated for those aged  $\geq 65$  and those with chronic diseases. The restriction was later extended to include children and young people aged  $< 20$ . A call was made not to travel outside the country and not to leave the house unless required (6).

All kinds of scientific, cultural, artistic and similar meetings and activities were postponed with the Presidential Circular published on 20 March (5,6).

On the same date, all hospitals with level 3 adult intensive care units, including at least two of the infectious diseases and clinical microbiology, chest diseases and internal medicine specialists, were defined as “pandemic hospitals” by the Ministry of Health. In the next period, all hospital staff went through very difficult times. All hospitals made pandemic-related arrangements according to their own conditions (5,6).

With the circular issued by the Presidency on March 22, rotation and remote work in public institutions and organizations were allowed (1).

On March 23, Favipravir began to be used in Turkey (2).

The Minister of Health announced that healthcare workers would be paid additional wages for three months (6).

As of April 3, the Ministry of Health Scientific Board was expanded and the “Community Pandemic Management Board”, consisting of Public Health faculty members, held its first meeting.

Turkish Airlines stopped domestic flights on April 3 (6).

It was obligatory to wear masks in public areas such as markets and markets, and entry and exit to 30 metropolitan cities and Zonguldak were banned (6).

The Ministry of National Defense announced that all summons, dispatch and demobilization procedures in military barracks were delayed for a month.

The Council of Judges and Prosecutors announced that all hearings, negotiations and discoveries were suspended until 15 June, except for detained and urgent matters and cases of time out (4,6).

Airlines, especially Turkish Airlines, announced that have terminated all international and domestic flights until next notice (5,6).

The obligation to use masks in public areas such as markets and bazaars was put into effect.

Intercity travels were subject to the permission of the governor and the application of infrequent seating in public transportation was started.

Hundreds of settlements, villages and towns were quarantined under COVID-19 measures.

In order to minimize the economic effects of the pandemic, many regulations were made and support packages were announced.

Flexible working system with minimum personnel in private and public sector was introduced (5,6).

In accordance with the law, the Ministry of Family, Labor and Social Services imposed a three-month dismissal ban on employers.

On April 9, the treatment of patients with COVID-19 was included in the scope of emergency.

On the same date, it was announced that a 1.000-room field hospital would be established on the Atatürk Airport grounds and in Sancaktepe (5,6).

On 11-12 April 2020, a large-scale curfew was declared for the first time (5,6).

It was announced that the curfew would continue in thirty metropolitan cities and Zonguldak between April 23-26.

On April 29, the Minister of Health announced that 7.428 healthcare workers were infected.

A curfew was declared between 1-3 May (2).

The “normalization calendar” was announced on May 4. According to this calendar, it was announced that the travel restrictions in 7 provinces would be lifted and hairdressers, barbers and shopping centers would be opened on May 11.

It was announced by the President that the higher education institutions examination which was previously announced to be held at the end of July, would be held at the end of June by pulling forward one month (5,6).

In a statement, the Ministry of Foreign Affairs announced that 473 Turkish citizens died from CoV abroad. In addition, more than 65 thousand Turkish citizens from 103 countries were brought to Turkey by evacuation (5,6).

One hundred and sixteen countries requested help from Turkey. Medical aid materials including N95 masks, overalls, protective glasses, respirators, test kits and visors were sent to 44 countries,

including the United States of America, the United Kingdom, Spain, Italy and Iran, which were most affected by the epidemic (1,6).

Between 23-26 May 2020, curfews were imposed in all 81 provinces for four days, including Eve and Ramadan Feast.

In early June, after the decision to enter the normalization process and abolish the bans, it was observed that there was a relaxation and relief in the measures, despite giving continuous information on social distance and the use of masks in order not to increase the transmission. Due to the public's complacency in obeying the rules, a partial increase in the number of patients was observed in mid-June.

As of June 11, 2020 the total number of patients with COVID-19 was 174,023 and the number of patients who lost their lives due to COVID-19 was 4,763 in Turkey. Of the current patients, 643 patients are being treated in intensive care units, and 266 of them are receiving respiratory support. 147,860 patients recovered and were discharged (2).

Until June 11, 2020, 2,500,890 people were tested. While Istanbul was the city with the highest number of patients, it was followed by İzmir, Ankara, Kocaeli and Konya, respectively (5,6).

### **The Role of Media in Pandemic**

The media played a major role in the pandemic since the first patient was seen. In this process, the media was effective in informing the public and in managing the risk and motivating the public. The media opened the subject to discussion from different angles by presenting patient and death statistics and at the same time helped the audience/readers to be informed about the developments in the world (5).

In this process, it was seen that there was a large number of false information as well as correct information. Especially before encountering patients in Turkey, lots of news about ways to destroy the virus and to strengthen the immune system with non-evidence-based data, were given (4). In addition to expert scientists in this field, news, programs and broadcasts were made that included the opinions of physicians from different specialties making it difficult for the society to access correct and healthy information. Anxiety level increased in the society (5).

### **CONCLUSION**

Turkey is among the countries affected by the outbreak relatively late. The pandemic has led to many important effects and consequences in social, economic, political, economic, administrative, legal, military, religious and cultural areas in

Turkey. It is obvious that the COVID-19 pandemic will affect our country and our health system for a long time. During the COVID-19 pandemic, the Scientific Committee Guidelines have been taken as a basis for patient management and have been updated periodically. In the guide, last updated on June 1, 2020, information and recommendations are available on management of pandemic, strategies and practices to be followed when encountering a patient with COVID-19 or contact, COVID-19 infection chain (source, transmission route, susceptible people), patient definitions and diagnostic methods. The guideline has been mainly prepared in line with WHO recommendations and is updated in line with current WHO recommendations and scientific developments. In this process, contact tracing teams have been established in provinces under the organization of Provincial Health Directorates. In some provinces, Community Health Center employees mainly work in this task, while in some provinces oral and dental health workers or different healthcare workers are involved in contact tracing.

Guidelines are guiding on issues such as Return to Normalization Plan in Hospitals, Infection Control Measures, and Pandemic Management in the Community in the COVID-19 pandemic and are renewed within the framework of changing conditions.

Since the COVID-19 pandemic has not been completely terminated, the risk continues until an effective treatment and/or vaccine specific to the virus is found. During the pandemic period, the need for other health services has also increased. For this reason, taking into account that the pandemic continues, it is inevitable that other health services will start. This situation reveals the necessity of providing services within the same system for patients with and without COVID-19. Points to be considered here are ensuring the continuity of COVID-19-related precautions and healthcare services, keeping hospitals safe for patients with and without COVID-19, ensuring the safety of healthcare professionals, ensuring equal access and safety to all patients, and ensuring that personnel and healthcare services are to regulate gradually.

### **Ethics**

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# The Characteristics of SARS-CoV-2 Virus and Microbiological Diagnosis

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## Abstract

World Health Organization, named the disease caused by Severe Acute Respiratory syndrome-coronavirus-2 coronavirus on 11 February 2020 as Coronavirus Disease-2019 (COVID-19). A person who has clinical symptom and a history of contact with a patient with confirmed COVID-19 is identified as a “possible case” and is expected to be confirmed by laboratory test. A confirmed case is asymptomatic/symptomatic suspected individual with a positive molecular test. Specific diagnosis is made by specific molecular tests on respiratory samples (orofarengeal/nasopharyngeal swab/sputum/endotracheal aspirates and bronchoalveolar lavage). The virus can also be detected in the stool and in severe patients for a short time in the blood. The number of molecular tests that should be used in the case of a pandemic is rapidly increasing. At the beginning of the outbreak in Turkey, tests could only be performed in suspected patients in the central unit and then they began to be performed in other reference laboratories. Rapid antigen tests did not provide the desired performance, while rapid antibody tests were distributed to the field to support polymerase chain reaction tests and determine immunity. Microbiology Laboratory is indispensable in controlling the COVID-19 pandemic.

**Keywords:** SARS-CoV-2, COVID-19, microbiological diagnosis

## INTRODUCTION

World Health Organization (WHO), named the disease caused by Severe Acute Respiratory syndrome-coronavirus-2 (SARS-CoV-2) coronavirus on 11 February 2020 as coronavirus disease-2019 (COVID-19). A person who has fever, sore throat, cough, or shortness of breath and a history of contact with a patient with confirmed COVID-19 is identified as a “possible patient” and is expected to be confirmed by laboratory test. Among the patients that meet the “possible patient” definition, patients with SARS-CoV-2 detected by molecular methods are defined as definite or confirmed patients. Specific diagnosis is made by specific molecular tests on respiratory samples (orofarengeal/nasopharyngeal swab/sputum/endotracheal aspirates and

bronchoalveolar lavage). The virus can also be detected in the stool and in severe patients for a short time in the blood. Validated and certified tests are not common at this time. The number of molecular tests that should be used in the case of a pandemic is rapidly increasing. At the beginning of the outbreak in Turkey, tests could only be performed in suspected patients in the central unit and then they began to be performed in other reference laboratories. Rapid antigen tests did not provide the desired performance, while rapid antibody tests were distributed to the field to support polymerase chain reaction (PCR) tests and determine immunity. Microbiology laboratory is indispensable in controlling the COVID-19 pandemic. Molecular tests have become widespread in our country, the number of tests performed has gradually increased, and the results can be



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obtained rapidly. In this way, support has been provided to the clinic and contact tracing.

## Coronaviruses and SARS-COV-2

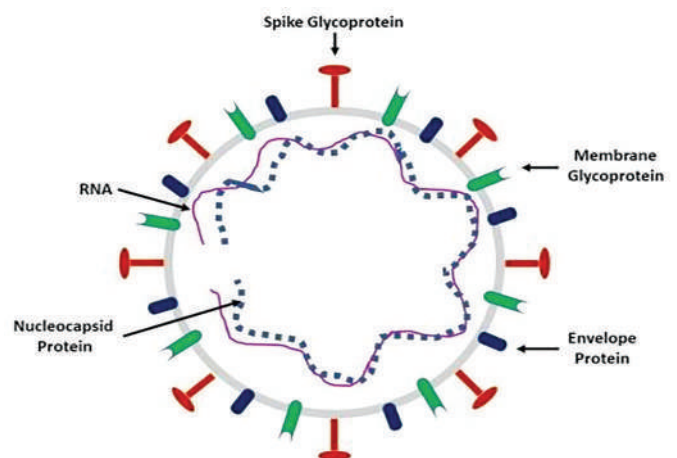
### History

In 1937, Beaudette and Hudson identified the first coronavirus to cause respiratory infection in chickens (1). The first patient with human coronavirus (HCoV) infection was reported in 1960. This patient was suffering from the common cold (2). These coronaviruses have been divided into two different antigenic classes as HCoV 229E and HCoV OC43 (3). HCoV NL-63 was defined in 2004 and HCoV HKU1 in 2005. In many studies, it was determined that especially HCoV NL-63 caused respiratory system infections in children (4). SARS caused by SARS-CoV-2, which alarmed WHO in February 2003, affected countries such as Hong Kong, Taiwan, Canada and Singapore the most after the Guangdong region of China. The disease, which is thought to be transmitted first from bats to palm musk cats and from them to humans, reached 8422 patients in an eight-month period, with most of the patients from China. Nine hundred sixteen deaths were recorded and the mortality rate was determined as 10.8%. After 2004, there has been no new case report related to SARS-CoV-2. Another coronavirus, Middle East respiratory syndrome (MERS)-CoV-2, was isolated in 2012 from the respiratory sample of a 60-year-old patient with acute pneumonia and kidney failure (MERS) in Saudi Arabia. Studies have found that dromedary camels act as reservoirs for this virus. As of February 14, 2020, it differs from other coronaviruses with more than 2.500 laboratory-approved patients and a high fatality rate of 34.4% (5). In late December 2019, Chinese health officials concentrated their work on the cluster of patients with atypical pneumonia occurring in people in a seafood and livestock market in Wuhan, Hubei Province of China. Fever, cough and chest discomfort and/or respiratory distress were reported most frequently in patients. The patients were diagnosed as having pneumonia with the help of radiological diagnostic tests such as chest X-rays and/or computed tomography. By sequencing the bronchoalveolar lavage samples taken from patients, a variable betacoronavirus (betaCoV) showing approximately 80% sequence homology with the bat SARS virus-like coronavirus was identified (6). The virus was then isolated in cell culture and, according to detailed genetic analysis results, it was reported to show 89% sequence homology with bat SARS-like-CoVZXC21, 82% with human SARS-CoV-2 and approximately 51.8% with MERS-CoV-2 (7). Variant CoV-2, named as SARS-CoV-2 by the International Committee of Taxonomy of Viruses, has been defined as the seventh CoV-2 that causes disease in humans and the third

CoV-2 that has been associated with severe respiratory diseases since 2003 (8,9). WHO named the disease caused by SARS-CoV-2 coronavirus as COVID-19 on February 11, 2020 (10).

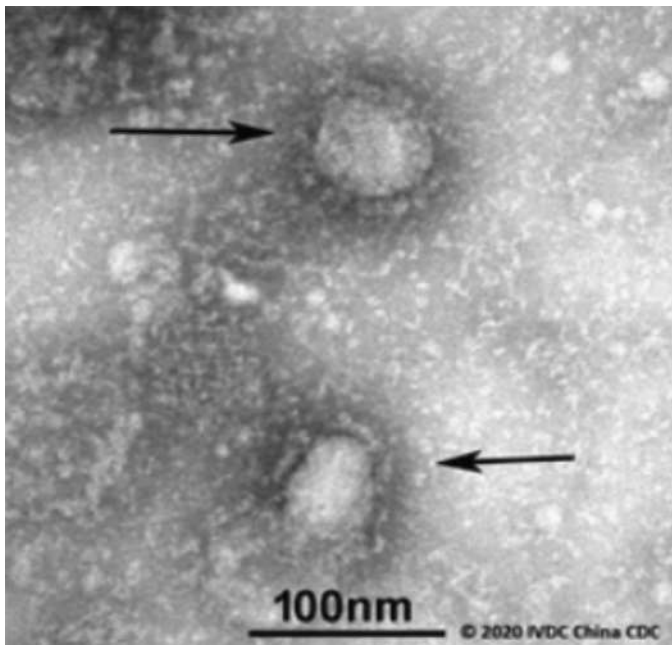
### General Features and Genome

Coronaviruses belong to the order Nidovirales, family Coronaviridae, and subfamily Orthocoronavirinae. The Orthocoronavirinae subfamily involves four genera and is classified into multiple subgenera under these genera: Alphacoronavirus (alphaCoV), betaCoV, deltacoronavirus and gammacoronavirus. Only alphaCoV and betaCoV are known to infect humans. The coronavirus family is an enveloped, positive-polar RNA virus family with helical symmetry that causes disease in mammals and birds such as camels, cattle, and cats. Coronaviruses are the largest RNA viruses detected so far in terms of genome size and genetic complex structure. The large genome makes the virus less dependent on the host during replication. Its replication occurs in the cytoplasm of respiratory and gastrointestinal epithelial cells. Because it is seen as a crown, it is called “corona”, which means crown in Latin (11). In Figures 1 and 2, the schematic view and electron microscopic view of SARS-CoV-2 are shown. SARS-CoV-2 is from betaCoV 2b lineage. Coronaviruses are 65-125 nm in diameter and contain single-stranded RNA as nucleic acid, approximately 30 kbs long. Like other CoVs, it is sensitive to ultraviolet light and heat. It can be inactivated with lipid solvents such as ether (75%), ethanol, chlorine-containing disinfectant, peroxyacetic acid and chloroform other than chlorhexidine. Its single-stranded RNA contains 29,891 nucleotides and encodes 9,860 amino acids. Coronaviruses are capable of replicating their own genomes without integrating into the host genome. They owe this ability to



**Figure 1.** Schematic view of SARS-CoV-2

SARS-CoV-2: Severe Acute Respiratory syndrome-coronavirus-2



**Figure 2.** Electron microscopic view of SARS-CoV-2 (source: <https://www.gisaid.org/> last access date: 25.05.2020)

SARS-CoV-2: Severe Acute Respiratory syndrome-coronavirus-2

the RNA-dependent RNA polymerase (RdRp) gene that they have. RdRp gene enables these viruses to replicate their own genomes in the host's cytoplasm (12-14).

SARS-CoV-2 has a typical coronavirus structure. The envelopes of coronaviruses are made up of lipids.

Their genomes consist of structural, non-structural and accessory genes. In this context, in addition to the leader sequence, it contains the gene encoding the replicase protein required in the replication and transcription processes of RNA, the ORF1a and ORF1b encoding non-structural proteins, the *S* gene encoding the spike (S) protein, the *M* gene encoding the membrane (M) protein, the *E* gene encoding the envelope (E) protein, the *N* gene encoding the nucleocapsid (N) phosphoprotein and various numbers of ORFs (replicase open reading frame), which encode genes of which functions are unknown.

Coronaviruses have four main structural proteins. These are S, M, E and N proteins. All of the structural proteins are encoded from the 3' end of the viral genome. The S glycoproteins are located outside the virion and give the virions their typical shape. By forming homotrimers, S proteins provide the formation of crown-shaped morphologies that give coronaviruses their name. The S protein is cleaved by the host cell's protease enzyme into two separate polypeptides S1 and S2. The S1 subunit forms a large part of the receptor

binding domain of the S protein, while the S2 subunit forms the stem of the S protein, which is likened to the spike model. S proteins bind to the virion membrane via their C-terminal transmembrane regions and also interact with M proteins. Virions bind to specific surface receptors on the plasma membrane of the host cell via the N-terminal of S proteins [this receptor for SARS-CoV-2 is the angiotensin-converting enzyme 2 (ACE2) receptor] (15).

The coronavirus M glycoprotein has 3 transmembrane regions. M proteins are glycosylated in the golgi apparatus. This modification of the M protein is important in the fusion of the virion into the cell and gaining antigenic properties of the protein. The M protein plays a key role in regenerating virions inside the cell. The N protein forms a complex by binding to genomic RNA, and then the M protein interacts with this complex in the endoplasmic reticulum-golgi apparatus intermediate compartment (ERGIC), triggering the formation of virions. This protein is important in the sensitization of the host cell by the virus, enabling the activation of the Interferon beta pathway by a toll-like receptor-dependent mechanism (16).

Coronavirus E proteins are small proteins that are approximately 76 to 109 amino acids long. Coronavirus E protein is an important virulence factor that plays a role in the accumulation of virions inside the cell and the separation of the virus from the cell by budding. It has been found that if there is no E protein in the virus, the viral load in the host is lower (17).

N protein is a helix and flexible phosphoprotein that can bind to viral genomic RNA. N protein has an important role in the structure of the virion, replication and transcription of coronaviruses; because it is localized both in the replication/transcription region of coronaviruses and in the ERGIC region where the virus is collected. As a result of the crystallization studies of the N protein of Avian infectious bronchitis virus and SARS coronaviruses, it has been shown that the N terminal of the protein binds to viral genomic RNA and the C terminal causes oligomerization during the accumulation of the virus (18). In addition, the C terminal of the N protein also interacts with the viral M protein. In studies, it has been observed that when viral M and N proteins are expressed together by means of mammalian expression vectors, M and N proteins interact in the cell to form structures similar to virions. The N protein also acts as an interferon antagonist, thereby inhibiting the virus from trying to be destroyed by the immune system (19).

The non-structural proteins (nsp) in the coronavirus genome are involved in a wide range from transcription of RNA to protein

synthesis and modification. They are listed between 1-16. Among these, 3CL-pro, PL-pro, RdRp and helicase are important targets for the development of small inhibitor molecules due to their functional structures and enzyme active sites.

1- Papain-like proteinase (PL-pro) is responsible for cleaving the N-terminal of the replication polyprotein to release nsp1, nsp2 and nsp3, which are responsible for correcting virus replication. In addition, studies have confirmed that PL-pro is important for antagonizing the innate immunity of the host. PL-pro, an indispensable enzyme during coronavirus replication and host infection, has been a popular target for coronavirus inhibitors (20).

2- 3C-like main protease (3CL-pro); 3CL-pro, also known as nsp5, first automatically separates from polyproteins to produce mature enzymes and then separates nsp at specific regions to release nsp4 and nsp6. 3CL-pro directly mediates the maturation of nsp, which is necessary in the life cycle of the virus (21).

3- RNA-dependent RNA polymerase; RdRp is required for the genome replication of coronaviruses. RNA viruses containing RdRp can reproduce independently of the host and therefore reside in the cytoplasm. The protein itself is highly conserved, meaning that its structure is similar in all viruses containing the enzyme. Nsp12, a protein conserved in coronaviruses, is an RNA-dependent RNA polymerase and is the most important enzyme of the coronavirus replication/transcription complex (22).

The main reason for transmission from animal to human is the ingestion of an infected animal, then the virus is passed from infected individuals to healthy individuals by close contact. The disease is mainly transmitted by droplets. In addition, the droplets emitted by sick individuals through coughing and sneezing are transmitted by touching the mouth, nose or eye mucosa after contact with other people's hands. Since viruses can be detected in respiratory tract secretions of asymptomatic people, it can be contagious (23).

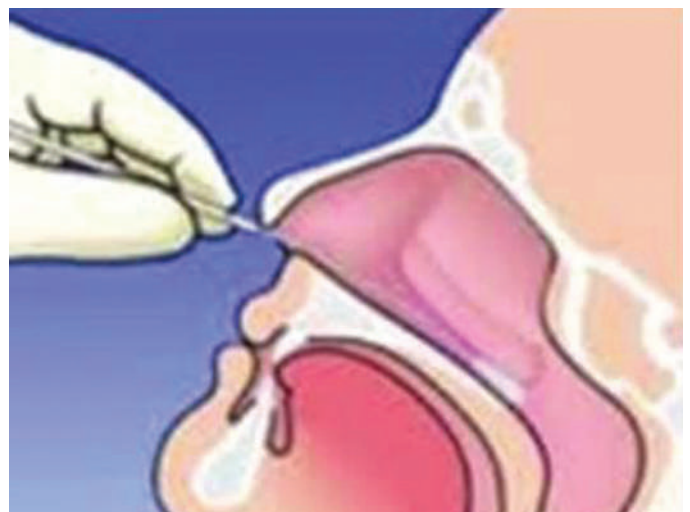
It binds to the ACE-2 receptor on the host cell surface via the virion S protein and enters the cell and leaves its genomic RNA to the cytoplasm. Primarily, two viral replicase polyproteins are synthesized. These two large proteins are transformed into 16 nsp with the help of proteases. These 16 nsp form double membrane vesicles and the replication and transcription complex. New virions are formed by combining newly formed structural proteins and genomic RNA in the ERGIC. The newly formed virions exit the cell using exosomes (24).

## Laboratory Diagnosis

### Sampling and Transport

Since it will cause aerosol scattering during the sampling process for molecular or other tests to be performed for the diagnosis of COVID-19, the personnel who will perform this procedure should use appropriate personal protective equipment (N95 mask, goggles, face protection). Health personnel assigned in this field are primarily informed by persons experienced in the prevention and control of infections (such as Infectious diseases specialist, microbiology specialist or infection control nurses). Training should be provided on infection control measures, use of personal protective equipment, appropriate sampling, storage and transportation of the sample under appropriate conditions. Ideally, it is recommended that first oropharyngeal sampling using oropharyngeal swab, then nasal sampling using the same swab should be performed and the swab should be placed in the same viral transport medium. Sputum, endotracheal aspirate samples and bronchoalveolar lavage samples can be used in patients with more severe respiratory disease. However, it should be kept in mind that the risk of transmission may be higher in this case (25). Figures 3 and 4 illustrate the nose and throat sampling using swab. Sampling and storage conditions are included in Table 1.

The fact that the if the first sample taken from patients who meet the definition of a possible case and whose infection findings continue worsening is an upper respiratory tract sample and the test result is negative, this does not exclude the suspicion of COVID-19 infection.



**Figure 3.** Taking a nasal swab

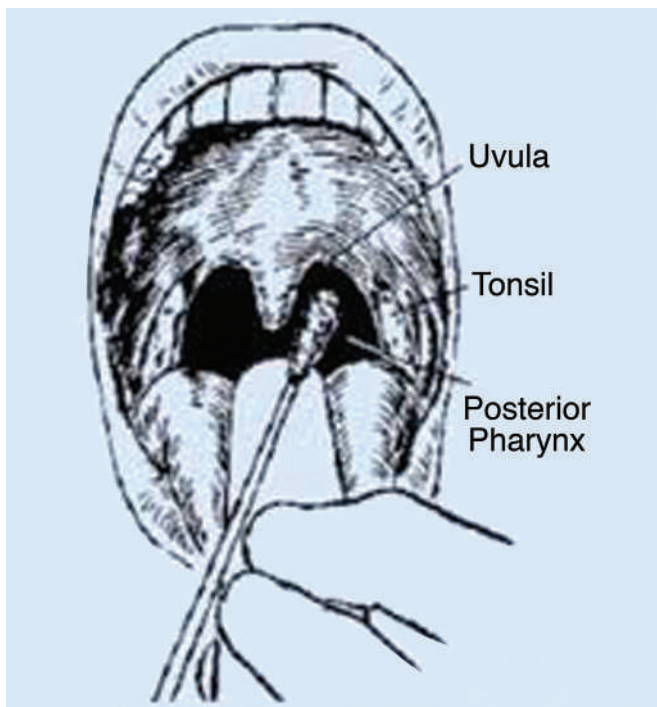


## Diagnostic Tests

In classical virology, diagnostic tests can be classified as cell culture, serology and molecular tests. Virus isolation is carried out under Biosafety level-3 (BGS-3) conditions. The WHO does not recommend virus culture and isolation for diagnostic purposes (27).

Today, there are 2 currently valid test methods for the diagnosis of COVID-19 (28).

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



**Figure 4.** Taking a throat swab

## 1- Rapid Diagnostic Tests Detecting Antigen

The antigen test, a type of rapid diagnostic test, is based on detecting the presence of viral proteins expressed by SARS-CoV-2 in the respiratory sample. Since the detected antigens only occur when the virus is replicated, they are used to identify acute or early infection. How well the test works depends on a variety of factors, such as when the sample is taken, the viral load, and the quality of the sample. The US Food and Drug Administration announced that it approved the first antigen test (Sofia 2 SARS Antigen FIA) on 8.05.2020. Detected in this test is the SARS-CoV-2 nucleocapsid protein. Rapid results are its most important advantage. However, reactive results do not exclude other coronaviruses and bacterial infections that cause cold. Tests with nonreactive results should be confirmed with a molecular test depending on the patient's condition (29). Advanced antigen-detecting tests with sufficient performance can be used as a pre-test to quickly identify patients who are likely to have potential COVID-19 and reduce the need for expensive molecular confirmatory testing. With the current limited data, WHO discourages the use of antigen tests to diagnose the disease.

## 2- Viral RNA Tests

The first preferred test method for the diagnosis of COVID-19 is viral nucleic acid determination with reverse transcription-PCR (RT) (30). RNA can be obtained from upper respiratory tract (oropharynx and nasopharynx) swabs as well as lower respiratory tract samples such as bronchoalveolar lavage and sputum. It has been observed that samples taken from the nasopharynx give two times better results than samples taken from the oropharynx (31). If both samples are taken, it is recommended to combine the samples in a common tube,

**Table 1. Sampling and storage conditions (26)**

Type of sampling	Collection of material	Conditions of transport of material	Storage
URT sampling (NP/OP swab and nasal swab)	Dacron or flocked swab (in VTM)	4 °C	Within 5 days: 4 °C More than 5 days: -70 °C
LRT sampling (sputum, tracheal aspirate)	Sterile container	4 °C	Within 48 hours: 4 °C More than 5 days: -70 °C
Lung biopsy	Sterile container with salt water	4 °C	Within 48 hours: 4 °C More than 5 days: -70 °C
Serum	Serum tube (duplicate samples are collected for serological tests. Acute phase: Within 7 days of symptom onset. Recovery period: 14 days after collection in the acute phase)	4 °C	Within 5 days: 4 °C More than 5 days: -70 °C

VTM (viral transport medium) containing antibacterial and antifungal must be used to transport samples. Repeated freezing and thawing should be avoided. If VTM is not available, sterile saline can also be used (In this case, the storage time at 2-8 °C may be shorter than stated above).

URT: Upper respiratory tract, LRT: Lower respiratory tract, NP: Nasopharyngeal, OP: Oropharyngeal, VTM: Viral transport media

and it is known that the best result will be obtained by joint testing of both the lower and upper airways. SARS-CoV-2 RNA can also be isolated from stool, urine and blood samples, but these samples are less reliable than respiratory samples. It is recommended that upper respiratory tract samples be collected within a few days of the onset of symptoms. It has been reported that the virus peaks in the upper respiratory tract at the end of the first week, and in the lower respiratory tract at the end of the 3rd and 4th weeks in more severe patients (32). PCR tests should be run under BGS-2 conditions and with personal protective equipment. It is known that the PCR test does not detect any viruses other than SARS-CoV-2 by cross-reaction, and therefore it is a highly specific test. Although a definite rate cannot be given for its sensitivity, it has been reported that it ranges between 63-78% (33). False negativities are common due to reasons such as low viral load or displacement of viral load, incorrect sampling, early or late sampling, antiviral use before testing, transport error, presence of PCR inhibitors in the environment, and viral genetic mutation. If the test is negative, repeating it at intervals is recommended to increase the sensitivity of the test (26,32-34). It is of great importance to evaluate the clinical findings of the patients together with the RT-PCR results. For example, in a study of 4.880 patients conducted in Wuhan, the city where the pandemic started, it was reported that diagnostic value of RT-PCR increased by 19% in the presence of fever, and the diagnostic value of the test increased in advanced age and male patients (35). Again in a clinical observation of 82 patients made in China, when evaluated together with computed tomography, it was found that the sensitivity of RT-PCR increased from 79% to 94%, and this situation was found to show that the presence of lung involvement like other clinical findings reduced the rate of false negativity of RT-PCR (36).

RT-PCR is a gold standard method used in the confirmation of COVID-19 infections despite its limitations (31). It enables the amplification of nucleotide sequences in the targeted regions of the RNA of the virus to become visible in real time with fluorescent dyes (37). *S* and *N* genes and non-structural RdRp and ORF 1a/b genes are often used as target regions because they are genes that are conserved in the evolutionary process, expressed and less involved in cross-reaction genes (38). When the diagnostic value of the RdRp/Hel region of SARS-CoV-2 is compared with the RdRp-P2 region, its sensitivity and specificity have been found to be higher (38,39). Various number of different gene regions are used in different test kits and RT-PCR protocols suitable for these gene regions are performed. International viral transport mediums and kit specific viral nucleic acid buffers can be used

for sample collection and transport. The samples taken should preferably be delivered to the laboratory at 4 °C and as soon as possible. The threshold cycle value (Threshold cycle/Ct) of target genes that can be evaluated at the end of PCR is below the limit value, indicating the presence of viral nucleic acid and means a positive result. The test results in an average of a few hours (34). Reactive reaction conditions, the number of genes analyzed can affect the sensitivity of the analysis. Optimization of PCR conditions by the laboratory is important. The clinical laboratory is required to perform a quality control in routine work using validated negative and positive samples. Apart from all these, the tested pathogen is an RNA virus. RNA is a molecule with low stability, it can be easily degraded by many enzymes after cell destruction, and it has a high risk of contamination. It is also known that RNA viruses are highly susceptible to mutation. Therefore, conducting the test on an RNA virus is an important factor that can highly affect the specificity of the test (40).

In conclusion, although real-time PCR is the first test used in the diagnosis of COVID-19, it should not be considered alone when making a decision for isolation and treatment due to false negative rates. Patients should be handled with a multidisciplinary approach and they should be evaluated together with all other data including clinical findings, lung CT, etc. (41).

### Sequence Analysis

The virus genome ranges between 26-32 kb, contains 14 ORFs regions and encodes 26 proteins. *S* surface glycoprotein, *E* protein, *M* protein, and *N* protein are its main proteins (40).

Similarity of previously known SARS-CoV-2 (79%) and MERS-CoV-2 (50%) has been demonstrated by sequencing the genome data of the virus. It has been observed that SARS-CoV-2 shows a high level of homology to SARS-CoV-2 except for the differences in ORF1a and *S* gene. The RNA sequence of the virus evaluated in phylogenetic studies have shown that the virus belongs to the betaCoV family. Thus, many information about the virus's origin, evolution, mechanisms, transmission routes and treatment could be predicted. The similarities and differences in the *S* gene encoding the *S* protein have given important clues about the binding of the virus to human ACE2 receptors and human-to-human transmission. By performing protein modeling studies of the obtained sequence, it has been reported that the *S* protein has a high affinity for ACE2 receptors. Data such as human-to-human transmission dynamics, immune response, viral replication rate and virus mutation rate were obtained by determining the virus genome (40,42). In another study, 10 SARS-CoV-2 sequences obtained from different countries of the world



were compared. No difference was observed in the sequences encoding the M and N proteins. Two amino acid variants in the S protein sequence, one mutation in the E protein in one sample, and two possible single nucleotide polymorphisms were detected in the ORF1ab and ORF8 regions (43).

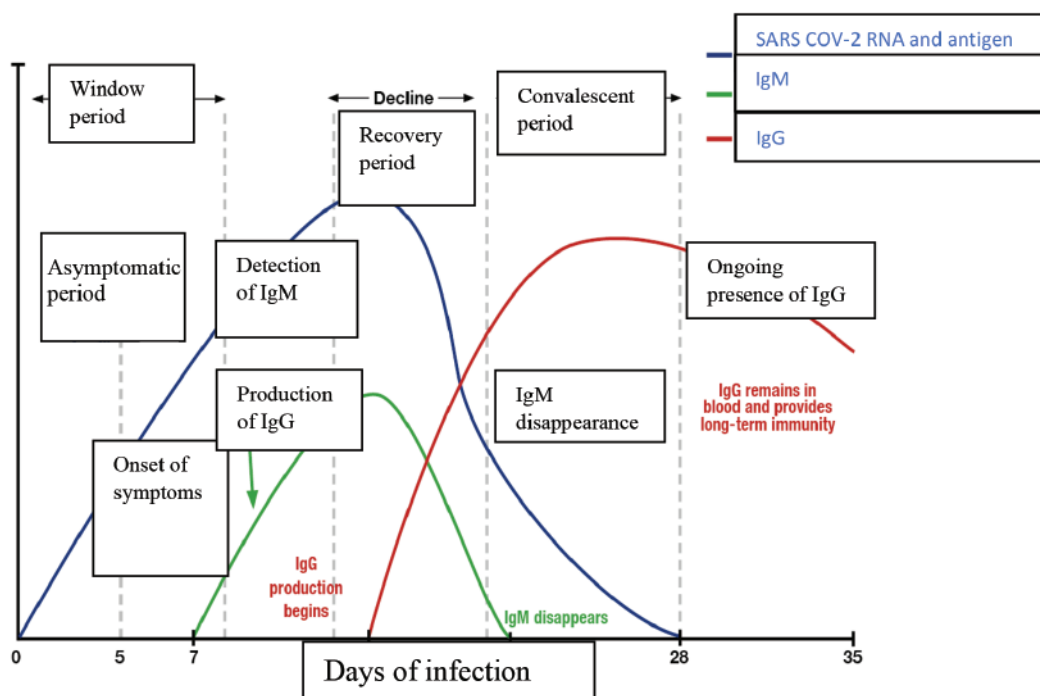
Similar studies of the RNA sequence of the virus are very valuable in terms of the course of the pandemic, prophylaxis and treatment of the disease (43). The genome sequencing of SARS-CoV-2 has also paved the way for vaccine technologies that can be developed against the virus. Vaccination studies on other viral pathogens, especially on DNA and mRNA, have paved the way for SARS-CoV-2 studies (44). The sequence of the ACE-Fc protein has been reported to be a candidate gene in studies to be performed (44-46).

### 3- Serology

Another broad category of tests in the diagnosis of Covid-19 are serological tests that detect Immunoglobulin M (IgM), IgA, IgG and total antibodies (in blood). The occurrence of an antibody response to infection depends on host immunity and requires a certain period of time. Therefore, the age of the patient, nutritional status, severity of the disease, diseases such as HIV and the drugs used may be important in the formation of immunity. Since antibody tests cannot be used in the early stage of acute infection and do not affect the duration of treatment, their use in clinical diagnosis is limited. Tests showing antibody

responses can be used for retrospective diagnosis by showing increased antibody levels in acute or convalescent periods in blood samples taken from patients with negative molecular test results for COVID-19 but with strong suspicion of COVID-19 (Figure 5). With current knowledge, time and more studies are needed on whether individuals infected with SARS-CoV-2 and have recovered later will be protected from SARS-CoV-2 in the future or how long protective immunity can last. Antibody tests for SARS-CoV-2;

- 1- It can be performed to monitor the contact person.
- 2- It can be used for serological monitoring at local, regional and national levels.
- 3- It is valuable in identifying people who have been exposed to the virus and may therefore be immune.
- 4- It can be used for diagnostic purposes to test individuals with clinical/radiological findings who are viral RNA-negative.
- 5- Information from serological tests can be used to guide decisions in individuals about returning to work, including individuals working in environments where they could potentially be exposed to SARS-CoV-2 (e.g. healthcare workers).
- 6- It can be useful in identifying individuals who may be sources for therapeutic or prophylactic neutralizing antibodies in plasma therapy.



**Figure 5.** Relationship between antibody levels and disease course SARS-CoV-2: Severe Acute Respiratory syndrome-coronavirus-2, IgM: Immunoglobulin M, IgG: Immunoglobulin G

7- It can be used to evaluate response in vaccine studies and to determine immunity levels in the population.

In bedside chromatographic tests, monoclonal antibodies (mAb) are used to detect viral antigens in clinical samples, or cloned viral antigens are used to detect antibodies against the virus. In the “lateral flow” test method, there is a strip embedded in the cassette and the reagent fixed on the nitrocellulose membrane (a mAb for a viral antigen or a viral antigen recognized by the patient’s antibodies). The patient’s sample is added to the strip and reacts with the previously immobilized reagent. The samples to be investigated may be serum, plasma or, in some cases, whole blood. The test can often be performed with two to three drops of blood taken from the patient’s fingertip. As a result of the positive reaction, a colored line is observed on the strip. Most tests also include a checkpoint or band so the results can be evaluated. Results are read visually and given qualitatively within minutes (47).

Enzyme immunoassay (EIA) tests, which take longer to develop, have less sensitivity and specificity than molecular methods, but they are easy to use and give results in a shorter time. However, the inability to reproduce the results obtained during their validation in clinical settings and the uncertainty of the results of the tests create serious diagnostic difficulties.

In the EIA method, the antibody bound to the antigen-antibody complex is marked with an enzyme and the enzyme activity is detected by measuring the intensity of the color change (enzyme-linked immunosorbent assay-ELISA) or the resulting light (chemiluminescent immunoassay-CLIA), and thus the antigen antibody reaction is detected. The direct method used in the search for antibodies by ELISA technique is also known

as the “sandwich” or “double antibody” method (48). Proteins frequently selected as targets in tests are the N protein, which plays an important role in replication and transcription, and the “S” protein that facilitates viral entry into airway epithelial cells by binding to ACE2 expressed on the host cell surface (S1 and S2 in some tests) (49). In the study performed by Jin et al. (50) using the CLIA method, they found that the sensitivity for IgM was 48.1%, the specificity for IgM was 100%, the sensitivity for IgG was 88.9%, and the specificity for IgG was 90.9%. In another study conducted by Pan et al. (51), it was stated that IgM, IgG and total antibody levels were at the highest level after the 15<sup>th</sup> day.

The SARS-CoV-2/COVID-19 tests and their use are shown in Table 2, and the clinical significance of the SARS-CoV-2/COVID-19 tests is shown in Table 3.

### COVID-19 Diagnostic Laboratory Studies and Test Algorithm in Our Country

The first patient in our country was observed on March 11 and until today, 2.070,719 tests were performed, 164 764 positive patients and 4563 deaths were reported (As of 01 June 2020).

First, PCR test for COVID-19 started to be performed in our country in only one test center (Public Health Agency of Turkey). With the increase in the number of tests, the number of test centers has also increased and as of 01 June 2020, 129 laboratories in 73 provinces have been authorized as COVID-19 Diagnostic Laboratories by the Ministry of Health. There are 2 types of PCR kits supplied to these laboratories by the Ministry of Health. The first of these is Biospeedy kit (Bioeks, Turkey) which targets viral RdRp. Virus RNA is isolated with VNAT solutions provided by the same brand. RT-PCR is provided

Test	Status of individual	Usage	Benefit
Viral nucleic acid (RNA) Amplification (nasopharyngeal swab, oropharyngeal swab, sputum, bronchoalveolar lavage, other)	SARS-CoV-2 infection	1- Infection and transmission status of the individual	Status of individuals, isolation and treatment
		2- Patient management and control screenings to prevent contamination	People staying or working in healthcare sector or care facilities for long-term
		3- In necessary procedures to prevent contamination	Contribution to public health by identifying the contacts
Antibody detection (Blood, plasma, serum, fingertip blood)	Prior SARS-CoV-2 infection	1- Identification of suspected patients (antigen, PCR negative and previously infected)	Identification of potential immune individuals
		2- Identifying individuals with neutralizing antibodies	Plasma therapy
		3- To facilitate contact tracing and surveillance	Contribution to public health by identifying the contacts

SARS-CoV-2: Severe Acute Respiratory syndrome-coronavirus-2, COVID-19: Coronavirus Disease-2019

Test result			Clinical significance
PCR	IgM	IgG	
+	-	-	The patient may be in the window period of the infection
+	+	-	The patient may be in the early phases of the infection
+	+	-/+	The patient is in the active phase of the infection
+	-	+	The patient may be in the late phase of infection or in recurrence phase.
-	+	-	The patient may be in the early phase of the infection (PCR result may be false negative)
-	-	+	The patient has had the infection and has recovered
-	+	+	The patient may be in recovery phase or the PCR result may be false negative

SARS-CoV-2: Severe Acute Respiratory syndrome-coronavirus-2, COVID-19: Coronavirus Disease-2019, PCR: Polymerase chain reaction, IgM: Immunoglobulin M, IgG: Immunoglobulin G

in a single step and the amplification of SARS-CoV-2 RNA is performed in a single tube with internal control and read in two different channels.

The second PCR kit is an imported kit called Direct Detect (Coyote Bioscience, China). Isolation is achieved quickly with the reagents provided by the kit, and RT and amplification are carried out in one step. Differently, two different regions are targeted for amplification (N and ORF1ab), and when internal control is considered, readings are made in three different channels, and positivity is diagnosed by observing amplification in both targeted regions. Observing amplification in only one region is not sufficient and requires repeating the test with the same or a different method.

Various antibody tests have also been distributed to laboratories authorized by the ministry of health in our country. Some of the kits can detect IgM and IgG type antibodies separately, while others detect total antibodies. Both of the two test categories for SARS-CoV-2 have been useful in this pandemic. If the rapid antigen test is represented by a product with increased sensitivity, it can be used in field pre-scans, in areas where PCR is impossible or inadequate. In breaking the pandemic, the power of the test is inevitable, and knowing the sensitivity of the diagnostic tests and increasing them if necessary will make valuable contributions to the clinic in terms of public health in starting contact tracing, follow-up of contacts and termination of contact tracing.

The first genome sequence of the SARS-CoV-2 shared in Turkey was provided open access by the Ministry of Health via GISAID database on March 25, 2020 (<https://www.gisaid.org/> last access date: 01.06.2020).

### **COVID-19 Diagnostic Laboratory Studies in Our Hospital**

In our hospital, after we started following up patients with COVID-19, respiratory samples of these patients were sent

to Public Health Laboratory no: 1, Kanuni Sultan Süleyman Training and Research Hospital, Turkey Institutes of Health Administration (TÜSEB), which started to perform SARS-CoV-2 PCR, and to COVID-19 PCR laboratories established in other training and research hospitals when necessary. Testing periods in external centers were 3-4 days on average. As a result of negotiations with TÜSEB in the first week of April 2020, a 3000-capacity COVID-19 PCR diagnostic center was established in our hospital. After the necessary logistical arrangements were made, this center started to work actively on 19 April 2020. While the preparations for the opening of the COVID-19 diagnostic center were continuing, 1,400 COVID-19 IgG and IgM rapid antibody card tests were sent to our hospital through the Ministry of Health. A special room and working team were established in the Infectious Diseases and Clinical Microbiology Outpatient Clinic. The training was completed by providing information on safe working principles and protection. Rapid antibody tests have started to be actively performed on April 14, 2020, and the personnel working in our hospital are still being screened. Seven biosafety cabinets, 4 PCR devices, other necessary PCR equipment and a young team of 10 people, experienced in biology, molecular biology and genetics departments of various universities, were sent to the COVID-19 diagnostic center established in our hospital. Initially, the Direct Detect (Coyote Bioscience, China) kit was used. Currently domestic Biospeedy (Bioeks, Turkey) kit is used. In our laboratory, samples from other hospitals affiliated to Beyoğlu Presidency are also studied. Our daily number of tests ranges from 300 to 800. Almost all of the tests are studied during the day, and the average time for giving result is less than 24 hours. In our laboratory, 1047 rapid antibody tests were performed during this period and the positivity rate was 19.2%. The number of SARS-CoV-2 PCR tests studied in the same period was 22 277. The positivity rate was on average 10.2% (the positivity rate, which was 23% at the beginning, decreased over time and fell below 5%).

## CONCLUSION

As a result, in the COVID-19 pandemic, with molecular and serological diagnostic tests, it is possible to verify the patients in accordance with national guidelines and to effectively isolate positive cases. Accurate and reliable test results make it possible to prevent the disease, to get it under control quickly and to provide the necessary support to the patient in a timely manner. The power of the test is inevitable in breaking the pandemic, and knowing the sensitivity of the diagnostic tests and increasing them if necessary will provide valuable contributions to the clinic in contact tracing, treatment initiation, follow-up and treatment termination in terms of public health.

## Ethics

**Peer-review:** Externally and internally peer-reviewed.

## Authorship Contributions

Surgical and Medical Practices: Ç.A., G.A.T., B.E.K., B.E., K.A., E.A., Concept: Ç.A., B.E.K., B.E., K.A., E.A., Design: Ç.A., G.A.T., Data Collection or Processing: Ç.A., G.A.T., B.E.K., B.E., K.A., E.A., Analysis or Interpretation: G.A.T., B.E., E.A., Literature Search: Ç.A., G.A.T., B.E.K., B.E., K.A., E.A., Writing: Ç.A., G.A.T., B.E.

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# Radiology Clinic Management in COVID-19 Pandemic

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## Abstract

After the outbreak of a Coronavirus Disease-2019 pneumonia occurred in Wuhan, China in December 2019, the disease first reached Iran, Europe and then our country on March 11, 2020, creating a pandemic. Our hospital and radiology clinic aimed to overcome the pandemic with minimum damage by taking the necessary precautions. The radiology clinic led treatment management with computed tomography which was stated to be of high diagnostic value. In this informative article, the studies carried out in the radiology clinic during the pandemic were conveyed for information and guidance.

**Keywords:** Coronavirus, COVID-19, pandemic, tomography, management

## INTRODUCTION

A new Coronavirus Disease-2019 (COVID-19) pneumonia emerged in Wuhan, China, in December 2019.

In this new disease, severe pneumonia symptoms with fever, fatigue, dry cough and respiratory distress were observed. A new corona virus named 2019 Novel Coronavirus Severe Acute Respiratory syndrome-coronavirus-2 (SARS-CoV-2) was declared by the World Health Organization (WHO) as the causative agent of pneumonia in the analyzes performed from samples taken from the lower respiratory tract. Since the incubation time of the virus was an average of 5.2 days and the disease did not show symptoms during the incubation period; its spread to the world was rapid, and WHO declared the outbreak as a global emergency on February 5, 2020 (1).

According to the guidelines in the current medical literature, the gold standard in the diagnosis of SARS-CoV-2 infection is the reverse transcriptase polymerase (RT) chain reaction (PCR) test performed in respiratory tract samples. In the first applications, the sensitivity of RT-PCR was found to be between 37 and 71%. Ai et al. (2) stated that the sensitivity of computed tomography (CT) was 97% and the specificity was 25% in a study which was

performed in 1014 patients in Wuhan, China and of which PCR results were shown as the reference standard. Similar results have been found in several other publications, and the results suggest that in patients with highly suspected COVID-19 pneumonia, CT imaging will be useful in early detection of interstitial pneumonia (3). It is stated that imaging is of great importance in evaluating the severity and progression of the disease in COVID-19 pneumonia (4). Therefore, radiologists should be aware of the imaging signs of the new COVID-19 pneumonia.

Generally, CT imaging findings are quite specific. However, there may be atypical involvement (single focus, single lobe) or non-specific findings. Again, it is not possible to distinguish COVID-19 pneumonia from other viral pneumonia caused by H1N1 influenza or cytomegalovirus or from atypical pneumonia in terms of CT findings. If the patient has a history of contact and the clinical course is compatible, the diagnosis is made by considering it in favor of COVID-19 pneumonia and by confirming with PCR test. Since the PCR test kits are not diagnostic at the desired level, it is of great importance to perform thoracic CT rapidly and interpret it.



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### Radiology Clinic During the Pandemic

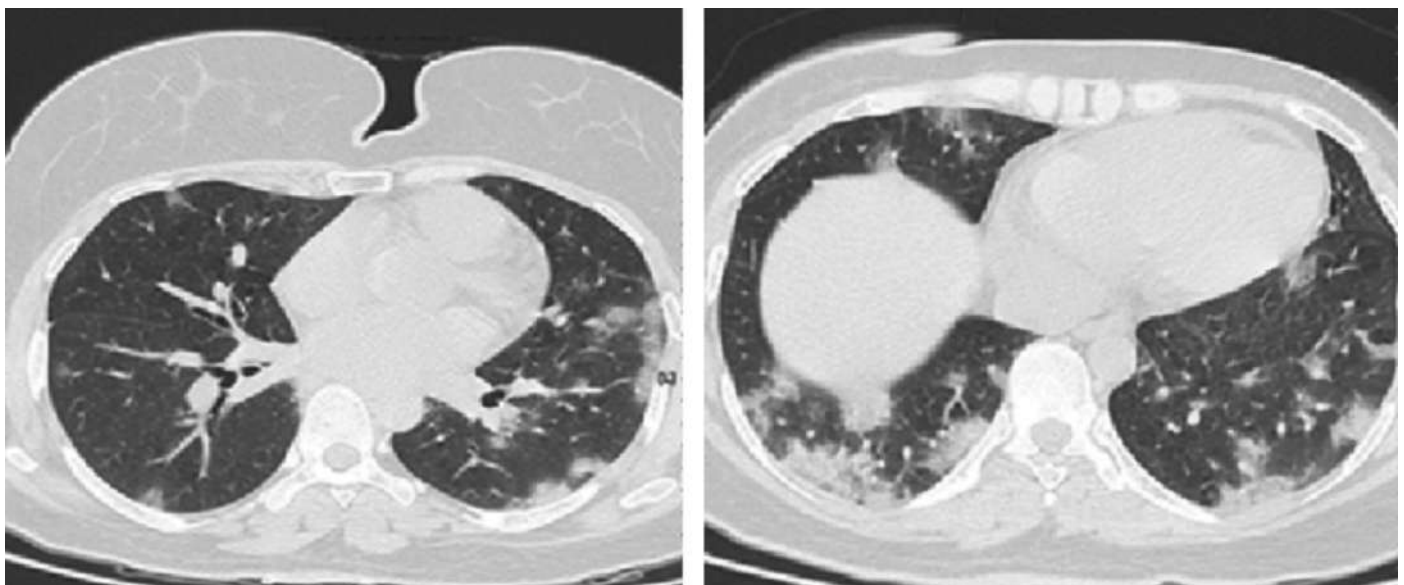
Approximately 1.5 months after the first patients in China, on February 19, 2020, the first patient with COVID-19 was reported in the city of Kum, Iran. Due to the fact that the city of Kum is a religious center and has many visitors around the world, it has been thought that this will have high effect on the spread of the disease. For this reason, considering that it would be inevitable to spread to our country, the planned seminar was immediately canceled due to the need to renew the knowledge of our residents and specialists in terms of this new disease with the leadership of the education supervisor in our clinic and instead, seminars about the danger of COVID-19 in the world, prevention methods and radiological findings in the literature were organized and awareness was raised among all radiologists working in the groups.

In the thorax CT obtained in the radiology clinic, images compatible with the findings of COVID-19 were observed for the first time on March 9 in a hospital employee, and it was reported to the infectious diseases clinic and taking necessary measures was recommended. (Figure 1). Although the first PCR test was negative for COVID-19, as stated in the literature, it was insisted that the findings could be related with COVID-19, and at the end of 10 days, the repeated PCR test was positive for COVID-19.

In our country, 6 days after the first patient was announced on March 11, patients began to come to our hospital, and CT findings of COVID-19 were observed and reported in the thoracic CT examination of 7 patients performed on March

17, the first day. Considering that the disease would spread due to the pandemic, it was decided that we, as the team reading thoracic CT scans, should assist the clinicians in terms of rapid diagnosis and treatment guidance. It was deemed a duty to help clinicians in this triage by realizing the difficulty of how to guide patients in this new unknown situation. For this purpose, in order to serve up CTs, which have a significant role in the differential diagnosis of patients, to clinicians a thoracic CT subgroup for the pandemic was established in the radiology clinic and started reading 24/7 thoracic CTs on March 17. In order to be effective, an instant messaging group was created and it was named "Thorax CT-Vigilance Group". Radiologists, emergency physicians and infectious diseases specialists were added to the group at the first stage. Thus, interactive communication was provided between the emergency service, internal departments and radiology. The first admission examination, clinical findings and thoracic CT of the patients were evaluated quickly. Thus, the patient's CT scan was immediately evaluated by the radiologist from the system. The relevant radiologist was able to report his/her first finding to the group on his/her mobile phone and sent it to the clinician within half an hour.

Stating that this task will be difficult with only the thorax team due to the increase in the number of patients, our clinical management planned to form a strong union with all radiologists working in the clinic to participate in this important task. Sub-branches of radiologists such as "abdomen", "neurology" and "musculoskeletal" were temporarily suspended, and all



**Figure 1.** The imaging of the first patient diagnosed as having COVID-19; a 45-year-old female patient, findings consistent with specific viral pneumonia in both lungs, mostly peripheral and subpleural localized, irregularly demarcated multiple consolidation and ground glass opacity areas  
COVID-19: Coronavirus Disease-2019

radiologists and residents took the task of reading and reporting thoracic CTs in a very short time and providing guidance.

In our clinic, 7 radiologists, 2 at night and 5 during the day, actively evaluated and reported on thoracic CTs in three shifts over 8 hours. In addition, on-call duties were created for ultrasonography, magnetic resonance imaging, and interventional radiological procedures in the clinic. In hospitals that did not read and report CTs on-site and only received services, such as our hospital, the difficulty in setting up a team in emergency situations and communicating with the consultation team, and the difficulties that clinicians had because of staying away from radiologists who were their deep eyes, were observed. During this pandemic, which was not experienced before and was rare, the handicaps and difficulties of remote radiological reading and reporting were also clearly noticed.

Due to the growth of the group reading thoracic CTs, the reading method and performing criteria were updated (Table 1).

Radiology clinic workers are in the group of healthcare professionals who will be affected first in the pandemic since they encounter patients who have made the first admission and have not been diagnosed (4). Therefore, it is important to protect employees. At the beginning of the pandemic process, all employees were trained by the infectious diseases clinic about general information about COVID-19, ways of transmission and ways of protection, and which personal protectors to use. Again, the working conditions were arranged taking into account the declarations of the Turkish Radiology Association. Our technicians who greeted the patient protected themselves with overalls, masks, gloves, goggles or visors while performing CT scan. The environment of CT device, on the other hand, was ventilated as much as possible, and by cleaning the surface by cleaning staff trained for this pandemic provided by the hospital

administration department for each CT device, it was tried to prevent contamination from the environment. At the end of this process, only one of our young CT technicians had the disease.

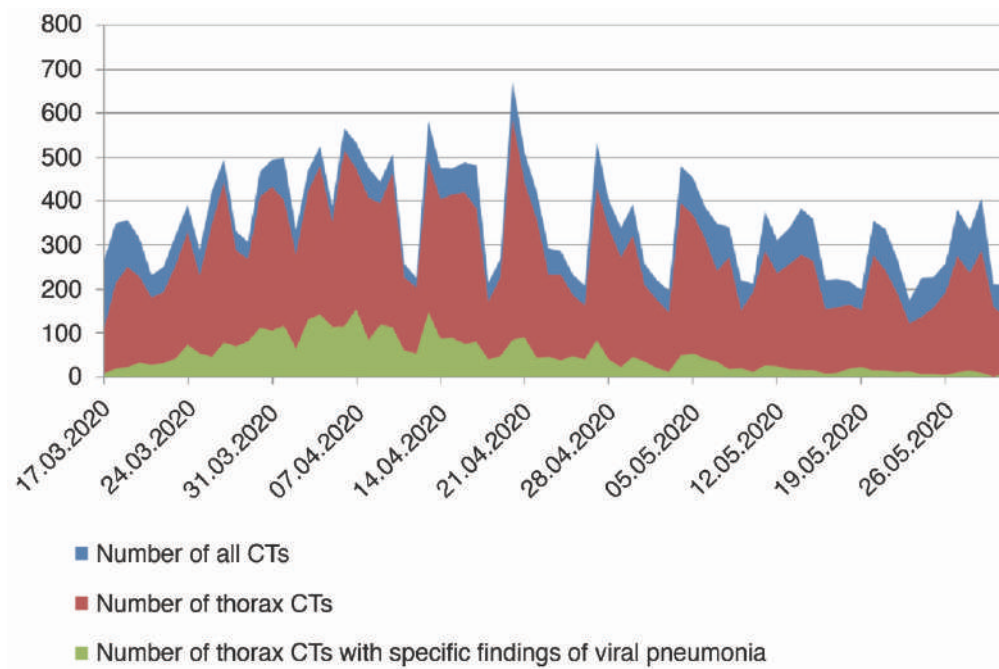
Our thorax CT protocols were performed in accordance with the guidelines with a standard dose at first and low dose protocol was not applied. Thin section axial plan imagings with 120 kV and 200-250 mAs and without using intravenous contrast agent were performed. In our hospital, according to the guidelines, very few pediatric patients received CT suitable for automatic child doses (5).

In the following days of the pandemic, in accordance with the guidelines published by the Ministry of Health and with the knowledge of the hospital's scientific committee, low-dose protocol was started to be performed in patients under 20 years of age in the first scan and even in the control scans (COVID-19 guide-12.04.2020) (6).

Interpretation of 3700 CTs with specific viral pneumonia findings with the evaluation of 21,000 thorax CTs performed in our hospital between 17 March 2020-17 May 2020 with 3 different CT devices (Philips Ingenuity core 128 sections, Philips Brilliance 40 sections and Toshiba Alexion 16 sections), were reported to clinicians to contribute to their diagnosis. While the findings compatible with specific viral pneumonia were few in the early days, it peaked in mid-April 2020 and reached up to 152 CTs per day and gradually decreased to 10 new patients a day at the end of April. Meanwhile, on the days of curfew, sharp declines were observed in both the number of CTs and the number of those with findings (Chart 1). Another CT device (Toshiba Aquillion LB 16 slice), also available in the radiation oncology clinic in our hospital, was kept ready and clean for possible chaos. Also in our hospital, another tomography device (Philips Brilliance Big Bore) serves for radiotherapy applications.

**Table 1. Thoracic computed tomography reporting principles of radiologists in pandemic duties**

Our principles of assessing emergency thoracic computed tomographies during COVID-19 pandemic
1- Since early ground glass opacifications may be missed in laptops or normal PC monitors, CTs should be read from medical monitors in workstations in the hospital
2- The evaluating radiologist should photograph the patient's name and the part of the CT scan date and send it to the Thorax CT-vigilance group, and write briefly whether there is findings of viral pneumonia or write information briefly with his/her own sentence
3- If there is a finding in the evaluated CT, "viral pneumonia (+)" should be written briefly in the radiology interpretation section of PACS
4- CT reports should be dictated as quickly as possible (we have a 24/7 reporter) and written reports should be approved quickly (half an hour on average)
5- After the delivery of the duty to the next colleague, the monitor should be left unattended
6- If the radiologist's opinion is requested, the opinion of the radiologist should be reported in other urgent nighttime examinations during the period of duty. CTs that are not asked for opinion will be read by the radiologist who will arrive in the morning
7- In this period, thoracic CTs performed in another hospital and uploaded to the system should also be reported
COVID-19: Coronavirus Disease-2019, CT: Computed tomography, PACS: Picture archiving and communication system



**Chart 1.** The distribution of thorax CTs with specific viral pneumonia findings within the all tomographies over a 43-day period. The sharp declines on the days of the curfew are evident in the chart

CT: Computed tomography

## CONCLUSION

The COVID-19 pandemic that shakes the world is also very effective in our country and has deeply shaken our daily lives. With the fast, effective and sharing approach of our health system, the deadly effects of the pandemic have been slightly overcome and the pandemic has been taken under control.

Our hospital and radiology clinic have played a very effective role in the fight against the pandemic with their pioneering behavior towards the pandemic and their applications in parallel with the practices of our country. In this process, the radiology clinic has coordinated quickly with emergency clinic and infectious diseases clinic with a multidisciplinary approach and has made a great contribution to the triage and treatment of patients. The importance of the effectiveness of communication between clinics has been observed clearly in this process.

In hospitals that did not read and report CTs on-site and only received procurement (teleradiology) services and reportings of cross-sectional images such as our hospital, the difficulty in setting up a team in emergency situations and communicating with the consultation team, and the difficulties that clinicians had because of staying away from radiologists who were their deep eyes, were observed.

Radiologists should work with clinicians as part of a team while helping clinicians by showing them the invisible side of the iceberg. Administrative and academic arrangements should be made for this.

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## Ethics

**Peer-review:** Externally and internally peer-reviewed.

## Authorship Contributions

Concept: R.Y.B., S.D.Ö., D.K., H.Y., Design: R.Y.B., K.H., H.Y., Data Collection or Processing: R.Y.B., Analysis or Interpretation: R.Y.B., S.D.Ö., K.H., D.K., Literature Search: R.Y.B., D.K., Writing: R.Y.B., K.H., H.Y.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study received no financial support.

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# Emergency Management Planning in COVID-19 Pandemic Period

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## Abstract

Coronavirus Disease-2019 was first reported in the city of Wuhan, Hubei Province of China, and has spread worldwide. The World Health Organization reported that this epidemic is a global public health problem. In our country, the first case was reported on March 11, 2020. Many changes were made in our hospital. We made one of the most radical changes in our emergency room. These changes included both work plan and physical changes. We think that these changes will be a guide in the later pandemic periods.

**Keywords:** COVID-19, pandemic, emergency department, management

## INTRODUCTION

Coronavirus Disease-2019 (COVID-19) was first reported in Wuhan city of Hubei Province of China, and today it has spread all over the world (1). The disease spread around the world, and on March 11, 2020, the World Health Organization (WHO) reported that the outbreak became a pandemic (2). In our country, the first patient was reported by the ministry of health on March 11, 2020. Until this date, many measures were taken early against the disease seen in many surrounding countries. At our hospital, we have taken many safety measures in all departments ranging from the hospital administration department to the smallest department and have made some changes. The most radical changes were made in our emergency department. These changes have included both work plans and physical changes. For this reason, we believe that defining these changes along with the reasoning behind them will be fundamental in later pandemic periods.

### Physical Changes

Since COVID-19 is a respiratory and contact disease, pre-hospital planning should be at the forefront. The emergency service of our hospital was divided into two areas, clean and dirty. The triage area established in front of emergency services was designated to welcome all incoming patients. The patients were divided into

two groups, those with suspected COVID-19 and those without suspected COVID-19, per recommendations from the ministry of health. Suspected patients were taken into the hospital through a separate door and those without suspected disease through another separate door. The area where patients with suspected COVID-19 were taken was named as the dirty area. These patients had a high fever and cough, had contact with people from abroad in the first days of the disease entering our country, or were abroad in the last 14 days. On days when the number of our patients increased, patients with fever, cough, or shortness of breath were directed to the dirty area without seeking foreign contact (3). Let's define these areas now.

### Contagious Area

Patients are guided from the triage area to the dirty area. The first application to be applied to patients with symptoms specified in the triage area is to wear a surgical mask. Vital signs such as fever, arterial blood pressure, pulse, and saturation are measured immediately afterward. Subsequently, patients who receive the triage card are directed to the dirty area. The entrance to the dirty area is from the outside. Patients are directed to the outside clinic for examination with two security guards and a nurse at the door.



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There are three examination rooms, one resuscitation room, and one observation room in the dirty area. Patients who are referred to our hospital by ambulance are taken to the resuscitation room. There is an ambient sterilization device in this room to clean the air. This device filters the dirty air in the room and releases it back into the environment. In this way, the virus load to which people will be exposed to is reduced.

A section should be created in the observation vicinity for patient blood sample collection in the dirty area. Outpatients should be taken to the waiting room with at least 1-2 meters between them after their blood sample is collected. The waiting room should be constantly ventilated. Blood sample collection, electrocardiography, or treatment should be performed at the bedside of patients whose general condition is between moderate to poor. Computed tomography of the thorax, as well as the reverse transcriptase-polymerase chain reaction test, are useful for diagnosis in COVID-19 disease (4). Tomography scans of these patients should be performed by taking precautions. Patients should not come into contact with other patients while being transferred to the radiology unit. For this, we use a separate corridor in our hospital while transferring the patients. Masks and gloves must be worn during the transfer of the patients. If intubated patients have to go by ambulance, an effective filter against both bacteria and viruses should be connected to an Ambu® mask.

### **Clean Area**

The physical conditions of the clean area do not differ from the conditions before the COVID-19 pandemic. Surgical masks should be worn only by patients who come or are brought to this area. The clean area consists of three parts, clean green, yellow, and red areas. Patients who are thought not to have COVID-19 as a result of the triage performed in front of the clean green area are taken in for necessary examination. Patients who need to go from the green area to the yellow area should be taken to the yellow or red area without coming into contact with the dirty area. Those who need to be hospitalized among the patients who have undergone the necessary examinations and tests should be hospitalized in beds reserved as clean areas in the hospital in consultation with the relevant departments. Meanwhile, resuscitation equipment should be complete in each clean area. We manage our clean area in our hospital by taking all the precautions mentioned above.

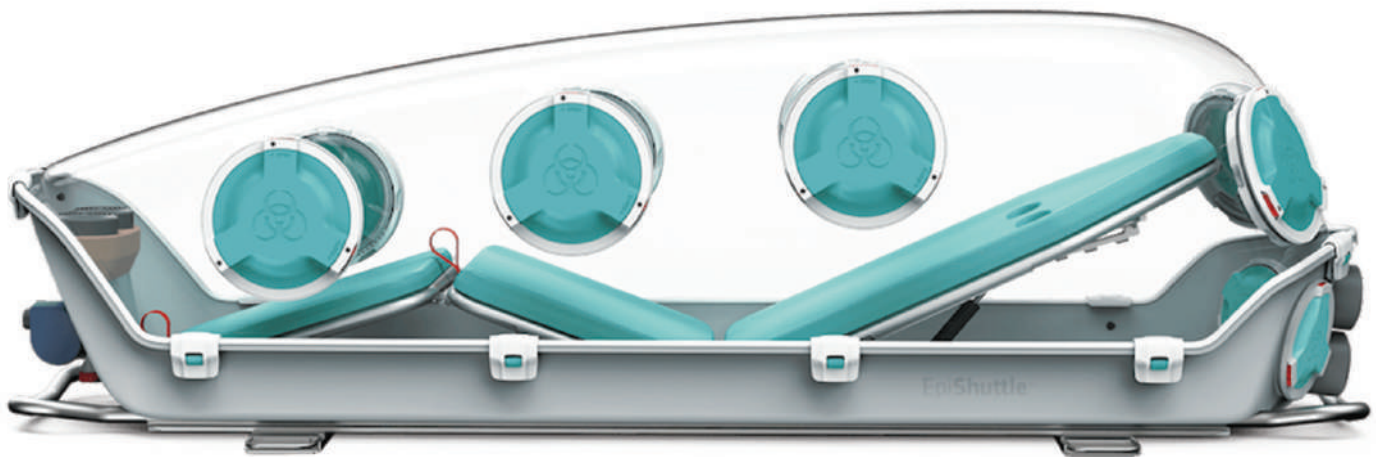
### **Changes in Work Plan**

Staff working in pandemics should be exposed to the virus load as little as possible. For this, it is very important to use personal

protective clothing carefully, especially during working hours. One of the best measures to reduce the virus load is to reduce working hours. In addition, the importance of shift work in terms of employee health and comfort should not be overlooked. We have started to work in shifts in the emergency department of our hospital. We have created 12-hour shifts in the dirty area of our emergency department. Although some publications indicate that an 8-hour shift would be more appropriate, this should be shaped according to the number of staff in the hospital (5).

### **Contagious Area**

We have adjusted the working order in two shifts in the dirty area. A total of four physicians, two of whom are experts and two of whom are assistants, have worked in each shift. According to the patient volume, these physicians have been recommended to work in groups of two among themselves. The physicians who have worked for two hours have been allowed to rest for two hours. Thus, a physician works for about 6 hours a day. Physicians have been allowed to rest for at least 3 days between their duties. A specialist physician has been appointed in the field of resuscitation in the dirty area. The main reason for this is to prevent loss of time in difficult intubations. Video laryngoscope should be used first while performing intubation in line with the current literature and experience (6). We have also used a video laryngoscope during intubation in our hospital. We have placed an application that we guess to be overlooked by many physicians, into our routine practice. Namely, clamping the tip of the intubation tube before intubation reduces virus aerosolization. It is necessary to post important warnings in the form of instructions in the resuscitation room and attract the attention of the physician. Intubation should be performed in a closed area called the respiratory protection unit where the patient's body is located. There are ready-made stretcher-shaped units, as well as a closed unit that the hospital can make with its own means (Figure 1) (7). These units should be transparent and we should be able to see all the procedures we will do to the patient from the outside. Intubation can be performed with the video laryngoscope by inserting hands through two holes on the part of the unit over the head of the patient. We also use a protection unit in our hospital that we have built with our own means. It should not be forgotten that virus filters are attached to the end of the intubation tubes of intubated patients. Video laryngoscopes to be used in this pandemic should also have some features. The current video laryngoscopes are of two types, the first one is mounted on a small monitor laryngoscope. In the second, the monitor is larger than the laryngoscope. The second video laryngoscope is more suitable for use in this pandemic. Because it is easier to use and provides less approach to the



**Figure 1.** Completely closed stretcher with openings on the front and sides for patient intervention

patient. We use the second type of video laryngoscope in our hospital (Figure 2).

Transfer of intubated patients to the intensive care unit should also be done through a separate corridor and in closed units. Thus, virus aerosolization will be prevented.

It is necessary to make the nurses and allied health personnel work in shifts. The number of nurses working in the dirty area has been increased. According to patient volume, 12 or more nurses have been placed in each shift. The nurses, like physicians, have been allowed to work at 2-hour intervals. Two personnel shifting every 2 hours have been set to deal with patient services. These personnel have also been provided with personal protective clothing while working in the dirty area. Of course, all personnel have been trained in their work before moving on to this working order. In particular, we think that the training to be given to the allied health personnel in advance is very important in terms of reducing virus transmission.

### Clean Area

Before the pandemic, the patient volume in yellow and red areas was very high. Since it has been thought that the number of patients coming to these areas will decrease with the pandemic, the number of working physicians has been reduced. Working hours in these areas have been set as 24 hours. Although there is no study on this subject yet, we have thought that there would be problems about consultation in these areas. The main reason for this is that all physicians would be on duty in COVID-19 patient wards. Normally, all departments are on duty in teams in our hospital. This problem has been overcome by decreasing the number of teams and placing an on-duty physician every day. We think



**Figure 2.** Video laryngoscope with monitor separate from laryngoscope

that every hospital should arrange a consultant physician duty list according to its internal dynamics.

## CONCLUSION

As a result, we have made arrangements for work in the emergency department of our hospital accordingly and have accelerated patient evaluation and hospitalization. The number of our patients, which was around 40,000 between February 11, 2020, and March 11, 2020, before the pandemic, decreased to 26,000 between March 11 and April 11, 2020. However, from March 11 to the beginning of May 2020, we consulted approximately 8,000 patients to the infectious diseases clinic. The main reason for the decrease in the number of patients can be attributed to the protective measures taken by the ministry of health. As a last word, we think that every hospital should make its own management plan according to its internal dynamics and physical conditions.

## Ethics

**Peer-review:** Externally and internally peer-reviewed.

## Authorship Contributions

Concept: A.K., Design: E.B.K., İ.K., A.K., Data Collection or Processing: E.B.K., S.K., İ.K., Analysis or Interpretation: S.K., İ.K., Literature Search: E.B.K., S.K., İ.K., Writing: A.K.

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**Financial Disclosure:** The authors declared that this study received no financial support.

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# Responsibility and Work Procedure Order of Infectious Diseases Clinic in Our Hospital in the First Period of COVID-19 Pandemic

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## Abstract

In this section, we aimed to share the experience of infectious diseases and clinical microbiology clinic during the Coronavirus Disease-2019 outbreak. The processes experienced in the first trimester from the beginning of the outbreak were evaluated. Our contribution to the fast, flexible and strong response to the epidemic in the institutional structure of our hospital was emphasized. The 3-month experiences of other countries shed light on us in the diagnosis and treatment of this disease, which was originally new to all of us. The decisions and algorithms of the Scientific Committee of the Ministry of Health guided us. All branches, especially department of emergency, internal diseases, intensive care, radiology, family medicine, clinical microbiology, have made important contributions in patient monitoring and management. Multidisciplinary cooperation in patient management and combating the infectious disease has enabled us to make an important institutional contributions to healthcare in this challenging period.

**Keywords:** Coronavirus Disease-2019, infectious diseases and clinical microbiology, medical care

## INTRODUCTION

Coronavirus Disease-2019 (COVID-19) emerged in Wuhan City, Hubei Province of China in December 2019 and reached a dimension that affected the whole world. The World Health Organization defined this outbreak which more than 118,000 patients were detected in 114 countries and 4,291 deaths were recorded, as a pandemic on March 11, 2020 (1). The first patient diagnosed with COVID 19 was announced on 10 March 2020 in Turkey (2).

The institutional pandemic plan was updated before the pandemic in the Prof. Dr. Cemil Taşçıoğlu City Hospital, a large tertiary health institution. Before the pandemic in our country, we did due diligence with the hospital administration department, urgent needs for the upcoming COVID-19 pandemic were determined and quickly completed. A patient with pneumonia was admitted to our clinic on March 9, 2020 and was followed as having COVID-19 as of March 10 due to the

findings of computed tomography (CT) of thorax and became our first patient with definitive diagnosis. In this patient, the clinic of radiology warned the clinician due to lung CT findings, which enabled the patient to be recognized early on March 10. The radiology clinic made important contributions to patient follow-up with the instant lung CT reporting method in shifts. Patient follow-ups were initiated in accordance with the frequently updated recommendations of the Ministry of Health Scientific Committee (3). The instructions of the Provincial Health Directorate and the General Directorate of Public Health were followed (4).

**Clinical Infrastructure and Capacity:** Infectious Diseases department was serving in a single-storey building with 17 beds in total, separate from the hospital main building. There were two outpatient clinic rooms. There were also patient beds in the clinic belonging to the department of pediatric infectious diseases. In-clinic staff training on the disease was conducted,



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and appropriate personal protective equipment (PPE) was used. Our other patients were discharged or transferred to other clinics. The clinical medical staff consisted of 5 specialist physicians, 5 residents and 2 internal diseases residents, 5 nurses, 5 assistant staff and a secretary. Routine outpatient clinic services were closed to the appointment system. Patients with possible COVID-19 referred from the department of emergency were examined 24/7 by this team in our outpatient clinic. Hospitalization, home treatment and quarantine decisions were made. Records of patient information and all consent forms were arranged. All patients with COVID-19 pre-diagnosis were hospitalized on behalf of infectious diseases and clinical microbiology department. A follow-up form was created to facilitate the follow-up of inpatients. Initially, nasal and throat swab samples for viral polymerase chain reaction (PCR) were taken by our resident physicians, barcoded and recorded in the Public Health Management System. Virology analysis request form, COVID-19 patient information form and contact follow-up forms were filled for each patient. The samples were delivered to the relevant external molecular diagnostic laboratories by courier. Results were followed. Our clinical microbiology and biochemistry laboratories made the provision, maintenance and timely reporting of the necessary laboratory tests in patient follow-up. In the light of clinical findings, radiological and laboratory data, basic data about the severity of the disease, patient approach options and prognosis were obtained from the very beginning.

#### **Dynamic Functional Structuring and Capacity Utilization Throughout the Hospital in the First Phase of the Pandemic:**

The first phase of the pandemic was accepted to start on March 11, 2020. Its end was June 5, 2020 when the curfew was lifted at the weekend (5). Istanbul was the city where approximately 60% of the patients were detected during this phase and the pandemic was the most intense (6). When the pandemic started, the COVID-19 scientific board was established with the participation of relevant clinics in our hospital and gathered every morning as of March 16, the problems in the field were reviewed, dynamic decisions were made and implemented. COVID-19 patient management in our hospital was given under the responsibility and with coordination of infectious diseases and clinical microbiology department. Healthcare professionals were trained on PPE use and isolation precautions. Approximately 1,700 healthcare professionals were reached in these trainings. Infected health workers were recorded and followed up by the infection control team with the follow-up form prepared. Our infectious diseases clinic capacity could not be sufficient due to the rapidly increasing

number of patients. The staff support, which started with three chest physicians and an increasing number of internal medicine residents, was strengthened by the participation of family medicine residents in the duty and outpatient clinic services. Our retired education officer colleague, who joined us upon our invitation, gave us an important support during clinical visits. Patients were hospitalized with a maximum of two people in the wards of the clinics that were evacuated in the old building starting from the 2<sup>nd</sup> floor, except for the 5<sup>th</sup> and 8<sup>th</sup> floors. A patient accompanist was not taken with the patients, except in compulsory cases. Since the capacity of our existing hospital was not sufficient, the opening of our new hospital building, which was built in the same area, was quickly made on April 5. Because of this newly opened hospital building, the name of our hospital was renamed as Prof. Dr. Cemil Taşcıoğlu City Hospital. The infectious diseases clinic, located in a separate single-storey building, was evacuated on April 5. In the new hospital building, 15 wards in total, starting from the top 7<sup>th</sup> floor were opened as infectious diseases wards to hospitalize patients with COVID-19. Infectious diseases COVID-19 first admission outpatient clinic was reorganized extensively. The new hospital started operating on April 7 in the fully equipped section on the ground floor. The service continued uninterruptedly for patients who came from emergency department triage or referred from other hospitals. Physicians and auxiliary health workers from all other clinics participated in COVID-19 clinical duties. Those with medical conditions were excluded from these duties with the medical board report. Infectious diseases and chest diseases specialists made morning visits of the inpatients, and the treatment and discharge decisions were made by these physicians. Patients with severe comorbidities or pregnant women were followed separate clinics by relevant specialists. Protective low molecular weight heparin was applied starting from the first days. Hydroxychloroquine tablet, which was expected to be used in treatment, arrived at our hospital pharmacy on March 19. We used hydroxychloroquine and lopinavir/ritonavir for antiviral treatment in our previous hospitalized patients. The use of favipiravir sent by the ministry of health, in selected patients started on March 24. Immune plasma treatment prepared by the “Kızılay” was started on April 14<sup>th</sup>. At the same time, rapid antibody kits purchased by the ministry of health for healthcare personnel reached our hospital and started to be used. As of March 20, immunoglobulin G (IgG)/IgM antibody detection with rapid antibody kit was started in our patients. Tocilizumab treatment was started on April 9 in selected patients. Interleukin-6 kit was purchased by our hospital and

it was put into use as of April 15, and it became a guide for our patients who needed tocilizumab. Shift laboratories were assigned by the clinical microbiology department in order to take samples for PCR properly and without interruption. The samples were delivered to authorized external laboratories by couriers. Turkey Institutes of Health Directorate on 19 April 2020 Severe Acute Respiratory Syndrome-Coronavirus-2 PCR diagnostic laboratory was set up in our new hospital and PCR assays began to be performed in our hospital. PCR results were reported daily by our genetics and microbiology experts. Due to the decrease in the pandemic rate, the wards in the old hospital building were evacuated except for the 2<sup>nd</sup> floor and were given to the use of patients of other clinics other than COVID-19. The COVID-19 first admission outpatient clinic, which was organized on the ground floor of the new hospital building, was closed and moved to the COVID-19 area held in the emergency room in the old building. In our new hospital, a COVID-19 follow-up outpatient clinic was opened on May 31 in order to monitor patients discharged from infectious diseases wards. During this period, approximately 2,250 patients were hospitalized and more than 4,000 outpatients were followed up. The hospital pharmacy and medical equipment warehouse did not let any interruption in the supply and maintenance of the necessary medicines and protective materials. The follow-up and treatment of more than 500 inpatients per day was arranged during the periods of the most intense admission. In about 80 days (11 March 2020-1 June 2020), a total of 16.000 bed/day (average 200/bed/day) patients with COVID-19 were visited by infectious diseases and chest diseases specialists. Patient follow-ups were carried out by the day's on-duty assistants and responsible duty specialist physicians. In the 48-bed intensive care unit allocated to COVID-19 patients, daily consultations were held by infectious diseases specialists. Infectious diseases or chest diseases specialists were on-duty every day. In addition, infectious diseases consultation services were continued for non-COVID-19 patients in emergency, intensive care unit and clinics.

## CONCLUSION

### Challenges Awaiting Solutions in the Ongoing Pandemic

Institutional arrangements are made in order to meet the demands changing according to the pandemic course. In this process, dynamic decisions have been taken in the face of unforeseen developments in our hospital, directing the practices, and health services have continued with a capacity utilization and extraordinary work determination. In other countries facing the pandemic, it is observed that similar multidisciplinary

practices are performed under the leadership of the infectious diseases department in competent health institutions (7). In this pandemic, which is not known when it will end, the following problems are expected in the transition to the normalization period after the first wave:

- Various complaints of the patients may continue after discharge (8).
- How will the follow-up, treatment by other clinics and consultation regulation of patients with confirmed or suspected COVID-19 be provided?
- How will the protective measures taken be managed on the basis of clinics and procedures?
- How can difficulties and deviations in ordinary healthcare delivery be minimized while protecting patients and healthcare professionals? Guidelines are being developed on this subject (9).

We know that all these difficulties will be overcome with reason, science, effort and patience. Our effort to reach our goal of providing a fast and effective health service that takes patient and employee safety into consideration is carried out under the common responsibility of all healthcare professionals.

## Ethics

**Peer-review:** Internally peer-reviewed.

## Authorship Contributions

Surgical and Medical Practices: M.T.Y., F.Ş., A.K., M.O., S.B., E.A., Concept: M.T.Y., Design: M.T.Y., Data Collection or Processing: M.T.Y., Analysis or Interpretation: M.T.Y., Literature Search: M.T.Y., Writing: M.T.Y.

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# COVID-19 Patient Management in Intensive Care

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## Abstract

The World Health Organization (WHO) declared the coronavirus outbreak as an international public health emergency (pandemic) on January 31, 2020. In line with WHO recommendations, in order to guide the Coronavirus Disease-2019 (COVID-19) agent, transmission routes, case definitions, diagnosis and treatment methods, strategy and application methods, Turkish Ministry of Health, General Directorate of Public Health has prepared guidelines. Management of patients with COVID-19 includes epidemiological risk assessment and patient isolation; general and optimized supportive care, symptomatic treatment, respiratory support, nutritional support, psychological intervention etc. for infection prevention and control. The prognosis of patients depends on the severity of the disease, the age of the patient, their underlying diseases and their general medical condition. Patients with severe COVID-19 should be treated in the critical care unit.

**Keywords:** COVID-19, intensive care, supportive therapy

## INTRODUCTION

In December 2019, a new coronavirus was detected in Wuhan, China, which was widespread, highly contagious and caused a high rate of acute respiratory disease. The World Health Organization (WHO) declared the coronavirus outbreak to be an international public health emergency (pandemic) on January 31, 2020.

In line with the recommendations of WHO, guidelines were prepared in order to guide about the Coronavirus Disease-2019 (COVID-19) agent, transmission routes, case definitions, diagnosis and treatment methods, strategy and implementation methods, especially by the Ministry of Health, General Directorate of Public Health [COVID-19 Severe Acute Respiratory syndrome-coronavirus-2 (SARS-CoV-2) Infection Guide 14.04.2020] (1).

Management of patients with COVID-19 includes epidemiological risk assessment and patient isolation; general and optimized supportive care, symptomatic treatment, respiratory support,

nutritional support, and psychological intervention, etc for infection prevention and control (2).

COVID-19 may present with severe pneumonia, Acute Respiratory Distress syndrome (ARDS), sepsis, septic shock, myocarditis, arrhythmia and cardiogenic shock, and multiple organ failure.

Respiratory failure is often hypoxemic respiratory failure, less commonly in the form of hypercapnic respiratory failure. The prognosis of patients depends on the severity of the disease, the patient's age, underlying diseases, and general medical condition. Severe patients with COVID-19 should be treated in a critical care unit [intensive care unit (ICU)].

**COVID-19 Management in the Intensive Care Unit of the Ministry of Health Prof. Dr. Cemil Taşcıoğlu City Hospital and Okmeydanı Training and Research Hospital**

### Infection Control and Tests

During aerosol-generating procedures (Endotracheal intubation, open aspiration, nebulized treatments, manual ventilation before



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intubation, taking the patient into the prone position, leaving the patient from the ventilator, non-invasive positive pressure ventilation, tracheostomy and cardiopulmonary resuscitation), healthcare workers wear gloves, overalls, safety glasses or face shield, N95 mask, FFP2 or equivalent. Endotracheal intubation, if available, is recommended to be performed with video-laryngoscopy instead of direct laryngoscopy by a healthcare professional with the most experience in airway management to minimize the number of attempts and the risk of contamination.

In order to protect healthcare professionals and other patients in the hospital by preventing the spread of infectious airborne pathogens from room to room or open areas in our ICU, the entire 48-bed ICU, each room of which is an isolated single room, has been turned into a negative pressure room. Contamination between the rooms has been prevented, and the risk of infection in the patients and employees outside the room has been reduced when aerosol-forming processes are performed in the room such as tracheal intubation, bronchoscopy and a non-invasive ventilation. In addition, unnecessary staff has not been allowed in the patient room.

### Support Therapy

The clinical spectrum of COVID-19 ranges from mild illness to ARDS with a high risk of mortality, with early markers of disease severity not yet fully established. Current evidence suggests that patients with advanced age, pre-existing comorbidity or dyspnea should be closely monitored, especially 1 to 2 weeks after symptom onset. More studies are needed to understand the incidence and consequences of COVID-19 ARDS, and to conduct critical care management and resource planning (3).

### 1. Hemodynamic Support

ARDS, severe pneumonia, sepsis, and septic shock are the life-threatening forms of SARS-CoV-2 infection and are indicative for treatment in the ICU (4). The prevalence of shock in adult COVID-19 patients is highly variable (1-35%) depending on the patient population, the severity of the disease, and the definition of shock.

In the meta-analysis of 660 articles (1/1/2020-2/23/2020) by Rodriguez-Morales et al. (5), 20.3% of the patients needed intensive care, and 32.8% of these patients were admitted to ICU in ARDS and 6.2% in shock. Average hospital mortality rate was 13.9%. In a study conducted with 44.415 patients, 2087 (5%) patients were defined as critical patients with other organ failure, including severe hypoxemia and shock (6). It is probably more common in hospitalized patients and can reach 20-35% in patients in ICUs (7). It should be kept in mind that patients may

have myocarditis and related arrhythmia and cardiogenic shock. Cardiac damage was found between 7% and 23% of patients with COVID-19 in Wuhan (7). They suggested that advanced age, low lymphocyte count, high D-dimer level were risk factors for possible cardiac damage.

Between 20 March and 15 May 2020, 1910 patients were admitted to our hospital, 9.1% of them (175 patients) were admitted to ICU and advanced hemodynamic support was required.

### 2. Fluid Therapy

In order to evaluate the fluid response in patients with COVID-19 and shock, it is recommended to use dynamic parameters (body temperature, capillary refill time and serum lactate levels) instead of static parameters. In acute resuscitation, conservative approach rather than liberal fluid strategy, using buffered balanced crystalloid instead of colloid is appropriate. Gelatins and dextrans should not be used. It is recommended to administer 30 mL/kg isotonic crystalloid fluid (saline or ringer's lactate) in the first hour, however, fluid therapy should be carried out carefully and hypervolemia should be avoided in patients with ARDS. Albumin should not be used routinely for initial resuscitation. In patients with COVID-19, despite fluid resuscitation, vasopressor support should be given in the presence of shock or in very deep hypotension, with an average arterial pressure of 65 mmHg and the first choice is the vasoactive agent norepinephrine. When not available, it is appropriate to use vasopressin or epinephrine as the first choice instead of other agents. Subsequent treatment is determined by the patient's cardiac output and fluid responsiveness. Dopamine should not be used. In case of persistence of cardiac dysfunction despite adequate fluid resuscitation and norepinephrine and ongoing signs of hypoperfusion, it is appropriate to add dobutamine instead of increasing the norepinephrine dose. Lactate monitoring should be done. In patients with refractory shock, daily intravenous 200 mg hydrocortisone can be used as a low-dose infusion or as an intermittent dose instead of giving corticosteroid therapy. Our practice in the clinic has been in this direction.

### 3. Respiratory Failure Management

In SARS-CoV-2 infection, acute hypoxemic respiratory failure requiring mechanical ventilation develops due to many underlying mechanisms such as pulmonary edema, hemoglobinopathy, vascular occlusion and ventilation/perfusion mismatch (7). If peripheral oxygen saturation ( $SpO_2$ ) is <90%, oxygen therapy should be initiated. Recent guidelines recommend a target oxygen saturation of 92-96% in adults with COVID-19 using



supplemental oxygen as needed. If acute hypoxemic respiratory failure develops despite conventional oxygen therapy, high frequency nasal oxygen [high flow nasal cannula (HFNC), up to 60 L/min] can be used instead of noninvasive mechanical ventilation (NIMV). NIMV should be administered with intensive care ventilators or dual circuit ventilators. A viral/bacterial filter should be added to the inspiratory and expiratory outputs of the circuits. It should be applied with maximum personal protective equipment (PPE) in negative pressure rooms if possible, and in single rooms if possible, especially due to the risk of aerosol creation of high flow oxygen application and NIMV (8). Patient selection is important; those with moderate to severe hypoxaemia are unlikely to receive sufficient oxygen through HFNC and usually require intubation. Stable patients with mild to moderate hypoxaemia can be given oxygen via nasal cannulas, but should be carefully monitored for signs of deterioration. Patients should be evaluated for worsening of respiratory failure at close monitoring and at short intervals. In case of worsening in breathing, early intubation should be considered (Appendix 1).

Although the actual incidence of hypoxic respiratory failure in patients with COVID-19 is not known, approximately 14% of the patients will be in a serious condition that requires oxygen therapy and 5% will need mechanical ventilation and intensive care (6). Of the patients hospitalized in our hospital, 9.1% needed mechanical ventilation and intensive care.

Controversies against early intubation remain unresolved, largely due to lack of good evidence. Those recommending early intubation recommend avoiding the risk of self-induced lung injury. Those who oppose early intubation note the high mortality rates reported among intubated patients with COVID-19 and claim that ventilator-induced lung injury is a contributing factor. The best approach will depend on the patient. A single approach is unlikely to work in a disease as heterogeneous as COVID-19 (9).

Although the current histopathology shows widespread alveolar damage consistent with ARDS, Gattinoni et al. (9) has stated that COVID-19 pneumonia is a specific disease with distinctive phenotypes with relatively well preserved respiratory mechanics despite the severity of hypoxemia.

There are two types of patients with different pathophysiologies who are clearly distinguishable by computerized tomography scan;

Type 1: Approximately 2/3 of the patients who do not have ARDS and whose compliance is preserved are in this form.

Type 2: ARDS, low compliance.

Type 1 patients: In patients with high pulmonary compliance (static  $>40$  mL/cmH<sub>2</sub>O), positive end-expiratory pressure (PEEP) levels should be kept low, tidal volume should not exceed 6 mL/kg, respiratory frequency should not exceed 20/min.

### Acute Respiratory Distress Syndrome

- Respiratory distress that occurs or worsens in the last week
- Radiologically pleural effusion, collapse or nodular bilateral opacities
- Respiratory failure that cannot be explained by heart failure or volume excess
- Mild ARDS:  $200 < \text{PaO}_2/\text{FiO}_2 \leq 300$  (PEEP  $\geq 5$  cmH<sub>2</sub>O)
- Moderate ARDS:  $100 < \text{PaO}_2/\text{FiO}_2 \leq 200$  (PEEP  $\geq 5$  cmH<sub>2</sub>O)
- Severe ARDS:  $\text{PaO}_2/\text{FiO}_2 \leq 100$  (PEEP  $\geq 5$  cmH<sub>2</sub>O)

Since ARDS (Type 2) caused by COVID-19 is similar to ARDS due to other causes, the principles supporting ventilation should also be similar. Standard therapy should be used for severe ARDS; low tidal volume (Vt 4-8 mL/kg) instead of higher tidal volume (Vt  $>8$  mL/kg), plateau pressures (Pplat)  $<30$ cmH<sub>2</sub>O, driving pressure (driving pressure=plateau pressure - PEEP)  $<14$  cmH<sub>2</sub>O, it is recommended to use a higher PEEP strategy rather than a low PEEP strategy. In moderate-severe patients ( $\text{PaO}_2/\text{FiO}_2 <200$ ), PEEP, which provides the best compliance and oxygenation without impairing hemodynamics, should be applied. In cases of pH  $<7.15$  and hypercapnia, tidal volumes can be increased to 8 mL/kg, and respiratory rate can be up to 30/min. Otherwise, permissive hypercapnia may be allowed. It is sufficient to have PaO<sub>2</sub> of 60-85 mmHg and SO<sub>2</sub> of 88-95% (10). Despite ventilation optimization, recruitment maneuvers can be used in case of hypoxemia. The use of neuromuscular blocking agents (NMBA) is not recommended routinely, but can be applied in the presence of ventilator incompatibility, persistent hypoxemia or hypercapnia despite sedation. Excessive sedation should be avoided or sedation should be light (Figure 1). Thrombosis and associated ischemic events are very common in this disease. Anticoagulation should be initiated when necessary and daily coagulation parameters, especially D-dimer levels should be checked.

### 3.1. Prone Position

Uncertainty about how best to optimize respiratory support has led to increased use of the awake prone position for non-intubated patients. Lying prone improves ventilation-perfusion matching and is associated with reduced mortality in patients with ARDS compared with supine positioning. The positive effects of daily

COVID-19 (+) mild ARDS	COVID-19 (+) moderate/severe ARDS	Rescue/Support treatment
<p>✓ Perform</p> <p>4-8 mL/kg tV and P<sub>platue</sub> &lt;30 cm H<sub>2</sub>O</p>	<p>! Consider</p> <p>Higher PEEP</p>	<p>? Unclear</p> <p>Antiviral agents, hydroxychloroquine, anti-IL6</p>
<p>✓ Perform</p> <p>Search for presence of bacterial infection</p>	<p>! Consider</p> <p>Neuromuscular blocker agent boluses to facilitate ventilation targets</p>	<p>! Consider: High P<sub>platue</sub> and asynchrony despite prone</p> <p>Neuromuscular blocker agent infusion for 24 hours</p>
<p>✓ Perform</p> <p>Target SPO<sub>2</sub> is 92-96%</p>	<p>! Consider: (If there is response to PEEP)</p> <p>Conservative recruitment maneuvers</p>	<p>! Consider</p> <p>Prone ventilation for 12-16 hours</p>
<p>! Consider</p> <p>Conservative liquid strategy</p>	<p>! Consider</p> <p>Prone ventilation for 12-16 hours</p>	<p>! Consider</p> <p>Prone ventilation for 12-16 hours</p>
<p>! Consider</p> <p>Empiric antibiotic therapy</p>	<p>! Consider: High P<sub>platue</sub> and asynchrony despite prone</p> <p>Neuromuscular blocker agent infusion for 24 hours</p>	<p>! Consider: Stop if there is no rapid response</p> <p>Nitric oxide inhalation</p>
<p>? Unclear</p> <p>Systemic corticosteroids</p>	<p>! Don't do it</p> <p>Stepwise recruitment</p>	<p>! Consider: See the ECMO criteria</p> <p>V-V ECMO or send to an ECMO center</p>
	<p>! Consider</p> <p>Short-term administration of systemic corticosteroids</p>	
	<p>? Unclear</p> <p>Antiviral agents, hydroxychloroquine, anti-IL6</p>	

**Figure 1.** Patients with mild/moderate/severe COVID-19 and Rescue/Support therapy (10)

ARDS: Acute Respiratory Distress syndrome, IL: Interleukin, COVID-19: Coronavirus disease-2019, ECMO: Extra-corporeal membrane oxygenation, PEEP: Positive end-expiratory pressure, SPO: Oxygen saturation

prone position application on hypoxia have been demonstrated in non-intubated patients with pulmonary involvement. For type 2 patients, the prone position can be used as long-term therapy (for 12-16 hours) as with any severe form of ARDS. However, in type 1 patients, prone positioning should be considered as a rescue maneuver to facilitate the redistribution of pulmonary blood flow rather than opening up collapsed areas. Prolonged prone positioning/supine cycles provide little benefit in patients with high lung compliance and result in high levels of stress and fatigue in staff (9). While it is appropriate to use intermittent boluses of NMBA instead of continuous infusion of NMBA when necessary to facilitate protective lung ventilation; in the presence of ventilator desynchronization, ongoing deep sedation, prone ventilation, or continuous high plateau pressures, continuous NMBA infusion up to 48 hours may be required (10). In the ICUs of our hospital, prone position was provided in all patients with P/F <150 and the duration was programmed to be 12-16 hours according to the response, and even we had applications that lasted 24 hours in some patients.

Although the ventilation is optimized by using rescue therapies and prone positioning in adults with COVID-19 who are mechanically ventilated; in case of refractory hypoxemia, it is recommended to perform venovenous extra-corporeal membrane oxygenation (ECMO) or refer the patient to an ECMO center. ECMO should only be considered in carefully selected patients with COVID-19 and severe ARDS (Figure 2, our ECMO application).

**3.2. Application of Tracheostomy**

Since tracheostomy is one of the processes that create aerosol, care should be taken in its timing. The general approach is to



**Figure 2.** ECMO application  
ECMO: Extra-corporeal membrane oxygenation

avoid tracheostomy before the 14<sup>th</sup> day of intubation. Some authors recommend not to make a tracheostomy decision before the 21<sup>st</sup> day. These applications are also aimed at reducing the patient’s viral load. Repeating the polymerase chain reaction (PCR) or antibody test before tracheostomy and a negative result are recommended by some authors, but repeating the PCR test before tracheostomy is not an accepted practice (1). Maximum PPE (N95/FFP3 mask, goggles/face protection, liquid impermeable surgical gown/overalls, double-layer gloves and, if possible, powered air-purifying respirator) should be used for healthcare worker safety. Tracheostomy should be performed by the most experienced physician. Tracheostomy should be performed in a negative pressure operating room or a negative pressure patient room. The choice of percutaneous or surgical tracheostomy method should be decided based on hospital resources and experience. The general approach is to prefer surgical tracheostomy (Appendix 2. Tracheostomy protocol. Our percutaneous tracheostomy applications in the clinic; Figures 3a, 3b, 3c, 3d).

**4. Medical Treatment of COVID-19**

**Anti-cytokine and Anti-inflammatory Treatments**

Tocilizumab, which blocks interleukin (IL)-6, has been reported to have a positive effect on COVID-19 related Macrophage Activation syndrome. In our unit, tocilizumab treatment is preferred in our patients under the guidance of infectious diseases clinic



**Figure 3a.** Percutaneous tracheostomy; puncture





**Figure 3b.** Percutaneous tracheostomy; dilatation



**Figure 3c.** Percutaneous tracheostomy; insertion of tracheostomy cannula

when necessary. Excessive immune response to infection with the SARS-CoV-2 virus has been blamed for respiratory distress and multiorgan failure, referred to as “cytokine storm” in some patients. High levels of IL-6 and other cytokines have been shown.

In a study conducted with 21 patients with severe COVID-19 symptoms who were given IL-6 blocker tocilizumab; fever and elevated C-reactive protein (CRP) levels improved and levels of IL-6 and other proinflammatory cytokines decreased within 24 hours of tocilizumab therapy. Additional oxygen use decreased in 15 patients, and oxygen saturation levels stabilized in all patients. Two patients were removed from the mechanical ventilator (11). Our practices in our clinic have also been in this direction. Tocilizumab is administered at a dose of 8 mg/kg (maximum 800 mg). It can be administered as a single dose of 400 mg or 800 mg intravenously, depending on the severity of the patient’s symptoms. When the first dose is 400 mg, taking into account the changes in clinical and laboratory findings, a dose of 200-400 mg can be repeated within 12-24 hours (Appendix 3. ICU COVID-19 Treatment algorithm). Tocilizumab should not be used in the presence of pregnancy, neutropenia ( $<500/\text{mm}^3$ ), active tuberculosis, active hepatitis B or C, allergy, and hypersensitivity. Liver functions and thrombocyte count should be monitored. Patients with diverticulitis history should be monitored closely for perforation. Since CRP values may



**Figure 3d.** Percutaneous tracheostomy; connecting to a mechanical ventilator

decrease after tocilizumab treatment, regardless of the clinical efficacy of the drug, additional examinations (such as serum IL-6 levels) should be used in the follow-up of the acute phase response. It should be known that the decrease in ferritin values will not be rapid when there is a response to the treatment, and if the values remain high for a while, it should not be considered as treatment failure. In addition, signs of inflammation (fever, leukocyte, CRP, ferritin, etc) must be taken into consideration as well as signs of hypoxia, respiratory failure, shock, and multiple organ failure in evaluating the effectiveness of treatment.

## CONCLUSION

As a result; COVID-19 is a systemic infection that has an important effect on hemostasis and currently has no effective treatment. Multiple organ failure with severe pneumonia, ARDS, sepsis, septic shock, myocarditis, cardiogenic shock can be encountered. Respiratory failure is often in the form of hypoxemic respiratory failure. Management of patients with COVID-19 requires patient isolation, infection prevention and control, optimized supportive care, symptomatic therapy and respiratory support. The prognosis of patients depends on the severity of the disease, the patient's age, underlying diseases, and general medical condition. Patients with severe COVID-19 should be treated in the ICU.

## Ethics

**Peer-review:** Externally peer-reviewed.

## Authorship Contributions

Concept: Ş.V., E.A.T., F.G., F.U., T.M., O.O., C.P., N.T., Design: Ş.V., E.A.T., T.M., O.O., C.P., N.T., Data Collection or Processing: Ş.V., E.A.T., N.T., Analysis or Interpretation: Ş.V., N.T., Literature Search: Ş.V., E.A.T., F.G., F.U., T.M., C.P., N.T., Writing: Ş.V., E.A.T., F.G., F.U., T.M., O.O., C.P., N.T.

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**Appendix 1. Endotracheal intubation protocol (10)**

1. It should be applied with a rapid sequential intubation protocol by trained and experienced people.
2. Intubation should be performed with a video laryngoscope, if possible. Patients who are thought to have difficult airway can be intubated by flexible bronchoscopy. However, bronchoscopy is also a procedure with a high risk of creating aerosol.
3. Intubation should be applied with maximum personal protective equipment (PPE) in rooms with negative pressure if possible due to the risk of creating aerosol, and if not in single rooms.
4. If possible, the use of balloon-mask should be avoided during preoxygenation. A filter should also be used in balloon mask application.
5. A neuromuscular blocker can be used to suppress cough before intubation. Positive pressure ventilation should not be initiated until the endotracheal cuff is inflated. A heat-moisture exchanger (humidifier) filter can be used, but active humidification should be preferred in cases of dense plugging and dead space increase.
6. Unless necessary, the connection should not be cut in the mechanical ventilator circuit, if it is necessary, PPE must be used.
7. If possible, closed system aspiration method should be used.
8. Bronchoscopic procedures should be avoided unless absolutely necessary, and metered dose inhaler should be preferred instead of nebulization in bronchodilator therapy.

**Appendix 2. Tracheostomy protocol in intensive care unit in our hospital (1)**

- Patients who will undergo tracheostomy should have mechanical ventilation values of  $FiO_2 \leq 50\%$  and positive end-expiratory pressure  $\leq 10$  mmHg.
- In the case of prolonged intubation, daily endotracheal tube cuff pressure measurement is recommended until the tracheostomy is opened. The cuff pressure should be kept in the range of 20-30 cm H<sub>2</sub>O to prevent air leaks.
- Tracheostomy cannula should be fenestrated and a cuffed cannula. It is useful to have several sizes of tracheostomy cannula ready. In addition, the integrity of the cuff should be checked before the procedure.
- There should be a minimum of healthcare workers in the operation room or the patient's room and all necessary materials should be prepared in the room before.
- Before application,  $FiO_2$  should be adjusted to 100%.
- A full dose of neuromuscular block and deep sedation should be applied in the patient at a level to prevent coughing and straining.
- During the opening of the tracheostomy, the use of electrocautery or aspirator should be avoided as much as possible, as they create aerosol.
- During tracheostomy, the cuff of the tube should be fully inflated and adjusted to avoid leakage, and care should be taken not to damage the cuff during surgery.
- When the front wall of the trachea is seen, cutting the cuff should be prevented by pushing forward the anesthesia tube as deep as possible towards the bronchi. Make sure that the cuff of the tube is fully inflated. The surgeon should make the incision and open the tracheal window without damaging the head.
- The most risky time in tracheostomy is the stage of pulling the endotracheal tube and placing the tracheostomy cannula. During this period, if the patient's condition allows (no critical hypoxia), ventilation is stopped at the end of expiration. The endotracheal tube is pulled up to the incision, but is not completely removed, the tube is clamped at this stage.
- Heat and moisture exchanger filter and mechanical ventilation circuit are placed on the tracheostomy cannula. As soon as the cannula is placed, the cuff must be inflated before ventilation is initiated and then the patient must be ventilated. The endotracheal tube should be pulled out and placed in a plastic bag for disposal.
- The location of the tracheal cannula should be verified with end-tidal CO<sub>2</sub> measurement, and verification by auscultation with a stethoscope is not recommended in terms of spread of infection.
- If a percutaneous tracheostomy method is used, it can be applied without using bronchoscopy to minimize aerosol generation. In addition, if the patient's condition is suitable (if there is no critical hypoxia) after the guidewire is placed, mechanical ventilation should be stopped at the end of expiration and the operation area should be covered with gauze before starting tracheal dilatation.

**Appendix 3. COVID-19 Treatment algorithm in intensive care unit in our hospital**

**Intensive care- before connecting to a mechanical ventilator:**

- The tube will be clamped, the breathing circuit will be connected and then ventilation will be connected.

1. Invasive and non-invasive monitoring will be done
2. Routine cultures will be taken
3. All routine laboratory blood samples will be taken

In Addition:

Ferritin

D-dimer

Fibrinogen

Lactate dehydrogenase (LDH)

Alanine aminotransferase (ALT)/aspartate transaminase (AST)

CRP

TRIGLYCERID

4. SOFA and APACHE II scores will be recorded

**COVID-19 Medical Treatment (the treatment that the patient received in the ward will be considered)**

**Day 1: Hydroxychloroquine 2x2 tb, first day**

2x1 tb maintenance, 4 days

In addition to hydroxychloroquine, at the end of the 3rd day, according to the patient's clinical status

Hydroxychloroquine + Favipravir

Clarithromycin 2x500 from day 1/Azithromycin 1\*500

If community-acquired pneumonia is considered, ceftriaxone should be started, and if hospital-acquired pneumonia is considered, piperacillin/tazobactam should be started. In case of an increase in infection parameters at any stage of the treatment process, cultures are sent from all invasive and suspicious areas and the opinion of the infectious diseases clinic is obtained for antibiotherapy/tocilizumab treatment.

NOTE: QT should be monitored and drug interactions should be evaluated on electrocardiogram.

**Tocilizumab**

With fever monitoring, in case of refractory fever exceeding 39 °C, tocilizumab may be given after blood sample for IL-6 is taken.

**IVIg**

It may be considered if the blood IgG level is low. In patients within 7-15 days, if it exceeds 10 days, it is given in the dose of 0.5 mg/kg per day.

**COVID-19 ARDS Treatment**

Prone Position: When FiO<sub>2</sub> is 60%, Pplateau is 28 and PEEP is 12, if the P/F ratio is <150, the prone position is provided (12-16 hours).

If mean arterial pressure is below 60 mmHg and there is no response to 30 mL/kg fluid resuscitation, vasopressor is started.

1. Option inotrope is dobutamine + additional noradrenaline as needed

CORTICOSTEROID: (+) inotrope dobutamine can be started with low dose hydrocortisone (200 mg/day 5-7 days) in patients without contraindication.

Sedative agent: OPIOID or OPIOID + Midazolam

If spontaneous breathing is not suppressed despite deep sedation, neuromuscular blocker infusion can be given in the supine and or position.

**Other Supportive Medical Treatment**

Vitamin D3, 1 amp per week

Magnesium (with blood level monitoring)

Zinc

N-Acetyl-Cysteine

C Vit (between 2-5 g/day) (3\*1.5 g)

Nutrition: Calorie calculation will be made by dividing the hours in the supine position, prokinetic agent will be used when necessary).

**COVID-19 Diagnostic Tests and Patient Management**

- If the PCR result is negative, a control PCR should be sent no earlier than 24 hours. The control PCR result should be consulted with infectious diseases clinic in order to send an antibody test (rapid test) from the patient who is negative for COVID-19 in the PCR test.

- If 10 days are not exceeded in a patient with negative PCR test who has transferred from the ward, PCR will be performed in tracheal aspirate.

- If PCR test is positive; antibody test will not be done.

Monitoring of negativization in PCR (+) Patient: If the PCR test is negative in the 14th day, the PCR test is repeated after 24 hours. And if it is negative again, the patient is considered COVID-19 negative.



# During COVID-19 Pandemic Anesthesia Practices and Operating Room Management of Our Anesthesiology and Reanimation Clinic in the University of Health Sciences Turkey, Prof. Dr. Cemil Taşcıoğlu City Hospital

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## Abstract

Coronavirus Disease-2019 (COVID-19), which emerged in China in December 2019, was announced by the World Health Organization as a pandemic in March 2020. Many institutions and organizations in the world and Turkey have made recommendations on measures that will protect both medical personnel and the patient in cases requiring emergency or elective surgery in patients with suspected or confirmed COVID-19 and are still continuing to update their recommendations. In this article, we planned to convey our experiences regarding anesthesia and operating room practices that we carried out in line with the recommendations of the Ministry of Health Science Committee and other important health institutions in the world during this extraordinary period we passed.

**Keywords:** COVID-19, coronavirus, anesthesia, operating room, personal protective equipment, pandemic

## INTRODUCTION

The world became aware of the Coronavirus Disease-2019 (COVID-19) outbreak for the first time when China reported to the World Health Organization (WHO) that patients with pneumonia of unknown origin occurred in the city of Wuhan, Hubei province on December 31, 2019. A process that had not been experienced before for the whole world began when the outbreak, which was perceived as a regional epidemic, initially affecting China and its surroundings, rapidly crossed Asian lands and began to threaten public health globally. In this period, we started our work in our hospital, of which name was Okmeydanı Education and Research Hospital before the pandemic and which was named as Prof. Dr. Cemil Taşcıoğlu City Hospital after the precious lecturer of İstanbul University Faculty of Medicine lost his life in the pandemic, primarily by holding informative meetings for the staff of our clinic and other

employees in the operating room. In these meetings, we shared up-to-date information on transmission routes and prevention methods. Each meeting was held repeatedly at different times so that all personnel could attend. In the continuation of the process, we have completed our preparations for protection plans that develop when needed. In this review, we have planned to transfer our experiences regarding our anesthesia and operating room practices during the COVID-19 pandemic process by dividing the process into three periods from the beginning of the pandemic. Because we think that since the announcement of "International Public Health Emergency" by WHO on January 30, three separate periods, which are different from each other in terms of dynamics, have been passed both in our own hospital and other regional hospitals. We have described these three periods as the first period from the announcement of the epidemic in China to the announcement



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of pandemic, the second period we have called the pandemic period and the third period when the normalization process has started.

### **Our Anesthesia Practices and Operating Room Management During the COVID-19 Pandemic Process**

#### **Period I (December 2019 - March 11, 2020)**

In this process, from the endemic announcement in China to the pandemic announcement, which we considered as the first period, we tried to have the most detailed and accurate information about the general risks that might be encountered in these patients by evaluating the literature available for that period, mostly from China. Our aim was to make the right arrangements in order to protect all operating room health personnel and other patients from contamination, while providing the necessary treatment to the patients in line with their needs in case the pandemic started to rise in our country and İstanbul and the number of patients increased. In this period, we could make the training meetings more frequently and we could rarely made them in the period II and III due to the workload and protective measures by providing the social distance and protection rules. Starting most of the trainings in the first period provided a very positive contribution to the system as it provided the basis for the team to protect itself and its surroundings in future periods which would be very busy. In the first period of the epidemic, all elective interventions in and out of the operating room continued routinely in our hospital, as in other hospitals. Since there was no patient volume outside of working hours during this period, the healthcare personnel in our clinic continued their normal working hours. In addition, we completed our workforce and equipment planning in case of an increase in patient volume during this period. We thought that this first period was a preparation period for pandemic for our hospital and clinic and this preparation period contributed a lot to the successful management of the pandemic.

#### **Period II: The Pandemic Period (March 11, 2020 - June 1, 2020)**

Along with the determination of the first patient in our country and the announcement of the pandemic, a Scientific Board was created for COVID-19 in many medical institutions and our hospital, especially the Ministry of Health. As the Anesthesiology and Reanimation Clinic, we determined the personal protection equipment (PPE) (N95/FFP2 or N99/FFP3 mask, waterproof apron, coveralls, gloves, bonnets, boots, and galoshes) which were required to protect the health of all employees who would support the treatment of patients with COVID-19 and prevent contamination. Then we conveyed the missing ones to the hospital administration department (Figure 1) (1). During this

extraordinary period, we observed that close contact of the field with hospital administrations was necessity in order to meet urgent needs quickly. During this period, we experienced that the complete provision of these equipment, which we determined for the safety of medical personnel and patients, made a very positive contribution to the morale and motivation of our working staff by making them feel safe. Since it is important to learn how to put on and remove these materials as well as procuring PPE in order to prevent contamination, and since contamination is reported especially during removal, we have given priority to giving recurrent simulation training to all personnel in the operating room on putting on and removing PPE (Figure 2) (1,2). During these trainings, we have paid special attention to the participants being in small groups, maintaining social distance and being masked. For PPE putting on and removing, we have made visual videos filmed in our own clinic to be shared on the common social networks of our clinic's health workers. In March 2020, the Science Board of the Ministry of Health recommended that planned surgeries and endoscopic interventions should not be performed during this period due to the increased perioperative risks in patients undergoing surgery, even if they were asymptomatic and to ensure the controlled consumption of resources. These suggestions were discussed



**Figure 1.** Personal protection equipment

in the Scientific Committee of our hospital and as of March 21, elective surgeries and endoscopic interventions were postponed. Operations classified as urgent or emergent by various surgery societies including emergency cesarean section, acute abdomen, bleeding, orthopedic emergencies, large vessel emergencies, emergency bypasses, neurosurgeries and transplantations that could not be postponed were performed (3). In this period before the transition to normalization, all urgent surgeries of patients with and without COVID-19 were continued uninterruptedly in our hospital. In this period, while making the operation order

of emergent patients, care was taken to start with patients with lower risk of operation, under 60 years of age and without comorbidity, in line with the recommendations (4-7).

**Period III: Normalization Process (June 1, 2020 - )**

Following the publication of the Scientific Committee of the Ministry of Health on a June 2020 “Working Guideline in Health Institutions During the Normalization Period”, the process of returning to normal throughout our country has started. During this period, we started to gradually withdraw our human resources, which we had previously directed to our intensive care units, back to the operating room due to the increased surgical procedures. During this period, we did all planning in our clinic, within the scope of the requests and the possibilities we had, by following the recommendations of the Ministry of Health’s Scientific Board’s current guides. The “Working Guideline in Health Institutions During the Normalization Period”, which was last updated on July 7, 2020, emphasizes a planning to manage the increasing demand due to the postponed planned procedures in this process and ensuring the safety of patients and healthcare workers. Also it is emphasized that the COVID-19 related measures should be continued within this planning (8). In the same guideline, it is stated that it is necessary to observe a steady decrease in the incidence of COVID-19 for at least the last 14 days in order to start healthcare services to be provided especially to planned surgical patients at the provincial level, and it is appropriate to prioritize the operations by evaluating the patient, disease and surgical procedure factors when starting elective surgeries (Table 1) (8). In the current guideline, it is also recommended to establish a committee



**Figure 2.** Simulation trainings

**Table 1. Factors belonging to the patient, disease and surgical procedure that should be considered in the prioritization of the operations in the normalization period**

<b>Patient</b>	<ul style="list-style-type: none"> <li>- Age</li> <li>- Chronic diseases (COPD, asthma, CVD, CAD, malignancy, DM)</li> <li>- Immunosuppression (chemotherapy, immunosuppressive therapy for other reasons)</li> <li>- Presence of COVID-19 or flu-like symptoms</li> <li>- History of contact with a patient with COVID-19 in the last 14 days</li> </ul>
<b>Disease</b>	<ul style="list-style-type: none"> <li>- Whether there is a non-surgical treatment option</li> <li>- The effect of delayed surgery on disease progression</li> <li>- Whether the delay of the surgery will cause difficulty in the surgical technique</li> </ul>
<b>Surgical procedure</b>	<ul style="list-style-type: none"> <li>- Operation time</li> <li>- Possibility of intubation</li> <li>- Risk of the surgical area (head, neck, nose-throat, respiratory tract, thoracic surgery, etc.)</li> <li>- The amount of blood loss predicted during surgery</li> <li>- Number of people in the surgical team</li> <li>- The necessity of postoperative intensive care follow-up</li> <li>- Postoperative anticipated length of stay</li> </ul>
<p>COVID-19: Coronavirus Disease-2019, COPD: Chronic obstructive pulmonary disease, CVD: Cerebrovascular disease, CAD: Coronary artery disease, DM: Diabetes mellitus</p>	



consisting of administrative directors and representatives of infectious diseases, surgical departments, anesthesia, pathology, gastroenterology and other necessary disciplines in order to determine the planned surgical procedures to be performed in the hospital and to determine the priority surgical procedures to be performed for each unit by this committee (8).

### **Workforce Planning in Our Anesthesia and Reanimation Clinic During the Pandemic Period**

In our clinic, especially with the announcement of the pandemic and the decision to cancel the elective surgeries, the patient load in the operating room decreased relatively, so our anesthesiologists, residents and technicians were divided into groups and included in shift-based working programs in order to employ the least number of personnel required. During this period, the patient load of our intensive care units was too high, so the working programs of our anesthesiologists, residents and technicians were mainly arranged to spend their shift in our intensive care units. In this period, the introduction of a flexible working system for all healthcare workers made it easier for us to plan working shift. In the first periods when the number of patients started to increase, the shifts continuing with 24-hour active 48-hour rest (24/48) periods were changed and reorganized as 24-hour active 72-hour rest (24/72) shifts, as it was stated that they were too consumer to be tolerated according to the feedback. During this period, all operating room employees were asked to evaluate themselves every day in terms of COVID-19 symptoms and contact history and to inform if they were symptomatic.

### **Preoperative Evaluation of Patients Planned to be Operated During the Pandemic Period**

Patients with confirmed or suspected COVID-19 were identified before surgery and it was deemed appropriate to be taken into operation after two preoperative triages were made in line with the decisions of our hospital's Pandemic Scientific Committee in order to protect the safety of both themselves and healthcare professionals. The first and second triages are continued as follows.

**First Triage:** An anamnesis is taken by the relevant surgical service physician, and after physical examination (PE), personalized tests are requested. In terms of symptoms of COVID-19 (fever, cough, breathlessness, weakness, diarrhea, abdominal pain, muscle pain, sore throat, vomiting, loss of sense of taste and smell, etc.), the patient, and the people living in the same house and working in the same workplace with the patient and person who will accompany the patient in the hospital are questioned for the last 14 days, in terms of symptoms of COVID-19 (fever,

cough, breathlessness, weakness, diarrhea, abdominal pain, muscle pain, sore throat, vomiting, loss of sense of taste and smell, etc.) (1). At the end of the evaluations, elective surgeries of the patients with suspected COVID-19 are canceled and they are referred to infectious diseases. If it is necessary to test for COVID-19 in line with the recommendations of the scientific board guide of the Ministry of Health, the sample is taken by the unit to which the patient is admitted. Until the test result is obtained, the patient is informed about isolation at home. The interventional procedure should be planned within three days at the latest after a negative test result (8).

In the current guideline, the conditions that require polymerase chain reaction (PCR) testing as soon as possible (48 hours) before the planned treatment or procedure are stated as follows;

- Patients with suspected COVID-19 or the contacts of these patients,

- If the frequency of new patients in the last 14 days (total number of new patients/population at risk in the last 14 days) is above 2%, patients who are asymptomatic and even if there is no suspicious contact.

Regardless of the frequency of new cases in the last 14 days;

- Patients who have undergone chemotherapy and radiotherapy, solid organ transplantation, or bone marrow transplantation

- Patients using >15 mg prednisolone or equivalent glucocorticoid and/or small molecule or biological agent with immunosuppressive effect in the last three months,

- Group A surgeries of all surgical branches,

- Patients of Otorhinolaryngology and Plastic Surgery departments requiring head and neck surgery,

- All patients of Cardiac Surgery Department requiring access to the cardiopulmonary pump,

- Patients requiring thoracic surgery,

- Patients scheduled for jaw surgery,

- Patients scheduled for airway surgery,

- Patients scheduled for cancer surgery,

- All patients who will undergo transplantation,

- Surgical patients with an American Society of Anesthesiologists score of III or above and requiring general anesthesia.

If the first test result is negative but the suspicion of COVID-19 is high, it is recommended to perform the second test at least 24 hours later. If the incidence of new patients in the last 14

days is below 2%, testing is not recommended in patients who are asymptomatic and have no suspicious contact, except for the above-mentioned conditions.

The patient with a positive test result is managed according to the Ministry of Health COVID-19 Guidelines. Even if the test result is negative, N95/FFP2 mask, goggles/face protector should be used in processes that generate aerosol (1). Planned surgery should be postponed if the patient has positive test and/or symptoms compatible with COVID-19. The procedure of the patient should be performed as soon as possible (on the same day, if possible) after hospitalization, and the pre- and post-procedure periods should be kept short (8). The second triage of the patients is performed by the anesthesiologist before the intervention.

**Second Triage:** After anamnesis and PE, patients who do not have clinical suspicion of COVID-19 and whose PCR result is negative, are planned to sign a specially prepared patient consent form for COVID-19 and undergo interventional treatment as soon as possible. For all patients who are planned to undergo anesthesia, it is also required to fill the COVID-19 Hospitalization Pre-Form (Form 1) prepared by the Scientific Committee of our hospital by the relevant services. We experienced that the use of this simple form, which was prepared in this period when our work intensity increased, was very useful in determining the details about patients that could be overlooked.

### **Our Operational Order in the Operating Room for Patients with Confirmed or Suspected COVID-19 Planned for Surgical Intervention During the Pandemic Period**

During the pandemic, all patients are required to come to the operating room with a mask. The fever of the patients is measured again at the entrance of the operating room and they are accepted inside (1). In our operating room, one of the rooms at the closest possible distance to the entrance and exit has been determined as the COVID-19 room. In this room where patients with COVID-19 are taken, all materials and tools except the necessary materials are emptied. There is always a warning sign on the door of this room. Entries and exits to this room are prevented unless required during surgery. If a material outside the operation room is required, an outside staff brings it. The anesthesia machine, monitor, video laryngoscope, microscope and other space-occupying materials in the COVID-19 room where the patient will be operated are covered with transparent nylon bags to prevent the risk of contamination (Figure 3). Transparent covers are always kept backed up in an anesthesia emergency cabinet or in an accessible cabinet. Chief technicians and nurses in charge

of the operating room are responsible for monitoring the PPE, transparent covers and protective measures to be used in the operating room.


Since the initial symptoms of COVID-19 infection are nonspecific and there is no high sensitivity test to rule out the presence of infection, personnel should wear PPE in all operations such as intubation/extubation/tracheotomy/tracheostomy, aspiration of respiratory secretions, mask-pouch ventilation, nasogastric catheter insertion/irrigation, cardiopulmonary resuscitation, bronchoscopy and endoscopy, which are known to cause aerosolization in the operating room (1,2,9).

In order to put on and take off the PPE in the correct order, attention should be paid to the following steps:

**Sequence for Putting on the PPE:** All accessories except glasses are removed outside the operation room. Key, wallet, phone, etc. must be left out. Hair should be bulk. It should be remembered that the beard prevents the mask from fitting the face. Hand hygiene is provided after wearing disposable bonnets and foot protectors. Standard surgical hand washing/rubbing is performed after N95/FFP2 mask, goggles and face protector are worn. In the operating room, sterile surgical gowns and double layers of gloves are worn (1,2).



**Figure 3.** Protection of medical devices from contamination in operation rooms where patients with COVID-19 will be taken  
COVID-19: Coronavirus Disease-2019

Form 1. Prof. Dr. Cemil Taşçıoğlu City Hospital COVID-19 Hospitalization pre-protocol form		
	Prof. Dr. Cemil Taşçıoğlu City Hospital, COVID-19 Hospitalization Pre-protocol Form	
CODE: HB. FR.01-68 PUB. DATE: 12.05.2020      REV. DATE: -      REV. NO: 00		
Name-surname:	ID number:	
Age:	Gender:	<input type="checkbox"/> Female <input type="checkbox"/> Male
Fever:		
Heart rate:		
Tension:		
Saturation:		
Ventilation rate:		
Additional disease:		
<input type="checkbox"/> HT	<input type="checkbox"/> CHF	<input type="checkbox"/> DM <input type="checkbox"/> COPD
<input type="checkbox"/> Other:		
1. Have you had any of the following complaints in the last 14 days?		
<input type="checkbox"/> Fever	<input type="checkbox"/> Diarrhea	<input type="checkbox"/> Rapid breathing
<input type="checkbox"/> Coughing	<input type="checkbox"/> Myalgia	<input type="checkbox"/> Wheezing
<input type="checkbox"/> Shortness of breath	<input type="checkbox"/> Loss of taste-smell	
<input type="checkbox"/> Weakness	<input type="checkbox"/> Headache	
2. Have any of the people with whom you share the same house been diagnosed as having COVID-19?		
<input type="checkbox"/> Yes	<input type="checkbox"/> No	
3. Is there rales and rhonchi in the lungs, is wheezing heard?		
<input type="checkbox"/> Rales	<input type="checkbox"/> Rhonchi	<input type="checkbox"/> Wheezing <input type="checkbox"/> Normal
4. Is there any infiltration on the PA chest X-ray? (will be performed if there is evidence of abnormal lung sounds)		
<input type="checkbox"/> Yes	<input type="checkbox"/> No	
5. Is there an image compatible with viral pneumonia on thorax CT?		
<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> No need for tomography
6. Is PCR result positive? (for patients scheduled for operation)		
<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> No need for PCR
7. Was COVID-19 considered with the current findings?		
<input type="checkbox"/> Yes	<input type="checkbox"/> No	
8. Was the patient diagnosed as having COVID-19 in the system?		
<input type="checkbox"/> Yes	<input type="checkbox"/> No	
COVID-19: Coronavirus Disease-2019, HT: Hypertension, CHF: Congestive heart failure, DM: Diabetes mellitus, COPD: Chronic obstructive pulmonary disease, PA: Posteroanterior, CT: Computed tomography, PCR: Polymerase chain reaction		

**Sequence for Removing the PPE:** In the operating room, hand hygiene is provided after removing galoshes, gloves and aprons. Outside the operation room, hand hygiene is provided after each of the glasses, face protector and bonnet is removed and then hand hygiene is provided again after the mask is removed. In the dressing room, the uniform is removed and a shower is taken if possible (1,2,8). In particular, the last removal of the mask and providing hand hygiene after it should not be neglected. Non-disposable material (glasses and face protector) can be disinfected with 70% alcohol and reused. In the removal process, we should not be contacted with the dirty surface and hands should be washed with soap or a disinfectant should be used at every stage (1,2,8).

Since intubation and extubation are among the procedures that create aerosolization, only the anesthesia team should be present in the room while performing these procedures, and healthcare workers who do not participate in the procedure should not be in the room (1,2). The surgical team should enter the room 10 minutes after the procedure (1,2). While the surgical team and operating room nurse leave the room before extubation, only the anesthesia team should stay in the room and extubation should be performed (1,2).

If surgery can be performed with regional anesthesia, the first choice should be regional anesthesia. During regional anesthesia, oxygen should not be given with a mask, but if necessary oxygen should be given via nasal cannula, not more than 4 mL/min. Regional anesthesia and PPE should be worn in peripheral nerve blocks in patients with confirmed or suspected COVID-19 (9).

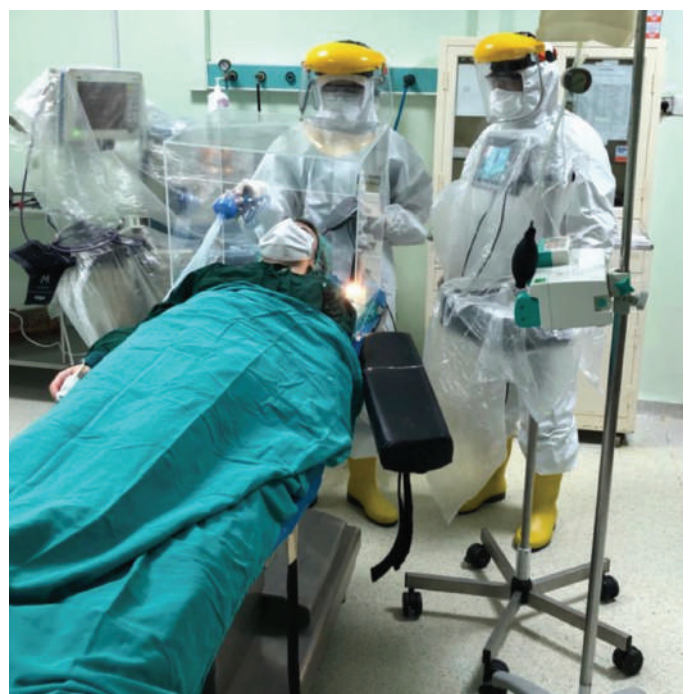
### Endotracheal Intubation

In order to minimize aerosolization and droplet spread, intubation should be performed by the most experienced anesthesiologist and appropriate PPE should be worn. Awake fiberoptic intubation is avoided unless there is a specific indication. Rapid serial induction is recommended to avoid manual ventilation and aerosolization (9).

### Preoxygenation

Preoxygenation can be performed with nasal oxygenation by giving 3 lt/min 100% O<sub>2</sub> under the mask during the apneic phase before intubation or by giving 5-8 breaths with 100% O<sub>2</sub> from the mask that is held with two hands under the transparent cover placed before induction. Endotracheal intubation should be administered as rapid serial intubation, and mask ventilation should be avoided as much as possible to prevent aerosolization. Cricoid pressure is not recommended in this period, intubation

should be performed with a video laryngoscope at the first attempt, and a tube with appropriate size with a stylet should be ready (10). Oxygenation with low tidal volume/pressure is provided between unsuccessful attempts. If a straight tube is used, the endotracheal tube cuff is clamped so that the pilot is not damaged. The clamp should be opened and ventilation should be started only after the cuff is inflated and the system is switched to the closed system (10). It is important to inflate the cuff quickly and completely without any leakage. If intubation is unsuccessful for the second time, it is preferable to switch to supraglottic airway devices through which intubation can be performed. In the respiratory system, filters are attached at least to the expiration arm, preferably to both the inspiration and expiration arms and just after the intubation tube (10). If the breathing circuit is to disconnect from the tube, ventilation should be stopped first and the heat and moisture exchanger filter should be adjusted to remain at the patient side while the system is disconnected (10). There may be many barriers that can be used to prevent aerosolization during preoxygenation, intubation and ventilation. Transparent covers covered on the patient and intubation boxes called transparent 'aerosol boxes' (Figure 4) are among the most frequently used ones (11). It is important that the barrier used in these applications does not interfere with the interventions and that it is removed from the environment in a way that does not cause contamination after use (11).



**Figure 4.** Transparent aerosol box used to prevent aerosolization in patients with COVID-19

COVID-19: Coronavirus Disease-2019



## Extubation

In order to restrict aerosolization during extubation, the mask can be taken under a transparent cover, and only the connector part can pierce the bag so that the mask remains under the cover. All aspirations of the patient are made with closed system aspiration, if possible. The transparent cover with the mask is brought closer to the patient's face and the patient is extubated. The intubation tube is thrown into the COVID-19 waste without contacting it.

If the patient is ventilated enough, the patient is ventilated with mask manipulations (such as head tilt - chin lift maneuver) without placing an airway in order to avoid coughing. If the patient needs respiratory support, he/she is ventilated with a circuit connected to the mask and with both hands. When the patient has sufficient vital capacity, an oxygen mask is put on his/her face. The patient, whose respiration is considered to be safe, is transferred from the operating room to the room in the service directly with an oxygen tube. All personnel who will participate in the transfer of patients with suspected or confirmed COVID-19 should wear PPE (1,2). All patients with COVID-19 are transported with a special stretcher with a transparent tent barrier. Care should be taken to leave the stretcher ready for the next patient by wiping and cleaning it with 1/100 diluted bleach after each patient (1). After the patient leaves the room, the room and devices are cleaned. Video laryngoscope plates are cleaned with surface disinfectant cleanser and put into the box. Then, depending on the urgency, it is sterilized with savlon or surface disinfectant and used again. If it is to be disinfected in savlon, the area that needs to be closed in order not to damage the video laryngoscope blade is closed in accordance with the instructions and thrown into the savlon. In cases where the video laryngoscope is not used, surface disinfectant is sprayed on top of the materials such as laryngoscope blades and similar materials before they are being washed. Then, they are kept in a pre-prepared dirty box for at least two minutes and then sent to sterile processing department. In order to prevent contamination caused by dirty tools, boxes with lids which can be covered should be kept in every room, into which used dirty tools can be put and into which the chuck, mask, airway and blade of the laryngoscope can fit. The lids should be closed after spraying surface disinfectant on the materials placed in the dirty box, and diluted washing water or surface disinfectant should be sprayed on the box again (1,2,9). Ensure that all contaminated equipment is placed in an appropriately labeled bin for support personnel who collect and dispose of the equipment.

## CONCLUSION

As stated by the Scientific Advisory Board of the Ministry of Health in the "Working Guideline in Health Institutions During the Normalization Period" published in July 2020; due to the fact that the COVID-19 pandemic does not end completely, the risk continues until an effective treatment and/or vaccine specific to the virus is found. According to the same guide, it should be remembered that the flattening of the pandemic curve is not an indication that the total number of patients will decrease, it only indicates that the disease burden will spread over a longer period, and it is emphasized that health services should be initiated and maintained considering the continuity of the pandemic. It is important to make dynamic planning in order to manage the increasing demand due to the planned transactions delayed in this process. As long as the process continues, it is necessary to continue all protective measures, especially to prevent the loss of health employees' workforce.

## Ethics

**Peer-review:** Externally and internally peer-reviewed.

## Authorship Contributions

Surgical and Medical Practices: S.K., E.A.T., Concept: S.K., E.A.T., O.O., Design: S.K., E.A.T., O.O., T.M., İ.G., Data Collection or Processing: S.K., E.A.T., O.O., İ.G., Analysis or Interpretation: S.K., E.A.T., O.O., T.M., İ.G., Literature Search: S.K., E.A.T., O.O., T.M., İ.G., Writing: S.K., E.A.T., O.O., İ.G.

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# COVID-19 in Pregnancy and the Pandemia Process in Gynecology and Obstetrics Clinic

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## Abstract

The clinical symptoms of Coronavirus Disease-2019 (COVID-19) in pregnant women are similar to those of non-pregnant individuals. A positive test for Severe Acute Respiratory syndrome-coronavirus 2 usually confirms the diagnosis of COVID-19, but it should be known that there may be false positive and false negative results. Pregnancy does not increase susceptibility to infection and does not worsen the clinical course. The incidence of preterm delivery and cesarean delivery is high in infected pregnant women with pneumonia. It is recommended for use in standard indications in pregnant women with suspected or diagnosed COVID-19, since pregnant women between 24+0-33+6 weeks of gestation and with high risk of preterm delivery within seven days have proven benefits of antenatal betamethasone administration. The mode of delivery is determined by standard obstetric indications, including the mother's acute decompensation. There are advantages of preferring euro axial anesthesia. Late clamping of the umbilical cord is not recommended. During the pandemic period, the necessary precautions were taken in line with the commendations of the Scientific Committees in the Gynecology and Obstetrics Clinic, as in our entire hospital, and the pregnancy follow-up and birth processes of our mothers were tried to continue in a healthy manner.

**Keywords:** Pregnancy, COVID-19, pandemia

## INTRODUCTION

Coronaviruses are a large family of viruses that can cause disease in animals or humans. In humans, it is known to cause common cold or more severe respiratory infections such as Middle East Respiratory syndrome and Severe Acute Respiratory syndrome (SARS). The most recently discovered coronavirus causes Coronavirus Disease-2019 (COVID-19). COVID-19 has become a pandemic that affects the whole world today (1).

### Prevention

Pregnant women should also follow recommendations such as social distance, hand hygiene, wearing a mask in order not to be exposed to the virus. Women with an epidemiological history of contact should be monitored. Pregnant women with children should pay more attention. COVID-19 in children can usually be mild or asymptomatic. The possibility of transmission

of the disease to pregnant women from asymptomatic or presymptomatic individuals in the incubation period should be considered (2-4).

### Clinical Features

All pregnant women should be monitored in terms of the development of COVID-19 symptoms and signs, especially if they are in close contact with people who have been diagnosed as having COVID-19 or investigated for COVID-19. In a systematic review of 356 pregnant women, the most common symptoms were; fever (67%), cough (66%), shortness of breath (7%), sore throat (7%), fatigue (7%), and myalgia (6%). Rhinorrhea/nasal congestion, loss of appetite, nausea/vomiting, headache, and odor and/or taste abnormalities were also among the symptoms. Laboratory findings were; lymphopenia (14%), mild increase in liver enzymes (5%), and thrombocytopenia (1%). Clinical findings were similar to those who were not pregnant (5). According to



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the National Institute of Health, the disease was classified as asymptomatic or presymptomatic infection, mild, moderate, severe, and critical disease (6). In the study in which 147 pregnant women were included, 8% of the pregnant women were in the severe disease group and 1% were in the critical disease group (7). According to the available data; pregnancy and childbirth do not increase the risk of SARS-coronavirus 2 (CoV-2) infection and do not worsen the course of the disease compared to non-pregnant women of the same age. Most infected mothers (>90%) recover before giving birth (8,9).

### **Pregnancy Complications**

The possibility of preterm birth and cesarean delivery increases. In a systematic review including 252 pregnant women with COVID-19, the birth rate before 37 weeks was reported as 15% and the cesarean rate as 70%. Hypoxemia caused by maternal fever and severe pneumonia may cause preterm labor, preterm membrane rupture and abnormal fetal heartbeat patterns. However, preterm birth can occur without serious respiratory disease. Another reason for the high rate of cesarean section may be the belief that maternal condition will improve by terminating the delivery by elective cesarean section in pregnant women with findings of severe respiratory disease. Although the data on first trimester are limited, the risk of spontaneous abortion does not appear to increase. Although there is anxiety that hyperthermia due to the disease may cause an increase in anomalies such as neural tube defect in pregnant women with COVID-19 in the period of organogenesis, theoretically, this situation has not been observed. More than 95% of newborns are in good condition. Complications related to the newborn are mostly related with preterm birth and adverse intrauterine environment resulting from critical maternal disease (5,10-12).

Possible vertical transmission of peripartum maternal infection (transmission from mother to fetus) has been reported in the third trimester. Vertical transmission is possible but rare. Neonatal results are generally good unless there are problems such as preterm delivery or placental abruption. Data on fetal sequelae due to maternal infection in the first and second trimesters are insufficient. There are no accepted criteria for vertical transmission. Assessment of virus IgM level in cord blood and sampling of neonatal nasopharynx, amnion-chorion and placental tissue using aseptic technique immediately after birth have been recommended. Amniotic fluid obtained during cesarean section can also be tested. Vaginal and amniotic fluid samples have been found to be negative in women with positive test for SARS-CoV-2 in the nasopharynx. Viremia rates in patients with COVID-19 appear to be low (1%) and transient,

suggesting that vertical transmission will not be common. In the studies conducted, viruses were detected in a few patients, but no evidence of infection was found in the placentas. The extent and clinical significance of the vertical transmission remain unclear. A few patients with possible vertical contamination were reported based on the laboratory and/or clinical findings of the newborn (13-16).

### **Diagnosis**

In patients with new onset of fever, chills and/or respiratory symptoms, (e.g. cough, shortness of breath) the possibility of COVID-19 should be considered. It should also be considered in patients with severe lower respiratory tract disease with no apparent cause. Being in or traveling to an area where there has been close contact with a confirmed or suspected patient with COVID-19 in the past 14 days should raise suspicion. In case of doubt, a nasopharyngeal swab sample should be taken and the SARS-CoV-2 RNA test should be performed with RT-PCR. It usually confirms the diagnosis of COVID-19, although a positive reverse transcription-polymerase chain reaction (RT-PCR) result may rarely be false positive. False negative tests were reported more frequently in the first day of symptoms and in the previous four days and in pregnant women. If the first nasopharyngeal test is negative but the suspicion of COVID-19 persists, the test should be repeated 24 hours later or within a few days. Infection control measures for COVID-19 should continue while reassessing. The next two negative samples usually rule out infection. In most patients hospitalized with a diagnosis of COVID-19, a chest x-ray is sufficient for the initial assessment of lung complications. A single chest X-ray has a very low fetal radiation dose of 0.0005 to 0.01 mGy. Computed tomography (CT) can be used by taking the necessary precautions when necessary. Fetal radiation dose for a routine lung CT is also low and not associated with an increased risk of fetal anomalies or pregnancy loss. In pregnant women with COVID-19 with pneumonia, if pulmoner sonography is performed during obstetric ultrasonography, it can be helpful in making early diagnosis. Some laboratory abnormalities (hemolysis, elevated liver enzyme levels, thrombocytopenia) associated with COVID-19 in pregnant women are as in severe preeclampsia and HELLP syndrome. These diagnoses should be considered and it should be remembered that they may be found with COVID-19 (17-20).

### **Antenatal Care**

Pregnant women with a history of epidemiological contact with a person with suspected or confirmed COVID-19 should be isolated and monitored for symptoms. The further

evaluation and treatment of patients who become symptomatic depends on the severity of the disease, comorbidities and clinical condition. Patients with at least moderate illness are hospitalized. Professional organizations such as the American College of Obstetricians and Gynecologists (ACOG), The Society for Maternal-Fetal Medicine, and the Royal College of Obstetricians and Gynaecologists have published their recommendations on prenatal care during the COVID-19 pandemic including; restriction of visitors during examinations, wearing at least surgical masks by all patients and healthcare workers, reducing the number of prenatal visits especially in pregnant women without high risk pregnancy, taking measures to ensure that pregnant women, including high-risk pregnant women, stay less time in the office (75 g oral glucose tolerance test (OGTT) instead of two-stage 50 g OGTT), using the cell-free DNA test instead of combined test in screening for Down syndrome, duration and frequency of obstetric ultrasonography, biophysical profile, and Nonstress test (NST) (20-24).

### Medical Management of Pregnant Women with COVID-19

Most pregnant women with confirmed or suspected COVID-19 are in a mild form of illness and do not need hospital care if there are no obstetric problems such as preterm birth. During home care, pregnant women should count fetal movements and report them in case of a decrease. Pregnant women with mild disease and comorbidity or with moderate/critical disease should be hospitalized in multidisciplinary 3<sup>rd</sup> or 4<sup>th</sup> level hospitals with obstetric and intensive care units (ICU). Fetal monitoring is an important issue in pregnant women during viability weeks. The frequency of fetal follow up depends on gestational age, stability of maternal vital findings, and maternal comorbidities. NST can be performed once or twice a day in patients with a stable general condition. In patients whose condition is not stable, continuous fetal monitorization is preferred, as emergency caesarean delivery may be required. An abnormal fetal heart trace can indicate the need for maternal oxygen therapy. Monitoring pregnant patients for signs and symptoms of preterm birth is a routine component of obstetric care (25).

The general supportive care of a patient with critical COVID-19 pneumonia is similar to that of patients with Acute Respiratory Distress syndrome (ARDS) for other reasons. Common complications of COVID-19-related ARDS include acute kidney damage, elevated liver enzymes, and heart damage (e.g. cardiomyopathy, pericarditis, pericardial effusion, arrhythmia, sudden cardiac death). During pregnancy, maternal peripheral oxygen saturation (SpO<sub>2</sub>) should be kept >95%. If the SpO<sub>2</sub> drops below 95%, an arterial blood gas is taken to measure the partial

oxygen pressure (PaO<sub>2</sub>). Maternal PaO<sub>2</sub> greater than 70 mmHg is desirable to maintain a proper oxygen diffusion gradient from the maternal side of the placenta to the fetal side. In the ICU, severely ill patients with COVID-19 are generally recommended to be placed in the prone position. Some ICUs have applied this approach to pregnant women, but even the semi-prone position in the later weeks of pregnancy can be difficult for pregnant women. Permissive hypercapnia (PCO<sub>2</sub> <60 mmHg) and extracorporeal membran oxygenation do not appear to be harmful to the fetus if indicated for ARDS management, but the data are limited (26,27).

Direct data between COVID-19 and thromboembolic risk are limited, but suggest an increased risk. Routine pharmacological prophylaxis for venous thromboembolism (VTE) is recommended in all hospitalized patients with COVID-19 without contraindications (bleeding, severe thrombocytopenia). For antepartum prophylaxis, unfractionated heparin 5000 U subcutaneously every 12 hours is a reasonable dose (28).

Several agents (Remdesivir, lopinavir-ritonavir, ribavirin, baricitinib) are being evaluated for COVID-19 treatment. Some observational studies suggest that the administration of hydroxychloroquine or chloroquine is generally not beneficial, has adverse maternal effects such as abnormal heart rhythms (ventricular tachycardia), especially when taken in conjunction with other QTc prolonging drugs. Therefore, these drugs should not be used for COVID-19 treatment outside of ongoing randomized trials. Hydroxychloroquine crosses the placenta. In animal studies, accumulation in fetal ocular tissue has been observed. However, no increase in fetal ocular abnormality has been observed in the treatment of pregnant women with malaria and systemic lupus erythematosus. However, the available data are limited and the risk to the fetus cannot be excluded when used at different doses for other indications. Many other drugs are used in research. One such drug is lopinavir-ritonavir, which is used primarily for the treatment of HIV infection also in pregnancy. It crosses the placenta and may increase the risk of preterm birth, but no increased teratogenic risk has been observed in humans. Investigational drugs for COVID-19, which are known to be teratogenic, include ribavirin and baricitinib (29).

### Drugs used in pregnancy complications

**Betamethasone:** Since antenatal betamethasone administration has proven benefits in pregnant women with high preterm birth risk within seven days between 24+0 -33+6 weeks of gestation, ACOG recommended its use in standard indications in pregnant women with suspected or confirmed COVID-19 (25).

**Low-dose aspirin:** The decision to continue the drug in pregnant women with suspected or confirmed COVID-19 should be personalized. For example, use for preeclampsia prophylaxis is probably not beneficial in pregnant women with severe or critical illness or near term (25).

**Non-steroidal anti-inflammatory drugs:** There is no clinical or population-based direct data. Therefore, World Health Organization (WHO) does not recommend avoiding these drugs in patients with COVID-19 in the presence of clinical indications (30).

**Tocolysis:** The tocolytic agent preferred in pregnant women with confirmed or suspected COVID-19 is nifedipine.

### **Delivery Timing in Infected Women**

If pregnant women with mild COVID-19 do not have medical and obstetric problems, it is ideal to have the delivery on time after negative test results are obtained following isolation. Thus, the risk of postnatal infection of the newborn is minimized. In those with medical and obstetric (membranoplasty, preeclampsia, etc.) complications, the time of delivery is individualized according to the protocols available for the specific medical problem. In those with severe and critical illness, whether the mother's respiratory disease will recover with birth and the risk of postnatal transmission is uncertain when maternal symptoms are in the acute period. As a result of increased normal oxygen consumption and decreased functional residual capacity in pregnant women, the general condition may deteriorate rapidly in patients with pneumonia. In the third trimester, in the presence of multiple pregnancy or polyhydramnios, excessive uterine dysfunction may impair respiratory function. For some patients with COVID-19 with a pregnancy of >32-34 weeks who are hospitalized due to pneumonia but not intubated, it is recommended to perform delivery before deterioration of pulmonary condition and development of fetal distress. It is recommended postponing delivery due to high morbidity and mortality risk in pregnancies <32 weeks. It is difficult to decide on the timing of delivery in pregnant women intubated due to COVID-19. Although delivery is advocated in pregnant women >32-34 weeks if the patient's condition is stable, it should not be forgotten that it may worsen the mother's condition. In pregnant women <32 weeks, fetal monitoring is generally recommended for perinatal benefit as long as the maternal condition remains stable or improves (21,25,31).

### **Management of Delivery**

All patients admitting for delivery should be questioned and controlled for symptoms and signs of COVID-19 and suspected

contact. Suspected pregnant women should be given priority in terms of testing. Two hundred and fifteen pregnant women who were admitted for delivery in New York were screened for COVID-19, and 33 (15%) pregnant women tested positive. Four of these pregnant women were symptomatic and 29 pregnant women (13.5%) were asymptomatic. Healthcare professionals should use their personal protective equipment when dealing with confirmed or suspected COVID-19 pregnant women. Strong exhalation, especially during active labor, may reduce the effectiveness of the mask the patient uses to prevent the spread of the virus. The follow-up and treatment of pregnant women with suspected or confirmed COVID-19 should be done in isolated rooms with negative pressure in the hospital and surgical masks should be worn during labor. In pregnant women with COVID-19, the type of delivery is determined according to the standard obstetric indications, including the acute decompensation state of the mother. Pregnant women who will undergo planned induction or cesarean section should be hospitalized the day before and be screened for COVID-19. In patients with confirmed or suspected COVID-19, neuraxial anesthesia is not contraindicated and has several advantages in patients giving birth such as it provides good analgesia and thus reduces cardiopulmonary stress caused by pain and anxiety. If general anesthesia is applied (intubation and extubation), special personal protective equipment (N-95 masks, etc.) should be used by all relevant healthcare providers during cesarean delivery due to the risk of aerosolization. The use of magnesium sulfate for maternal eclamptic seizure prophylaxis and/or neonatal neuroprotection in suspected or confirmed COVID-19 positive pregnant women should be decided in consultation with maternal-fetal medicine, respiratory diseases and ICUs, considering the risk of respiratory depression. Labor management usually does not change in pregnant women with asymptomatic or mild COVID-19. Personal contact in the maternity unit should be limited as much as possible. Balloon catheters can be used for cervical ripening when necessary. Induction can shorten labor time. Continuous fetal monitoring is recommended during labor. In more severe patients with respiratory distress or pneumonia, fluid intake and output should be carefully monitored, and aggressive hydration should be avoided as pulmonary edema may worsen maternal oxygenation. Oxygen therapy for fetal resuscitation should be abandoned, as intrapartum oxygen has no proven fetal benefit. The nasal cannula and face mask used are in contact with the maternal respiratory tract and secretions, so the use of such equipment increases the risk of contamination between



patients and healthcare providers. ACOG does not recommend delayed clamping of the umbilical cord because of the risk of transmission of pathogens from an infected mother to the fetus (32-35).

### **Postpartum Care**

In postpartum women with COVID-19, VTE prophylaxis should be considered based on individual risk assessment. In the mild disease group, vital signs should be evaluated in the first 24 hours after normal birth and every 4 hours during the first 48 hours after cesarean. For those with moderate illness, monitoring with pulse oximetry is recommended for the first 24 hours or until symptoms resolve. Serious or critical illness requires very close maternal follow-up in the ICU. Babies of mothers with COVID-19 are considered at risk of COVID-19. The test is performed in them and they are isolated from other healthy babies and followed up by taking infection control measures. The risk of transmission of SARS-CoV-2 through breast milk is uncertain. More data are needed to assess the risk of viral transmission. There is a general consensus that breastfeeding should be encouraged, as it has many benefits for mother and baby. Since breast milk is a source of antibodies, it can protect the newborn from the virus like other anti-infective factors (21,35,36).

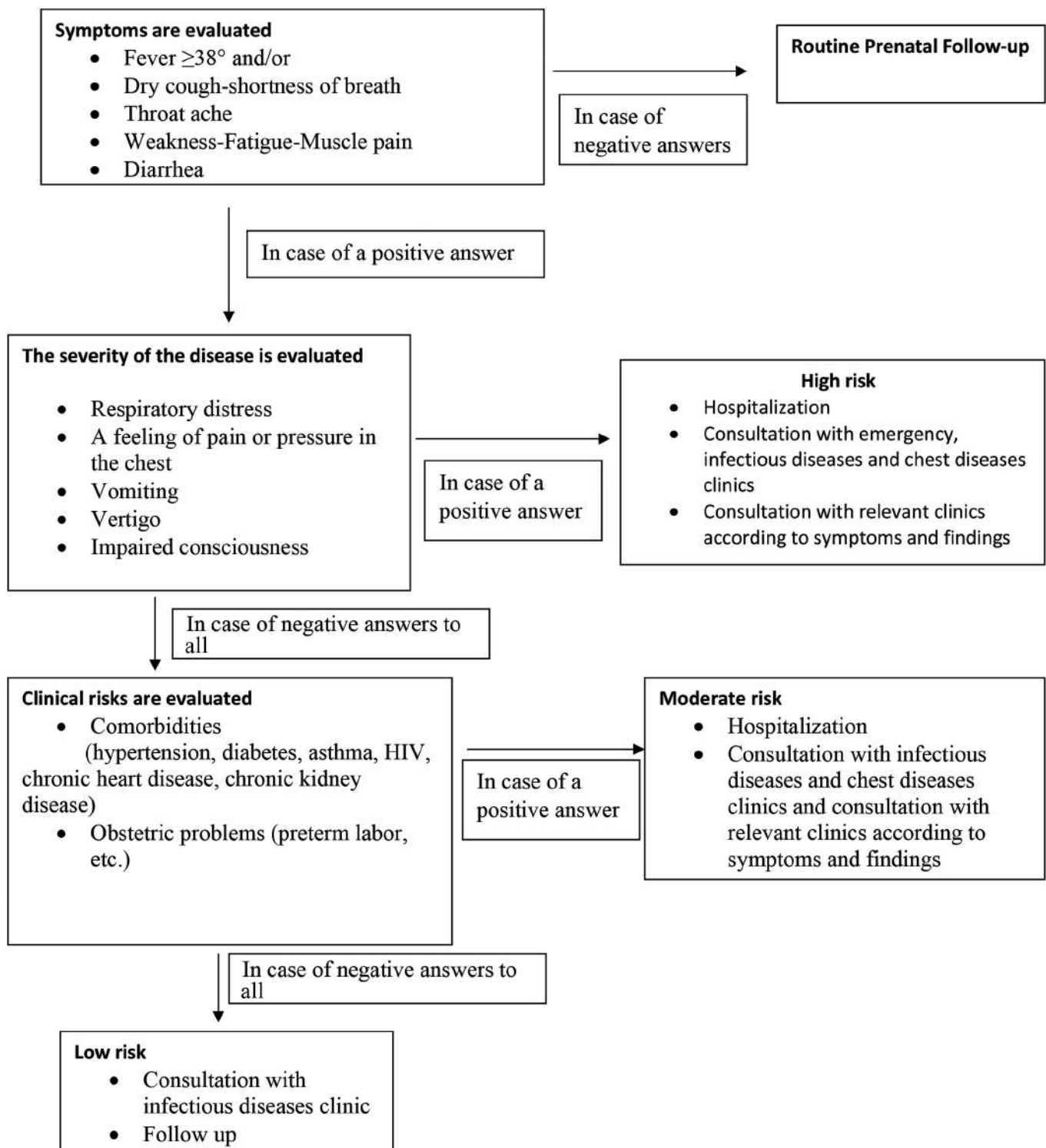
### **Pandemic Process in the Gynecology and Obstetrics Clinic**

The WHO defined the COVID-19 outbreak as an “international public health emergency” on January 30. WHO declared on March 11 that it was a pandemic due to the spread and severity of the coronavirus, which emerged in China, called SARS-CoV-2 and spread to many countries. The first patient with COVID-19 in our country was also detected on March 11. As in our entire hospital, necessary measures were taken in the gynecology and obstetrics clinic in line with the recommendations of the scientific committees. Antenatal follow-up of all pregnant women including mother candidates with suspected or confirmed COVID-19 was performed. Routine outpatient clinic services continued with reducing the number of outpatient clinic rooms. Elective surgeries were postponed, except for emergent ones. Endoscopic operations were not performed due to the risk of aerosolization. In order to provide birth and care services to patients with suspected or confirmed COVID-19 without any complications, especially in terms of preventing disruption in antenatal examinations of pregnant women; we have worked in coordination with the Infectious diseases clinic, pediatric health and diseases clinic, neonatal unit and anesthesiology-intensive care clinic. A separate outpatient clinic with ultrasonography and NST device and a separate ward for antenatal and postpartum patients in which the

health care was provided by physicians, midwives and nurses with personal protective equipment provided and where visitors were not allowed, were organized. A separate delivery room and cesarean operating room have been created for patients with suspected or confirmed COVID-19. After normal delivery or cesarean delivery, the baby is taken to the newborn ICU with a transport incubator and is isolated from other babies and followed up. On March 31, 2020, a symptomatic pregnant woman was diagnosed as having COVID-19 by the infectious diseases clinic in our hospital. The patient was hospitalized and treatment was started. In the following days, the follow-up and treatment of the pregnant women with suspected or confirmed COVID-19 have been made in the ward allocated to them. A specialist resident has been appointed by the hospital senior management for this ward every day. The transfer of the patients scheduled for a cesarean section to the operating room and surgeries have been carried out by taking appropriate precautions (Algorithm 1). Every pregnant who has been admitted to the outpatient clinic and emergency delivery clinic has been evaluated for COVID-19 (Figure 1). Suspected patients have been consulted with the infectious diseases clinic and related clinics according to their symptoms/findings. Pregnant women who have been admitted directly to the infectious diseases clinic through the emergency unit and hospitalized, have been treated by hospitalization in the ward prepared for the pregnant women with suspected or confirmed COVID-19 and their obstetric follow-up has been made. All patients hospitalized in this ward have been evaluated daily by infectious diseases and, when necessary, chest diseases and internal medicine specialists, and their treatments have been arranged. Patients whose general condition has deteriorated, who have had dyspnea and increased respiratory rate and whose oxygen saturation could not achieve desired values despite nasal oxygen support have been evaluated by intensive care specialists. The treatment of patients in need of intensive care has been continued in the ICU.

### **CONCLUSION**

Clinical signs of COVID-19 in pregnant women are similar to clinical signs of non-pregnant individuals. A positive test for SARS-CoV-2 usually confirms the diagnosis of COVID-19, but it should be noted that there may be false positive and false negative results. Pregnancy does not increase susceptibility to infection and does not worsen the clinical course. The incidence of preterm birth and cesarean delivery is high in infected pregnant women with pneumonia.



**Algorithm 1.** Evaluation of pregnant women with suspected or confirmed COVID-19  
 COVID-19: Coronavirus Disease-2019, HIV: Human Immunodeficiency virus



**Figure 1.** Transfer of a pregnant woman with COVID-19 to the operating room and cesarean operation  
 COVID-19: Coronavirus Disease-2019

## Ethics

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# Pandemic Process in the Department of Pediatrics

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## Abstract

Very recently, a new coronavirus causing a serious, atypical pneumonia cluster that was life-threatening in humans was discovered in December 2019. The virus detected in China spread to 188 countries/regions all over the world in a short period of six months, and it was declared by the World Health Organization to cause pandemics. In Coronavirus Disease-2019 (COVID-19), the main route of transmission is directly from person-to-person transmission by droplets and contact. In the reported publications, the disease related to Severe Acute Respiratory Syndrome-coronavirus-2 is more common in adults and causes a serious life-threatening disease, especially in the elderly. It is observed that it causes milder clinical presentation in children than adults. Fever and cough are also the most common symptoms in children. In the pandemic course, the department of pediatrics started the training, planning and preparation process before the acceptance of positive patients under the leadership of the Ministry of Health's constantly updated guide and the established multidisciplinary science committee of our hospital. The treatment of COVID-19 positive pediatric patients has been carried out for most up-to-date and successful manner. The protection both of our healthcare personnel and other pediatric patients who had to use same health care facility during the pandemic course was provided within the framework of the taken infection control measures. While applying the current scientific data and the guide of the Ministry of Health, it was aimed to emphasize that it is important to make decisions in accordance with the dynamics of the process, organized with team spirit.

**Keywords:** Children, pandemic, COVID-19, single center

## INTRODUCTION

Very recently, in December 2019, a new coronavirus (CoV) was discovered in the city of Hubei, Wuhan province, in the Republic of China, causing a severe, atypical pneumonia cluster in humans. Chinese scientists revealed the genome sequence of this virus, which they isolated from a patient, on January 7, 2020, in a short time. This new CoV was named 2019-new CoV by the World Health Organization (WHO) on January 12<sup>th</sup>, 2020 (1,2).

In order to determine the relationship of the new CoV with other CoVs, the genomic structure was first tried to be determined. In a study examining the 2019 new CoV genome obtained from a patient, nucleotide similarity was found with bat Severe Acute Respiratory Syndrome- (SARS)-like CoVZXC21 at a rate of 89% and with human SARS-CoV-2 BJ01 2003 at a rate of 82% (3). On February 11<sup>th</sup>, 2020, the name of the new CoV was changed to

SARS-CoV-2 by the International Virus Taxonomy Committee Coronavirus Working Group. The WHO announced the name of the new disease caused by this virus as Coronavirus Disease-2019 (COVID-19) on the same date (4). The disease spread all over the world in a short time. And ultimately, it was declared a pandemic by the WHO on March 11<sup>th</sup>, 2020 (5).

CoVs are enveloped, single-stranded RNA viruses belonging to the *Coronaviridae* family within the *Nidovirales* family. In humans, it usually causes a mild cold but sometimes severe acute lower respiratory tract infection. In the current taxonomy, CoVs have been classified into four genera; alpha, beta, gamma and delta CoVs, according to sequence and antigen-based studies. SARS-CoV-2, which was detected in 2002 and Middle East respiratory syndrome coronavirus (MERS-CoV-2), which was detected in 2002, which in the past crossed the species barrier and caused



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serious respiratory disease epidemics, are included in the beta CoV group. SARS-CoV-2 is also a beta CoV group member and is recorded as the seventh CoV that infects humans (causing mild disease; HKU1, NL63, OC43 and 229E, and severe disease-causing SARS-CoV-2, MERS-CoV-2 and currently detected SARS-CoV-2) (6-8).

At the beginning of the pandemic, the seafood market, where illegal livestock was sold, was shown as the place where the contamination took place. The fact that most of the people who got sick were people working in or visiting this market suggested that the virus was transmitted from animals to humans. However, as the pandemic progressed, person-to-person transmission became the main mode of transmission. It is still not clear what the source of the virus is (8,9).

In COVID-19 disease, where direct person-to-person transmission is the main route of transmission, transmission occurs mainly through droplets and contact. When an infected person coughs, sneezes, or even talks, the virus in the droplets are emitted. If these droplets come into contact with the respiratory tract and mucosal membranes (mouth, eyes and nose) directly with the hands, it may lead to the emergence of the disease. Droplets are typically thought to be spread no more than two meters away, thus it is necessary to maintain a social distance of at least two meters with sick people (8,10,11).

Under normal circumstances, whether SARS-CoV-2 is transmitted by air or not remains controversial. SARS-CoV-2 virus has also been detected in samples other than respiratory secretions, including feces, blood, tears and semen. However, the role of the virus detected in these regions in transmission is not certain. Although difficult to confirm, fecal-oral transmission has not been clinically defined. Likewise, although virus RNA is detected in the blood, it is thought that there is a very low probability of transmission through the blood. Transfusion transmission has not been reported with SARS-CoV-2 or previously with MERS-CoV-2 or SARS-CoV-2 (8,10-15).

The incubation period for COVID-19 disease is thought to be 2-14 days after the virus is taken, and most of the patients have been found to be symptomatic about 4 to 5 days after exposure. The contagious period of COVID-19 is not known exactly. It is thought that it starts 1-2 days before the symptomatic period and ends with the disappearance of symptoms. Although symptomatic infection is on a spectrum between mild and life-threatening disease, most infections are not severe (8,10,16). Disease spectrum of 44,415 confirmed patients in a report from the Chinese Center for Disease Prevention: 81% mild (no pneumonia and mild pneumonia), 14% severe (dyspnea, respiratory rate >30/

min, blood oxygen saturation <93%, more than 50% increase in lung infiltration within 24-48 hours) and 5% critical (respiratory failure, septic shock and/or multi-organ dysfunction or failure) (17). In another study reported, asymptomatic patients and patients with mild or moderate disease constituted 98% of the pediatric patients, while severe or critical disease was found in the remaining 2% (18).

The most common form of transmission in children is intra-familial transmission. Most patients are exposed to adult patients through household contact. The role of children in infecting others is not clear. Infected children can spread the SARS-CoV-2 virus around them. Infection by children is thought to be less common, due to their milder symptoms. However, the risk of transmission from infected children to adults cannot be neglected. Therefore, it is very important for those who provide care for infected children to take personal medical protection measures (10,16).

The presence of pneumonia characterized by fever, cough, shortness of breath, and bilateral infiltrates on chest X-ray is the most common severe presentation of COVID-19 disease. However, other clinical features are also common, including upper respiratory tract symptoms, myalgia, diarrhea, and smell or taste disturbances. Children have fewer symptoms than adults. Fever and cough are the most common symptoms in children. Although severe clinical course is less common in children compared to adults, the risk of severe disease is higher in children with underlying diseases. Younger age, underlying lung disease and conditions with immunodeficiency are associated with worse clinical outcomes in children (8,16,19).

Reported publications indicate that the disease caused by SARS-CoV-2 is more common in adults and causes a very severe disease that threatens life especially in the elderly. As of June 21<sup>st</sup>, the Johns Hopkins Coronavirus Research Center reports that 8,918,101 people worldwide were infected with COVID-19 disease and 467,611 deaths occurred due to this disease (20). In children, the disease is generally less common and is reported to be milder. Among 1,932,051 patients with COVID-19 whose age data were reached in the United States, [the data were updated by the Center for Disease Control (CDC) as of June 21<sup>st</sup>], the number of children between the ages of 0-17 was 99,618 (0.05%) (21). Intensive care requirement in children is less common compared to adults, and information is shared that especially infants have a more severe course (16,17).

The first patient with COVID-19 in Turkey was reported on March 11<sup>th</sup> 2020, and the first deaths were reported on March 17, 2020 (22). A total of 198,284 confirmed patients and 5,097 deaths have

been reported by the Turkish Ministry of Health as of June 28, 2020 (23). However, it has not been stated what percentage of these patients are pediatric patients. The reported mortality rate has been relatively low compared to most countries, and Turkey has been the 13<sup>th</sup> country in the world based on confirmed patients reported in the world as of June 21<sup>st</sup> (20).

Our hospital, located in a central location in Istanbul, is University of Health Sciences Turkey, Prof. Dr. Cemil Taşçıoğlu City Hospital, as a general pediatrics and infectious diseases clinic, has 61 beds, additionally 20-bed hematology-oncology service, 30-bed level 2 and three neonatal intensive care unit and 10-bed pediatric intensive care unit. In addition, the hospital has a children's emergency service with 16 conservation beds. For outpatients, four general pediatric outpatient clinics, as well as most of the sub-branches' outpatient clinics (infection, endocrinology, gastroenterology, cardiology, metabolism, nephrology, neurology, healthy child, newborn) provide services.

Before the first patient was detected in our country, a scientific committee consisting of a deputy head physician, family physicians, pediatric and adult infectious diseases, pediatric and adult intensive care, anesthesia, emergency, internal medicine and hematology-oncology specialists was established in our hospital under the leadership of the chief physician. In this scientific committee, decisions on various issues such as the protection and precautions to be taken of our healthcare workers working within our hospital, the use and provision of necessary personal protective equipment, in-hospital trainings regarding the pandemic, the management of patients with and without COVID-19 who will be admitted to our hospital, and making the physical conditions suitable, were made. While these decisions were made guidelines shared since the beginning of the pandemic and updated from time to time by the Turkish Ministry of Health, General Directorate of Public Health, were taken into consideration (8). The pandemic was managed in our hospital by reviewing many issues in the guide which were changed and developed as the data about the virus and disease increased, including possible case definitions and treatments, and the conditions of discharge and isolation in patients with COVID-19.

During the pandemic process, in-service theoretical and practical trainings were given to healthcare professionals in our pediatric clinic before the positive patients were accepted. The pediatric emergency outpatient clinic and service, where the patients would be admitted, were divided into two as dirty and clean areas. A separate triage outpatient clinic was established. It was ensured that the health worker working in the triage outpatient

clinic was provided with a full personal protective equipment including N95 mask. In line with the guide published by the Ministry of Health, possible patients were directed from the triage outpatient clinic to the dirty area. Surgical masks were provided for patients and their caregivers who were directed to the dirty area. Nasopharyngeal samples were taken from the patients who were evaluated in the dirty area in special cabinets. The nasopharyngeal sampling area was disinfected with ultraviolet (UV) light before being used for another patient. The UV light emitting device used is shown in Figure 1. Dirty and clean observation areas were created for patients who would be subject to observation for a certain period of time. Two COVID wards were created for patients who needed to be hospitalized. Patients with positive SARS-CoV-2 polymerase chain reaction (PCR) test were followed up and treated as much as possible in single isolated rooms with bathroom and toilet. Healthcare professionals working in the hematology-oncology service and neonatal intensive care units were assigned only in these departments. Health workers in these departments were not allowed to work in the dirty area. The work of the healthcare professionals was arranged in 24-hour shifts, separating the dirty and clean areas alternately. In this way, both the risk was shared and the exposure to risk was tried to be reduced. Until May 15<sup>th</sup>, more than 1,500 patients with possible COVID-19 were admitted



**Figure 1.** Device that emits UV light

UV: Ultraviolet

to our pediatric emergency outpatient clinic, and SARS-CoV-2 PCR positivity was detected in 160 of nasopharyngeal samples taken from these patients. In our hospitalized and treated patients, the number of positive patients was thirty. The number of positive patients followed in the pediatric intensive care unit was five, and no patient died. None of our pediatric patients required the use of hydroxychloroquine, favipiravir or lopinavir/ritonavir treatments specified in the guideline.

As the pandemic progresses, information on how the virus affects children's health is constantly reported, and new features are learned to emerge. In April, patients resembling incomplete Kawasaki disease or toxic shock syndrome, thought to be associated with COVID-19 disease have begun to be observed in children from the UK. Then, an increase has been observed in the reporting of similar patients from various countries around the world, especially in New York (USA). In mid-May, a new form of presentation of COVID-19 has been announced for the first time by the US CDC and Prevention. This condition has been called multiple systemic inflammatory syndrome (MIS-C) possibly associated with COVID-19 in children (24-27).

## CONCLUSION

As a result, the COVID-19 pandemic emerges as a dynamic process that is constantly evolving and changing. Here, the role of mankind's first confrontation with a CoV pandemic is great. In the process, as the information about SARS-CoV-2 and the disease it causes increases, changes in our approach may occur. It is very important to take adequate and appropriate infection control measures to prevent possible transmission from children with COVID-19 to other people, especially healthcare workers. It is obvious that it will contribute to preventing the spread of the disease in the community and in the hospital. Although the disease has a mild course in children, it is vital to follow up patients closely in terms of clinical features that may emerge and may be life-threatening (such as MIS-C).

## Ethics

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## Authorship Contributions

Surgical and Medical Practices: A.K., D.K.İ., E.T., M.T.P., Concept: A.K., Design: A.K., Data Collection or Processing: A.K., D.K.İ., E.T., M.T.P., Analysis or Interpretation: A.K., Literature Search: A.K., Writing: A.K.

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# Importance of Family Medicine Clinic in COVID-19 Pandemic

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## Abstract

Pandemics are global events that have always existed in the history of the world and that can cause profound changes. The Severe Acute Respiratory syndrome-coronavirus-2 pandemic, which appeared in China in December 2019, was also a current pandemic that affected life all over the world and in our country. Like many countries, Turkey has directed its existing strong health system to fight this pandemic. Family physicians who are the first to encounter pandemics have taken an important place in this fight by taking part in every step of the work to combat the Coronavirus Disease-2019 (COVID-19) pandemic. In this study, it was aimed to examine the duties and responsibilities of Okmeydani Family Medicine Clinic in COVID-19 pandemic both in the 1<sup>st</sup> and 3<sup>rd</sup> step health care.

**Keywords:** COVID-19, family physicians, pandemic,

## INTRODUCTION

Coronavirus Disease-2019 (COVID-19), which has created a widespread pandemic worldwide since December 2019 and which we are still struggling with in our country, continues to seriously threaten life.

Pandemic means “affecting all people” consisting of the words “pan” meaning “all” and “demos” meaning “people” in the Ancient Greek language. Considering the history of the pandemic, it is seen that 21 pandemics have occurred that have affected humanity so far. Endemics and pandemics, which cause unforgettable pain and death in humans and animals, have deeply affected health, psychology and life in every age, leading to the collapse of states and large social migrations. Although infectious diseases have always existed in the world throughout human history, the increasing human mobility and the ease of interaction with different human and animal populations across continents have facilitated the formation and spread of pandemics. Plague, cholera, influenza, AIDS and now COVID-19 are among the pandemics that have resulted in the death of a large number of people and affect the world the most (1,2).

Today, accepting an outbreak as a pandemic depends on the approval and acceptance of the World Health Organization (WHO). According to WHO, for an infection to be a pandemic, it must meet the following three conditions:

- 1- The emergence of a previously unknown outbreak.
- 2- Disease agent infecting people and causing a dangerous disease.
- 3- Easily and continuously spreading of the cause of the disease (1).

In December 2019, a large number of patients with pneumonia of unknown cause were reported in a seafood market in Wuhan, China’s Hubei province. The WHO first announced that the reason for these complaints was a new type of coronavirus (2019-nCoV) on January 12, 2020, and on February 11, 2020, this new virus was named Severe Acute Respiratory syndrome-coronavirus-2. The WHO named this pandemic as the “COVID-19” pandemic on March 11, 2020. According to the WHO, there have been 4,735,622 patients diagnosed and 316,289 deaths as of 20.05.2020 (1,3,4).



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Turkey is one of the earliest countries in the world to take measures regarding COVID-19. The Scientific Committee was established by the Ministry of Health on January 10. Various administrative measures were taken in line with the recommendations of the Scientific Committee, and the updated diagnosis and treatment guideline of COVID-19 was created by the board according to the developments. Elective examinations, procedures and surgeries were postponed. It was recommended that non-urgent patients receive service from their family physicians first. The first patient was detected in Turkey on 10.03.2020 (3,5). Since then, measures have been increased across the country to prevent and reduce the spread of the virus in the society. Measures for the source of the disease have been taken and continue to be taken in subjects such as finding the source, reporting the disease, definitive diagnosis, treatment of the patients, isolation, searching for carriers and following the patients with suspected COVID-19. Measures for the healthy persons have been taken and continue to be taken in subjects such as quarantine and observation.

Contact tracing is of great importance in protecting against COVID-19 in our country. In other words, screening the contact chain related to an infectious disease and/or finding the source of the disease and taking the measures before it spreads have an important place in the fight against the disease. At this point, the field work of the family physicians and district health directorates, who provide health services in the first step, constituting the contact tracing team, is of great importance. Screening people with whom they come into contact around patients with COVID-19 and diagnosing the disease in these people in the early period, giving treatment, following up and preventing the spread of the disease define the contact tracing (3).

Family medicine assistants working in 6 units of Education-Family Health Centers (E-FHC) affiliated to the family medicine clinic of our hospital have also been a part of contact tracing in this process. People with a positive polymerase chain reaction (PCR) test fall on the Public Health Management System screen of their family physician. After this point, the patients are called and the people they are in contact with are identified and screened one by one. While the PCR sample is taken from the symptomatic contacts, the family physicians call the asymptomatic contacts every day to ask whether they have symptoms and if they develop symptoms, they are referred to the relevant hospital by referring to 112, and this process and follow-up are meticulously continued for 14 days. Contacts with a positive PCR result and with good general condition are

treated at home in the early period and are followed up by their family physicians for 14 days at weekends and weekdays in terms of symptoms and drug use. Isolation training of patients and contacts at home and follow up of isolation are managed by family physicians. In this process, approximately 250 patients have been followed up in our E-FHCs with the method of contact tracing, and preventive medicine, one of the main duties of family medicine, has been performed by providing isolation training. Considering that the most effective and fastest solution against the COVID-19 pandemic is social isolation, which is an anti-infectious activity, as in all infectious diseases, the key importance of family physicians who provide primary health care services to follow up and inform them is once again understood.

While all these continue, normal outpatient clinic services continue at E-FHC for emergency and non-postponable situations. At this point, the triage system application has been initiated. Contacts with a COVID-19 positive patient, who have symptoms (such as fever, cough, etc.) are identified, the detected patients are immediately put on a mask and isolated, and the district health directorates are notified and the patient is brought to the nearest COVID-19 outpatient clinic. In addition, people who are monitorized due to pregnancy or having adolescents, infants or children have been called and appointments have been made at intermittent hours, thus reducing the number of outpatient clinic volume and contact. In order not to increase the risk against other infections while protecting the society from a source of infection, childhood vaccinations have been administered without delay, and babies who could not be reached for vaccination have been vaccinated by home visits. See Table 1 for the status of other outpatient clinic services (6).

In this process, the number of nine Family Medicine Outpatient Clinics within the Family Medicine Clinic of Prof. Dr. Cemil Taşcıoğlu City Hospital has been reduced to three. As Family Medicine and adult vaccine outpatient clinic, we have continued to serve in the institution. By closing smoking cessation outpatient clinics and other family medicine outpatient clinics, we have been clinically involved in the fight against the COVID-19 pandemic. Family medicine clinic specialists and residents have been involved in 24-hour quarantine duties since the first day of the quarantine services opened in our hospital on 20 March 2020. As of March 24, 2020, all other branch residents have been included in these duties. In the beginning, 2 family medicine specialists and 40 family medicine residents were on duty at regular intervals, while this number reached 55 resident physicians with the new starters. During the duties, 1 family

**Table 1. Status of Education-Family Health Centers outpatient clinic services**

The reason for the patient's arrival at E-FHC	Management of health care services implemented in E-FHC
Prescribing medicine with report	Directed to the pharmacy in accordance with the Ministry of Health circular
To be examined Getting a marriage/military report To get mental report for use in notary and deed transactions Get vaccinated	The individual is directed family physician to whom he/she is registered
Getting a driver report To have a laboratory examination Getting screened for cancer	Temporarily postponed except in compulsory cases
Follow-up of babies, children, adolescents and pregnant women	The individual is directed to the family physician to whom he/she is registered, if the appointment day and time are suitable
E-FHC: Education-Family Health Centers	

medicine resident has been responsible from 1 ward and follows up an average of 25 patients with COVID-19. Every day, 8 family medicine residents have been on duty in quarantine wards, one in the infectious diseases service. From the beginning until June 15, approximately 490 duties were held by family medicine residents. During the duty; family medicine residents have had a one-to-one active role in the hospitalization of the patient from the emergency department, arranging the rooms, providing isolation, taking swab samples, requesting the examinations, planning and starting their treatments with the Infectious Diseases on-duty specialist, re-evaluating other chronic diseases, if any, and making the necessary consultations and in the process until discharge. By carefully following the symptoms and signs of the patients, they organize the referral of the patients whose general condition deteriorates to the intensive care unit. Resident and specialist physicians of the family medicine clinic evaluate family medicine in the best way as a specialty branch that can take a holistic approach and evaluate the human body, regardless of age, gender and disease, without separating human body according to its organs and systems. Rotations, which are also a part of family medicine residency training, have been stopped except for emergency room rotation in order to reduce the virus load and take an active role in combating the pandemic. The rotations of our family medicine residents in the Emergency Department have continued.

## CONCLUSION

During this whole process, Prof. Dr. Cemil Taşçıoğlu City Hospital Family Medicine Clinic, both by tracing for isolation for the prevention of contamination in the contact tracing team in E-FHC in primary care, and by being involved in the diagnosis, treatment and hospitalization process of patients with COVID-19

in the emergency service, outpatient clinic and quarantine services in the third step hospital has taken its place in the front lines in combating the pandemic.

## Ethics

**Peer-review:** Externally and internally peer-reviewed.

## Authorship Contributions

Surgical and Medical Practices: H.R.S., S.A., Concept: H.R.S., S.A., Design: H.R.S., S.A., Data Collection or Processing: H.R.S., S.A., Literature Search: H.R.S., S.A., Writing: H.R.S., S.A.

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# The First Patient with COVID-19 in Our Hospital and the Clinical Results of the Approaches at the Beginning of the Pandemic

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## Abstract

Severe Acute Respiratory syndrome coronavirus firstly appeared on December 2019 in Wuhan, China then It started to spread whole world and became a global epidemic in a very short time. On March 11, 2020, It is declared as a pandemic by the World Health Organization and within the same day, the first case o the new Coronavirus Disease-2019 (COVID-19) in Turkey was detected and declared by the Turkish government. In this case report, we examined the hospitalization and diagnosis process of our hospital's first COVID-19 case who was being followed up firstly at the internal medicine clinic outside of the pandemic area. Moreover, we aimed to note the results of our first approaches to cases in the early stage of the pandemic and its effects on our all health personnel team.

**Keywords:** COVID-19, SARS-CoV-2, health personnel

## INTRODUCTION

The new Coronavirus Disease-2019 (COVID-19) is a viral illness that has a clinical course ranging from simple cold to severe acute lung failure. It's agent is Severe Acute Respiratory syndrome coronavirus, which has a newly defined enveloped virus structure. This virus is transmitted from person to person through droplets and contact (1).

Since it is a newly described virus, the dynamics of the virus cannot be fully characterized, so the risk of being infected in the pandemic is high. The control of the pandemic and the steps taken in this regard are handled nationally, institutionally and individually. Healthcare workers are at risk of being infected in such pandemics and are also a risk factor in terms of contagion. With this case report, we examined the hospitalization process of the first patient with COVID-19 in our hospital, who was admitted to our internal medicine clinic and diagnosed in our clinic before the first case was identified in our country. We evaluated the results of our approaches in the early stages of

the pandemic in terms of healthcare personnel through this phenomenon.

## CASE PRESENTATIONS

A 81-year-old female patient, who complained of shortness of breath and general deterioration, was admitted to the emergency room on 8 March 2020. She was hospitalized in the internal medicine clinic to investigate the etiology of dyspnea and hypoxia. The patient, who had a history of hypertension and ischemic cerebrovascular disease, was dyspneic and disoriented, and had difficulty in establishing cooperation during the examination. In physical examination; blood pressure was 110/80 mmHg, pulse 88/min and rhythmic, fever 36.5 °C, and blood oxygen saturation 82% (at room air). In respiratory system examination; bilateral respiratory sounds were reduced and no features were detected in other system examinations. In laboratory examinations; white blood cell count was  $6.97 \times 10^3/\mu\text{L}$  (3.8-10), lymphocyte count  $3 \times 10^3/\mu\text{L}$  (1.18-3.74), hemoglobin



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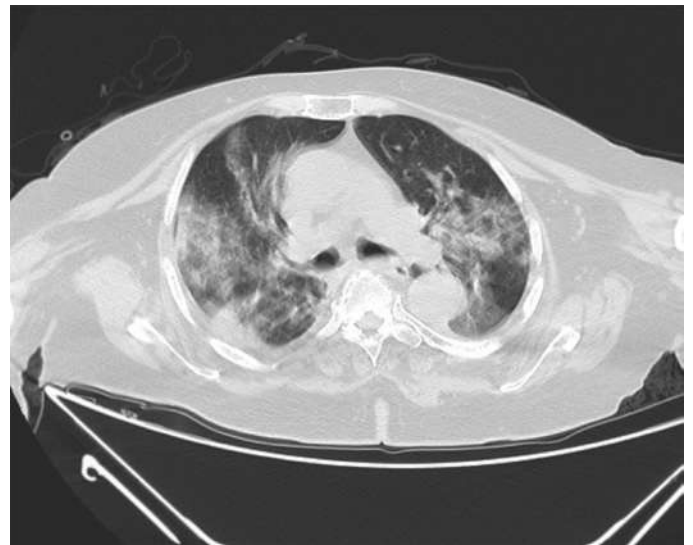
11.4 g/L (115-155), C-reactive protein (CRP) 33.5 mg/L (0-5), procalcitonin <0.12 µg/mL (0-0.12), ferritin 320.7 µg/L (11-306.8), lactate dehydrogenase 206 U/L (0-248), and in arterial blood gas under oxygen; pH 7.51 (7.37-7.45), SO<sub>2</sub> 95.3% (95-99), partial pressure of oxygen 66.3 mmHg (70-100), partial pressure of carbon dioxide 32.2 mmHg (35-46), and Bicarbonat-actual 25.6 mmol/L (21-26). Electrocardiogram was in sinus rhythm.

The computed tomography (CT) of the patient who was desaturated without oxygen, did not have an infiltration suggesting infection and/or malignancy. In transthoracic echocardiography; ejection fraction was 60%, pulmonary artery pressure was 30 mmHg and left ventricular hypertrophy, valve degeneration, mild aortic and mitral valve insufficiency were detected. Considering the patient's comorbid diseases and general condition, CT angiography was performed for the etiology of hypoxia to exclude pulmonary embolism. In angiography; upon detection of a filling defect consistent with embolism in the lower lobe posterior segment branch of the right pulmonary artery, enoxaparin 2x6000 IU was initiated subcutaneously. In bilateral lower extremity venous Doppler ultrasound imaging performed for etiology, no finding of thrombus was detected.

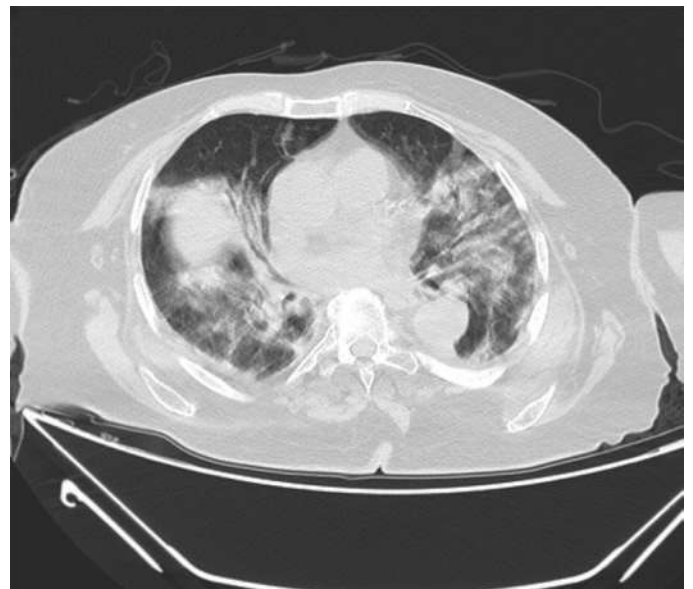
On March 11, 2020, the first patient with COVID-19 was detected in our country and a pandemic was also declared. Meanwhile, fever occurred in our patient, who was on the 3<sup>rd</sup> day of her hospitalization, and there was suspicion in terms of COVID-19. When the history of the patient was deepened, it was learned that on February 26, 2020, family members had contact with their relatives from abroad and some of these people developed symptoms of upper respiratory tract infection. In the examinations requested after emergence of fever; white blood cell count was  $4.43 \times 10^3/\mu\text{L}$ , lymphocyte count  $1.22 \times 10^3/\mu\text{L}$ , CRP 127 mg/L, and procalcitonin <0.12 µg/mL. Significant decrease in lymphocyte values compared to what was measured during hospitalization and no increase in procalcitonin level despite high CRP were common findings in COVID-19. There upon, control thorax CT of the patient was performed. On CT, a diffuse infiltration pattern accompanied by patched ground glass opacities was detected, unlike the CT performed in the emergency room before. Peripheral subpleural ground glass opacities and crazy-paving pattern suggested viral pneumonia (Figure 1, 2). The patient was consulted with the infectious diseases clinic on March 17, 2020. With the pre-diagnosis of COVID-19, a new nasopharyngeal CoV real time polymerase chain reaction (PCR) sample was taken. The patient whose general condition deteriorated was intubated and transferred to the intensive care unit on March 17, 2020 with a pre-

diagnosis of COVID-19. The PCR sample taken from the patient twice was negative and the rapid antibody test was positive (Figure 3). The patient, whose clinical, laboratory and imaging findings supported COVID-19, was started on lopinavir/ritonavir treatment with hydroxychloroquine. The patient, who developed a cardiac arrest on March 27, 2020, died in the intensive care unit.

Meanwhile, examinations were made in terms of COVID-19, as the family members complied with the possible case definition. Thoracic CT images supported viral pneumonia. These people, whose PCR samples were taken for COVID-19, were taken to home isolation.



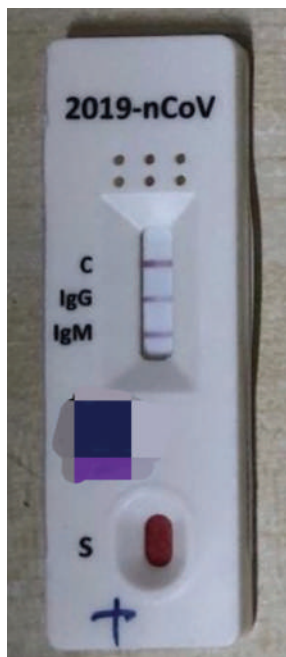
**Figure 1.** Thorax CT image-1 of our patient  
CT: Computed tomography



**Figure 2.** Thorax CT image-2 of our patient  
CT: Computed tomography



In line with the precautions taken within the scope of the pandemic in our hospital, the room where 3 more patients were staying together with the patient was isolated. Patient exit from the room and hospitalization in the room were not allowed. Symptom monitoring was initiated in accordance with the algorithms specified in the COVID-19 guide published by the ministry of health for the medical personnel and patients who were in the same room with the patient. The medical staff continued to work by wearing a surgical mask. During the process, symptoms developed in 11 individuals, including physicians and nurses who had multiple exposure with the patient and healthcare professionals in contact with patient



**Figure 3.** Rapid antibody test result of our patient

(Table 1). The individuals with symptoms were removed from the hospital environment by performing the necessary tests. The health care workers and medical personnel in our clinic with a diagnosis of COVID-19 were among the first ones identified in Turkey.

## DISCUSSION

The novel COVID is transmitted mainly by droplet and contact. It is transmitted by direct contact with the droplets emitted by the sick individuals by breathing, coughing, sneezing, or by bringing hands to the mouth, nose or eye mucosa after hand contact. Asymptomatic people are thought to be infectious, as viruses can be detected in their respiratory tract secretions (2).

At the time of our patient admission to our hospital, there were no defined patients in our country yet, and the number of patients was rapidly increasing all over the world. Considering the possibility of unidentified patients, patients who were admitted to the emergency service and outpatient clinics of our hospital were questioned about symptoms and abroad contact in terms of COVID-19. In our patient, COVID-19 was not considered in the foreground at the time of admission, because the patient's relatives did not give an anamnesis in the direction of abroad contact and there were no findings suggesting viral pneumonia in thoracic CT performed in the emergency service. After the diagnosis of this patient, 11 of our physicians and nurses, who had close contact with the patient, were diagnosed as having COVID-19 in the first 15 days. At the time of submitting our article to the journal, a period of approximately 3 months passed since the beginning of the pandemic in our country. There were 80 physicians and 35 nurses working under our clinic. While 11 personnel were diagnosed as having COVID-19

**Table 1. Clinical analysis of infected health workers**

	Duty	Symptom onset	Symptoms	Thorax CT	N-CoV real time PCR
1	Resident (1)	16.03.2020	Cough, subfebrile fever, headache	Viral pneumonia	Positive
2	Resident (2)	17.03.2020	Fever	Viral pneumonia	Positive
3	Nurse (1)	18.02.2020	Cough, fever, shortness of breath	Viral pneumonia	Negative
4	Resident (3)	20.03.2020	Cough, inability to taste or smell	Normal	Positive
5	Specialist physician	22.03.2020	Fever, cough	Viral pneumonia	Positive
6	Nurse (2)	22.03.2020	Fever, inability to taste and smell	Viral pneumonia	Negative
7	Nurse (3)	24.03.2020	Fever, cough, headache	Viral pneumonia	Negative
8	Resident (4)	25.03.2020	Cough, malaise, myalgia	Viral pneumonia	Negative
9	Nurse (4)	26.03.2020	Headache, myalgia	Viral pneumonia	Positive
10	Resident (5)	27.03.2020	Fever, myalgia, inability to taste or smell	Viral pneumonia	Positive
11	Resident (6)	29.03.2020	Fever, myalgia, shortness of breath	Viral pneumonia	Positive

CT: Computed tomography, PCR: Polymerase chain reaction, N-CoV: Noval coronavirus



in the first 15 days of the pandemic, the number of infected personnel in the next 2.5 months was only 2.

In our patient, the COVID-19 symptoms emerged simultaneously with the first confirmed patient in our country. The date of the patient's hospitalization coincided with a period when country-wide measures were not strictly implemented yet. With the first patient, personal protection was provided with surgical masks in clinics other than infectious diseases and intensive care units. Especially in the early days, due to both physical conditions and individual adaptation problems, the use of surgical masks and compliance with the distance rule were also hampered by the patients and their attendants. This patient, in whom the history of abroad contact was not given, also increased the risk in terms of transmission.

Considering these conditions, in the first days of the pandemic, the number of healthcare personnel who were initially infected in our clinic due to the lack of knowledge and experience was high. With the serious measures taken afterwards and the increase in our knowledge and experience regarding the disease, a significant decrease was observed in the number of infected healthcare workers. As a result, it is of great importance for the process to carefully comply with all precautionary suggestions of the ministry of health, to raise the awareness of the public and health personnel, and to implement the precautions completely.

## Ethics

**Informed Consent:** During the follow-up of the patient, consent form could not be obtained due to the death in the intensive care unit.

**Peer-review:** Externally peer-reviewed.

## Authorship Contributions

Concept: H.A.M., Y.A., M.A., Design: H.A.M., Y.A., T.Y., M.A., Data Collection or Processing: H.A.M., Y.A., T.Y., M.A., Analysis or Interpretation: H.A.M., Y.A., M.A., Literature Search: H.A.M., Y.A., M.A., Writing: H.A.M., Y.A., M.A.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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# An Afebrile and Severe COVID-19 Case That was Admitted Before the First Case Report in Our Country

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## Abstract

Typical symptoms in Coronavirus Disease-2019 (COVID-19) pneumonia are fever, cough and shortness of breath. These findings may not always coexist. Patients can apply with atypical or less common complaints. In the days when the disease had not been detected in our country, the diagnosis and treatment process of a COVID-19 case presenting with findings suggesting community-acquired lower respiratory disease is presented.

**Keywords:** COVID-19, afebrile, case, quantitative lung CT

## INTRODUCTION

In the early stages of the Coronavirus Disease-2019 (COVID-19) pandemic, there were difficulties in detecting patients before a case report was made in a country. When epidemiological, clinical and laboratory data are not distinctive, patients may be overlooked or cannot be definitively diagnosed. If the patient is also a health worker, there is a risk that the disease will be transmitted to other employees and patients. In this context, the process experienced in a health worker who had been admitted and monitored on suspicion of atypical pneumonia will be discussed.

## CASE PRESENTATION

### Case

A 44-year-old female patient, whose complaints of weakness, anorexia, sweating, muscle joint pain and cough had started a week ago, was admitted on March 9, 2020 with a prediagnosis of lower respiratory tract infection. When examined three days ago, vital functions were found to be normal, crackles and

increased density in the lower zones on Posteroanterior chest X-ray were observed. The infection parameters were as follows: White blood cell: 5.290/mm<sup>3</sup>, PNL: 64%, and C-reactive protein (CRP): 9 mg/L (normal <5). Complaints of dry cough increased under outpatient clarithromycin 500 mg 2x1 treatment. It was understood from the detailed anamnesis of the patient, who worked as a staff in our hospital's infectious diseases clinic, that her complaints had started four days after her relatives from the Netherlands attended the funeral ceremony held in Antalya. There was no feature in her family history, it was learned that she had no additional disease and she took no medication continuously. Examination findings revealed the followings: Fever: 36 °C, pulse: 91/min rhythmic, respiratory rate: 18/min regular, diffuse crepitant rales in the middle lower zones in both hemithoraces. Other examination findings were normal. Piperacillin/tazobactam and oseltamavir were added to her treatment. Lung computed tomography (CT) was requested. One day later, the radiology clinic specialist verbally reported that CT findings were compatible with COVID-19. Diarrhea started on the 2<sup>nd</sup> day of her hospitalization. No pathogen was detected in stool microscopy and culture. In the first CT scan, crazy-



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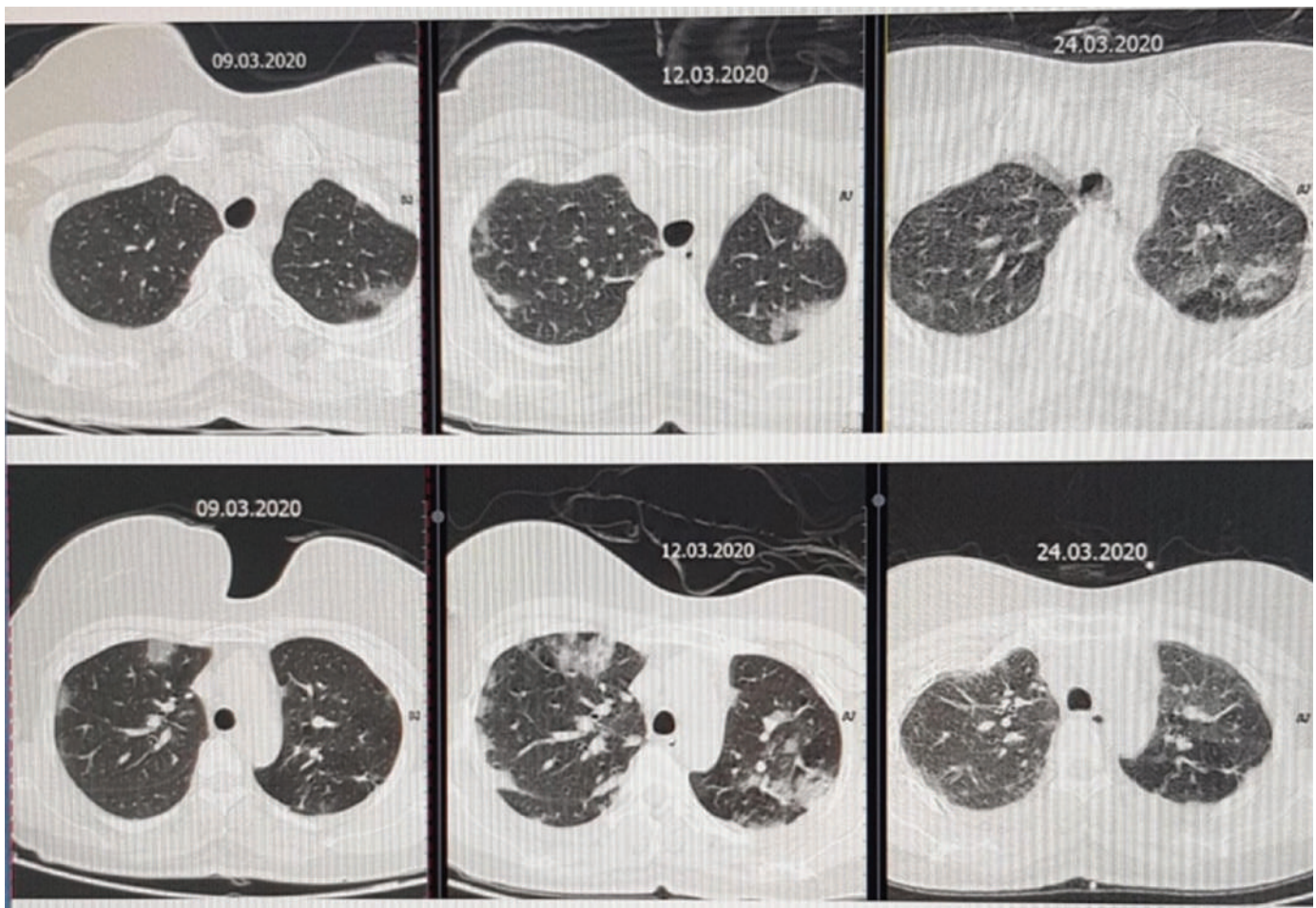
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paving pattern characterized by diffuse patch-like ground-glass opacities and interlobular septal thickening were observed in all lobes of both lungs in the lower zones and peripheral areas suggesting a viral pneumonia. Due to progressive and unresolved clinical findings, it was rechecked with CT on the 3<sup>rd</sup> and 15<sup>th</sup> days of hospitalization. Hydroxychloroquine (Hq) 200 mg tbi 2x1 and lopinavir/ritonavir (LPV/r) 200 mg tbi 2x2 combined with nonspecific supportive therapy were initiated. Hq was given for 5 days and LPV/r for 14 days. She did not have any fever in the clinical course. On the 3<sup>rd</sup> day of treatment, an increase in the density of the infiltration areas and the diffusion of ground glass opacities were observed on control CT. Figures 1 a and b show the changes in lung parenchyma involvement during the disease process. Quantitative lung involvement volume was calculated. Total lung volume was 2932 cc, COVID-19 uptake volume was 665 cc, COVID-19/lung volume ratio was approximately 22.6% (Figures 2 a and b). The mean density of the COVID-19 uptake area was calculated to be -285 Hounsfield units (HU) (normal -1000 HU).

The patient's complaints started to regress from the 7<sup>th</sup> day of hospitalization. The most challenging clinical finding was severe cough and shortness of breath. Bloody sputum was observed for two days. Supportive treatment was continued by providing nasal oxygen support and hydration. Normal flora bacteria grew in sputum culture, mycobacteria were not detected. Influenza A/B antigen was found negative in throat swab. Blood type was A Rh (-). Changes in the patient's specific laboratory values are shown in Table 1.

The patient was discharged on the 16<sup>th</sup> day of hospitalization. Although her cough complaint decreased when she was discharged, it continued. The throat-nose swab polymerase chain reaction (PCR) test taken on the 9<sup>th</sup> day of the complaints was found to be negative, and the rapid antibody test for immunoglobulin G (IgG) and IgM performed on the 17<sup>th</sup> day was found to be strongly positive (Figure 3). The positivity of second PCR test performed on the 10<sup>th</sup> day of her complaints was learned long after she was discharged, since the result of the test was delayed. Although the patient was a clinical staff, no illness



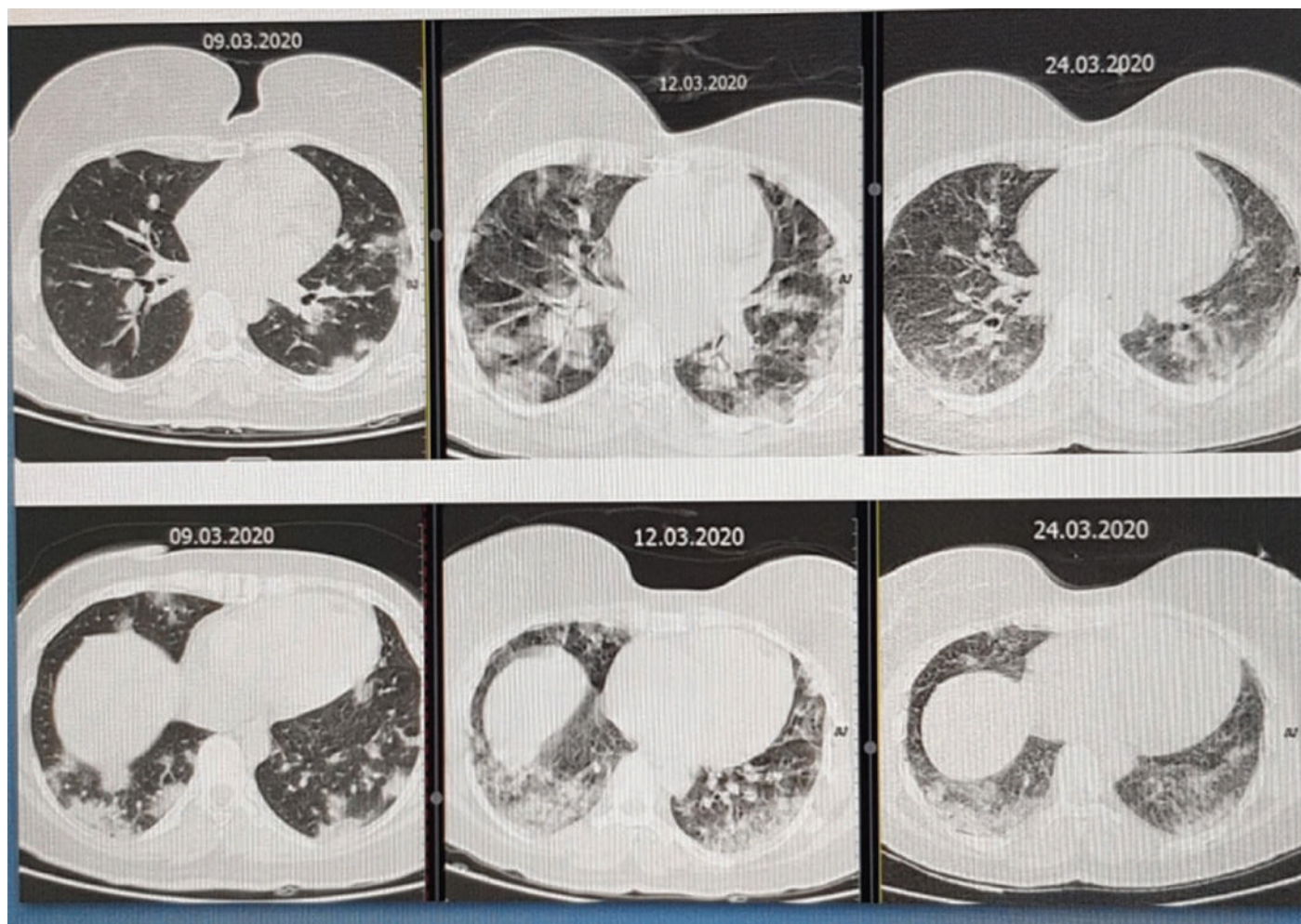
**Figure 1a.** Appearance of pneumonic involvement in different axial sections in lung CT performed at three different dates during the disease process  
CT: Computed tomography



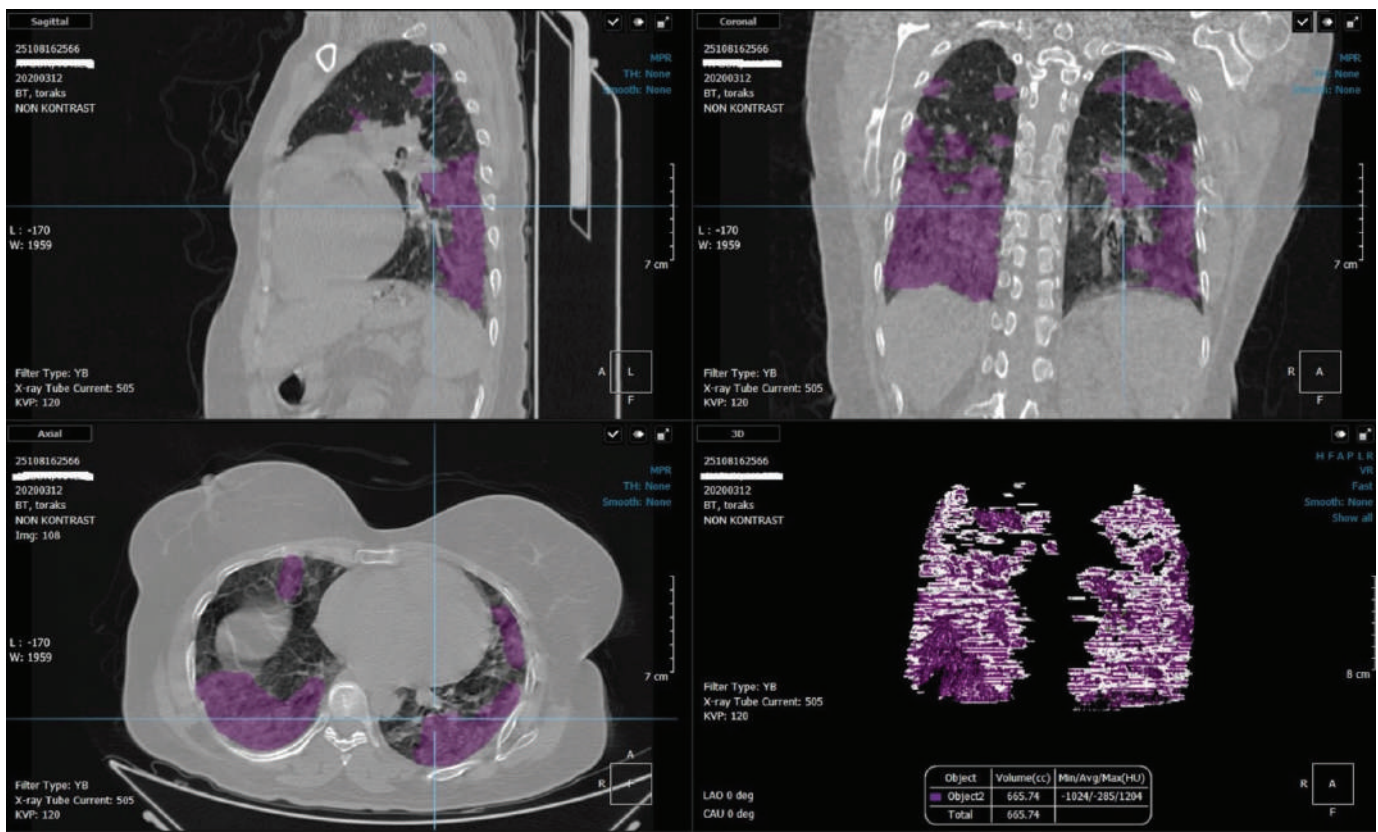
**Table 1. Change in the patient’s laboratory values**

Laboratory finding (normal range)	First admission (4 <sup>th</sup> day*)	Hospitalization (7 <sup>th</sup> day)	Maximum value	Discharge (20 <sup>th</sup> day)
WBC (3.8-10 10 <sup>3</sup> /μL)	5.29	5.14	6.91	5.64
Lymphocyte (1.18-3.74 10 <sup>3</sup> /μL)	1.17	1.44	2.40	2.09
Hgb (115-155 g/L)	125	121	101	111
Platelet (150-400 10 <sup>3</sup> /uL)	257	204	473	417
CRP (<5 mg/L)	9	88	148	3.5
Sedimentation (1-15 mm/h)		37		
Procakitonin (<0.12 μg/L)		<0.12	2.6	<0.12
D-dimer (80-500 μg/L)		797	5950	5950
Fibrinogen (2-4 g/L)		3.87	3.61	
INR (08-1.2)		0.93	1.1	
LDH/ALT/AST (<248/0-50/<35 U/L)	188/36/31	344/38/51	450/61/51	325/61/39
Creatin Phosphokinase (CPK) (0-145 U/L)	68	130	488	53

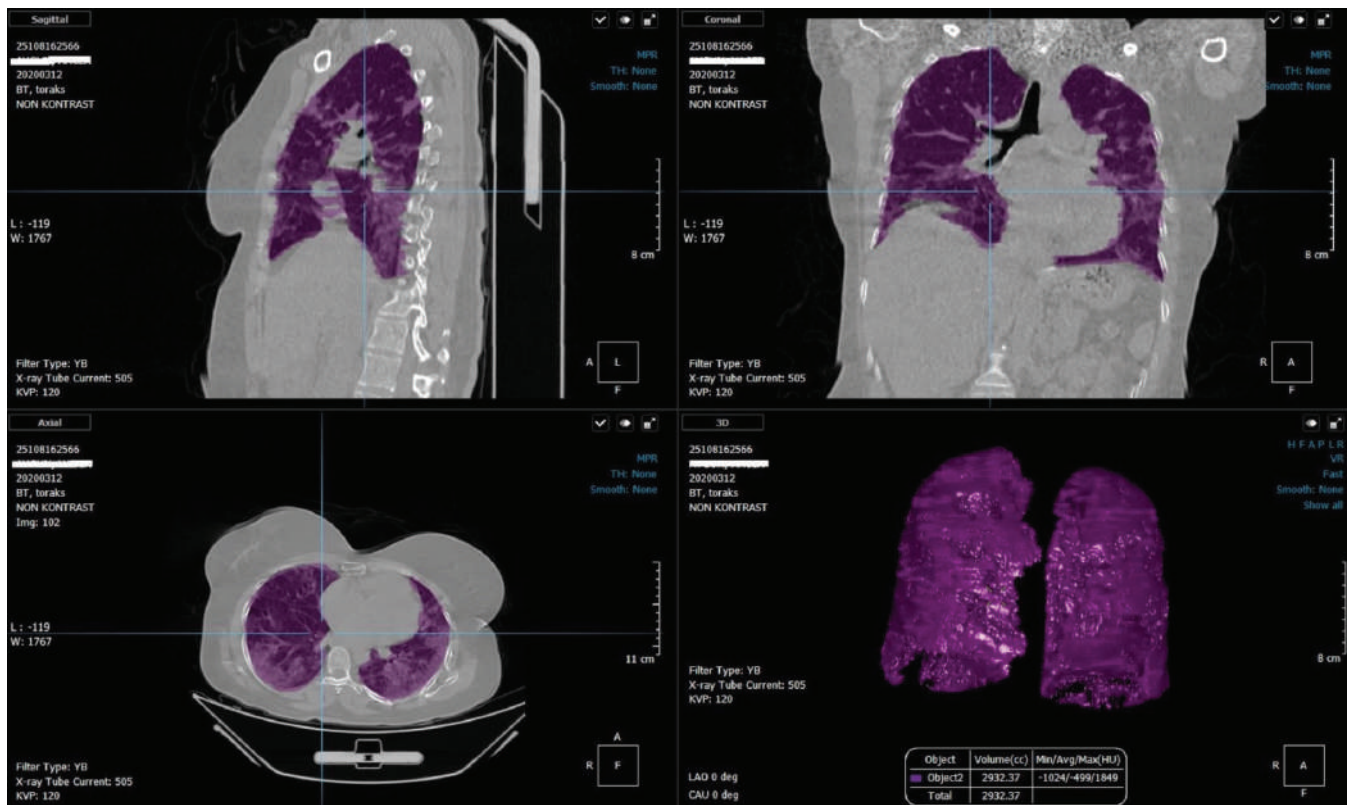
\*The number of days refers to the duration of symptoms  
WBC: White blood cell, Hgb: Hemoglobin, INR: International normalized ratio, LDH: Lactate dehydrogenase, ALT: Alanine aminotransferase, AST: Aspartate transaminase, CRP: C-reactive protein



**Figure 1b.** Appearance of pneumonic involvement in different axial sections in lung CT performed at three different dates during the disease process  
CT: Computed tomography

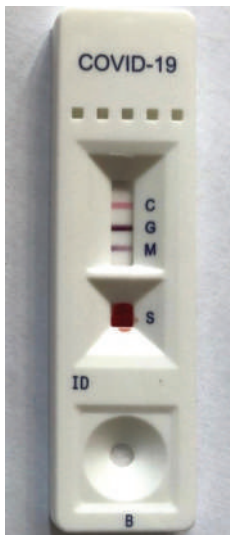


**Figure 2a.** Volumetric evaluation of areas affected by COVID-19 on lung CT shown in purple  
 COVID-19: Coronavirus Disease-2019, CT: Computed tomography



**Figure 2b.** Color image of the patient's entire lung volume





**Figure 3.** COVID-19 IgG and IgM positivity detected in the whole blood antibody test on the 17<sup>th</sup> day of symptoms

COVID-19: Coronavirus Disease-2019, IgG: Immunglobulin G, IgM: Immunglobulin M

was found in other healthcare workers who worked together in the same environment, and her written consent was obtained from her for this case report.

## DISCUSSION

Among the symptoms at first admission in patients with COVID-19, fever is detected at a rate of 43.8% and increases to 88.7% after hospitalization. Cough takes the second place with a rate of 67.8%, and diarrhea may occur less frequently in 3.8% (1). Our patient had a very severe and persistent cough, but body temperature was always found to be normal. In the laboratory tests, the most striking increase was seen in D-dimer, accompanying low fibrinogen was not detected. The mild lymphopenia observed at the beginning gradually returned to normal. The increase in CRP was remarkable, the increase in procalcitonin was mild and short-lived. During clinical follow-up, serum D-dimer, CRP, lactate dehydrogenase, and creatin phosphokinase values increased to levels of severe disease. At the first admission of the patient, COVID-19 was diagnosed due to the clinical findings as well as supportive lung CT findings. There is increasing data stating that quantitative measurement of pneumonia involvement volume and rate and pneumonia density in units of HU will have clinical prognostic value in patients with COVID-19 (2). In our patient, there was widespread involvement in the cross-sections in thorax CT findings in addition to persistent and severe clinical findings. Later, it was understood that the calculated volumetric involvement was low at 22.6% and the mean

HU value of the pneumonic areas was not at the level of severe pneumonic score. The patient's first Severe Acute Respiratory syndrome-coronavirus-2 PCR test was negative. In addition to the positive rapid antibody test, the diagnosis was confirmed by excluding other reasons. Although PCR is deemed necessary in the definitive diagnosis of COVID-19, it is known that it is not always sufficient on its own and does not rule out the disease. Antibody tests taken at the appropriate period are supportive of the diagnosis (3). The sensitivity and specificity of the rapid diagnostic antibody test (Healgen®) we used were predicted to be 97.2% and 100% for IgG, 87.9% and 100% for IgM.

## CONCLUSION

This patient was initially diagnosed as having COVID-19 with radiological findings and rapid antibody test and it was learned that repeated PCR test was positive in the late period. The evaluation of laboratory tests together considering clinical compliance is guiding in the early differential diagnosis of COVID-19.

## Ethics

**Informed Consent:** Written consent was obtained from the patient for this case report.

**Peer-review:** Internally peer-reviewed.

## Authorship Contributions

Surgical and Medical Practices: M.T.Y., K.H., S.K., M.O., Concept: M.T.Y., Design: M.T.Y., Data Collection or Processing: M.T.Y., K.H., S.K. D.K., Analysis or Interpretation: M.T.Y., K.H., S.K., Literature Search: M.T.Y., Writing: M.T.Y., S.K.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study received no financial support.

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