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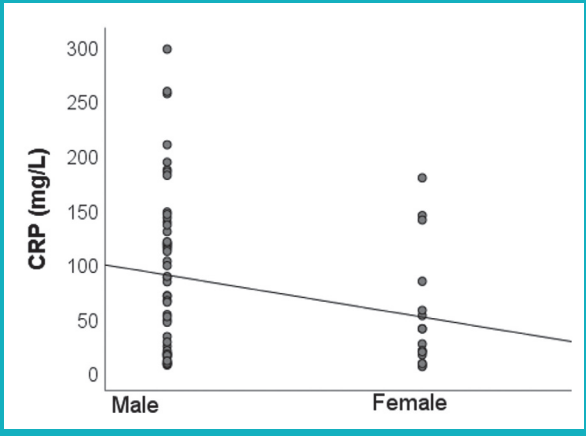
Covid-19; Experiences and Future Prospects

-Part II-



Original Article

Investigation of C-reactive Protein and D-dimer Findings in Patients with COVID-19
Hayrullah YAZAR, Yıldırım KAYACAN, Mehmet ÖZDİN; Sakarya, Turkey

Health Care Professionals' Views on Healthcare Provision During the COVID-19 Pandemic: A Descriptive Study
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The journal Bezmialem Science is an international periodical published in electronic format in accordance with the principles of independent, unbiased, and double-blinded peer-review. Four issues are published per year, in January, April, July and October.

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Pharmaceuticals should be specified with their generic names, and medical products and devices should be identified with brand name and company name, city and country.

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Scientific or Technical Report: Smith P. Golladay K. Payment for durable medical equipment billed during skilled nursing facility stays. Final report. Dallas (TX) Dept. of Health and Human Services (US). Office of Evaluation and Inspections: 1994 Oct. Report No: HHSIGOE 169200860.

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Manuscripts published in electronic format: Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis (serial online) l995 Jan-Mar (cited 1996 June 5): 1(1): (24 screens). Available from: URL: http:/ www.cdc.gov/ncidodlElD/cid.htm.

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EDITORIAL

COVID-19; Experiences and Future Prospects

Part II

In the third part of our attempt to publish the efforts of Turkish clinicians and scientists in fight against the SARS-CoV-2 pandemic, here we publish studies collected from various fields of the health sciences as the second special issue with the topic of "Experiences and Future Prospects" and the third special issue about COVID-19.

The most important topic in the COVID-19 treatment; "COVID-19 and Influenza Coexistence" is being discussed by Uslu Ersoz et al. in our first article. This article is followed by investigations on the very important factors in diagnosis of this disease such as "Investigation of C-reactive Protein and D-dimer Findings in Patients with COVID-19" and "Microbiological Diagnosis of COVID-19" which, are being discussed by Yazar et al. and Sumbul et al. respectively.

In this special issue, we also tried to cover the impact of the pandemic on healthcare professionals. Arslan et al. studied and reported the "Evaluation of Perceived Stress Levels of Radiology Workers Regarding COVID-19 Outbreak" while, a survey study is reported by Korkusuz et al. dealing with "The Importance of Healthcare Workers to Comply with Infection Prevention and Control Instructions During COVID-19 Outbreak". Similarly, a descriptive study is reported by Guner et al. emphasizing the "Health Care Professionals' Views on Healthcare Provision During the COVID-19 Pandemic".

The risk factors in COVID-19 virus infection are being discussed by several authors. High body mass and its impact on the infection is discussed in two different perspectives by Bolukcu et al. and Keskin et al. with the topics "Investigation the Relationship Between Body Mass Index and Mortality in COVID-19 Patients" and "Is High Body Mass Index a Risk Factor for COVID-19?" respectively. Another risk factor, ocular contamination is discussed by Ekinci and Ozdemir in the article entitled "Coronavirus (COVID-19) and its Relationship with Ocular Surface".

Prof. Kirpinar shared his very precious experiences during the pandemic with the readers in the article entitled "COVID-19 Pandemic: Stress and Psychiatric Disorder".

Treatment of pregnant and lactating mothers, which is the most delicate issue in the development of any kind of treatment, is discussed in two articles. These are "Is Online Pregnant School Training Effective in Reducing the Anxiety of Pregnant Women and Their Partners During the COVID-19 Pandemic?" by Merih et al. and "Evaluation of Updated Therapeutic Options For COVID-19 in Pregnancy and Lactation" by Dr. Tirmikcioglu.

Technological Innovations in New Type Coronavirus and Health System" is discussed by Guner et al and "Precautions Prior to the Treatment in Oral and Maxillofacial Surgery in the Reopening Period during COVID-19 Pandemic" is described widely by Doganay and Dolanmaz. Finally, two case reports are presented by Hamidi et al. and Yenigun et al., indicating "Clinical Course of COVID-19 in a Thalassemia Major Patient Who Underwent Haematopoietic Stem Cell Transplantation" and "Nursing Care of Patient with COVID-19" respectively.

As guest editor and on behalf of all editors of Bezmialem Science journal, I would like to thank to our sponsors for their financial and moral support in publishing this special issue.

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EDITORIAL

Special thanks to the Gilead Sciences, Inc. for their very generous donation to our special issue. Here I would like to include the sentences of Mr. Dr. Tahsin Gokcem Ozcagli, the Medical Director of Gilead Turkey;

"For 33 years, Gilead has focused on developing innovative treatments for invasive fungal infections, HIV/AIDS, Hepatitis B, Hepatitis C, hematology, inflammation, and oncology, supporting efforts to transform these diseases from deadly diseases into manageable diseases.

Gilead, headquartered in Foster City, California, operates in more than 38 countries around the world. Since 2007, Gilead Turkey is also dedicated to operating invasive fungal infections.

The story of our treatment for invasive fungal infections began in 1983 with the discovery of AmBisome®. Amphotericin B was one of the few treatment options available for the treatment of invasive fungal infections in the 1980s and has been used since the 1950s. However, these older formulas were associated with severe renal toxicities and infusion reactions. Upon this, the inspiring Research Scientist, Professor Jill Adler-Moore, began working in 1983 to develop an Amphotericin B formulation with a tolerable side effect profile. Its aim was to find a long-term solution to invasive fungal infections. His bold step and transformational discovery marked the way in the treatment of invasive fungal infections. Thus, patients at risk of contracting a life-threatening fungal infection, resulting in less toxicity; He started to benefit from this treatment, which has broad spectrum activity against most fungal pathogens, including those that cause rare and difficult to treat infections. Our product, which is licensed in 63 countries around the world, has been used in the treatment of nearly 2 million patients since its launch.

There are different treatment options that are used by physicians both in the world and in our country in the treatment of invasive fungal infections. When we look at AmBisome®, in 2010, it was recommended as the preferred first-line treatment by the World Health Organization's Expert Committee for visceral leishmaniasis in the Indian subcontinent and visceral leishmaniasis in HIV-co-infected patients in East Africa. It remained on the Essential Medicines List for more than 10 years. We are extremely proud to see AmBisome® stand shoulder to shoulder with today's most important and life-changing treatments.

We are extremely proud of all the achievements we have achieved with AmBisome® over the past 30 years. Approximately 2 million people have been treated with AmBisome® to date. It allowed mothers, fathers, children, siblings to reunite with their families who had a life-threatening invasive fungal infection. We now have footprints on almost every continent. This makes us very proud. AmBisome® is currently available in 63 countries around the world, and it is anticipated that it will be approved elsewhere in the coming years. Foreseeing the needs of physicians and patients in this regard, Gilead invested more than $ 500 million in La Verne facilities in an area of 32,500 square meters in California in order to increase production volumes between 2015-2019. With this new production facility, whose approvals have been recently completed in many countries, we will continue to benefit patients for decades to come."

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EDITORIAL

Special thanks to UPTODATE, the only clinical decision support resource associated with improved outcomes, for their very kind sponsorship to our special issue. Here it is my honor as guest editor to share the very precious message of "Wolters Kluwer" with dear readers;

Support from Wolters Kluwer in the global fight against COVID-19

We are grateful to all healthcare providers for coming forward and fighting on the front lines during the COVID-19 pandemic. Like you, our top priority has been to protect the health of our communities and equip healthcare professionals with the latest evidence and expert advice on the point of care.

We made our COVID-19 content available for free and gained access to clinical topics, drug monographs and patient education materials from our globally trusted resources UpToDate, Lexicomp and Emmi.

In the first six months of the pandemic, our editorial team developed 50 topics dedicated to COVID-19. During this time, the content was viewed over 11.4 million times by clinicians around the world looking for quick answers in a time-critical situation.

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EDITORIAL

We would like to thank to the WILEY Publications, one of the largest and most authoritative collections of online journals, books, and research resources, covering life, health, social, and physical sciences for their very kind donation to our special issue.

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During the publication of our three special issues in the fight with SARS-CoV-2 pandemic, many of our professors and health professionals in Bezmialem Vakif University got infected by COVID-19 virus. It will be our honor to dedicate these special issues to those devoted individuals. These heroes will remain in mind and documents of history as unforgettable figures.

Guest Editor

Assistant Prof. Dr. Fatemeh Bahadori
Bezmialem Vakif University
Faculty of Pharmacy
Department of Pharmaceutical Biotechnology

Original Article

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COVID-19 and Influenza Coexistence

COVİD-19 ve İnfluenza Birlikteliği

Ayşe Betül USLU ERSÖZ[1], Sibel BOLUKÇU[1], Nurgül ANDİÇ[1], Dilara KARAKUŞ[1], Gülay OKAY[1], Bilge SÜMBÜL[2], Asiye Bahar KAÇMAZ[3], Bülent DURDU[1], Yasemin AKKOYUNLU[1], Meliha MERİÇ KOÇ[1]

[1]Bezmialem Vakıf University Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, İstanbul, Turkey
[2]Bezmialem Vakıf University Faculty of Medicine, Department of Medical Microbiology, İstanbul, Turkey
[3]Bezmialem Vakıf University, Dragos Hospital, Clinic of Infectious Diseases and Clinical Microbiology, İstanbul, Turkey

ABSTRACT

Objective: Viral pneumonia cases occur quite frequently in the community. The rate of viral infections in community-acquired pneumonia is about 25%. severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and influenza are also viruses that can cause pneumonia. In this study, we aimed to determine the rate of influenza co-infection in Coronavirus disease-19 (COVID-19) cases.

Methods: The data of adult patients who applied to Bezmialem Vakıf University Hospital between March 6, 2020, and May 21, 2020, which were positive with the SARS-CoV-2 polymerase chain reaction (PCR) test and influenza antigen test were retrospectively scanned from the hospital automation system.

Results: SARS-CoV-2 PCR test was found positive in 498 adult patients who applied to our hospital. Two hundrend-sixty of these patients were hospitalized and 238 were followed up on an outpatient basis. In 88 patients SARS-CoV-2 PCR and influenza antigen were studied, and 6 of them had positive influenza antigen. COVID-19 and influenza co-infection was not detected.

Conclusion: In order to determine the exact rate of influenza and COVID-19 co-infection, it is necessary to evaluate the patients who applied with the appropriate clinical picture from the beginning of the seasonal influenza period by using reverse transcription-PCR for these two viral infections, if possible. Further research is needed in this area.

Keywords: COVID-19, influenza, co-infection

ÖZ

Amaç: Viral pnömoniler toplumda oldukça sık görülür. Toplum kökenli pnömonide viral enfeksiyonların oranı yaklaşık %25'tir. Şiddetli akut solunum yolu enfeksiyonu-2 (SARS-CoV-2) ve influenza da pnömoniye neden olabilen virüslerdendir. Bu çalışmada Koronavirüs hastalığı-19 (COVİD-19) olgularında influenza ko-enfeksiyonu oranını belirlemeyi amaçladık.

Yöntemler: 6 Mart 2020-21 Mayıs 2020 tarihleri arasında Bezmialem Vakıf Üniversitesi Hastanesi'ne başvuran, SARS-CoV-2 polimeraz zincir reaksiyonu (PZR) testi ve influenza antijen testi pozitif olarak sonuçlanan erişkin hastaların verileri retrospektif olarak hastane otomasyon sisteminden tarandı.

Bulgular: Hastanemize başvurmuş olan erişkin hastaların 498'inde SARS-CoV-2 PZR testi pozitif bulundu. Bu hastaların 260'ı hastaneye yatırılarak, 238'i ayaktan takip edilen hastalardı. SARS-CoV-2 PZR ve influenza antijeni çalışılmış olan toplam 88 hasta mevcuttu ve bunların 45'inde influenza antijeni pozitifti. COVİD-19 ve influenza ko-infeksiyonu saptanmadı.

Sonuç: İnfluenza ve COVİD-19 ko-enfeksiyonu oranını tam olarak belirlemek için mevsimsel influenza döneminin başından itibaren uygun klinik tablo ile başvuran hastaları bu iki viral enfeksiyon yönünden mümkünse gerçek zamanlı-PZR ile değerlendirmek gereklidir. Bu alanda daha fazla çalışmaya ihtiyaç vardır.

Anahtar Sözcükler: COVİD-19, influenza, ko-enfeksiyon

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Address for Correspondence: Ayşe Betül USLU ERSÖZ, Bezmialem Vakıf University Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, İstanbul, Turkey
E-mail: aysebetuluslu@gmail.com **ORCID ID:** orcid.org/0000-0001-8235-6083

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Introduction

Viral pneumonia cases are quite common in the community. The rate of viral infections in community-acquired pneumonia is approximately 25% (1). Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and influenza are viruses that can cause pneumonia (2,3). Seasonal influenza is a public health problem affecting approximately 5-10% of adults worldwide each year and is responsible for significant morbidity and mortality, especially in high-risk groups (4). Patients with influenza infection generally present with cough, fever, headache, weakness, muscle pain, runny nose, and sweating. Patients without influenza pneumonia tend to have the same symptoms, but dyspnea is more common in patients with pneumonia (3).

Ground glass opacities, consolidation, and nodular opacities can be seen in the thorax computed tomography (CT) of patients with viral pneumonia. Generally, patients present with weak opacities defined as ground glass. The second most common finding is consolidation. Nodular opacities are less common. Opacities are usually unevenly distributed and bilateral involvement is quite common (3).

In Coronavirus disease-19 (COVID-19) patients, the most common symptoms are fever, weakness, and dry cough, followed by other symptoms such as headache, nasal congestion, sore throat, myalgia, and arthralgia. Some patients may experience shortness of breath usually accompanied by hypoxemia in the second week of the illness (5).

86.2% of COVID-19 patients have abnormal findings on thoracic CT images, and more than 75% of these findings are in the form of bilateral lung involvement with a peripheral distribution. In mild patients, ground-glass opacities that were initially unilateral and focal gradually progress to bilateral or multilobular lesions. As the disease progresses, ground-glass opacities turn into consolidations (6).

In Turkey, influenza infections are most common between November and March (4). The first COVID-19 case in Turkey was detected on March 10, 2020 (7). Clinical findings, routes of transmission, and thoracic CT findings are similar in both viral infections. The coincidence of the COVID-19 pandemic with seasonal influenza also suggests the possibility of co-infection. There are various publications about the coexistence of COVID-19 and other respiratory viruses (8-10). The aim of this study was to determine the rate of influenza co-infection in the COVID-19 cases we followed-up.

Method

Between March 6, 2020 and May 21, 2020, patients admitted to Bezmialem Vakıf University with symptoms suggesting COVID-19 infection were included. Combined nasal and pharyngeal swabs were obtained and studied with SARS-CoV-2 reverse transcription-polymerase chain reaction (RT-PCR) test using Biospeedy COVID-19 SARS-CoV-2 qPCR Detection Kit (Bioeksen, Turkey). For influenza diagnosis, nasopharyngeal swab samples were obtained, and an influenza antigen test was performed with ichroma TRIAS Influenza A+B (Boditech, Kore) test kit using ichroma II device. During the pandemic period, the data of adult patients whose SARS-CoV-2 PCR test and influenza antigen test were positive were retrospectively scanned from the hospital automation system.

Results

The SARS-CoV-2 PCR test was found to be positive in 498 of the adult patients who applied to our hospital between March 6, 2020, and May 21, 2020. Two hundred and sixty of these patients were hospitalized and 238 were outpatients.

Influenza antigen was found positive in 45 (21%) of 212 adult patients whose influenza antigen was studied. Seven of the cases were influenza A positive, and 38 of them were influenza B positive.

During the pandemic, both SARS-CoV-2 PCR and influenza antigen were studied in 82 patients. The average age of these patients was 54.45±16.6 and 50% (n=44) of them were males. All of those were hospitalized patients. Thoracic CT findings were found to be compatible with viral pneumonia in 82 of 88 patients. CT findings of 17 patients were mild, and the CT findings of 65 patients were moderate/severe. However, COVID-19 and influenza co-infection were not detected in any patient.

Discussion

Influenza viruses are known to cause many pandemics. Although there are 3 different influenza viruses -A, B, and C- antigenically, influenza A virus is responsible for the vast majority of mortality and morbidity in humans (11). In 1918, the influenza A/H1N1 (Spanish flu) pandemic killed nearly 40 million people worldwide (11). In 2009, a new pig-derived H1N1 strain was identified in Mexico. In June 2009, the World Health Organization (WHO) declared the beginning of this epidemic and reported a total of 18,631 deaths with confirmed H1N1pdm09 disease (12). In 2012, WHO confirmed 610 cases infected with the influenza A/H5N1 virus. Most of these cases had close contact with infected birds, and 360 mortality occurred (11). Influenza B virus, unlike influenza A, almost exclusively infects humans and is therefore not associated with a pandemic. Also, influenza B is less diverse as it undergoes slower antigenic drift (4).

In Turkey, influenza infections are most common during November-March (4). A study conducted in Turkey between 2003 and 2016 found that except 2009-2010 pandemic, an average of 32% of influenza cases was associated with influenza B (4).

The SARS-CoV-2 virus caused a pandemic that started in Wuhan, China in December 2019 and spread to the whole world (5). To date (27.06.2020), 491.128 deaths have been reported worldwide by WHO (13). In Turkey, the first COVID-19 case was seen on March 10, 2020, (7) and COVID-19 so far (06.27.2020) caused the deaths of 5,065 patients (13).

Diseases caused by influenza and SARS-CoV-2 virus have similar characteristics and their seasonal preferences coincide which suggested the possibility of these infections being seen together. Our aim was to determine the rate of this coincidence.

In the literature, rates of influenza co-infection in COVID-19 case series vary between 0-5% (8-10,15-17). We didn't detect any influenza and COVID-19 co-infection. We think this may be due to three factors. In Turkey, COVID-19 cases first appeared at the end of the influenza season. Also, measures to prevent COVID-19 might have prevented the transmission of influenza. In addition, the lower sensitivity of the influenza antigen test (75.6% for influenza A, 63.6% for influenza B) (14) we used for the diagnosis of influenza compared to the RT-PCR method may have led to the absence of any co-infected patients.

Conclusion

In conclusion, in order to determine the rate of influenza and COVID-19 co-infection precisely, patients presenting with an appropriate clinical picture from the beginning of the seasonal influenza period should be evaluated with RT-PCR for these two viral infections, if possible. Further studies on this subject are required.

Ethics

Ethics Committee Approval: Bezmialem Vakıf University Clinical Research Ethics Committee (no: 71306642-050.05.04-)

Informed Consent: Retrospective study.

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: A.B.U.E., S.B., N.A., D.K., G.O., B.S., A.B.K., B.D., Y.A., M.M.K., Design: A.B.U.E., S.B., N.A., D.K., G.O., B.S., A.B.K., B.D., Y.A., M.M.K., Data Collection or Processing: A.B.U.E., S.B., N.A., D.K., G.O., B.S., A.B.K., B.D., Y.A., M.M.K., Analysis or Interpretation: A.B.U.E., S.B., N.A., D.K., G.O., B.S., A.B.K., B.D., Y.A., M.M.K., Literature Search: A.B.U.E., S.B., N.A., D.K., G.O., B.S., A.B.K., B.D., Y.A., M.M.K., Writing: A.B.U.E., S.B., N.A., D.K., G.O., B.S., A.B.K., B.D., Y.A., M.M.K.

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Original Article

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Investigation of C-reactive Protein and D-dimer Findings in Patients with COVID-19

COVİD-19 Hastalarında C-reaktif Protein ve D-dimer Bulgularının İncelenmesi

Hayrullah YAZAR[1], Yıldırım KAYACAN[2], Mehmet ÖZDİN[3]

[1]Sakarya University Faculty of Medicine, Department of Medical Biochemistry, Sakarya, Turkey
[2]Yaşar Doğu Sports Science Faculty, Coaching Training, Samsun, Turkey
[3]Sakarya Training and Research Hospital, Clinic of Biochemistry, Sakarya, Turkey

ABSTRACT

Objective: The purpose of this study is to examine the levels of C-reactive protein (CRP) and D-dimer by age and gender in the pandemic caused by the new coronavirus.

Methods: Coronavirus disease-19 (COVID-19) diagnoses were made according to the results of real-time polymerase chain reaction and lung computed tomography (n=70). In the study, CRP and coagulation were examined as indicators of inflammation, and D-dimer was examined as an indicator of fibrinolytic system activity. Patients' age, gender, and CRP and D-dimer values were analyzed with Spearman's rho correlation, whereas the gender factor was analyzed with the Mann-Whitney U test.

Results: Although D-dimer levels were high in women, there was no statistical significance. A correlation was identified between CRP and gender, and the levels in male patients were higher (p=0.049). A positive correlation was found between the patients' age and CRP and D-dimer findings.

Conclusion: There are two main findings in this study. First, age and gender are essential parameters in disease findings due to the COVID-19 pandemic. Their importance overlaps with the finding that inflammation is severe in elderly males and that the mortality is higher than in younger individuals. Second, the CRP and D-dimer test results can be used as practical and reliable biomarkers for COVID-19. We propose that if these two tests, which are already used routinely, are interpreted with consideration of age and gender, they can be used more efficiently in early diagnosis and isolation.

Keywords: SARS-Cov-2, COVID-19, C-reactive protein, D-dimer

ÖZ

Amaç: Bu çalışmanın amacı, yeni koronavirüsün neden olduğu pandemide ilk tanı konulduğu anda C-reaktif protein (CRP) ve D-dimer düzeylerinin yaş ve cinsiyete göre incelenmesidir.

Yöntemler: Gerçek zamanlı polimeraz zincir reaksiyonu ve akciğer bilgisayarlı tomografi (n=70) sonuçlarına göre COVİD-19 tanıları konuldu. CRP inflamasyonun göstergeleri olarak, D-dimer ise fibrinolitik sistem aktivitesinin bir göstergesi olarak incelendi. Hastaların yaşı, cinsiyeti, CRP ve D-dimer değerleri Spearman'ın rho korelasyonu ile analiz edilirken cinsiyet faktörü Mann-Whitney U testi ile analiz edildi.

Bulgular: Kadınlarda D-dimer düzeyleri yüksek bulundu, ancak istatistiksel olarak anlamlılık tespit edilmedi. Erkek hastalarda ise CRP düzeyleri anlamlı olarak yüksek bulundu (p=0,049). Hasta yaşı ile CRP ve D-dimer arasında pozitif korelasyon bulundu.

Sonuç: Çalışmada iki ana sonuç ortaya çıktı. Birincisi, yaş ve cinsiyetin COVİD-19 salgını nedeniyle gerçekleşen hastalıkta önemli bir parametre olduğudur. Bu bulgu, yaşlı erkeklerde inflamasyonun şiddetli olduğu ve gençlere göre ölüm oranının daha yüksek olması bulgusuyla örtüşmektedir. İkinci sonuç ise, CRP ve D-dimer testlerinin COVİD-19 için pratik ve güvenilir bir belirteç olabileceğidir. Zaten rutin olarak kullanılan bu iki testin yaş ve cinsiyet dikkate alınarak yorumlanması halinde erken teşhis ve izolasyonda daha verimli kullanılabileceğini öneriyoruz.

Anahtar Sözcükler: SARS-Cov-2, COVİD-19, C-reaktif protein, D-dimer

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Address for Correspondence: Hayrullah YAZAR, Sakarya University Faculty of Medicine, Department of Medical Biochemistry, Sakarya, Turkey
E-mail: drhyazar@hotmail.com **ORCID ID:** orcid.org/0000-0001-9447-6322

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Introduction

New coronavirus disease (COVID-2019) was first seen in the city of Wuhan in Hubei State in China. According to the World Health Organization, a single-stranded RNA virus, named SARS-CoV-2, was identified as a pathogen in patients with unexplained pneumonia since December 2019 (1). This pandemic spread worldwide in a short amount of time. A study showed that the new coronavirus infects humans through an incubation period of 1-14 days (2). It was stated that the new coronavirus infections could trigger not only respiratory tract diseases but also inflammation, high fever, cough, acute respiratory tract infection, and dysfunction of internal organs leading to death. The new coronavirus is first attacked by mast cells found in the submucosa of the respiratory tract and nasal cavity that act as a protective barrier against microorganisms (2). In the early stages of COVID-19, the benefits of C-reactive protein (CRP) level measurements were revealed in a study. In the study, lung lesions and CRP levels were associated. A positive correlation was found between the diameter of lung lesions and CRP levels. Since there is no treatment for COVID-19 disease, research on biomarkers has been brought to the forefront (3). CRP and D-dimer were the prominent ones in the search for biomarkers. (CRP), which is referred to as an acute-phase reactant (APR), was first discovered in the sera of pneumococcal pneumonia patients (4). The increase of APR concentration due to inflammation and tissue damage was identified in the serum level (5,6). Undoubtedly, the increase of CRP in the serum a few hours after the inflammation led to it being one of the first biomarkers considered in COVID-19.

Another biomarker associated with COVID-19 sepsis is D-dimer, which is a product resulting from D-dimerfibrin destruction. It is the smallest protein fragment identified in blood when a blood clot is degraded (fibrinolysis). Its name derives from the two cross-linked D fragments of fibrin protein. D-dimer is a reliable test and has been preferred for patients with a suspected clotting disorder since the 1990s (7). D-dimer measurements and monitoring gained importance with the occurrence of sepsis-induced coagulopathy in COVID-19 patients. Some clinicians eliminated this situation by using heparin to reduce the risk of the spread of intravascular clotting and venous thromboembolism (8). In our study, we investigated whether there was a relationship between CRP, D-dimer, and COVID-19. In addition, we considered age and gender factors. Our literature search showed that no other study had evaluated these four parameters at the same time. Our study will contribute to the more efficient use of CRP and D-dimer tests that are widely and routinely used in all healthcare institutions and will accelerate the process, enabling the early diagnosis of COVID-19.

Method

The patients' information on gender and age were obtained from the Hospital Information Management System. The diagnoses of all the patients included in the study with COVID-19 were made based on the results of a real-time polymerase chain reaction and lung computed tomography. Twenty-four patients were admitted to emergency rooms, whereas 41 patients were admitted to the infectious disease department, and five were admitted to pediatric polyclinics (n=53 males and n=17 females). The mean ages of patients were 55.11±2.92 for males and 55.18±5.80 (± SEM) for females. Patient samples were collected by phlebotomists from venous blood. Biochemical tests were performed in the emergency labs using plasma samples for D-dimer and serum for CRP.

Statistical Analysis

For analyzing the data, SPSS v.21 (IBM, USA) was used. The patient findings did not show a normal distribution (Shapiro-Wilk test, p=0.000), so Spearman's rho was used for correlation analyses, whereas the Mann-Whitney U test was used to identify the differences between genders. A significance level of $p<0.05$ was accepted. The study was approved by the Medical School Ethical Committee (ethical number: 050.01.04/106).

Biochemical Analyses

CRP Latex

Cold centrifuge procedures were performed at 5,000 rpm for 10 minutes to obtain serum. The device used in the study was a Beckman Coulter AU5800 Clinical Chemistry Fully Automatic System (The Fastest AU Analyzer Ever. Serial Number: 2016022598. Tokyo/Japonya). The accepted normal range for CRP was 0.00-5.00 mg/L.

Collinearity: The test was collinear in the concentration range of 0.2-480 mg/L for a normal application and the concentration range of 0.08-80 mg/L for a very sensitive application.

Sensitivity: The lowest levels that could be identified were 0.20 mg/L for normal and 0.05 mg/L for very sensitive. The lowest level that could be identified represents the lowest CRP level measured and distinguished from zero. The standard deviation was calculated as the absolute mean of 20 repetitions of a sample that does not contain analytes plus three.

Accuracy: Accuracy was obtained using three serum pools analyzed over 20 days for CRP (Latex) normal and high-level sensitive tests. The cofficient of variation % value in the study was found to be very sensitive, with a total of 3.48.

D-dimer

Measurements were performed using the fragmental improved immunoturbidimetric test. Normal values for D-dimer were accepted as 0-500 μg FEU/mL. A D-dimer test was performed using venous blood plasma. Plasma was obtained after centrifuging for 20 minutes at 3200 rpm and then run on the Diagon Coag XL (SN: 30115-03082015), which was followed by D-dimer measurements. All patient samples were run with the same lot numbers in the same Diagon XL coagulation device.

Measuring range: The test was developed to identify D-dimer concentrations between the measurement range of 0.22-8.0 μgFEU/mL. When the values were above this range, the samples were diluted.

Specificity: Dia-D-dimer is an immunological test unique for human D-dimer because of its antibodies. No interaction with rheumatoid factor up to 50 IU/mL was observed.

Cut-off value: The lowest identification threshold is 0.22 µg FEU/mL.

Results

The descriptive statistical findings for CRP (mg/L), D-dimer (µgFEU/mL), age (years), and gender are presented in Table 1. When differences were examined based on gender (Mann-Whitney U test), it was found that the CRP level was higher in male patients than female patients ($p<0.05$; Table 2). A positive correlation was identified between patient age and CRP ($p=0.000$) and D-dimer ($p=0.028$). It was observed that as age increases, both CRP and D-dimer findings increase.

Table 1. Descriptive statistics and Mann-Whitney U findings of the parameters

Parameters	Gender	N	Mean	SD	SEM	Min	Max	P
CRP (mg/L)	Male	53	89.29	73.4	10.08	6.84	296.86	**0.049**
	Female	17	50.70	54.14	13.13	5.28	178.64	
D-dimer (µgFEU/mL)	Male	53	1969.96	3339.94	458.77	519	22400	**0.468**
	Female	17	3159.58	7951.72	1928.57	511	33400	
Age (years)	Male	53	55.11	21.27	2.92	2	86	**0.732**
	Female	17	55.18	23.87	5.79	15	83	

There are descriptive statistical findings according to the gender of the patients. It is seen in the table that the average age is very close in the two genders. CRP findings were detected at a high level in men and D-dimer in women. It was determined that CRP value was significantly higher in male patients.
SD: Standard deviation, CRP: C-reactive protein, Min: Minimum, Max: Maximum

Table 2. Findings of Spearman's rho correlation analysis detected in patients

Parameters*	Age (years)	CRP
CRP	0.263	
	0.028	
D-dimer	0.434	0.249
	0.000	0.037

According to the analysis, a positive correlation was found among age, CRP and D-dimer findings. In other words, it is seen that these data increase as age increases. Also, there was a correlation between CRP and D-dimer. (*: The top line shows the r values and the bold numbers indicate the p values.)
CRP: C-reactive protein

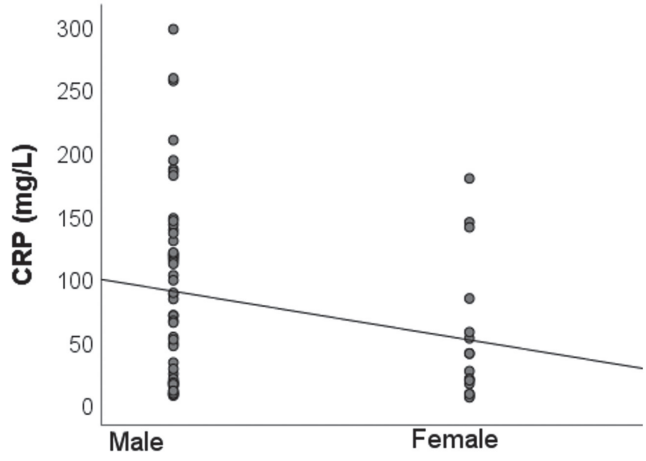


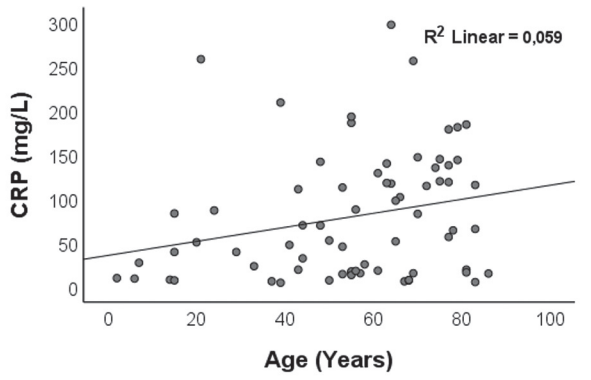
Figure 1. The comparison of the CRP by gender
CRP findings were found as 89.29±10.08 in men and 50.7±13.13 (SEM) in women. This value was found to be significantly higher in men with COVID-19
CRP: C-reactive protein, COVID-19: Coronavirus disease-19, SEM: Scanning electron microscope

Discussion

On March 10, 2020, the World Health Organization declared a global pandemic because of the widespread infection of the COVID-19. The first COVID-19 case in Turkey was seen on March 11, 2020. The late start compared with other countries was considered as a pleasant development. However, the speed at which the virus spread, particularly in the young population, was remarkable. Germany and South Korea are considered as the countries that fight COVID-19 the best because of early diagnosis. Our study emphasizes that using easy and practical tests for routine use by developing an algorithm for pre-diagnosis would result in a more successful fight against the virus in many countries.

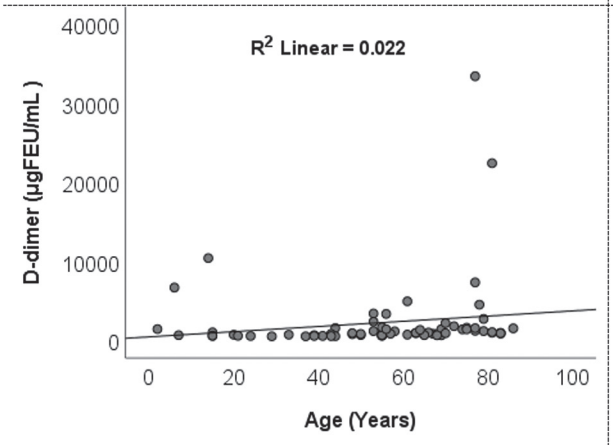
In this study, we found that advanced age was effective in the prognosis of this disease. There is a limited number of studies in the literature because this virus is novel. Saghazadeh and Rezaei (18) found that the older population has a higher risk of catching COVID-19. In our study, 47.8% of the patients admitted to our hospital were in the 60 and older age group. Tolia et al. (9) reported that most patients they received and diagnosed with COVID-19 were males.

Similarly, it was significant that 53 of the diagnosed patients with COVID-19 were males in this study (9). In a study conducted with 140 COVID-19 patients in China, the distribution of the two genders was found to be equal. In contrast, another study conducted on critical patients showed that women were affected by COVID-19 67% more than men (10). A recent report



D) **Correlation graph determined between CRP 9nda ge**

It can be seen that the CRP values detected in patients are higher than 60 years of age. There was a significant relationship between age and CRP (R^2= 0.059)



B) Correlation graph determined between D-dimer 9nda ge

D-dimer data is observed to be significantly concentrated in patients aged 60 and over (R^2= 0.022).

Figure 2. Correlations of CRP and D-dimer with age (years)
CRP: C-reactive protein

stated that 58% of the 1,099 patients with COVID-19 in 552 hospitals in 30 cities in China were males (11). These data show that COVID-19 may show gender tendency and that men are more prone to be affected. This gender tendency may be due to men's high levels of smoking compared with women in China (in 2018, the number of smokers was 288 million for men and 12.6 million for women). In the current study, we could not obtain data on patients' smoking habits, but we believe that smoking may be a factor in the density of the male population.

In the current study, we examined the CRP and D-dimer parameters by gender and age. No other studies in the literature with the patient population of our study examines gender/age factors. Mi et al. (12) examined CRP and D-dimer values in patients in their 40s who were diagnosed with COVID-19. Their findings showed high levels of CRP and D-dimer in all patients (12). Similarly, Chen et al. (13) found that CRP and D-dimer values were high in their study, consisting of 21 (17 male and four female) patients diagnosed with COVID-19. The low number of patients in these two studies prevents making a general evaluation. Our study, which consists of more patients with COVID-19, supports the high levels of C-reactive and D-dimer in COVID-19 patients. According to the findings of a study conducted by Wang (3), CRP may positively correlate with lung lesions in the early diagnosis of COVID-19 and reflect the severity of the disease. In addition to the similar findings we obtained in our study, a relationship between an increase in CRP mainly and gender and age was found. Tang et al. (14) evaluated the D-dimer test parameter in identifying low molecule weight heparin effectiveness in their study. Their results showed that the 28-day mortality of heparin users was lower than those who did not use heparin. They also found high D-dimer levels in COVID-19 patients. However, in our study, we evaluated CRP and D-dimer together. Yu and Yang (15) conducted a study on COVID-19 cases and found that a significant number in society continue to live asymptomatically. According to them, this puts the whole society at risk. The data in our study clearly showed the relationship between CRP and D-dimer tests and COVID-19.

If the two tests used in our study are used for screening purposes, it is possible to identify cases early. Furthermore, the examination of four parameters simultaneously is unique. Not having easy access to COVID-19 tests and definitive diagnosis kits being time-consuming leads to the question, "Can a new algorithm be developed by evaluating CRP, D-dimer, age, and gender?" CRP and D-dimer tests are practical tests being used routinely in all healthcare institutions. Evaluation of these two tests with age and gender can accelerate the path to early diagnosis of the disease and contribute positively to the fight against COVID-19.

Conclusion

A relationship between the COVID-19 pandemic due to new coronavirus and age and gender was found. Particularly in elderly male patients, it is possible to use CRP and D-dimer monitoring as biomarkers of inflammation. The low mortality rate in those with high disease resistance highlights the need to examine patients' lifestyles who are affected by this disease. Germany and South Korea are the two countries that receive attention for their successful handling of COVID-19. Since these two countries are test manufacturers led to the early diagnosis and isolation of more people. The speed of disease spread was significantly below the world average. Other countries may not have tests that provide comprehensive and fast results for a confirmed diagnosis of COVID-19. However, they have CRP and D-dimer options that are easily accessible, practical, and routinely used. We recommend developing a new algorithm for testing CRP and D-dimer in individuals regardless of age and gender. People with high results on the test would be isolated fast as "suspected cases" to reduce the spreading speed of COVID-19.

Ethics

Ethics Committee Approval: The study was approved by the Medical School Ethical Committee (ethical number: 050.01.04/106).

Informed Consent: Retrospective study.

Peer-review: Externally peer reviewed.

Authorship Contributions

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

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

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Original Article

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Investigation the Relationship Between Body Mass Index and Mortality in COVID-19 Patients

Vücut Kitle İndeksi ile COVİD-19 Hastalarının Mortalitesi Arasındaki İlişkinin İrdelenmesi

Sibel BOLUKÇU[1], Mehmet Emin ÖZMEN[1], Çağla EKŞİ[1], Gülay OKAY[1], Bilge SÜMBÜL[2], Asiye Bahar KAÇMAZ[3], Bülent DURDU[1], Yasemin AKKOYUNLU[1], Meliha MERİÇ KOÇ[1]

[1]Bezmialem Vakıf University Faculty of Medicine Training and Research Hospital, Department of Infectious Diseases and Clinical Microbiology, İstanbul, Turkey
[2]Bezmialem Vakıf University Faculty of Medicine Training and Research Hospital, Department of Medical Microbiology, İstanbul, Turkey
[3]Bezmialem Vakıf University, Dragos Hospital, Clinic of Infectious Diseases and Clinical Microbiology, İstanbul, Turkey

ABSTRACT

Objective: Obesity might be a risk factor for patients with Coronavirus disease-19 (COVID-19). We aimed to investigate the association of the obesity with intensive care need and mortality caused by severe acute respiratory syndrome-CoV-2 (SARS-CoV-2) infection in this retrospective cohort.

Methods: Between March 11th and May 1st, 135 patients, who were treated in our clinic, were enrolled in the study. Body mass index (BMIs) of the patients were grouped according as WHO criteria (<25 kg/m^2: normal, 25 30 kg/m^2: overweight, >30 kg/m^2: obese).

Results: Of our patients, 34.1% (n=46) were obese. Mean BMI of the mortality group was 31.2 kg/m^2 and was not different from that of the survivors (p=0.09), However, mean BMI of the patients, in whom intensive care was needed, was 31.2 kg/m^2 and higher than that of those intensive care was not needed (p=0.04). In subgroup analyses, obesity (BMI >30 kg/m^2) was more common among mortality group versus survivors in males older than 60 years old (p=0.03).

Conclusion: Obesity with associated disorders are negative prognostic factors for COVID-19 and should be tackled as the end of the pandemic is obscure.

Keywords: COVID-19, obesity, Turkey

ÖZ

Amaç: Obezitenin, Koronavirüs hastalığı-19 (COVİD-19) olguları için olumsuz bir risk faktörü olabileceği görülmektedir. Bu retrospektif kohortta, şiddetli akur solunum enfeksiyonu-CoV-2'nin (SARS-CoV-2) sebep olduğu mortalite ve yoğun bakım ünitesinde takip edilme gereksinimi ile vücut kitle indeksi ilişkisini değerlendirmeyi amaçladık.

Yöntemler: 11 Mart-1 Mayıs 2020 tarihleri arasında kliniğimizde takip edilen 135 hasta çalışmaya dahil edildi. Hastaların VKİ değerleri Dünya Sağlık Örgütü'nün belirlediği değerlere göre gruplandırıldı (<25 kg/m^2 = normal, 25-30 kg/m^2 =kilolu ve 30 kg/m^2 =obez).

Bulgular: Buna göre olguların %34,1 (n=46) obezdi. Ölen olguların, vücut kitle indekslerinin ortanca değeri 31,2 kg/m2 idi ve sağ kalan grupla benzerdi (p=0,09). Buna karşılık yoğun bakım ünitesinde takip edilen olguların, vücut kitle indeksilerinin ortanca değeri 31,2 kg/m^2 ve yoğun bakım ünitesinde takip edilmeyen olgulardan daha yüksekti (p=0,04). Alt grup analizlerinde >60 yaş erkek cinsiyet olanlarda sağ kalanlara göre ölenler obezdi (vücut kitle indeksi >30 kg/m^2) (p=0,03).

Sonuç: Obesite, kendisi ve beraberinde getirdiği hastalık yüküyle COVİD-19 gibi bir çok hastalıkta kötü prognostik faktördür. COVİD-19 salgınının ne zaman sonlandırılacağı bilinmezken obezite gibi hastalığın seyri açısından olumsuz faktörlerle mücadele edilmesi gerektiği açıktır.

Anahtar Sözcükler: COVİD-19, obezite, Türkiye

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Address for Correspondence: Sibel BOLUKÇU, Bezmialem Vakıf University Faculty of Medicine Training and Research Hospital, Department of Infectious Diseases and Clinical Microbiology, İstanbul, Turkey
E-mail: saydinbolukcu@yahoo.com **ORCID ID:** orcid.org/0000-0001-6475-3894

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Introduction

Since severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) first appeared in Wuhan, China, 7,039,918 people around the world have been diagnosed with COVID-19 and 404,396 of them died [World Health Organization (WHO); accessed on 9th June 2020]. Again, according to WHO data, the first case in Turkey was confirmed on 11th March 2020, a total of 171,121 cases were diagnosed which corresponds to 2029 cases per 1 million population and 56 deaths per 1 million population.

Studies during the early period of the pandemic suggested that the disease had a more severe course in the elderly population, men, and those with comorbidities (1). Abdominal obesity is known to cause abnormal synthesis of adipokines and cytokines such as tumor necrosis alpha (TNF-alpha) and interferon, causing a chronic low-level inflammation that can damage the lung parenchyma and bronchi (2,3). Obesity appears to be a risk factor for COVID-19 cases.

The aim of this retrospective cohort study was to evaluate the relationship between the mortality caused by SARS-CoV-2 and the need to be followed in the intensive care unit (ICU) and body mass index (BMI).

Method

This retrospective cohort study was conducted in a single center. Starting from the first case on 11th March, 2020, all cases followed at the Infectious Diseases Clinic of Bezmialem Vakıf University Faculty of Medicine until 1st May 2020 were included. The diagnosis was made taking into account the updates of the Ministry of Health's National COVID-19 Guide. The microbiological examination was performed by reverse transcription-polumerose chair reaction (RT-PCR) analysis of nasopharyngeal swab samples. From the database gender, age, BMI, RT-PCR result of nasopharyngeal swap samples, and follow-up and survival data in the ICU were analyzed. BMI values were grouped according to WHO criteria (<25 kg/m^2= normal, 25-30 kg/m^2= overweight, ≥30 kg/m^2= obese) (4).

Statistical Analysis

Chi-square test and Fisher's exact test were used to analyze the difference between the percentages of categorical data. The significance of the difference between the mean ages of the dead and survived patients was evaluated with the Student t-test and the significance of the difference between the medians of BMI was analyzed using the Mann-Whitney U test. Whether the BMI groups showed a trend in survival and follow-up in the ICU was analyzed with the chi-square trend and post-hoc z test.

Results

This study included 135 patients. Among them 57.8% (n=78) were males and the mean age was 52.5±16.1 years. The median BMI value was 27.7 (interquartile range: 24.1-31.2). The highest BMI was 56 kg/m^2. In 39.3% (n=53) of the cases RT-PCR was positive in a nasopharyngeal swap and/or there were radiological findings + clinical features were compatible; in other cases, radiological and clinical findings were compatible. Fifteen cases were followed in ICU and 13 cases died (Table 1).

According to WHO classification 27.4% (n=37) were <25 kg/m^2, 38.5% (n=52) were between 25-30 kg/m^2 and 34.1% (n=46) were >30 kg/m^2. Obesity (BMI >30 kg/m^2) was more common among females (n=28, 49.1%) (p=0.002).

The median BMI value of cases followed in ICU (31.2 kg/m^2) was higher than cases who were not followed in ICU (p=0.04). In addition, their mean age was (61.6±14.9) higher than cases followed at a ward (p=0.02). Comparison of the BMI groups according to follow-up in the ICU revealed that obese patients were followed in the ICU more than the other two groups (p=0.03).

The median BMI value of dead cases was (31.2 kg/m^2) similar to the BMI value of survivors (p=0.09). The mean age of dead patients (62.9±14.5) was higher than survivors (p=0.01).

Subgroup analyses of dead cases revealed that the mean BMI value of females ≥60 years of age was similar to survivors (p=0.97). Among males in this age group, died cases were more frequently obese (BMI >30 kg/m^2) than survivors (p=0.03) (Table 2). In both sexes, no mortality was observed in normal weight, overweight, and obese groups. In females, mortality was in cases above 50 years of age.

Table 1. Features of dead and survived patients

	Survived patients (n=122)	Dead patients (n=13)	p
Sex (n;%)			
Female	53; 93	4; 7	0.3
Male	69; 88.5	9; 11.5	
Mean age ± SD	51.4±16.01	62.9±14.5	**0.01***
Median BMI (IQR)	27.6 (24.1-30.8)	31.2 (25.5-34.3)	0.09
BMI groups (n;%)			
Normal	35; 94.6	2; 5.4	
Overweight	48; 92.3	4; 7.7	0.1
Obese	39; 84.8	7; 15.2	
RT-PCR positivity n;%	41; 77.4	12; 22.6	**0.0001***
ICU follow up n;%	3; 20	12; 80	**0.0001***

SD: Standard deviation, BMI: Body mass index, RT-PCR: Reverse transcription-polymerase chain reaction, ICU: Intersive care unit, IQR: Inter quantile range

Discussion

COVID-19 continues to be an important health problem in Turkey as well as all over the World. Particular attention should be paid to elderly people with co-morbidities due to severity of illness, need for ICU, and the high risk of death in this group.

Table 2. The distribution of BMI groups according to sex and age

	Normal	Overweight	Obese	p
Males, age groups				
<30	NA	NA	NA	
30-40	0	1; 7.7	0	
40-50	0	1; 20	1; 20	0.6
50-60	1; 20	0	1; 20	1
>60	0	2; 20	2; 50*	0.03
Females, age groups				
<30	NA	NA	NA	
30-40	NA	NA	NA	
40-50	NA	NA	NA	
50-60	NA	0	1; 14,3	1
>60	1; 20	0	2; 15.4	0.97

NA: Not applicable
*Chi-Square trend analysis (z test), BMI: Body mass index

Obesity is known to be associated with many comorbid conditions. The aim of our study was to examine the effect of obesity in terms of survival and follow-up in ICU, considering age groups and gender.

There is an obesity epidemic all over the World. Obesity is also a growing health problem in Turkey. In the recent national health statistics data, it has been emphasized that the rate of obese people in both genders has increased (females 24.8% males 17.3%) (accessed from http://www.tuik.gov.tr/PreHaberBultenleri.do?id=33661). In 2017-2018 the prevalence of obesity in the USA was 42.4% and among them, 9.2% had BMI >40 kg/m^2 (accessed from https://www.cdc.gov/obesity/data/adult.html). Obesity has negative consequences on the lives of individuals and communities. It is associated with many comorbidities (5). Obesity is accompanied by several COVID-19 risk factors (e.g diabetes mellitus, hypertension) (6). Obesity was observed to be associated with severe disease during the H1N1 epidemic (7). Experiences gained in the H1N1 epidemic can also provide insight into COVID-19 cases. Given the growing COVID-19 outbreak in countries with a high prevalence of obesity such as the USA, UK, and Mexico, clarification of the relationship between obesity and COVID-19 severity seems to be very important (8-11). A study conducted in France found that after standardization according to age and gender, the prevalence of obesity in severe COVID-19 patients was 1.35 times higher than the general French population (8). In contrast, obesity was not associated with mortality in the Chinese case series (1). However, although the rate of diseases associated with obesity such as diabetes, hypertension, and coronary artery disease was high in some case series reported from China, obesity was not reported among the underlying conditions (12,13). We couldn't find a study from Turkey about the course of obesity in COVID-19 cases in our literature scan. The median BMI of the patients who died in our study was not different from the survivors.

In addition, according to the WHO classification, mortality rates in the obese group were not higher than in the surviving group. Simonnet et al. (14) demonstrated a relationship between obesity and disease severity in patients followed with a diagnosis of COVID-19 (14). In a study examining the recent national data in Mexico, higher mortality rates (13.5% vs 9.4%), hospitalization, and pneumonia were observed in obese COVID-19 cases. In addition, they noted that obese patients were followed in the ICU at a higher rate (5.0% versus 3.3%) and needed mechanical ventilation at a higher rate (5.2% versus 3.3%) (10). Similarly, another study demonstrated that the rates of being followed in the ICU in the presence of obesity were 1.89 times higher (8). In our study, the mean BMI of patients followed in the ICU was higher than those followed in the ward and the rate of obesity was higher in patients followed in ICU. A previous study demonstrated that mortality increased in the presence of obesity in patients <40 years old. In the same study obesity, early-onset diabetes mellitus, and accompanying co-morbidities also increased mortality (10). Unlike this, we did not observe the effect of obesity on mortality in young patients.

In a study examining New York City data, BMI >30 kg/m^2 in COVID-19 cases <60 years of age was a risk factor for follow-up in the ICU (9). In the subgroup analysis of our study, mortality in >60 years of age males was higher than other age groups and females. This result suggested that factors affecting mortality in young patients should be evaluated.

Conclusion

In conclusion, the obesity epidemic in many countries, including the USA and Turkey, should cause worry as much as the COVID-19 pandemic. Obesity, by itself and with accompanying diseases, is a poor prognostic factor for many diseases including COVID-19. Therefore, it is clear that short and long-term national and international strategies should be determined in the fight against obesity.

Ethics

Ethics Committee Approval: Bezmialem Vakıf University Clinical Research Ethics Committee (no: 71306642-050.05.04-)

Peer-review: Externally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: A.B.K., Concept: S.B., Design: S.B., Data Collection or Processing: M.E.Ö., Ç.E., Analysis or Interpretation: S.B., Literature Search: S.B., G.O., A.B.K., B.D., Y.A., M.M.K., Writing: S.B., M.E.Ö., Ç.E., G.O., B.S., A.B.K., B.D., Y.A., M.M.K.

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

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Original Article

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Is Online Pregnant School Training Effective in Reducing the Anxiety of Pregnant Women and Their Partners During the COVID-19 Pandemic?

COVİD-19 Pandemi Döneminde Online Yapılan Gebe Okulu Eğitimleri Gebelerin ve Eşlerinin Anksiyetelerini Azaltmada Etkili Midir?

Yeliz DOĞAN MERİH[1], Özlem KARABULUT[2], Aytül SEZER[3]

[1]University of Health Sciences Turkey Hamidiye Faculty of Nursing, Lecturer, İstanbul, Turkey
[2]University of Health Sciences Turkey, Zeynep Kamil Women's and Children's Diseases Training and Research Hospital, Pregnancy School, İstanbul, Turkey
[3]University of Health Sciences Turkey, Zeynep Kamil Women's and Children's Diseases Training and Research Hospital Coordinator Nurse, İstanbul, Turkey

ABSTRACT

Objective: The aim of this study was to determine the views of pregnant women and their spouses on the coronavirus disease-19 (COVID-19) pandemic process, to support pregnant women and their spouses through online pregnancy school training, and to decrease their anxiety levels.

Methods: The universe of this semi-experimental study with pre-and post-training model consisted of all pregnant women presenting at the pregnancy monitoring service of an Obstetrics and Pediatrics Training and Research Hospital in the Anatolian side of Istanbul between April and May 2020. 90 people (45 pregnant women and 45 spouses) who met inclusion criteria were included in the study. Data were collected using a questionnaire including the demographic of the participants as well as their views on the COVID-19 process and the Beck Anxiety Inventory. Study data were evaluated using percentages, mean values, the chi-square test, and one-way ANOVA.

Results: In the study, the anxiety scores in both groups were found to decrease (the pre-education score of the mothers is 9.05±7.29 and the post-education score is 5.56±5.38, the pre-education score of the fathers is 3.13±3.60 and the post-education score is 2.02±2.49) significantly after training ($p<0.05$).

Conclusion: Online pregnancy school for pregnant women and their spouses during the COVID-19 pandemic period was effective in reducing the anxiety levels of the parents.

Keywords: Anxiety, COVID-19 training, pregnancy, pandemic

ÖZ

Amaç: Çalışma, pandemi döneminde gebelerin ve eşlerinin koronavirüs hastalığı-19 (COVİD-19) pandemi sürecine yönelik görüşlerini belirlemek, online yapılan gebe okulu eğitimleri ile gebe ve eşlerini destelemek, anksiyete oranlarını azaltmak amacıyla gerçekleştirilmiştir.

Yöntemler: Eğitim öncesi-sonrası modelli yarı deneysel çalışmanın evrenini, İstanbul ili Anadolu yakasında bulunan kadın ve çocuk hastalıkları eğitim ve araştırma hastanesinin gebe izlemine Nisan-Mayıs 2020 tarihleri arasında başvuran gebeler oluşturmuştur. Örnekleme alınma kriterlerine uyan 90 kişi (45 gebe ve 45 eş) dahil edilmiştir. Veriler, katılımcıların demografik, COVİD-19 sürecine yönelik görüşlerinin yer aldığı anket formu ve Beck Ankisyete Ölçeği ile toplanmıştır. Araştırmadan elde edilen veriler, yüzde, ortalama, ki-kare testi, t-testi ve one-way ANOVA testleri ile kullanılmıştır.

Bulgular: Çalışmada her iki grupta da eğitim sonrası anksiyete puanlarının düştüğü (annelerin eğitim öncesi puanı 9,05±7,29 ve eğitim sonrası puanı 5,56±5,38, babaların eğitim öncesi puanı 3,13±3,60 ve eğitim sonrası puan 2,02±2,49) ve aradaki farkın istatistiksel açıdan anlamlı olduğu belirlenmiştir ($p<0,05$).

Sonuç: COVİD-19 pandemi döneminde gebe ve eşlerine uygulanan online gebe okulunun anne-baba adaylarının anksiyete düzeylerini azaltmada etkili olduğu belirlenmiştir.

Anahtar Sözcükler: Ankisyete, COVİD-19, eğitim, gebelik, pandemi

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Address for Correspondence: Yeliz DOĞAN MERİH, University of Health Sciences Turkey, Zeynep Kamil Women's and Children's Diseases Training and Research Hospital, Pregnancy School, İstanbul, Turkey, University of Health Sciences Turkey Hamidiye Faculty of Nursing, Health Care Services Manager, İstanbul, Turkey
E-mail: yelizmrh@gmail.com **ORCID ID:** orcid.org/0000-0002-6112-0642

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Introduction

Although pregnancy is a physiological process for women, it is a period in which important biological and psychosocial changes occur, and the risk of encountering factors that may cause stress and anxiety is high (1). Women perceive pregnancy as a source of joy, satisfaction, maturity, self-realization, and happiness, as well as a period in which negative psychological emotions such as stress, anxiety, anxious anticipation, and overloading can be experienced (2).

Anxiety is a disturbing feeling which is life-threatening or perceived to be life-threatening and expressed with words such as apprehension and worry. It is an emotional situation experienced in the face of the possibility of danger from the internal or external world or any situation perceived and interpreted as dangerous by the person (3). Most of the physiological conditions seen in pregnancy are very similar to anxiety symptoms, so anxiety disorders are masked in pregnant women. Clinicians need to be careful about this (4). The rates of depression and anxiety disorders in pregnancy reported in studies conducted in the last 30 years vary, but the rates generally reported are higher than the rates in the general population (5-7). Previous studies found that the frequency of depression and depressive symptoms during pregnancy varies between 5-51% (8). In one of the few studies on this subject in Turkey, according to the Beck Depression Inventory (limit 17 and above), the incidence of depressive symptoms was found between 10-15% (9).

Each woman's reaction to pregnancy varies according to her mental, socioeconomic, and cultural background. A pregnancy which increases the love between spouses and strengthens the foundations of marriage leads to hormonal changes that induces psychological changes in women (10). As a new stage in human life, parenting is a stressful situation for spouses. When this stress is combined with the possibility that everything will not go well during pregnancy, it creates a heavy burden for parents, thus affecting family and public health (10).

Since many of the symptoms seen during pregnancy are similar to anxiety symptoms, the anxiety may be masked (11). Since this situation creates a problem also for Turkey, comprehensive training that includes information about pregnancy, birth, and puerperium and support should be provided (12). Pregnancy education classes, which have an important place today, make it easier for parents to adapt to the periods of pregnancy, birth, and puerperium, prepare couples for the parenting process, increase the harmony between spouses, and reduce anxiety (13,14). In addition, women who get training during pregnancy, childbirth, and postpartum periods perceive a higher quality of life after pregnancy and postpartum, learn to cope with problems such as fear of childbirth and labor pain, and experience less stress related to pregnancy (15).

There are many factors affecting the anxiety levels of expectant mothers and fathers during pregnancy. In many studies, it has been shown that depression and anxiety during pregnancy can be related to age, marital status, number of children, education level, smoking, alcohol and substance use, the trimester of pregnancy, whether the pregnancy is voluntary, sociodemographic characteristics, and previous illnesses and crises (16-19).

Coronavirus disease-19 (COVID-19) has gradually spread around the world and turned into a pandemic. Its rapid spread, lack of a cure, and its fatality increase the effect of the disease. An increased sensitivity has not been reported in pregnant women compared to the general population. However, because pregnant women are more susceptible to diseases than non-pregnant women, their morbidity and mortality are higher, and similar viruses like severe acute respiratory syndrome-CoV (SARS-CoV) and Middle East respiratory syndrome-CoV (MERS-CoV) infections caused high mortality rates the management of suspicious or infected pregnant women should be done by a competent multidisciplinary team. Limited information is available on pregnant women and management is like non-pregnant women for now. Fetal distress and premature birth have been observed in some pregnant women. There is no evidence yet that it passes from mother to baby. In pregnancy and delivery management, isolation under appropriate conditions, aggressive infection control, early mechanical ventilation in progressive respiratory problems, oxygen therapy, avoiding excess fluid, and strict fetal, and uterine monitoring are necessary (20).

The COVID-19 pandemic caused an increase in anxiety rates in pregnant women and their families, especially in the risky group, as in the whole society. In this pandemic period where many physical, social, and psychological changes have been experienced, the effective use of infection control measures for the protection of physical and mental health, as well as the development of solution-oriented approaches, information sharing, and individual coping methods are of great importance.

Midwives and nurses are the closest healthcare personnel who determine the risk factors that may occur during pregnancy, create self-confidence in the mother with their knowledge and experience, provide awareness in maternal-fetal interaction, support the preparation of the pregnant for motherhood, help regulate family relations, and provide consultancy to women (21-23). Several studies indicated that pregnant women who have received antenatal training use less medication, have less anxiety, and have less depression in the postpartum period. According to the circular issued in 2014 by the Ministry of Health Public Health Agency of Turkey, to be informed during pregnancy is a right of motherhood. In this context, they recommended that pregnant information schools initiated as soon as possible in institutions affiliated with the Public Health Authority and the Association of Public Hospitals. With this circular, pregnancy schools have become widespread in Turkey (24,25). We believe that evaluating the contributions of the pregnancy school and determining women's opinions and suggestions about this training will contribute to those who plan to implement pregnancy schools.

During the pandemic, many processes were suspended due to the importance of home isolation. Pregnancy schools are among the suspended services. We planned our study considering the necessity of pregnancy schools and created live online pregnancy

schools. Pregnant women and their spouses were provided with pregnancy school services in safe home conditions. We designed a semi-experimental study with a pre-and post-training model without a control group to evaluate the effect of online pregnancy school on anxiety levels during the COVID-19 pandemic.

The Hypothesis of the Study

H0: Online pregnancy school training do not have a positive effect on reducing the anxiety rates of pregnant women and their partners.

H1: Online pregnancy school training has a positive effect on reducing the anxiety rates of pregnant women and their spouses.

Method

This study was performed between April and May 2020 at an Obstetrics and Pediatrics Training and Research Hospital in the Anatolian side of Istanbul.

Sample and Universe

The study universe consisted of pregnant women who applied to the pregnant follow-up clinic of the hospital during the study period. The study sample included pregnant women and their partners who were between 20-45 years old, whose pregnancy week was 30 or above, who could speak and understand Turkish, and who volunteered to participate in the live online pregnancy school. The study sample consisted of 45 pregnant women and their 45 partners.

Tools for Data Collection

Data were collected using a questionnaire containing demographic, individual, and obstetric characteristics of the participants, their opinions about the COVID-19 process, and the beck anxiety scale.

Pregnant data form: Pregnant data form which was prepared by researchers in accordance with the literature included 25 questions about socio demography (age, year of marriage, education, employment, economic status, family type, having a chronic illness) (1,2,10,15,16), obstetric history (pregnancy week, whether the pregnancy was wanted, route of conception, problems in pregnancy, training about pregnancy, opinions about pregnancy schools) (1,2,10,15,16), opinions about the COVID-19 pandemic, and evaluation of the training.

Spouse data form: Spouse data form which was prepared by researchers in accordance with the literature included 20 questions about socio demography (age, marriage year, education, employment, economic status, family type, having a chronic disease) (1,2,10,15,16), opinions about pregnancy school, opinions about the COVID-19 pandemic, and evaluation of training they received.

Beck anxiety inventory (BAI): This scale was given to pregnant women and their spouses at the first interview and at the end of the training. The scale was developed by Beck et al. (1988) and adapted to Turkish by Ulusoy et al. (26). The scale has been found to have sufficient reliability and validity (25). BAI evaluates the frequency of anxiety symptoms experienced by the individual. It is a self-rating scale, consisting of 21 items scored between 0 and 3. Questions are asked to understand the level of disturbance caused by distress feelings last week. The score range is between 0 to 63. The higher the score obtained from the scale, the more severe the anxiety experienced by the individual. For Beck Anxiety Inventory 0-7 points indicate minimal anxiety, 8-15 points indicate mild anxiety, 16-25 points indicate moderate anxiety, and 26-63 points indicate severe anxiety (26). Permission to use the scale was obtained.

Content of Online Birth and Baby Preparation Training

- **Scope of Training**: The training was planned as 6 sessions of online meeting and training program (a 6-day program was designed, all sessions were attended by pregnant women and their spouses together).

- **Training hours**: Each session was 3 hours, with 10 minutes breaks in between.

- **Training program**: The training program was shared with the participants in advance (birth preparation training in the 1st and 2nd sessions, preparation to breastfeeding training in the 3rd session, baby care training in the 4th session, adaptation to the postpartum process, parenting process, reproductive health and sexuality, family planning and evaluation of the whole training program and opinions and suggestions in the 5th and 6th sessions). Online Birth Preparation training was enriched with supportive meditation, imagination, presentations, videos, games, painting works that support the expression of emotions, and drama games for expectant mothers and fathers.

- **Educator:** Training was provided by Zeynep Kamil Hospital Pregnancy School Educator Midwife Özlem Karabulut.

Data Collection

- The pregnant women who came to the pregnant follow-up department of the hospital for control and who met the sampling criteria were informed about the study, the pregnant women who agreed to participate in the study were informed about the online education process, and their consents were obtained.

- The pregnant women and their spouses who would participate in the live online (zoom) pregnancy school training group were informed by the researchers about the content and program.

- On the first day of training, the relevant data forms were first sent to the participants by e-mail and they were asked to fill them out.

- After the data forms were filled, training including pregnancy, birth, postnatal process, and baby care processes were given by the maternity school educator with the interactive participation of the participants. At the end of the training, feedback was received.

➢ After the completion of the training, the training evaluation form and Beck Anxiety form were given again and the process was evaluated.

Ethical Aspect of the Research

Institutional permission from the institution where the research was conducted and approval from the ethics committee was obtained. Written consent was taken after the pregnant women participating in the study and their spouses were informed about the purpose of the study and it was explained that the obtained information would only be used for this study.

Analysis of Data

The socio-demographic and obstetric characteristics of the pregnant women participating in the study were evaluated using the percentage, the chi-square test was used to test the relationships between categorical variables, t-test for independent groups and the One-Way ANOVA parametric test were used to analyze normally distributed data. SPSS 15 package program was used in the analysis of the data and the level of significance was taken as 0.05.

Results

The mean age of the pregnant women participating in the study was 29.44±4.43, the mean age of the spouses was 32.58±5.37, and the duration of marriage was 3.01±1.91 years. Most of the pregnant women (97.8%) received high school or higher education, 73.4% were employed, 60.0% evaluated their income as moderate, 77.8% did not have a chronic disease, 84.4% did not smoke, 73.3% did not use alcohol, and 71.2% their mental state as good. All of the spouses (100.0%) received high school or higher education, most (95.6%) worked, 51.1% evaluated their income as moderate, 88.9% did not have a chronic disease, 77.8% did not smoke, 86.7% did not use alcohol, 86.7% evaluated their mental state as good. 93.4% of the participants had social security, and most (97.8%) had a nuclear family structure (Table 1).

The obstetric characteristics of pregnant women participating in the study are given in Table 2. Among the pregnant women, 73.3% were primiparous, 93.4% got pregnant voluntarily, 88.9% had their pregnancy without any problems, most (91.2%) attended to regular pregnancy control visits, 37.8% had received information during a previous pregnancy, and in 44.4% primary source of information was TV and internet.

Participants' views on the functioning of the pregnancy school are given in Table 3. Most of the participants (77.8% of the pregnant women, 82.2% of the fathers) found themselves competent in pregnancy, childbirth, and puerperium, they had attended a limited number of pregnant school training before and stated that it was not good to suspend the birth preparation training (62.2% of the pregnant women, 71.1% of the fathers). They mostly wanted preparatory education to be delivered online as remote education (95.6% of the pregnant women, and 100.0% of the fathers).

Table 1. Distribution of participants by demographic and health histories

Individual features		Mother		Father	
		N	%	N	%
Age distribution	20-25 years	7	15.5	2	4.4
	26-31 years	**24**	**53.3**	**18**	**40.0**
	32-37 years	12	26.6	21	46.6
	38-43 years	1	2.2	4	8.8
Education status	Primary school	1	2.2	-	-
	High school and above	**44**	**97.8**	**45**	**100.0**
Employment status	**Employed**	**33**	**73.4**	**43**	**95.6**
	Unemployed	12	26.6	2	4.4
Monthly income	Good	16	25.6	20	44.4
	Moderate	**27**	**60.0**	**23**	**51.1**
	Bad	2	4.4	2	4.4
Health history		**Mother**		**Father**	
N		**%**	**N**	**%**	
Chronic disease	Yes	10	22.2	5	11.1
	No	**35**	**77.8**	**40**	**88.9**
Smoking	Yes	2	4.4	10	22.2
	No	**38**	**84.4**	**35**	**77.8**
	Stopped due to pregnancy	5	11.1	-	-
Alcohol use	Yes	-	-	6	13.3
	No	**33**	**73.3**	**39**	**86.7**
	Stopped due to pregnancy	12	26.7	-	-
Mental self-evaluation	Good	**32**	**71.2**	**39**	**86.7**
	Moderate	2	4.4	6	13.3
	Bad	11	24.4	-	-
Total		**45**	**100.0**	**45**	**100.0**

Topics that the participants want to be included in the online birth preparation training is given in Table 4. Both the pregnant women and their spouses wanted all issues regarding the pregnancy process and baby care to be included in their training.

Table 5 includes the opinions of the participants about COVID-19 infection control measures. Participants generally knew COVID-19 infection control measures (93.3% pregnant women, 93.3% fathers), applied protection measures at high rates (97.8% of the pregnant women, 93.3% of the fathers), and could apply social distance and isolation rules at home conditions (77.8% of the pregnant women, 80.0% of the fathers).

The concerns of the participants during the COVID-19 pandemic are evaluated in Table 6. Pregnant women stated that during the pandemic period their concerns were the absence of spouse or a relative at birth (86.2%), the risk of contracting COVID-19 infection from healthcare workers (82.2%) and experiencing pain with a mask (82.2%). Concerns of the fathers

Table 2. Distribution of mothers by obstetric characteristics

Features		N	%
Number of pregnancies	**1**	**33**	**73.3**
	2-3	12	26.7
Was the latest pregnancy wanted?	**Yes**	**42**	**93.4**
	No	13	6.6
Was there a problem with the latest pregnancy?	Yes	5	11.1
	No	**40**	**88.9**
Attended to routine controls during the latest pregnancy	**Yes**	**41**	**91.2**
	No	4	8.8
Got training/information during pregnancy	Yes	17	37.8
	No	**28**	**62.2**
Source of information/training about post-natal care in pregnancy	**TV, internet**	**20**	**44.4**
	Relative, friend	10	32.2
	Doctor	5	11.1
	Nurse, midwife	2	4.4
	Book	11	24.4
Total		**45**	**100.0**

Table 3. Opinions of the participants about pregnancy school

Individual characteristics		Mother		Father	
		N	%	N	%
Feels sufficient about pregnancy, childbirth, and puerperium	Yes	10	32.2	8	17.8
	No	**35**	**77.8**	**37**	**82.2**
Previously attended pregnancy training	Yes	9	20.0	6	13.3
	No	**39**	**86.7**	**36**	**80.0**
Opinion about the suspension of birth preparation training	Good	7	15.6	2	4.4
	Indecisive	10	22.2	11	24.4
	Bad	**28**	**62.2**	**32**	**71.1**
Requesting that the childbirth preparation training be given online	**Yes**	**43**	**95.6**	**45**	**100.0**
	No	2	4.4	-	-
Total		**45**	**100.0**	**45**	**100.0**

were not being with their wives during birth (82.2%), getting COVID-19 infection from another patient (80%), or from healthcare workers (75.6%).

Opinions of the pregnant women and their spouses about the education were taken after the live online pregnancy school training (Table 7). 88.9% of the pregnant women and all of the spouses were very satisfied with the training. Participants were asked about what they were most satisfied with during the online birth preparation training. Both the pregnant women and their spouses (33.3% of the pregnant women, 31.1% of the spouses) stated that being together with different families and sharing their experiences made them happy, and also receiving counseling relieved the participants and reduced their stress (28.9% of the pregnant women, 31.1% of the spouses).

The mean BAI score of the pregnant women before the training was 9.05±7.29, and the mean BAI score of the fathers was 3.13±3.60. Anxiety scores decreased after the education in both groups. After the training, the mean BAI score of the pregnant women was 5.56±5.38 and the fathers was 2.02±2.49 and the difference was statistically significant ($p<0.05$) (Table 8).

Discussion

Good mental health during pregnancy is important for maternal and fetal health. It is known that mental illnesses can affect the mood of the mother and cause negative consequences related to pregnancy and increase maternal and fetal morbidity and mortality rate in those who do not receive treatment (27). It is important to recognize and prevent psychosocial reactions as well as physiological reactions during pregnancy, to reduce their effects on maternal and child health and to improve preventive mental health services. Thus, psychological evaluation as well as physical evaluation during pregnancy follow-up is important for a holistic approach (28,29). Psychosocial health and social support, which may affect the pregnant woman's adaptation processes to pregnancy, birth and parenthood, should have an important place in the nursing care of the pregnant woman and her family (10,30). During prenatal follow-up, nurses and midwives often play the roles of educators and counselors to identify, protect and improve the psychosocial health status of pregnant women. It is important to evaluate the psychosocial health as well as physical health during the nursing and midwifery process, which includes the follow-up and care of the pregnant woman, to determine the effects of family, culture, religion and other factors during pregnancy, and to reveal the social support of prospective parents (30,31).

We planned our study considering the necessity of pregnancy schools and provided pregnant women and their spouses pregnancy school online in safe home conditions. Our aims were to determine the opinions of pregnant women and their spouses about the COVID-19 process during the pandemic period, to create awareness about the process, to support pregnant women and their spouses with online pregnancy school trainings, and to reduce anxiety rates.

The amean age of the pregnant women participating in our study was 29.44±4.43, the mean age of the spouses was 32.58±5.37, and the mean duration of marriage was 3.01±1.91 years. Most of the participants received high school or higher education, did not have chronic illnesses, did not smoke and drink alcohol, and evaluated their mental state as good. 93.4% of the participants had social security and most (97.8%) of them had nuclear family structure (Table 1).

Similar results have been reported in other studies conducted with pregnant women (32-34). In these studies, Özkan and Arslan (32) reported that 79% of the pregnant women were between 20-29, Tunç et al. (35) reported that 33% of the pregnant women were between 23-27, Demirbas et al. (36) reported that 56.2% of the pregnant women were between 18-29 (36) and Ozcelik and Larch (33) reported that 56.5% of the pregnant

Table 4. Distribution of the topics that the participants wanted to be included in online birth preparation training

Topics Related to pregnancy	Mother				Father			
	Necessary		Unnecessary		Necessary		Unnecessary	
	N	%	N	%	N	%	N	%
Pregnancy-related changes	41	91.1	4	8.9	40	88.9	5	11.1
Nutrition	39	86.7	6	13.3	45	100.0	-	-
Hygiene	38	84.4	7	15.6	43	95.6	2	4.4
Sleep and rest	39	86.7	6	13.3	42	93.4	3	6.6
Excretory habits	44	97.8	1	2.2	44	97.8	1	2.2
Perineum care	45	100.0	-	-	45	100.0	-	-
Pregnancy follow-ups	44	97.8	1	2.2	45	100.0	-	-
Infection control measures	45	100.0	-	-	45	100.0	-	-
Physical activity and exercises	42	93.3	3	6.7	45	100.0	-	-
Emotional coping methods	44	97.8	1	2.2	45	100.0	-	-
Parent role and family communication process	44	97.8	1	2.2	44	97.8	1	2.2
Topics related to baby	**N**	**%**	**N**	**%**	**N**	**%**	**N**	%
Breastfeeding	44	97.8	1	2.2	44	97.8	1	2.2
Bathing	42	93.3	3	6.7	40	88.9	5	11.1
Babycare	44	97.8	1	2.2	43	95.6	2	4.4
Dressing	42	93.3	3	6.7	39	86.7	6	13.3
Sleep	43	95.6	2	4.4	42	93.4	3	6.6
Burping	44	97.8	1	2.2	44	97.8	1	2.2
Vaccination	43	95.6	2	4.4	42	93.4	3	6.6
Routine controls	43	95.6	2	4.4	43	95.6	2	4.4
Excretory problems	44	97.8	1	2.2	44	97.8	1	2.2
Infections	45	100.0	0	0	45	100.0	0	0.0
Total	**45**	**100.0**	**45**	**100.0**	**45**	**100.0**	**45**	**100.0**

women were between 28-32 years old. In our study most of the participants received high school and higher education. In other studies conducted with pregnant women in Turkey, majority of women were primary school graduates (2,9,12,15,37). The higher education level of the participants in our study compared to other studies was due to the fact that the participants who cared about pregnancy school training and wanted to receive education were included in our study. In addition, the presence of participants with a high level of education will be effective in their better adaptation to pregnancy process. In this study, 73.3% of the pregnant women were primipars, 93.4% of them got pregnant willingly, and most of them (91.2%) attended to regular pregnancy controls (Tablo 2). The high education level of the participants was effective in the high rate of receiving antenatal care (ANC).

The rates of ANC varies in different countries (38). According to Turkey Demographic Health Survey, 90% of women recieved 4 or more times antenatal care (39). Among similar field studies conducted in Turkey, all pregnant women in Burdur received ANC at least once, while 1.7% of pregnant women in Adiyaman, and 0.6% in Istanbul didn't to receive ANC from their obstetrist or primary care physician (40).

The opinions of the participants about the functioning of the pregnancy school are given in Table 3. Participants mostly (77.8% of the pregnant women, and 82.2% of the fathers) considered themselves competent in pregnancy, birth, puerperium, and stated that suspending the birth preparation trainings during the pandemic period was not good (62.2% of the pregnant women, 71.1% of the fathers). Most of them (95.6% of the pregnant women, 100% of the fathers) wanted to get birth preparation training online.

Although birth is a natural process, women have significant fears about childbirth and prenatal training is required to cope with these fears (41,42). In order to protect and improve psychosocial health, a nurse becomes an important member of the healthcare team that allows the pregnant women and her families to express their feelings and concerns, use positive coping strategies, and regulate family relationships during prenatal follow-up. In addition, it is among the duties of the nurse to determine the existing social support systems in this process and to ensure that the pregnant women and their families use them effectively (30,31). Pregnancy schools have important roles in protecting and improving the psychosocial health of both pregnant women and their families. At first, pregnancy schools were opened to encourage normal birth, but later on prenatal, birth and postnatal

Table 5. Participants' opinions on COVID-19 infection control measures

Opinions	Mother						Father					
	Yes		Indecisive		No		Yes		Indecisive		No	
	N	%	N	%	N	%	N	%	N	%	N	%
Do you know what a COVID infection is?	42	93.3	3	6.7	-	-	42	93.3	3	6.7	-	-
Can COVID infection be prevented?	31	68.9	13	28.9	1	2.2	37	82.2	7	15.6	1	2.2
Is hand hygiene important to prevent COVID infection?	44	97.8	1	2.2	-	-	45	100.0	-	-	-	-
Should hand sanitizer be used to prevent COVID infection?	36	80.0	7	15.6	2	4.4	41	91.1	3	6.7	1	2.2
Should a mask be worn to protect against COVID infection?	40	88.9	5	11.1	-	-	44	97.8	1	2.2	-	-
Do you think home isolation is important to prevent COVID infection?	42	93.3	2	4.4	1	2.2	45	100.0	-	-	-	-
Do you know what social distance means to protect from COVID infection?	45	100.0	-	-	-	-	45	100.0	-	-	-	-
Do you implement precautions to protect against COVID infection during pregnancy?	44	97.8	1	2.2	-	-	42	93.3	3	6.7	-	-
Do you think you have enough information about measures to protect against COVID infection?	39	86.7	6	13.3	-	-	36	80.0	3	6.7	6	13.3
Can you apply social distance and isolation rules in home conditions?	35	77.8	4	8.9	6	13.3	36	80.0	3	6.7	6	13.3
Do you know the precautions that your relatives living at home should take for infection control?	42	93.3	3	6.7	-	-	41	91.1	1	2.2	3	6.7
Total	**45**	**100.0**	**45**	**100.0**	**45**	**100.0**	**45**	**100.0**	**45**	**100.0**	**45**	**100.0**

COVID: Coronavirus disease

care, healthy lifestyle habits, and reducing anxiety and depression levels began to be addressed (31).

In this study, both the pregnant women and their spouses wanted all subjects related to pregnancy process and baby care to be included in their training process (Table 4). Previous studies stated that pregnancy schools aim to provide expectant mothers with knowledge and skills on issues related to pregnancy, birth and the postpartum period, normal labor, pain management, and adaptation to new roles (43). Our results were in accordance with the literature.

We also evaluated the opinions and concerns of the participants about the COVID-19 pandemic. Based on the opinions and training needs, online pregnancy schools werte planned. The participants were generally (93.3% pregnant women, 93.3% fathers) knowledgeable about COVID-19 infection control measures and applied protection measures at high rates (97.8% of the pregnant, 93.3% of the fathers). When the concerns of the participants about the pandemic period were evaluated, pregnant women mostly worried from not to have a spouse or a relative at birth (86.2%), getting COVID-19 infection from healthcare workers (82.2%), and experiencing pain with a mask (82.2%). Concerns of the fathers were not being with their wives during birth (82.2%), getting COVID-19 infection from another patient (80%), or from healthcare workers (75.6%) (Table 6).

CoVs are important human and animal pathogens. In February 2020, the World Health Organization identified COVID-19 disease, which stands for 2019 coronavirus disease. Coronavirus infection spread around the world, causing a pandemic. Its rapid spread, lack of treatment and fatal course make the effects of the virus important. The high mortality and morbidity of the disease increases the clinical importance of this infection. There is limited information about infection in pregnant women and it is recommended that management be done like non-pregnant women for now. Fetal distress and premature birth have been observed in some pregnant women. There is no evidence yet for mother-to-baby transmission. Isolation under appropriate conditions, effective control and management of infection, early mechanical ventilation in progressive respiratory problems, oxygen therapy, avoidance of excess fluid treatment, and strict fetal and uterine monitoring are required in pregnancy and delivery management. Management of suspected or infected pregnant women should be done by a multidisciplinary team (20,44). The fact that the pandemic process is widespread and uncertain has increased the concerns of pregnant women and their families, especially in the risky group. During this period, it is important that all healthcare team members take a holistic role and activate support processes.

The status of the mother changes in the family and society with pregnancy and childbirth, she assumes new responsibilities and

Table 6. Participants' concerns about COVID-19 Infection

Concerns of mothers about COVID-19 infection	Yes		Unstable		No	
	N	%	N	%	N	%
I do not want to go to follow-ups just because I fear to get COVID-19 infection from hospitals	29	64.4	10	22.2	6	15.3
Have enough precautions been taken in the hospital where I am being followed up for the pregnancy? Are there any COVID-19 patients?	25	55.6	17	37.8	3	6.7
May I contract COVID-19 infection from healthcare workers?	37	82.2	8	17.8	-	-
My husband is working and I'm afraid he might bring home COVID-19	22	48.9	9	20.0	14	31.1
If I get COVID-19 infection during pregnancy, will my baby be harmed?	28	62.2	11	24.4	6	13.3
Even if I do not have an infection, is there a risk of transmission from another patient during or after birth in the hospital?	35	77.8	10	22.2	-	-
Do interventions increase in this period to accelerate birth?	25	55.6	14	31.1	6	13.3
I'm afraid of not getting physical support at birth	30	66.7	8	17.8	7	15.5
Not to have my husband or a relative with me during birth worries me.	39	86.2	6	13.3	-	-
Experiencing the pain with a mask worries me	37	82.2	3	6.7	5	11.1
Will they direct me for a planned cesarean instead of a normal delivery?	26	57.8	9	20.0	10	22.2
If I become COVID-19 positive, can I breastfeed my baby?	33	73.3	8	17.8	7	6.9
Who will take care of my baby if I am sick?	29	64.4	10	22.2	6	13.3
I will not be able to get support from elders after birth, I have fears about breastfeeding and baby care.	31	68.9	2	4.4	12	26.7
I am worried about going to the health institution for the vaccinations and control of my baby, how can I take precautions.	36	80.0	5	11.1	4	8.9
Fathers' concerns about COVID-19 infection	**Yes**		**Indecisive**		**No**	
	N	**%**	**N**	**%**	**N**	**%**
I do not want to take my wife to follow-ups just because we can catch COVID-19 infection from hospitals.	21	46.7	12	26.7	12	26.7
May I contract COVID-19 infection from healthcare workers?	34	75.6	10	22.2	1	2.2
I am working and I'm afraid I bring home COVID-19	30	66.7	5	11.1	10	22.2
Who cares for my family if I get COVID-19 disease?	20	44.4	12	26.7	13	28.9
If my wife gets COVID infection, will our baby be harmed?	29	64.4	9	20.0	7	15.6
Is there a risk my wife contracts COVID infection at a hospital during or after birth?	36	80.0	8	17.8	1	2.2
I am worried that I can't be with my wife during birth.	37	82.2	6	13.3	2	4.4
Will they direct me for a planned cesarean instead of a normal delivery?	15	33.3	14	31.1	16	35.6
If my wife becomes ill, who will take care of our baby?	18	40.0	13	28.9	14	26.7
We are afraid that we will not be able to get support from elders after birth	20	44.4	8	17.8	17	37.8
Total	**45**	**100.0**	**45**	**100.0**	**45**	**100.0**

COVID-19: Coronavirus disease-19

has to fulfill new roles. These mandatory roles and responsibilities that need to be fulfilled may lead to adaptation problems in some individuals. Also, pregnancy is an important time of psychosocial and developmental transition and adaptation. Adaptation to pregnancy and the changes it brings is perceived differently by every woman and family, and therefore different reactions and problems may arise in adaptation (45-47). Social support, spouse and marital harmony are of great importance in adaptation to pregnancy. Social support, which is defined as the total support provided by family members, friends and other social relationships, has positive effects on physical health and well-being (48) because social support systems make it easier to adapt to new situations (49). Considering that psychosocial and developmental transition and adaptation problems are experienced even during normal pregnancy, adjustment problems, anxiety, and increased need for social support may be expected during pandemic process. In our study, as expected pregnant women and their spouses had high anxiety rates regarding the COVID-19 pandemic process and expressed their needs in this regard.

The prevalence of psychosocial health problems such as depression, anxiety and stress is high during pregnancy and

Table 7. Participants' opinions on online birth preparation trainings

Opinions		Mother		Father	
		N	%	N	%
Did the online birth preparation training meet your expectations?	Yes, I was very pleased	**40**	**88.9**	**45**	**100.0**
	It met my expectations moderately	5	11.1	-	-
On which subject online birth preparation training pleased you the most?	I was able to get the information I needed	7	15.6	17	37.8
	Counseling relaxed me, my stress relieved	13	28.9	14	31.1
	It made me happy to be together with different families online and to share experiences.	**15**	**33.3**	**14**	**31.1**
	I learned more about COVID infection and prevention methods	9	20.0	-	-
	Other	1	2.2	-	-
Total		**45**	**100.0**	**45**	**100.0**

COVID: Coronavirus disease

Table 8. Comparison of participants' mean beck anxiety scale scores before and after training

Features		Mean ± SD	p
Mothers' BAI scores	Before training	9.05±7.29	0.000
	After training	5.56±5.38	
Fathers' BAI scores	Before traning	3.13±3.60	0.000
	After training	2.02±2.49	

(p<0.05), SD: Standard deviation, BAI: Beck anxiety inventory

these psychosocial health problems can negatively affect the health of both pregnant women and babies (50,51). In a study that wanted to draw attention to the psychosocial health status during pregnancy, the frequency of antenatal anxiety was 20.6% and there was a relationship between education level and anxiety prevalence (52). As can be seen in the study by Agostini et al. (53), another factor that is related to the occurrence of mental problems during pregnancy which has an important role in pregnancy, and significantly affects psychosocial health, is the level of social support the woman receives (54). Elsenbruch et al. (55) found that pregnant women who did not have sufficient social support had high depressive symptoms and low quality of life. Evaluation of the studies on social support during pregnancy revealed that, another factor that can turn pregnancy into a risky period is the lack of social support systems. In addition, it is stated that the lack of social support during pregnancy negatively affects the health of the mother, fetus, and baby (33,56). A study performed by Şen and Şirin (31) with pregnant women who had preterm labor found that adequate social support decreased the rate of depression and anxiety in women, and positively affected the course of pregnancy and the health of the baby.

The opinions of the pregnant women and their spouses about the education were received after online pregnancy school. The participants were very satisfied with the training provided, they stated that especially being together with different families, sharing experiences online made them happy, and getting consultancy reduced their stress (Table 7).

Physiological and psychological changes that occur in a woman's body during pregnancy can affect not only the mother but also the people around her, her husband, family, and friends in various ways. Labor, which is the transition period for being a parent, is a temporary situation that affects both parents (17). In a study conducted with 390 women in the prenatal period, women who received information about pregnancy were more compatible with pregnancy and motherhood. The study found that women's adjustment to pregnancy was affected by many variables and prenatal care is of great importance in achieving this adjustment (36).

Previous literature reported that there may be a relationship between prenatal distress levels and the health status of the pregnant (57,58) and the first pregnancy (59). The training women received at the pregnancy school benefited both during pregnancy and the birth process (coping with labor pain, decreased birth fears) (60,61), facilitated the adjustment to pregnancy and motherhood, positively affected motivation (62), pregnant women were mostly satisfied with these training, and their level of knowledge increased significantly (63). Literature suggests that pregnancy school program has significant contributions to the pregnancy, birth, and postpartum period, and increases the adaptation of women to pregnancy. We also found that online pregnancy school, which was provided in accordance with the literature, pleased the participants, increased their awareness, and decreased stress rates.

In our study, before the training, the mean BAI score of the pregnant women was 9.05±7.29 (mild anxiety), and the mean BAI for their spouses was 3.13±3.60 (minimal anxiety), and anxiety scores decreased after the education in both groups. After the education, the mean BAI score of the pregnant women was 5.56±5.38 (minimal level of anxiety), and the mean BAI for their spouses was 2.02±2.49 (minimal level of anxiety) and the difference between pre and post-training values was statistically significant (p<0.05) (Table 8).

Population-based studies found that during pregnancy the prevalence of affective disorders was 70%, anxiety was 15-29%, and depression was 17-18% (64). Studies investigating the prevalence of depression during pregnancy in different cultures often found similar results. Lancaster et al. (49) found 18%, a

Hungarian study found 17.9%, a study from the USA found 30-38%, and a Latin American study found approximately 30% (64). Reports from Turkey found the prevalence of anxiety as 12-34% and the prevalence of depression as 19-53% (65-68).

Studies investigating the prevalence of psychological distress during pregnancy demonstrated that 13-25% of women in developed countries experience clinically significant psychological distress attacks, especially depression or anxiety disorders (69,70). Another study found the prevalence of distress in pregnancy between 41.7% and 51% (71). Studies on this topic from Turkey are limited. Karacam and Ancel found the prevalence of depressive symptoms in pregnancy as 27.3% (72). Golbaşı et al. (73) used the Edinburgh Postnatal Depression Scale (EPDS) and found the prevalence of depressive symptoms during pregnancy as 28.6%. Lee et al. found anxiety in 54% of pregnant women and depression in 37.1% (74). Studies that investigated the prevalence of anxiety and depression in Turkey and in various cultures gave similar results (16,75).

In our study, anxiety level was mild in pregnant women and minimal in their spouses. With the training program and social support process, the anxiety levels decreased in both groups, and the difference was statistically significant. With these results H1 hypothesis, "Online pregnancy school education has a positive effect on reducing the anxiety rates of pregnant women and their partners" was accepted.

It is very important for a healthy mother, baby, and family that psychosocial health, which may affect the processes of pregnancy, birth, postpartum, and parenting is addressed by nurses. Nurses are the members of the healthcare team in the most appropriate position to provide opportunities for the pregnant woman and her family by preparing an environment for expressing feelings and concerns during pregnancy, using positive coping strategies, organizing family relationships, and activating existing social support systems effectively. In this adaptation process, nurses frequently support the needs of pregnant women and their families with their educator and counselor roles. In order to protect and improve the health of the woman and her family with a holistic approach in the nursing process during the care of the pregnant woman, it is important to determine the effects of psychosocial health on pregnancy experience and the support that prospective parents receive from their social environment (24,28,30,31). In this context, nurses may activate the existing social support of pregnant women and prevent possible psychosocial health problems.

Conclusion

We found that the participants were generally knowledgeable about COVID-19 infection control measures and applied protection measures. During the pandemic, the most common worries of the pregnant women and their spouses were not to have a spouse or a relative at birth, and contracting COVID-19 from healthcare workers or other patients ($p<0.05$). We found that the changes experienced during pregnancy and the pandemic period increased the anxiety levels and supportive needs of pregnant women and their spouses.

Pregnant women need support to maintain their balance during pregnancy and birth. Health personnel who will provide this assistance must be competent in the psychological and physiological changes that will occur during pregnancy and must have developed communication skills. Together with the pregnant woman, the family and especially her husband should be educated about the physiological and psychological aspects of pregnancy. National and international support groups and antenatal mental health units should be established to provide education, support, and professional assistance to women and their spouses. For this reason, anxiety symptoms should be taken seriously, evaluated well, and pregnant women and their families should be supported with training and holistic approaches, especially during periods of radical changes such as pandemic periods.

Ethics

Ethics Committee Approval: Institutional permission from the institution where the research was conducted and approval from the ethics committee was obtained.

Informed Consent: Written consent was taken after the pregnant women participating in the study and their spouses were informed about the purpose of the study and it was explained that the obtained information would only be used for this study.

Peer-review: Externally peer reviewed.

Authorship Contributions

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

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Original Article

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Evaluation of Perceived Stress Levels of Radiology Workers Regarding COVID-19 Outbreak

Radyoloji Çalışanlarının COVİD-19 Salgınıyla İlgili Algılanan Stres Düzeylerinin Değerlendirilmesi

Hatice Nilden ARSLAN[1], Ayşegül İdil SOYLU[2]

[1]Ondokuz Mayıs University Faculty of Medicine, Department of Public Health, Samsun, Turkey
[2]Ondokuz Mayıs University Faculty of Medicine, Department of Radiology, Samsun, Turkey

ABSTRACT

Objective: The purpose of this study is to investigate the perceived stress levels of radiology workers and associated factors during the Coronavirus disease-19 (COVID-19) outbreak.

Methods: A descriptive questionnaire prepared by the researchers was completed online by employees who work in the radiology department of various health institutions in Turkey. In our study, the perceived stress scale was used. The necessary ethics approval was obtained for the study. SPSS Statistics for Windows, Version 22.0 (Armonk, NY: IBM Corp) was used for statistical analysis of the data.

Results: The average age of 573 radiology workers participating in the study was 34.0±9.3 years and 50.1% were women. The scores received by radiology workers from the perceived stress scale were 27.8±6.4 (median: 27.0, minimum-maximum: 6-50). In our study, it was determined that the perceived stress score was statistically significantly higher ($p<0.05$) in women and in those who lived with individuals over the age of 60, those working as radiology technicians, those who had a chronic disease, those who increased smoking, those who used social media more often than before, those who had not received training on COVID-19 infection, those who thought that the measures taken against COVID-19 infection were insufficient, and those who had contact with a patient with COVID-19.

Conclusion: In our study, we identified the perceived high stress-related factors that we thought could be useful for psychological support during the COVID-19 outbreak. With early detection of radiology workers at risk, we believe that both the mental health of the employees can be protected and workload loss can be prevented.

Keywords: COVID-19, pandemic, perceived stress score, radiology workers

ÖZ

Amaç: Bu çalışmanın amacı koronavirüs hastalığı-19 (COVİD-19) salgını sırasında radyoloji çalışanlarının algılanan stres düzeylerini ve bununla ilişkili faktörleri incelemektir.

Yöntemler: 15 Nisan-18 Nisan 2020 tarihleri arasında araştırmacılar tarafından hazırlanan tanımlayıcı tipte anket Türkiye'deki çeşitli sağlık kuruluşlarının radyoloji departmanlarında görev yapan radyoloji çalışanları tarafından online doldurduldu. Çalışmamızda algılanan stres ölçeği (perceived stress scala) kullanıldı. Çalışma için gerekli etik izin alındı. Verilerin istatistiksel analizlerinde SPSS 22.0 paket programı kullanıldı.

Bulgular: Çalışmaya katılan 573 radyoloji çalışanının yaş ortalaması 34,0±9,3 yıl olup, %50,1'i kadındı. Radyoloji çalışanlarının algılanan stres ölçeğinden aldıkları puan 27,8±6,4 (median: 27,0, minimum-maksimum: 6-50) idi. Çalışmamızda kadınların, 60 yaş üstü bireylerle birlikte yaşayanların, radyoloji teknisyeni/teknikeri olarak çalışanların, kronik bir hastalığa sahip olanların, sigara kullanımı artanların, sosyal medyayı eskisinden daha sık kullananların, COVİD-19'lu hastayla teması olanların, COVİD-19 enfeksiyonu ile ilgili bir eğitim almayanların ve COVİD-19 enfeksiyonuna karşı alınan önlemlerin yetersiz olduğunu düşünenlerin algıladıkları stresin istatistiksel olarak anlamlı düzeyde daha yüksek olduğu belirlendi ($p<0,05$).

Sonuç: Çalışmamızda, COVİD-19 salgını sırasında psikolojik destek için kullanılabileceğini düşündüğümüz algılanan yüksek stres ile ilişkili faktörleri tanımladık. Risk altındaki radyoloji çalışanlarının erken tespit edilmesiyle hem çalışanların ruh sağlığının korunabileceğini hem de iş yükü kaybının önlenebileceğini düşünüyoruz. Bununla birlikte risk gruplarına yönelik yapılacak etkili müdahaleler için daha kapsamlı çalışmalara ihtiyaç vardır.

Anahtar Sözcükler: COVİD-19, salgın, algılanan stres ölçeği, radyoloji çalışanları

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Address for Correspondence: Hatice Nilden ARSLAN, Ondokuz Mayıs University Faculty of Medicine, Department of Public Health, Samsun, Turkey
E-mail: haticenilden.arslan@omu.edu.tr **ORCID ID:** orcid.org/0000-0002-3237-7123

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Introduction

In December 2019, a new outbreak of pneumonia occurred in Wuhan City, Hubei province of China, of unknown etiology. This disease, which was determined to be caused by a new coronavirus, was named Coronavirus disease-19 (COVID-19) by the World Health Organization (1,2). The virus, which is known as severe acute respiratory syndrome (SARS)-CoV-2 leads to an acute respiratory infection that spreads via droplets, respiratory secretions, and direct contact (3,4). Transmission during health care also plays an important role in the spread of the disease (5).

The reverse transcriptase-polymerase chain reaction test (RT-PCR) is the gold standard in the diagnosis of COVID-19. However, the changes in the incubation period of the disease, low patient viral load, or variable positivity rates of the tests caused by disruptions in taking the test sample have increased the importance of radiological findings in diagnosis. In their research comparing the sensitivity of thorax computed tomography (CT) and RT-PCR, Fang et al. (6) reported that RT-PCR sensitivity was 71% for COVID-19 infection, whereas CT sensitivity was 98% ($p<0.001$). The study supported the use of thorax CT for COVID-19 screening, especially in patients with a negative RT-PCR test where clinical and epidemiological features are compatible with COVID-19 infection (6,7). Radiology personnel are at risk for COVID-19 infection due to increased CT examinations because of the increased importance of imaging methods in diagnosis (8).

Outbreaks are known to cause problems such as anxiety, depression, and post-traumatic stress disorder (9,10). In the studies conducted during the SARS epidemic, it was observed that especially healthcare workers were adversely affected due to the risk of infection and increased workload, and they had anxiety over the possibility of infecting their relatives (11-13). Factors such as the increasing number of cases and lack of personal protection and medications cause a psychological burden on healthcare workers due to the pandemic (14,15). The aim of this study is to investigate the perceived stress levels of radiology workers and related factors during the COVID-19 outbreak.

Method

The universe of this descriptive study constitutes radiologists and radiology technicians working in the radiology department at various health institutions in Turkey. The data were collected on social media (WhatsAPP, Twitter, Linkedin) using the online questionnaire prepared by the researchers. An information note explaining the purpose of the research was added to the questionnaire form, and a check box was added to the questionnaire that they cannot continue without giving consent that they voluntarily participated in the study. Necessary ethical permission was obtained for the study. The perceived stress scale (PSS) and questions about sociodemographic features were used in the questionnaire.

The PSS was developed by Cohen, Kamarck, and Mermelstein, and was adapted to Turkish by Eskin et al. (16,17). Consisting of 14 items in total, the PSS is designed to measure how stressful some situations in a person's life are perceived to be. The participants evaluate each item on a 5-point Likert scale ranging from "Never (0)" to "Very often (4)." A high score indicates the excessive perception of stress by the person.

Statistic Analysis

SPSS Statistics for Windows, Version 22.0 (Armonk, NY: IBM Corp) was used for statistical analysis of the data. The Kolmogorov-Smirnov test was used to evaluate the conformity of the quantitative data to the normal distribution. On this basis, nonparametric tests were chosen. In pair group comparisons, a Mann-Whitney U test was used. For comparisons of more than two groups, first a Kruskal-Wallis Test and then a Bonferroni-Corrected Mann-Whitney U test were used. Values of $p<0.05$ were considered statistically significant for all tests.

Results

The average age of 573 radiology workers participating in the study was 34.0±9.3 years and 50.1% were women. In all, 59% of the participants were married and 51.8% had at least one child. The frequency of those living with individuals over the age of 60 was 15.4%. A total of 82.0% of the participants worked in pandemic hospitals, 18.0% in other health institutions (Integrated hospital, Branch hospital, Cancer early diagnosis and training center, Tuberculosis dispensary, etc.). Average working time was 10.72±8.6 years, 19.7% were radiologists, and 80.3% were radiology technicians. The distribution of the participants according to some sociodemographic characteristics is shown in Table 1.

While 79.9% of radiology workers did not have any known chronic diseases, there was hypertension in 3.7%, COPD or asthma in 3.8%, diabetes in 1.7%, immunosuppressive disease in 1.9% and other diseases (mental illness, musculoskeletal system diseases, peptic ulcer etc.) in 9.2%. In all, 90.8% of participants stated that they did not have any mental illnesses diagnosed previously, while 3.0% had a previous mental illness, 3.7% had an ongoing mental illness, and 2.4% started to experience mental problems after the COVID-19 outbreak.

A total of 62.0% of the participants did not smoke cigarettes, and 80.6% did not use alcohol. When participants were asked about changes in these habits since the COVID-19 outbreak; 41.7% of smokers had not made any changes, 35.3% had decreased, 11.9% had increased, and 11.0% had quit. Likewise, 51.4% of alcohol users stated that their habits had not changed, 36.9% had decreased their alcohol consumption, 6.3% had increased, and 5.4% had quit.

Of all the participants, 59.9% stated that they had received training on COVID-19 disease in the institutions in which they worked. Of these trainees, 80% were working in a pandemic hospital. A total of 207 (36.1%) people answered yes to the question: "As far as you know, have you ever had contact with a COVID-19-positive patient?" When asked whether they were tested due to contact with a patient with COVID-19, it was determined that 51 (24.6%) people were tested, and 4 (7.8%) of

Table 1. Distribution of radiology workers according to sociodemographic characteristics

Variables	N (%)
Age (year)	34.0±9.3
Gender	
Female	287 (50.1)
Male	286 (49.9)
Marital status	
Married	235 (41)
Single (including widow or divorced)	338 (59)
Place of residence	
City center	419 (73.1)
Town	154 (26.9)
Profession	
Radiologist	113 (19.7)
Radiology technician	460 (80.3)
Working time (year)	
1-10	322 (56.2)
11 and more	251 (43.8)
Place of work	
Pandemic hospital	470 (82.0)
Other health institutions*	103 (18.0)

* Integrated hospital, Branch hospital, Cancer early diagnosis and training center, Tuberculosis dispensary, etc

them were found to be positive.

In answer to the question "What measures do you implement related to COVID-19 in your daily life outside the workplace?" 96.3% of participants stated that they washed their hands frequently, 84.6% of them used hand disinfectant/alcohol, 86.4% of them applied social isolation, and 83.2% of them ventilated their environment frequently. In answer to the question: "What measures do you implement in your professional life regarding COVID-19?" 98.3% of them stated that they wore masks, 96.9% of them washed their hands frequently, 89.7% of them wore gloves, 78.7% of them wore aprons, 89.9% of them used hand disinfectants/alcohol, 78.4% of them applied social isolation, and 74.2% of them ventilated their environment frequently. When asked, 27.6% of the participants stated that the measures taken against COVID-19 in their institution were "sufficient," 54.1% stated that the measures were "partially sufficient," and 18.3% stated that they were "insufficient." Of those who stated that the measures taken were sufficient and partially sufficient, 78% were working in a pandemic hospital.

The scores received by radiology workers from the PSS were 27.8±6.4 (median: 27.0, minimum-maximum: 6-50). Statistical comparisons were made according to some features of the employees. According to this; it was determined that the perceived stress was statistically significantly higher ($p<0.05$) (Table 2) in women and those living with individuals over the age of 60, those working as radiology technicians, those with a chronic disease, those who increased smoking, those who used social media more often than before, those who had contact with a patient positive for COVID-19, those who did not receive training on COVID-19, and those who thought that the measures taken against COVID-19 were insufficient.

Table 2. Comparison of perceived stress scores of radiology workers according to some variables

Variables Mean ± SD		Perceived stress score	Min-Max median	p
Gender	Male	26.4±6.0	6-50 27.0	0.000
	Female	29.1±6.5	6-50 29.0	
Marital status	Married	27.7±6.4	6-50 28.0	0.875
	Single	27.9±6.4	6-50 27.0	
Place of residence	City center	28.0±6.5	6-50 28.0	0.132
	Town	27.2±6.2	12-50 27.0	
Children	Present	27.8±6.4	6-50 28.0	0.910
	Absent	27.8±6.4	6-50 27.0	
>60 elderly individuals living together	Present	29.8±6.1	15-50 28.0	0.005
	Absent	27.4±6.41	6-50 27.0	
Profession	Radiologist	26.4±6.2	6-44 26.0	0.007
	Radiology technician	28.1±6.4	6-50 28.0	
Working time (year)	1-10	27.4±6.2	12-44 27.0	0.825
	11 and over	28.2±6.7	6-50 28.0	
Place of work	Pandemic hospital	27.7±6.3	6-50 27.0	0.399
	Other health institutions	28.2±6.7	6-50 28.0	
Chronic illness	Present	28.9±6.7	6-44 29.0	0.010
	Absent	27.0±6.0	6-50 27.0	

Cigarette consumption	Never smoked	27.8±6.4	6-50 27.0	0.009
	Did not change	26.3±6.5	6-43 27.0	
	Increased	31.7±7.1	20-50 32.0	
	Decreased	28.3±5.9	11-41 29.0	
	Quitted	27.6±5.3	16-39 28.0	
Alcohol consumption	Never used	27.8±6.4	6-50 27.0	0.945
	Did not change	27.5±7.4	6-50 27.0	
	Increased	28.2±4.3	21-34 29.0	
	Decreased	28.4±5.8	12-41 28.0	
	Quitted	27.6±2.0	24-30 28.0	
Social media usage	Increased	28.7±6.1	12-50 28	0.026
	Decreased	26.7±8.5	12-43 27	
	Did not change	27.2±6.3	6-50 27.0	
COVID-19 training	Present	27.4±6.6	6-50 27.0	0.045
	Absent	28.4±6.1	6-44 28.0	
Contact with a patient positive for COVID-19	Present	28.5±6.9	6-50 28.0	0.020
	Absent	27.4±6.0	6-50 27.0	
Measures taken against COVID-19	Sufficient	26.1±6.0	12-42 26.0	0.000
	Partially sufficient	28.0±6.5	6-50 28.0	
	Insufficient	29.8±6.2	13-44 29.0	

SD: Standard deviation, Min: Minimum, Max: Maximum, COVID-19: Coronavirus disease-19

Discussion

COVID-19 is an atypical pneumonia pandemic that has caused the most cases and deaths in the world after the SARS outbreak in 2003 (18,19). As the infection may be asymptomatic, with the progression of atypical pneumonia, approximately 2% of cases are lost due to acute respiratory distress syndrome (20,21). Clinical and radiological findings and diagnostic tests are used for the diagnosis of the disease. The role of thorax CT for the diagnosis and follow-up in individuals infected with COVID-19 has led radiology clinics to take an active place in the field (22-23).

People complied with social isolation and, to avoid becoming infected, did not leave their homes. However, healthcare workers, who assumed the most important task in the outbreak, were unable to cut off contact with the outside and with patients. Close contact and a high-risk of transmission threaten the mental and physical health of healthcare workers. During the SARS outbreak in 2003, 89% of healthcare workers in high-risk situations were reported to develop psychological symptoms (24,25).

Although the best approach to struggling with outbreaks is still uncertain, maintaining the mental health of healthcare workers is a requirement for better control of infectious diseases (26,27). Most research on the COVID-19 outbreak has focused on virus characterization, disease progression, and outbreak management (20,21,28). Sterilization of the radiology department, methods of personnel protection and the provision of an optimal safe working environment have been addressed in many scientific articles (29,30). However, there is no study in the literature about the psychological effects of this pandemic on radiology staff. This study provides an overview of the evaluation of the stress levels perceived by radiology workers during the COVID-19 pandemic. At the same time, it is the first study to assess the psychological status of employees working in radiology units during the COVID-19 outbreak in Turkey.

Compared with other outbreaks, the high transmission rate of COVID-19, in addition to the prevalence of asymptomatic patients, makes it difficult to control the outbreak (3,31). The most commonly used imaging method in diagnosis is thorax CT. Tomography rooms are closed areas, so radiology workers often have to be in close contact with the patient during tomography and positioning. Because of this, they cannot maintain their social isolation distance. In addition, it may be necessary to evaluate COVID-19 patients with other imaging methods and perform interventions during their follow-up in the hospital (32). In our study, 36.1% of the participants had a direct contact history with COVID-19-positive patients. The perceived stress level was found to be higher in those working in the pandemic hospital and in the group who came into contact with patients. We believe that this is due to the fact that radiology workers experience significant stress about becoming ill and transmitting the disease. In the study by Wang et al. (33), it was reported that more than 70% of the participants believed that they would recover after becoming infected, but they were concerned about their family members because they could not discontinue contact with them. In addition, epidemiological studies have shown that the disease progresses with higher mortality and morbidity rates in the elderly and the infection is associated with higher mortality in individuals with chronic disease (20,21,34). In our study, PSS

scores were higher in both those living with individuals over the age of 60 and those with a chronic disease. It can be interpreted that these people were concerned not only for their own health but also for that of their relatives.

Our sociodemographic data showed that the perceived stress level was higher in those of the female gender, those who were married and parents. This finding is parallel with previous epidemiological studies that found women to be at higher risk for depression (33,35). This situation may be attributed to female healthcare workers' concerns about becoming ill and carrying the virus to their families and children. Moreover, it can be related to their concerns about the disruption of family lifestyle or the care of their children if they are isolated/quarantined due to their own infection.

In our study, it was determined that 59.9% of the participants received training about COVID-19 disease in the institution where they work and the perceived stress level in the educated group was lower than those who were not trained. Similarly, the perceived stress level of radiologists was lower. Although the contents of these trainings are not known exactly, it can be assumed that the course of the disease, its clinical features, and the means of prevention are described. We believe that physicians, who have greater knowledge about diseases and means of prevention, and radiology workers who have gained knowledge through the training they have received, act more consciously during the hours they spend in the hospital and feel more secure. In an article emphasizing the personal protection problems of healthcare workers in China, it was reported that infection rates increased during the pandemic because healthcare workers did not have enough time for systematic training and practices (36). During the course of the pandemic, the diagnosis, treatment strategies, and protection recommendations of the healthcare workers have changed in the light of new data and the guidelines of health authorities have been revised. In previous studies, it has been reported that health authorities providing accurate and sufficient information in the outbreak are associated with lower stress, anxiety, and depression levels during the outbreak (33,37).

Social media pollution is an important cause of stress during outbreaks. It is known that the increasing number of new cases and deaths day by day, disinformation and false reports increase anxiety. During the COVID-19 outbreak, in their study of Chinese citizens over the age of 18, Gao et al. (38) reported that 82% of participants were exposed to social media a lot and had symptoms of high anxiety and depression. In our study, it was observed that the perceived stress was higher in the group using social media intensively. We believe that information pollution in social media negatively affects radiology workers in our country as well as all over the world.

It is important to limit transmission from person to person in order to reduce secondary infections among healthcare workers. Personal protective equipment is an important component that protects personnel from COVID-19, and correct use significantly reduces the risk of viral contamination (39,40). It has been reported by the China National Hospital Infection Management and Quality Control Center that the awareness of healthcare professionals about personal protection was inadequate due to the lack of recognition of the pathogen at the onset of the COVID-19 outbreak. As China was caught unprepared for the pandemic, long-term exposure to many patients and a lack of personal protective equipment increased the risk of infection in healthcare workers (36). During the 2003 SARS-CoV epidemic, researchers found that moderate anxiety levels were associated with participants taking more preventive measures. Regardless of the presence or absence of symptoms, special measures such as avoiding sharing items, hand hygiene and wearing a mask were associated with lower levels of depression, anxiety, and stress (33). In our study, radiology workers stated that they applied infection control measures both in their private lives and in the hospital. Despite contact with large numbers of patients, we think that the infection of only four radiology workers with COVID-19 was a result of correct and sufficient implementation of prevention methods. In addition, it was observed that most of the participants in the study were those working in hospitals designated as pandemic hospitals, and the scale scores of these people were similar to those of participants working in other health institutions. Although there is a higher risk of contact with COVID-positive patients, the lack of a high perception of stress can be attributed to the amount of protective equipment in these hospitals being more adequate than in other institutions or to the training provided to the personnel.

Study Limitations

This study has some limitations. In our study, the optional web-based survey method was used, because of this, the possibility of selection bias cannot be ignored. In addition, we tried to determine the participants' psychiatric conditions before the pandemic with only one question, but clinical evaluation could not be performed.

Conclusion

As a result, there are some risk groups among radiology workers who are known to have an increased risk of infection due to contact with patients as well as an increased workload due to the COVID-19 outbreak. These can perceive higher levels of stressors, resulting in deterioration of their mental health. These include some personal characteristics such as female gender, smoking, presence of chronic disease, or living with older individuals, as well as some professional characteristics such as occupational group, contact with COVID-19-positive patients, education and lack of personal protection. We think that early detection and intervention of those with high stress perception is important to reduce the psychological complaints of employees and to protect their mental health. It will also contribute to the reduction of workforce losses and the prevention of other staff's workload increases due to sick leave/medical reports in the current period of struggle with pandemics. However, more comprehensive studies are needed for effective interventions for high-risk groups.

Ethics

Ethics Committee Approval: OMU-CREC 2020/170.

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: H.N.A., A.İ.S., Design: H.N.A., A.İ.S., Data Collection or Processing: H.N.A., A.İ.S., Analysis or Interpretation: H.N.A., A.İ.S., Literature Search: H.N.A., A.İ.S., Writing: H.N.A., A.İ.S.

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Original Article

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The Importance of Healthcare Workers to Comply with Infection Prevention and Control Instructions During COVID-19 Outbreak-A Survey Study

COVİD-19 Salgını Sırasında Sağlık Çalışanlarının Enfeksiyon Önleme ve Kontrol Yönergelerine Uymalarının Önemi-Bir Anket Çalışması

Ramazan KORKUSUZ[1], Sevtap ŞENOĞLU[1], Özlem POLAT[2], Kadriye KART YAŞAR[1]

[1]University of Health Sciences Turkey, Bakırköy Dr. Sadi Konuk Training and Research Hospital, Clinic of Infectious Diseases and Clinical Microbiology, İstanbul, Turkey
[2]University of Health Sciences Turkey, Bakırköy Dr. Sadi Konuk Training and Research Hospital, Family Medicine, İstanbul, Turkey

ABSTRACT

Objective: Taking precations to prevent contamination and developing prevention programs play a key role in the outbreak. For this purpose, the use of personal protective equipment (PPE) of healthcare workers (HCWs) and their compliance with hand hygiene were investigated in the current Coronavirus disease-19 (COVID-19) outbreak.

Methods: In study, 117 HCW, who were diagnosed with COVID-19 between 11 March and 18 May 2020, and 117 HCW, who did not meet the case definition, 234 HCW were included in the study, A survey consisting of 28 questions was applied to obtain the research data. The survey consisted of multiple choice questions and was prepared by the researchers using the knowledge of the literature.

Results: It was determined that 65.8% of the participants were women, 41.9% were nurses, 82.1% did not have additional diseases and 62.8% did not smoke. Positivity was significantly higher in young patients aged 20-30 (p=0.05). In the use of PPE, the use of gloves as "always recommended" was found higher in infected HCW with 77.8% (p=0.012). The use of overalls/gowns was found to be statistically significantly lower in infected healthcare workers (p=0.01). In terms of the hand hygiene application variable after touching the patient between the groups,

ÖZ

Amaç: Salgın sürecinde sağlık çalışanlarında (SÇ) bulaşmayı önlemek açısından önlemlerin alınması ve önleme programlarının geliştirilmesi anahtar role sahiptir. Bu amaçla, halen yaşanmakta olan Koronavirüs hastalığı-19 (COVİD-19) salgınında, SÇ'nin kişisel koruyucu ekipmanları (KKE) kullanımı ve el hijyenine uyumu araştırılmıştır.

Yöntemler: Çalışmamızda 11 Mart-18 Mayıs 2020 tarihleri arasında laboratuvar tarafından doğrulanmış COVİD-19 tanısı alan 117 sağlık çalışanı ile olası olgu tanımını karşılamayan 117 sağlık çalışanı olmak üzere 234 sağlık çalışanı çalışmaya dahil edildi. Araştırma verilerini elde etmek için 28 sorudan oluşan anket uygulanmıştır. Anket, çoktan seçmeli sorulardan oluşmuş ve araştırmacılar tarafından literatür bilgisinden yararlanılarak hazırlanmıştır.

Bulgular: Katılımcıların %65,8'inin kadın, %41,9'unun hemşire olduğu, %82,1'inin ek hastalığının olmadığı, %62,8'inin sigara kullanmadığı saptanmıştır. Yirmi-30 yaş arası genç hastalarda pozitiflik anlamlı oranda yüksek saptanmıştır (p=0,05). KKE "her zaman önerildiği gibi" şeklinde eldiven kullanımı %77,8 ile enfekte SÇ'lerde daha yüksek bulunmuştur (p=0,012). Özellikle tulum/önlük kullanımı enfekte SÇ'lerinde istatistiksel açıdan anlamlı olarak düşük saptanmıştır (p=0,01). Gruplar arasında hastaya dokunduktan sonra el hijyeni uygulama değişkeni açısından

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Address for Correspondence: Ramazan KORKUSUZ, University of Health Sciences Turkey, Bakırköy Dr. Sadi Konuk Training and Research Hospital, Clinic of Infectious Diseases and Clinical Microbiology, İstanbul, Turkey
E-mail: ramazankorkusuz@hotmail.com **ORCID ID:** orcid.org/0000-0002-9988-9596

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ABSTRACT

compliance was found to be low in healthcare workers diagnosed with COVID-19 (p=0.005).

Conclusion: It was observed that the risks of healthcare workers getting COVID-19 decreased significantly if the infection control measures were followed. It is thought that it would be beneficial to investigate new methods to ensure that protective measures are fully implemented by HCW.

Keywords: Healthcare workers, COVID-19, personal protective equipment, hand hygiene

ÖZ

COVİD-19 tanılı SÇ'lerinde uyumun düşük olduğu saptanmıştır (p=0,005).

Sonuç: Enfeksiyon kontrol önlemlerine uyulduğu takdirde SÇ'lerin COVİD-19'a yakalanma risklerinin anlamlı olarak düştüğü gözlenmiştir. Buna rağmen, COVİD-19 pandemisi sürecinde, SÇ'lerin KKE kullanımındaki eksikliklerini görmek, KKE protokollerini iyileştirmek ve eğitimlerini yenilikçi yöntemler kullanarak geliştirmek için detaylı araştırmalara ihtiyaç vardır.

Anahtar Sözcükler: Sağlık çalışanları, COVİD-19, kişisel koruyucu ekipman, el hijyeni

Introduction

Healthcare workers (HCWs) are at risk of contracting life-threatening infectious diseases due to contact with patients' blood, mucus, discharge or aerosol droplets. Especially during epidemics, this risk is higher among HCWs compared to the general population. Due to the increase in the number of infected HCWs during epidemics, the overloaded healthcare system may be in a difficult situation due to the loss of workforce. In Wuhan, China, "severe acute respiratory syndrome coronavirus" (SARS-COV-2) with viral pneumonia started to appear in December 2019 (1). The World Health Organization (WHO) declared this disease, which spreads rapidly in the world, as "International Public Health Emergency" on January 30, 2020 and as a pandemic on March 11, 2020 (2,3). As of May 18, 2020; 4,618,821 cases in the world and in Turkey 150,593 cases have been reported (4,5). As of April 8, 2020, the number of HCWs diagnosed with Coronavirus disease-19 (COVID-19) in the world was reported as 22073 by WHO (6). In Turkey, according to the description of the the Ministry of Health, 7428 health care workers has been infected as of April 30, 2020 (7). Although the main transmission routes of COVID-19 disease are through droplets and contact, other transmission routes are also possible (8). Compliance with hand hygiene and the use of personal protective equipment (PPE) are the most important measures for HCWs exposure control. While overalls, gowns, masks, glasses and face shields prevent the skin and mucous from being contaminated, the mask prevents droplet inhalation. The indications for the use of PPE for HCW, which is and is not directly interested in the care of COVID-19 patients, have been specified by WHO (9). During the epidemic process, taking the necessary precautions and developing precaution programs to prevent contamination in the HCW has a key role. However, determining the contamination and protective measures by taking into account the characteristics of individual, procedural and health institutions will be effective in developing the targeted part of prevention programs. Our hospital, Istanbul/Turkey, as mandated by the Ministry of Health hospital pandemic and has been one of the centers most patients have been followed. Our hospital is a tertiary hospital with 612 beds and 2737 (724 physicians, 864 nurses, 10 pharmacists, 978 auxiliary health personnel, 161 technicians and technicians) HCW. In our study, the correct use of PPE and the effectiveness of hand hygiene by HCWs during the epidemic process were investigated.

Method

HCW with a laboratory-confirmed diagnosis of COVID-19 between March 11 and May 18, 2020, and HCW without any complaint and considered not to be infected, as a control group, were included in the study. The study protocol was approved by the Ethics Committee of Bakırköy Dr. Sadi Konuk Training and Research Hospital, University of Health Sciences Turkey (18.05.2020/2020-11). The study was a descriptive and cross-sectional study and was conducted as a single center study. Participants consisted of clinicians, nurses and assistant health personnel.

HCW working in the COVID service, providing care to the patient or entering the patient room, participated voluntarily in the study was included to the study. HCW that works in a non-COVID ward, does not provide care to the patient or does not enter the patient's room and does not approve the participation of the questionnaire were excluded from the study. Out of a total of 181 HCWs diagnosed with COVID-19, 117 HCWs meeting the inclusion criteria and 117 HCWs as control groups were included in the study. A total of 234 HCWs included in the study.

Due to the risk of contamination, approvals for participation in the study and questionnaire filling procedures were carried out by phone or online. A questionnaire consisting of 28 questions was applied to 234 HCWs to obtain research data. The questionnaire consists of multiple choice questions and was prepared by the researchers using the literature knowledge.

The questionnaire consists of multiple choice questions and was prepared by the researchers using the literature knowledge. Questions about socio-demographic characteristics (age, gender, comorbidities, occupational duty and working hours) in the first part of the questionnaire prepared in four parts; In the second part, the presence of domestic COVID-19 patients, contact with an out-of-hospital COVID-19 patient, application of aerosol-forming procedure to a COVID-19 patient (taking respiratory

tract samples, intubation, airway care and cardiac arrest), contact with biological material (contact of the patient with blood, body fluids, secretions); In the third part, the existence of protective equipment and in the last part, questions about hand hygiene compliance are given.

Statistical Analysis

The normality distribution of the data obtained from the participants (Kolmogorov-Smirnov) was made and it was determined that they were not distributed normally. For this reason, nonparametric tests were applied. Number and percentage distributions of the data obtained from the participants were made, and chi-square analysis was performed to test the difference between groups. The level of significance was taken as $p \leq 0.05$.

Results

It was determined that 34.2% of the participants were male, 65.8% were female, 73.1% were under the age of 40, 82.1% had no comorbidities, 62.8% did not smoke, 41.9% were nurses. Positivity was significantly higher in young patients between the ages of 20-30 (p=0.05). Socio-demographic variables in comparison of the groups are presented in Table 1.

The rate of diagnosing COVID-19 among family members is 35% in the infected HCWs group, and was higher than the control group (p<0.001). A statistically significant difference was found when compared to the other group in terms of face-to-face contact with the COVID-19 patient without a mask (p=0.024). In the control group, 52% of being in the same environment during the implementation of aerosol-forming procedures was detected, and this rate was found to be 18% higher than the rate we found in infected HCW (p=0.006). The clinical practice and contact variables of the healthcare professionals are presented in Table 2.

When the two groups were compared in terms of the use of PPE, the use of gloves as "always, as recommended" was found to be higher in infected HCW with a rate of 77.8% (p=0.012) (Table 3). Although there was no statistical difference between the two groups in terms of the use of N95 mask, face shield/glasses, it was observed that the compliance was lower in infected HCW as a percentage. Especially the use of overalls/aprons was found to be statistically significantly lower in infected HCW (p=0.01).

While there were no differences between the groups in the appropriate change of PPEs according to the procedure, before and after contact with the patient, before and after the aseptic

Table 1. Sociodemographic variables

			COVID		p
		Total	Negative	Positive	
Gender	Male	80 (34.2%)	46 (39.3%)	34 (29.1%)	0.098
	Female	154 (65.8%)	71 (60.7%)	83 (70.9%)	
Age	Between 20-30	114 (48.7%)	48 (41%)	66 (56.4%)	0.05
	Between 31-44	84 (35.9%)	50 (42.7%)	34 (29.1%)	
	≥45	36 (15.4%)	19 (16.2%)	17 (14.5%)	
	Average	34.1±9.61	34.2±9.8	34±9.47	
Additional disease	No	192 (82.1%)	95 (81.2%)	97 (82.9%)	0.909
	DM	3 (1.3%)	1 (0.9%)	2 (1.7%)	
	HT	6 (2.6%)	3 (2.6%)	3 (2.6%)	
	COPD	4 (1.7%)	3 (2.6%)	1 (0.9%)	
	Cancer	1 (0.4%)	1 (0.9%)	0	
	DM + HT	3 (1.3%)	1 (0.9%)	2 (1.7%)	
	HT + COPD	2 (0.9%)	1 (0.9%)	1 (0.9%)	
	Other	23 (9.8%)	12 (10.3%)	11 (9.4%)	
Cigarette	No	147 (62.8%)	72 (61.5%)	75 (64.1%)	0.075
	Yes	74 (31.6%)	42 (35.9%)	32 (27.4%)	
	Smoked before	13 (5.6%)	3 (2.6%)	10 (8.5%)	
Occupation	Doctor	62 (26.5%)	31 (26.5%)	31 (26.5%)	1
	Nurse	98 (41.9%)	49 (41.9%)	49 (41.9%)	
	Cleaning staff	74 (31.9%)	37 (31.6%)	37 (31.6%)	
Weekly working time (Hours) in COVID Unit	<40	86 (36.8%)	50 (42.7%)	36 (30.8%)	0.058
	≥40	148 (63.2%)	67 (57.3%)	81 (69.2%)	

DM: Diabetes mellitus, HT: Hypertension, COPD: Chronic obstructive pulmonary disease, COVID: Coronavirus disease

Table 2. Clinical practice and contact variables

	Total (n=234)	COVID Negative (n=117)	Positive (n=117)	p
Is there anyone at home diagnosed with COVID-19?	42 (17.9%)	1 (0.9%)	41 (35%)	0.000*
Have you had contact with a known COVID-19 patient outside the hospital in the last 14 days?	30 (12.8%)	19 (16.2%)	11 (9.4%)	0.118
Have you provided direct care without a mask for a COVID-19 patient?	13 (5.6%)	6 (5.1%)	7 (6%)	0.775
Have you contacted a COVID-19 patient face to face (within 1 meter) without a mask?	27 (11.5%)	8 (6.8%)	19 (16.2%)	0.024*
Have you been in the same area when the patient was given an aerosol-forming procedure?	101 (43.2%)	61 (52.1%)	40 (34.2%)	0.006*
What kind of procedure?				
Tracheal intubation	20 (19.4%)	14 (23%)	6 (14.3%)	
Nebulizer therapy	9 (8.7%)	5 (8.2%)	4 (9.5%)	
Aspiration	2 (1,9%)	2 (%3,3)	0	
Sputum collection	1 (1%)	1 (1,6%)	0	
Tracheostomy	1 (1%)	1 (1,6%)	0	0.328
Bronchoscopy	1 (1%)	0	1 (2.4%)	
Cardiopulmonary resuscitation	1 (1%)	0	1 (2.4%)	
Multiple transactions	59 (57.3%)	35 (57.4%)	24 (57.1%)	
Other	9 (8.7%)	3 (4.9%)	6 (14.3%)	

COVID: Coronavirus disease

procedure, and after contact with body fluids, compliance with the indication to perform hand hygiene after touching the positive patient's environment was found to be low in infected HCW (p=0.005). Differences between hand hygiene compliance are shown in Table 4.

No statistically significant difference was found between the groups in terms of infected patient excretions and having an accident (p>0.05) (Table 5).

Discussion

Usually, recall bias in questionnaires is a point of concern. However, it was thought that the questions were open and the requested information was about simple concrete behaviors and about recent events, so it was not at a level that would affect the results. When the socio-demographic risk factors in terms of SARS-COV-2 infection were compared in comparison of the HCW groups participating in the questionnaire, gender, comorbidities and smoking were found to be similar and no statistically significant difference was found (p>0.05). The more positivity in the young (20-30 years old) HC group (p=0.05), the milder course of the disease in the young people, and the experience of the senior HCW were evaluated as more adhering to the prevention methods.

It has been observed that having a smoking habit does not differ in terms of contamination. As far as we researched from the English literature, there are no studies evaluating the risk of SARS-CoV-2 infection among smokers. It was evaluated that more detailed studies should be done on this subject. In one study, it was stated that long working hours increased the risk of respiratory tract infection transmission, and moderate working hours were safer for HCWs (10). In terms of weekly working hours, the working time of 40 hours or more in infected HCW is more with a rate of 69.2%, but no statistical significance was found (p>0.05).

However, according to the characteristics of HCW, it has been evaluated that the hours he worked will be important in terms of viral transmission during the pandemic period. Due to the relatively small sample size of our study, it was thought that this variable might not have significance. The highest infection rate among HCW was observed in nurses. It was thought that this situation may be caused by nurses' closer and longer contact with patients.

During the pandemic process, HCWs can infect family members as well. In our study, it was observed that family members of 41 (35%) of infected HCW were also infected. In the control group, only 1 (0.9%) family member was found to have COVID-19 (p<0.001). This shows that there is an increased risk of disease transmission in family members of HCW diagnosed with COVID-19.

Ran et al. (11) stated in his research that the procedures that create aerosol in the use of appropriate PPE are not associated with the risk of infection transmission of HCWs. In our study, the fact that the application of the procedure that creates aerosol to the COVID-19 patient was higher in non-infected HCW,

Table 3. Use of personal protective equipment

	Total (n=234)	COVID		p
Have you used personal protective equipment during healthcare interaction with a COVID-19 patient?		Negative (n=117)	Positive (n=117)	
Gloves only				
Everytime, as suggested	162 (69.2%)	71 (60.7%)	91 (77.8%)	
Most of the time	60 (25.6%)	39 (33.3%)	21 (17.9%)	0.012*
Sometimes	9 (3.8%)	4 (3.4%)	5 (4.3%)	
Rarely	3 (1.3%)	3 (2.6%)	0	
Medical mask				
Everytime. as suggested	188 (80.3%)	88 (75.2%)	100 (85.5%)	
Most of the time	30 (12.8%)	19 (16.2%)	11 (9.4%)	0.212
Sometimes	6 (2.6%)	3 (2.6%)	3 (2.6%)	
Rarely	10 (4,3%)	7 (6%)	3 (2,6%)	
N95				
Everytime, as suggested	148 (63.2%)	77 (65,8%)	71 (60,7%)	
Most of the time	47 (20.1%)	24 (20.5%)	23 (19.7%)	0,642
Sometimes	18 (7.7%)	8 (6.8%)	10 (8.5%)	
Rarely	21 (9%)	8 (6.8%)	13 (11.1%)	
Face shield or goggles/protective goggles				
Everytime. as suggested	107 (45.7%)	61 (52.1%)	46 (39.3%)	
Most of the time	74 (31.6%)	37 (31.6%)	37 (31.6%)	0.066
Sometimes	26 (11.1%)	11 (9.4%)	15 (12.8%)	
Rarely	27 (11.5%)	8 (6.8%)	19 (16.2%)	
Overalls				
Everytime, as suggested	101 (43.2%)	61 (52.1%)	40 (34.2%)	
Most of the time	67 (%28.6)	29 (24.8%)	38 (32.5%)	0.01*
Sometimes	25 (10.7%)	14 (12%)	11 (9.4%)	
Rarely	41 (17.5%)	13 (11.1%)	28 (23.9%)	
During the healthcare interaction with the COVID-19 patient. did you remove and replace the Protective equipment according to the protocol (for example, wet PPE when the medical mask got wet)				
Everytime, as suggested	167 (71.4%)	80 (68.4%)	87 (74.4%)	
Most of the time	52 (22.2%)	29 (24.8%)	23 (19.7%)	0.575
Sometimes	14 (6%)	7 (6%)	7 (6%)	
Rarely	1 (0.4%)	1 (0.8%)	0	

COVID: Coronavirus disease, PPE: Personal protective equipment

showed the importance of compliance with infection prevention and control guidelines in preventing contagiousness.

The risk of SARS-COV-2 infection is highly dependent on the distance from the patient. Studies have reported that a physical distance of at least 1 meter with the patient can have a strong protective effect (12). During the pandemic, close contact of HCW with patients for a long time increases the possibility of transmission. In our study, the contact of infected HCW with a COVID-19 patient face to face (within 1 meter) without a mask was 16.2%, and it was found to be significantly higher than the control group (p=0.024). At the beginning of the pandemic process, it was thought that COVID-19 patients were hospitalized in different clinics with other diagnoses, and HCE was especially infected as a result of the use of unmasked or partial PPE in patient care.

Research has shown that since the transmission of SARS-COV-2 infection is through contact and droplets, medical masks (when combined with other PPEs, including face shields and hand

Table 4. Hand hygiene compliance

	Total (n=234)	COVID Negative (n=117)	COVID Positive (n=117)	p
Have you practiced hand hygiene before and after touching a COVID-19 patient?				
Everytime, as suggested	159 (67.9%)	88 (75.2%)	71 (60.7%)	
Most of the time	68 (29.1%)	26 (22.2%)	42 (35.9%)	0.057
Sometimes	7 (3%)	3 (2.6%)	4 (3.4%)	
Have you practiced hand hygiene before and after any clean or aseptic procedures during the period of healthcare interaction with the COVID-19 case?				
Everytime, as suggested	173 (73.9%)	88 (75.2%)	85 (72.6%)	
Most of the time	53 (22.6%)	24 (20,5%)	29 (24.8%)	0.787
Sometimes	5 (2.1%)	3 (2.6%)	2 (1.7%)	
Rarely	3 (1.3%)	2 (1.7%)	1 (0.9%)	
During the healthcare interaction with the COVID-19 case, did you practice hand hygiene after exposure to body fluid?				
Everytime, as suggested	214 (91.5%)	103 (88%)	111 (94,9%)	
Most of the time	16 (6.8%)	12 (10,3%)	4 (3,4%)	0.131
Sometimes	1 (0.4%)	0	1 (0,9%)	
Rarely	3 (1.3%)	2 (1,7%)	1 (0,9%)	
Have you practiced hand hygiene after touching the COVID-19 patient's surroundings (bed, door handle, etc.)?				
Everytime, as suggested	157 (67.1%)	90 (76.9%)	67 (57.3%)	
Most of the time	69 (29.5%)	23 (19.7%)	46 (39.3%)	0.005*
Sometimes	4 (1.7%)	1 (0.9%)	3 (2.6%)	
Rarely	4 (1.7%)	3 (2.6%)	1 (0.9%)	
Have surfaces with high risk contact with the COVID-19 case been disinfected frequently (at least three times a day)?				
Everytime, as suggested	116 (49.6%)	59 (50.4%)	57 (48.7%)	
Most of the time	82 (35%)	38 (32.5%)	44 (37.6%)	0,722
Sometimes	25 (10.7%)	13 (11.1%)	12 (10.3%)	
Rarely	11 (4.7%)	7 (6%)	4 (3.4%)	

COVID-19: Coronavirus disease-19

hygiene) are sufficient during non-aerosol care, and N95 masks are prominent compared to medical masks during routine care. It suggests that it does not provide any benefit (13).

In a study conducted in Hong Kong, 11 (2.7%) of a total of 413 HCWs used medical masks for routine care of COVID-19 patients and none of them developed infection (14). In our study, the compliance of infected HCW in the use of N95 mask "always, as recommended" is low as 60.7%. Although the compliance of the control group to use N95 mask was 5% higher, there was no statistically significant difference between the groups.

Studies have reported that the use of PPE reduces the risk of infection in HCWs (15-18). In the use of PPE, the rate of using gloves as "always, as recommended" between the two groups was found to be higher in infected HCW with 77.8-60.7% (p=0.012). While the rate of using face shield/glasses was low in both groups, the use of "always, as recommended" in infected HC was 13% lower. This rate was not statistically significant. Especially in the use of overalls/aprons, the use of "always, as recommended" was low in both groups, but a higher compliance was observed at a rate of 52.1% in the control group while it was 34.2% in infected HCWs (p=0.01). Our research suggests that no personnel will be infected if they use all four precautions as always recommended in the rules of wearing gloves, masks, eye protection and apron for PPE use.

The risk of disease transmission increases in case of unprotected contact with biological materials in HCWs (16,19). In our study, no significant difference was found between the groups in those who had unprotected contact with biological materials.

Another way of transmission of the SARS-COV-2 virus is through contact. The most important tool of the virus that facilitates indirect contact transmission is contaminated hands. In our study, in line with the answers given according to the "5-

Table 5. Contact with sick body fluid/respiratory secretions

	Total	COVID		p
		Negative	Positive	
Healthcare worker with a history of contact with biological fluid/respiratory secretions during the healthcare interaction period with a patient infected with COVID-19	10 (4.3%)	5 (4.3%)	5 (%4.3	1
Splash of biological fluid/respiratory secretions on the mucous membrane of the eyes	3 (30%)	3 (60%)	0	
Spatter of biological fluid/respiratory secretions on the oral/nasal mucosa	4 (40%)	1 (20%)	3 (60%)	0.115
Splash of biological fluid/respiratory secretions on intact skin	3 (30%)	1 (20%)	2 (40%)	

COVID: Coronavirus disease

step hand hygiene" rule, hand hygiene before and after touching the patient in infected HCW was found to be 60.7% as recommended, while it was higher in the control group with 75.2%.

Likewise, hand hygiene compliance after touching the patient's environment in the control group HC was found to be significantly higher with 76.9-57.3% compared to the infected HC (p=0.005). As a result, it has been observed that compliance with the "5-step hand hygiene" rule in line with the WHO recommendation to prevent the spread of the COVID-19 virus is extremely important in preventing infection transmission (20).

Study Limitations

The limitations of the study are that our study was single-centered, the number was relatively low, it was based on the questionnaire rather than direct observation, and the SARS-COV-2 polymerase chain reaction test of the HCW taken as the control group was not examined.

Conclusion

As a result, it has been observed that as the compliance with the infection control measures and directives decreases, the risk of contamination of COVID-19 to HCW increases. In addition, it has been observed that partial compliance with protective measures does not prevent the risk of disease transmission. It is noteworthy that there is an increased risk of disease transmission in family members of HCW diagnosed with COVID-19. This situation is important due to both employee and public health and prolonged labor losses. It is thought that it would be beneficial to research new methods that will ensure the full implementation of protective measures by the HCW and to provide training using innovative methods.

Ethics

Ethics Committee Approval: The study protocol was approved by the Ethics Committee of University of Health Sciences Turkey Bakırköy Dr. Sadi Konuk Training and Research Hospital(18.05.2020/2020-11).

Informed Consent: Signed informed consent was obtained from all participants before study.

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Authorship Contributions

Surgical and Medical Practices: R.K., Concept: Ö.P., K.K.Y., Design: R.K., K.K.Y., Data Collection or Processing: Ö.P., Analysis or Interpretation: S.Ş., K.K.Y., Literature Search: S.Ş., Writing: R.K.

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Is High Body Mass Index a Risk Factor for COVID-19?

Yüksek Beden Kitle İndeksi COVİD-19 için Bir Risk Faktörü Müdür?

Nilgün Seremet KÜRKLÜ[1], Ayşegül Seremet KESKİN[2], Merve TÜRKER[2]

[1]Akdeniz University Faculty of Health Science, Department of Nutrition and Dietetics, Antalya, Turkey
[2]University of Health Sciences Turkey Antalya Training and Research Hospital, Clinic of Infectious Diseases and Clinical Microbiology, Antalya, Turkey

ABSTRACT

Objective: The aim of this study is to evaluate the relation of body mass index (BMI) with Coronavirus disease-19 (COVID-19) and its effects on the course of the disease in COVID-19 patients.

Methods: The sample of the study consists of 97 adults who applied to our hospital COVID-19 triage clinic between 01.04.2020-01.06.2020. Patients' demographic data, symptoms, thorax computed tomography results, laboratory results, body weight, height, and need for intensive care therapy and mechanical ventilation were retrospectively screened. BMI was defined as normal if it was <25.0 kg/m^2, overweight if 25.0-29.9 kg/m^2, and obese if ≥30.0 kg/m^2.

Results: It was determined that 40.2% of the individuals participating in the study were overweight and 30.9% were obese. It was observed that obese individuals had more severe symptoms such as higher fever and poorer sense of smell, and higher thoracic bilateral involvement than those with normal weight (p<0.05). Similarly, the hospitalization rates of overweight and obese individuals (82.1% and 76.7%, respectively) (p=0,051), and the dependence rate of the latter on a mechanical ventilator (17.9%) were found to be higher (p<0.05). In the logistic regression analysis, it was found that a BMI of 25.0 and above increased the rate of hospitalization by approximately 3.5 times (p<0.05).

Conclusion: It was determined that increased BMI was an important risk factor for COVID-19 and increased hospitalization rates. In societies with high obesity rates, evaluation of obesity in COVID-19 patients is important to start treatment early and reduce hospitalization rates.

Keywords: Body mass index, COVID-19, obesity

ÖZ

Amaç: Bu çalışmanın amacı Koronavirüs hastalığı-19 (COVID-19) hastalarında beden kitle indeksinin (BKİ) COVİD-19 hastalığı ile ilişkisi ve hastalık seyrine olan etkilerini değerlendirmektir.

Yöntemler: Çalışmanın örneklemini 01.04.2020-01.06.2020 tarihleri arasında hastanemiz COVİD-19 triyaj polikliniğine başvuran 97 yetişkin birey oluşturmaktadır. Hastaların demografik verileri, semptomları, toraks bilgisayarlı tomografi sonuçları, hastaneye başvuru sırasında rutinde bakılan laboratuvar sonuçları, vücut ağırlığı, boy uzunluğu, yoğun bakım tedavisi ve mekanik ventilasyona ihtiyaç duyma durumları retrospektif olarak taranmıştır. BKİ'nin <25,0 kg/m^2 olması normal, 25,0-29,9 kg/m^2 arası hafif şişman ve 30,0 kg/m^2 olması ise şişman olarak tanımlanmıştır.

Bulgular: Çalışmaya katılan bireylerin %40,2'sinin hafif şişman ve %30,9'unun ise şişman olduğu saptanmıştır. Şişman olan bireylerde ateş ve koku alma bozukluğu gibi semptomların daha fazla ve toraks bilatertal tutulumun normal bireylere göre daha yüksek olduğu görülmüştür (p<0,05). Benzer şekilde hafif şişman ve şişman bireylerin hastaneye yatış oranlarının (sırasıyla %82,1 (p=0,051) ve %76,7) ve şişman bireylerin (%17,9) mekanik ventilatöre bağlanma oranlarının daha yüksek olduğu saptanmıştır (p<0,05). Lojistik regresyon analizinde BKİ'nin 25,0 kg/m^2 ve üzeri olmasının hastaneye yatış oranlarını yaklaşık 3,5 kat artırdığı saptanmıştır (p<0,05).

Sonuç: Artmış BKİ'nin COVİD-19 için önemli bir risk faktörü olduğu ve hastaneye yatış oranlarını artırdığı belirlenmiştir. Obezite oranlarının yüksek olduğu toplumlarda COVİD-19 hastalarının obezite açısından da değerlendirilmesi tedavinin erken başlaması ve hastaneye yatış oranlarının azaltılması açısından önemli olacağı düşünülmektedir.

Anahtar Sözcükler: Beden kitle indeksi, COVİD-19, obezite

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Address for Correspondence: Ayşegül SEREMET KESKİN, University of Health Sciences Turkey Antalya Training and Research Hospital, Clinic of Infectious Diseases and Clinical Microbiology, Antalya, Turkey
E-mail: aseremetkeskin@yahoo.com **ORCID ID:** orcid.org/0000-0002-9224-4699

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Introduction

Twenty-seven pneumonia cases of unknown etiology were detected on December 31, 2019, in Wuhan, China. The cause of this disease was named severe acute respiratory syndrome coronavirus (SARS-CoV-2) by the Chinese Center for Disease Control and Prevention on January 7, 2020, due to its similarity to SARS-CoV (1). The name of the disease was accepted as Coronavirus disease-19 (COVID-19) by the World Health Organization (WHO) and the COVID-19 epidemic was described as an "international public health emergency".

COVID-19 was declared as a global epidemic (pandemic) on March 11 due to the occurrence of COVID-19 in 113 more countries outside China, the spread and severity of the virus (2). Currently, according to WHO data, COVID-19 cases have been seen in 216 countries and the total number of cases is reported to be 7,094,473 (3). The first COVID-19 case in Turkey was detected on March 11, 2020. An increase in the number of cases has been observed in Turkey as in the whole world, and the total number of cases was 170,132 as of 08.06.2020 (4).

CoVs are single-stranded, positive polarity enveloped RNA viruses. The most important transmission route of COVID-19 infection is through droplets, touching surfaces containing the virus, and then touching the mucous membranes of the mouth, nose, and eyes. The contagious period of the disease is not known exactly; the average incubation period is 4-5 days but it extends up to 14 days (2). In mild cases of the disease, symptoms such as cough, fever, difficulty breathing, diarrhea, abdominal pain, taste and smell disorders, and widespread joint and muscle pain are observed; severe pneumonia and mortality can be seen in severe cases (5).

Obesity is increasing all over the world due to urbanization, economic development, and changes in lifestyle and is considered an epidemic problem. In recent years, one out of every two people is reported to be overweight or obese in industrial countries. Obesity prevalence is 34% in the US (6) and according to Turkey Nutrition and Health Survey-2010 data obesity prevalence was 30.3% in all adults in Turkey (7). Although the mechanism between obesity and COVID-19 is not known clearly, retrospective studies conducted on the influenza A virus H1N1 pandemic in 2009 emphasized that obesity was important in the course of the disease and mortality risk (8,9). Nowadays, obesity is also thought to be an important risk factor for COVID-19, and the increasing COVID-19 mortality in the United States is suggested to be due to the high prevalence of obesity in the country (10).

The increase in the consumption of refined carbohydrates, food with a high glycemic index, saturated fatty acids, processed foods, and red meat with the western-style diet, which is one of the most important causes of obesity, has a proinflammatory effect. In addition, due to insufficient intake of vitamins and minerals that act as antioxidants, antimicrobial agents cannot function adequately and the activation of macrophages is prevented (11). Secondary leptin insufficiency occurs in obesity due to leptin resistance. It is suggested that there may be susceptibility to infections in obese individuals due to the decrease in the immunomodulatory effect of leptin (12). In addition, low-level chronic inflammation caused by increased adipokines [tumor necrosis factor (TNF)-α, interleukin (IL) 6 and resistin, etc.) as a result of amyloid-A secreted by adipose tissue in obesity negatively affects the function of leukocytes and macrophages, altering the immune response and reducing the body's resistance to infections (13).

The number of studies examining the relationship between obesity and COVID-19 is limited in the literature. These studies found that increasing body mass index and obesity cause an increase in the severity of COVID-19 disease, the need for intensive care treatment, and mechanical ventilation (10,14). This study evaluates the relationship between obesity and COVID-19 disease and the effects of obesity on COVID-19 disease course in Antalya province.

Method

This study includes 19-83 years old adults (n=97) who were admitted to the COVID-19 triage outpatient clinic of a state hospital between 01.04.2020 and 01.06.2020 and had quantitative real-time PCR (reverse transcriptase polymerase chain reaction) test positivity in nasopharyngeal swab samples.

Demographic data of the patients, symptoms at hospital admission, thorax computed tomography (CT), routine laboratory test results at admission (leukocyte, platelet, hemoglobin, ferritin, etc.), need for intensive care unit (ICU) and mechanical ventilation, and duration of treatment at hospital and ICU were retrospectively scanned from the hospital data processing system. In order to determine the obesity status of the patients, height and body weight information were obtained from nurse observation forms and body mass index (BMI) was calculated with the formula [body weight (kg)/height (m^2)]. WHO criteria were used in body mass index classification; BMI of individuals below 25.0 kg/m^2 was considered normal, between 25.0-29.0 kg/m^2 as overweight, and 30.0 kg/m^2 and above as obese (15).

Before starting the study, permission was obtained from the Ministry of Health COVID-19 Scientific Research Platform Commission (project number: 2020-05-25T14_00_01); the study was also examined by the Health Sciences University Antalya Training and Research Hospital Ethics Committee, and approval was obtained on 03.06.2020 (decision number: 7-7)

Statistical Analysis

SPSS (Statistical Package for Social Sciences) Windows 22.0 package program was used for all statistical analyzes. For statistical significance, $p<0.05$ was accepted. Descriptive statistics were presented with frequency, percentage, mean ($\bar{X}$), standard deviation (SD), median, and interquartile range (IQR) values. Fisher's Exact Test or Pearson's chi-square test was used in the analysis of the relationships between categorical variables. Kruskal Wallis test was used for nonparametric comparison

Table 1. General characteristics of patients according to body mass index classification

	BMI			
	<25.0 kg/m² normal	25.0-29.9 kg/m² overweight	≥30.0 kg/m² obese	p
Gender, n (%)				
Male	13 (25.5)	20 (39.2)	18 (35.3)	0.640
Female	15 (31.1)	19 (42.2)	12 (26.7)	
Age, median (IQR)	47 (39-60)	39 (30-47)	52 (43-65.5)	0.002
Comorbidity, n (%)				
Hypertension	3 (11.1)	7 (17.9)	12(42.9)	0.012
Coronary artery disease	1 (3.7)	1 (2.6)	2 (7.1)	0.648
COPD	1 (3.7)	-	4 (14.3)	0.099
Asthma	-	5 (12.8)	2 (7.1)	0.149
Diabetes mellitus	2 (7.4)	4 (10.3)	9 (32.1)	0.019
Chronic kidney disease	-	-	1 (3.6)	0.304
Cancer	3 (11.1)	1 (2.6)	1 (3.6)	0.279

BMI: Body mass index, COPD: Choronic obstructive pulmonary disease, IQR: Inter quantile range

of biochemical findings of individuals according to BMI classification, and the ANOVA test was used when the assumption of normal distribution was confirmed. The effect of body mass index being normal (<25.0 kg/m²) or overweight/obese (25.0 kg/m²) on hospitalization, intensive care unit, and mechanical ventilator requirement was examined by logistic regression analysis. Hosmer-Lemeshow test was used for model fitness.

Results

Among the individuals (n=97) participating in the study, 52.6% (n=51) were men and 47.4% (n=46) were women. 40.2% of the individuals participating in the study were overweight, 30.9% were obese, and there was no difference between men and women according to BMI classification (p>0.05). The mean age of the participants was 48.4±15.0 years, the median age of the overweight group was 39 years and the obese group was 52 years.

The evaluation of the participants according to their accompanying diseases revealed that hypertension and diabetes were significantly higher in individuals with overweight and obesity compared to individuals with normal BMI (p<0.05).

Table 2 summarizes the initial symptoms, hospitalization, ICU, and mechanical ventilation needs of the individuals classified according to their BMI. Fever and impairment in olfaction were more common in obese individuals while the frequency of other symptoms was similar among the groups (p<0.05). Thorax CT results demonstrated that bilateral involvement in the thorax was more in overweight and obese individuals, and this difference was statistically significant (p<0.05). The hospitalization rate was higher in overweight and obese individuals (82.1% and 76.7%; respectively) (p=0.051) and obese individuals required mechanical ventilators more frequently (17.9%) (p<0.05). Although modestly significant statistically, one of every five obese individuals required ICU treatment and this rate was higher than normal weight or overweight individuals (p=0.051).

The evaluation of routine biochemical findings of the individuals revealed that platelet levels of overweight individuals were lower than the individuals with normal BMI. Although the levels of IL-6 increased as the BMI of individuals increased (p<0.05), there was no difference between other biochemical findings according to BMI groups (Table 3).

Table 4 shows logistic regression analysis of the relationship between being normal and overweight/obese and BMI, hospitalization, intensive care unit admission, and the need to use a mechanical ventilator. A BMI value of 25.0 kg/m² and above increased hospital admission rate approximately 3.5 times (odds ratio 3.494, 95% confidence interval 1.285-9.505, p<0.05).

Discussion

Changing dietary habits and increasing body fat tissue in recent years cause leptin resistance and inflammation, therefore, the immune response of obese individuals changes, and the body's resistance against infections decreases (11-13). Obesity prevalence is an important public health problem that is rapidly increasing in Turkey as well as in the whole World (7). Centers for Disease Control and Prevention (CDC) reports that individuals with asthma, chronic lung disease, diabetes, heart disease, and chronic kidney disease are in the risk group for many diseases. Obesity may be an important risk factor for COVID-19 disease as it plays a key role in the pathogenesis of these diseases (diabetes, heart diseases, asthma, etc.) specified by the CDC (16). In this study from Antalya, Turkey, more than half of adult patients detected to have COVID-19 positivity with real-time PCR were overweight or obese and a higher body mass index increased COVID-19 disease risk. In Shenzen, China, among 383 adult patients admitted within the first two months of the pandemic, 32% were overweight and 10.7% were obese (17). A study from the US found that among 5,700 COVID-19 cases 41.7% were obese and 19% were morbidly obese (18). In addition, two studies from China to determine the relationship between obesity and

Table 2. Symptoms, hospitalization, need to intensive care and mechanical ventilator according to the classification of body mass index

	BMI			
	<25.0 kg/m² normal	25.0-29.9 kg/m² overweight	≥30.0 kg/m² obese	p
Symptoms, n (%)				
Fever	17 (63.0)	32 (82.1)	25 (89.3)	0.047
Cough	11 (40.7)	22 (56.4)	16 (57.1)	0.373
Respiratory distress	6 (22.2)	7 (17.9)	10 (35.7)	0.236
Back pain	3 (11.1)	3 (7.7)	1 (3.6)	0.566
Muscle/joint pain	6 (22.2)	13 (33.3)	7 (25.0)	0.570
Headache	3 (11.1)	8 (20.5)	2 (7.1)	0.262
Sore throat	4 (14.8)	5 (12.8)	4 (14.3)	0.970
Diarrhea	-	2 (5.1)	2 (7.1)	0.397
Vomitting	-	3 (2.6)	4 (3.6)	0.637
Stomachache	-	2 (5.1)	2 (7.1)	0.397
Taste dysfunction	4 (14.8)	9 (23.1)	9 (32.1)	0.316
Smell dysfunction	-	5 (12.8)	6 (21.4)	0.045
Thorax CT, n (%)				
Unilateral involvement	6 (20.7)	12 (30.8)	8 (26.7)	0.032
Bilateral involvement	7 (24.1)	20 (51.3)	18 (60.0)	
No finding	16 (55.2)	7 (17.9)	4 (13.3)	
Hopitalization, n (%)	15 (55.6)	32 (82.1)	23 (76.7)	0.056
Hopitalization (day), Median (IQR)	6 (4-11)	6.5 (5-12.5)	8 (5-14)	0.364
Mortality, n (%)	2 (7.4)	3 (7.7)	4 (13.3)	0.134
Need ICU care, n (%)	2 (7.4)	5 (12.8)	6 (21.4)	0.051
Length of stay ICU (day), Median (IQR)	10 (8-10)	14 (9-19.5)	14.5 (11-20.5)	0.380
Need mechanical ventilator, n (%)	1 (3.7)	2 (5.1)	5 (17.9)	0.034
Mechanical ventilation (day), Median (IQR)	7	14 (8-14)	15 (7-23)	0.481

BMI: Body mass index, ICU: Intensive care unit, CT: Computed tomography, IQR: Inter quantile range

Table 3. Biochemical parameters of patients

BMI				
Biochemical parameters	<25.0 kg/m² normal	25.0-29.9 kg/m² overweight	≥30 kg/m² obese	p
	X ± SD	X ± SD	X ± SD	
Leukocyte (10³mm³)	6600.0±2724.1	6345.9±3070.9	5910.1±2209.1	0.656
Platelet (10³mm³)	271608.7±90995.3	220729.7±76162.3	230465.9±85958.9	0.023
Hemoglobin (g/dL)	13.2±2.0	13.4±1.5	112.8±2.2	0.442
Lymphocyte (10³mm³)	1508.7±822.9	1442.5±668.1	1321.4±565.9	0.607
N/L ratio	3.8±3.4	3.3±2.4	5.0±6.3	0.593
Ferritin (µg/L)	242.0±636.1	217.9±322.1	231.7±193.7	0.980
D-dimer	275.8±253.5	407.3±1206.5	262.6±274.9	0.788
Interleukin-6	17.4±31.7	25.9±28.4	70.9±53.8	0.014
C-reactive protein (mg/L)	33.3±71.1	36.8±50.1	56.1±81.8	0.455

BMI: Body mass index, N/L ratio: Neutrophil/lymphocyte ratio, SD: Standard deviation

COVID-19 found that the disease severity increased with higher BMI values in COVID-19 cases (17-19). In obese individuals, abdominal fat causes an increase in pleural pressure, a decrease in functional residual capacity, and expiratory reserve volume

Table 4. Logistic regression analysis of the relationship between normal and overweight/obesity according to body mass index for hospitalization, need to intensive unit care and a mechanical ventilator

	Odds ratio	95% CI	p
Hospitalization	3.494	1.285-9.505	0.014
Nedd to intensive unit care	1.188	0.122-11.550	0.882
Need to mechanical ventilator	2.196	0.102-47.126	0.615

CI: Confidence interval

(20). In retrospective studies conducted on the influenza A virus H1N1 pandemic, an increase in body weight caused pneumonia and severe lung infections (8,21). This study demonstrated that fever which is an upper respiratory infection symptom was more frequent in obese individuals and bilateral thoracic involvement was present in more than half of overweight and obese individuals which suggests that there was an association between obesity and disease severity. Other studies have also reported that obese individuals had more fever and cough symptoms compared to individuals with normal BMI (10,16).

In a study conducted in the USA, compared to individuals with a BMI <30 kg/m^2, the risk of hospitalization of individuals diagnosed with COVID-19 and with a BMI of 30-40 kg/m^2 was 4.3 times, and in those with a BMI ≥40 kg/m^2 was 6.2 times higher (10). Gao et al. (22) demonstrated that among hospitalized COVID-19 cases, obese individuals had longer hospital stays compared to non-obese individuals [median 23 (IQR: 17-30) and 18 (IQR: 13-24) days, respectively; p<0.05]. In the USA, 1428 COVID-19 cases admitted to hospital between 01 and 30 March 2020 were screened from the COVID-19-Associated Hospitalization Surveillance Network [COVID-NET] system. 90% of these cases had one or more comorbidities and 48.3% were obese (23). In this study, although the hospitalization rates of overweight and obese individuals were high, they were modestly significant. Logistic regression analysis in which individuals were classified as normal weight (BMI <25.0 kg/m^2) and overweight/obese (≥25.0 kg/m^2), BMI ≥25.0 kg/m^2 increased the rate of hospitalization approximately 3.5 times (odds ratio 3.494; 95% confidence interval 1.285-9.505, p<0.05). Knowing the risk for hospitalization is extremely important to start early treatment and estimate the need for hospital beds and personnel (10). Since obesity is an important factor affecting hospitalization status in COVID-19 cases, it should be evaluated in COVID-19 patients.

In a study conducted in England, which is one of the countries with high mortality due to the new type of coronavirus, 72% of the individuals receiving treatment in the intensive care unit due to COVID-19 were overweight or obese. Among 196 individuals participating in the study, 32% had BMI between 25-30 kg/m^2, 33% between 30-40 kg/m^2, and 7% 40 kg/m^2 and above (24). In a study conducted in the USA, individuals with BMI <30 kg/m^2 needed less ICU treatment compared to individuals with BMI 30 kg/m^2 and above (p<0.001) (25). In a similar study conducted in France (n=124), 48% of COVID-19 cases treated in the intensive care unit were obese (BMI >30.0 kg/m^2) and 28% were first degree obese (BMI >35.0 kg/m^2). An evaluation independent from age, diabetes, and hypertension mechanic ventilator requirement of COVID-19 cases increased with increasing BMI (p<0.050). In addition, the study found that individuals with first-degree obesity (BMI 30.0-35.0 kg/m^2) had a 7.36 times higher rate of mechanical ventilator requirement than individuals with normal body weight (26). In this study, although the number of patients who needed intensive care treatment was quite low (n=13), the number of overweight and obese individuals who needed intensive care treatment was higher than those with normal body weight (p=0.051). A small sample size may be responsible for modest statistical significance.

Biochemical findings such as lymphocyte, CRP, IL-6, and D-dimer evaluated at the time of admission to the hospital in COVID-19 cases were associated with the severity of the disease (10). Studies have demonstrated that as the severity of COVID-19 disease increases, the number of lymphocytes decreases, and the levels of CRP, IL-6, and D-Dimer increase (10,18). The increase in adipose tissue in obesity causes an increase in the levels of some proinflammatory markers [IL-6, (TNF-α), and CRP]. Therefore, obesity is considered a low-level chronic inflammatory condition (13). Increasing inflammation in obese individuals can also increase the severity of COVID-19 disease (18). In this study, higher IL-6 levels of obese individuals are thought to affect the severity and prognosis of the disease.

Study Limitations

This study has several limitations. The small sample size and the fact that it is a cross-sectional retrospective study are the most important limitations. In addition, since this was a retrospective study, the smoking status of the patients was not questioned. Smoking is also an important factor that can increase the severity and complications of COVID-19 disease.

Conclusion

In conclusion, this study found that increased BMI is an important risk factor for COVID-19 which increases hospitalization rates. Obesity rates are increasing day by day in Turkey. In societies with high obesity rates, evaluating obesity in COVID-19 patients is important for early initiation of treatment and reduction of hospitalization rates.

Ethics

Ethics Committee Approval: University of Health Sciences Turkey Antalya Health Application and Research Center (decision no: 7/7).

Informed Consent: Retrospective study.

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: A.S.K., M.T., N.S.K., Design: A.S.K., M.T., N.S.K., Data Collection or Processing: M.T., N.S.K., Analysis or

Interpretation: A.S.K., M.T., N.S.K., LiteratureSearch: A.S.K., M.T., N.S.K., Writing: A.S.K., M.T., N.S.K.

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Original Article

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Health Care Professionals' Views on Healthcare Provision During the COVID-19 Pandemic: A Descriptive Study

Sağlık Çalışanlarının COVİD-19 Salgını Sırasında Sağlık Hizmeti Sunumuna İlişkin Görüşleri: Betimleyici Bir Çalışma

Özgür TATLI[1], Perihan ŞİMŞEK[2], Yasemin GÜNER[3], Elif KILIÇ GÜNER[4], Abdülkadir GÜNDÜZ[1]

[1]Karadeniz Technical University Faculty of Medicine, Department of Emergency Medicine, Trabzon, Turkey
[2]Balıkesir University Faculty of Health Sciences, Balıkesir, Turkey
[3]Karadeniz Technical University, Faculty of Medical Science, Department of Medical Education, Trabzon, Turkey
[4]Karadeniz Technical University Faculty of Health Sciences, Education Coordinator, Trabzon, Turkey

ABSTRACT

Objective: The Coronavirus disease-19 (COVID-19) pandemic outbreak put a heavy burden on the health system. In this process, determining the difficulties faced by healthcare professionals is important in terms of making the necessary preparations for similar outbreaks and improving healthcare provision. The aim of the study was to determine the views of healthcare professionals about healthcare provision and the difficulties they faced during the COVID-19 pandemic period.

Methods: The descriptive study was carried out with the participation of 89 doctors and 58 nurses working in a university hospital in the Black Sea Region. In the study, the data form developed by the researchers and the job-related strain were used as data collection tools.

Results: While the psychological difficulty stated by the participants in the study was the anxiety of infecting the family/relatives (93.2%), the factor that made the service delivery the most participants was expressed as the discomfort (85%) caused by using personal protective equipment. It was found that the level of anxiety felt while providing healthcare services was higher in women compared to men (p=0.01) and nurses than physicians (p=0.001). The average score of the participants on the job-related strain was 37.51±5.80.

Conclusion: The concern of infecting relatives/family during the COVID-19 pandemic poses a psychological difficulty for healthcare

ÖZ

Amaç: Koronavirüs Hastalığı-19 (COVID-19) pandemisi sağlık sistemi için ağır bir yük getirmiştir. Bu süreçte, sağlık çalışanlarının karşılaştığı güçlüklerin belirlenmesi, benzer salgınlar için gerekli hazırlıkların yapılabilmesi ve sağlık hizmeti sunumunun iyileştirilebilmesi açısından önem taşımaktadır. Çalışmada sağlık çalışanlarının COVID-19 salgın döneminde sağlık hizmeti sunumuna ilişkin görüşlerinin ve bu süreçte karşılaştıkları güçlüklerin belirlenmesi amaçlandı.

Yöntemler: Tanımlayıcı nitelikte olan çalışma Karadeniz Bölgesi'nde bulunan bir üniversite hastanesinde çalışmakta olan 89 doktor ve 58 hemşirelerin katılımıyla gerçekleştirildi. Çalışmada veri toplama aracı olarak araştırmacılar tarafından geliştirilen veri formu ve işe bağlı gerginlik ölçeği kullanıldı.

Bulgular: Çalışmada en fazla katılımcı tarafından belirtilen psikolojik güçlük aile/yakınlara hastalık bulaştırma kaygısı (%93,2) iken hizmet sunumunu en fazla güçleştiren etmen kişisel koruyucu ekipman kullanmanın verdiği rahatsızlık (%85) olarak ifade edildi. COVID-19 salgın döneminde sağlık hizmeti verirken hissedilen kaygı düzeyinin kadınlarda erkeklere göre (p=0,01) ve hemşirelerde hekimlere göre (p=0,001) daha fazla olduğu bulundu. Katılımcıların işe bağlık gerginlik ölçeğinden aldığı ortalama puan 37,51±5,80 idi.

Sonuç: COVID-19 salgın döneminde yakınlar/aileye hastalık bulaştırma endişesi sağlık çalışanları için psikolojik bir güçlük

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Address for Correspondence: Yasemin GÜNER, Karadeniz Technical University, Faculty of Medical Science, Department of Medical Education, Trabzon, Turkey
E-mail: yasemin-kul@hotmail.com **ORCID ID:** orcid.org/0000-0003-4932-771X

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ABSTRACT

professionals. Using many personal protective equipments is a factor that makes service delivery difficult. The level of anxiety associated with providing health care is higher in nurses and women during this period.

Keywords: Anxiety, coronavirus disease, health care professionals, health services, pandemic

ÖZ

oluşturmaktadır. Birçok kişisel koruyucu ekipman kullanmak hizmet sunumunu güçleştiren bir etmendir. Hemşirelerde ve kadınlarda bu dönemde sağlık hizmeti sunma ile ilişkili kaygı düzeyi daha fazladır.

Anahtar Sözcükler: Anksiyete, koronavirüs hastalığı, sağlık profesyonelleri, sağlık hizmetleri, pandemi

"What is already known about the topic?"

- Healthcare professionals face many challenges providing healthcare during the COVID-19 pandemic.
- Healthcare professionals need accurate, reliable, and up-to-date information to deal with the COVID-19 outbreak.

"What this paper adds".

- Anxiety about infecting families and relatives was the major psychological challenge for healthcare professionals.
- Using personal protective equipment, which is essential for protecting healthcare workers, has made healthcare services difficult.
- Isolation measures were the main topic that healthcare professionals needed information on during the COVID-19 pandemic.

Introduction

On December 31, 2019, unexplained cases of pneumonia began to appear in Wuhan City, Hubei Province, China. The factor responsible for these cases was determined to be a new Coronavirus disease-19 (COVID-19), which was not previously detected in humans on January 7, 2020. The first case outside China was seen in Thailand on January 13, 2020, and the virus spread rapidly all over the world (1). As of June 28, while the number of confirmed COVID-19 infected cases worldwide was 9.95 million, 498,519 people died due to this infection (2).

Scientific studies are ongoing to prevent the disease spread. Research focuses primarily on disease transmission routes, vaccination, and measures that can be taken. One of the most emphasized measures in this regard is protective behavior (3). It was reported that vulnerability, perceived risk, and fear are among the most important factors in the individuals' engagement with protective behaviors (4). Although social rules and protective behavior can slow disease spread, the pandemic's effect is expected to continue for a long time (5,6).

During the COVID-19 pandemic, healthcare professionals try to fulfill their duties at a high risk of infection. During this period, more than 3,000 healthcare workers in China had a coronavirus infection (7). In Italy, 20% of healthcare professionals serving in the pandemic period were infected (8). During the COVID-19 pandemic, it was reported that 26% of COVID-19 cases in Spain (9) and 11% of cases in the United States (10) were healthcare workers. In a study conducted on an international basis, it was ascertained that 708 healthcare workers lost their lives due to COVID-19 infection until April 27, 2020; 51.5% were doctors, and 17.7% were nurses (11).

In addition to the risk of infection, uncertainties caused by the pandemic, stress factors associated with the pandemic, changes in social life, insufficient personal protective equipment, emotional breakdown due to infected co-workers, having to work long hours, and ethical dilemmas posed by the inability to provide the necessary health services to all patients because of insufficient intensive care conditions and the inadequate number of mechanical ventilators were listed among the difficulties faced by healthcare professionals in this process (12,13). All these challenges can negatively affect healthcare professionals psychologically, and this effect may last for a long time. It is determined that the stress and psychological distress experienced by the healthcare professionals continued even one year after the SARS (2002-2004) pandemic, which mainly affected Asian countries (14).

These difficulties may influence the motivation and willingness of healthcare professionals to perform their duties. According to the results of a meta-analysis evaluating the factors affecting the healthcare workers' willingness to work during the influenza outbreak, perceived personal security, pandemic risk awareness, and adequate clinical knowledge, role-specific knowledge, and confidence in personal skills associated with the pandemic were identified as factors that increase willingness to work in this process. The responsibility of childcare has been specified as a factor that lowers the willingness to work during the pandemic disease (15). Low work willingness is also a factor that reduces work efficiency (16). During the pandemic period, healthcare professionals are expected to perform their duties more efficiently.

During pandemics, it is essential to determine the experiences of healthcare professionals and examine their opinions about the difficulties they experienced, to both increase the willingness of the workforce and ensure the safety of employees.

Method

Design

The study was designed as a descriptive research study.

Recruitment of the Participants

The research was conducted at a university hospital in Turkey in a province in the Eastern Black Sea region. The province where

the research was conducted was among the top 10 provinces with the highest number of deaths and the top 15 provinces with the highest number of cases in the peak period of the COVID-19 pandemic. In addition, the center where the research was performed serves as an education research center and is where patients with special treatment and care needs are referred from neighborhood provinces. Individuals involved in this study consisted of physicians and nurses working at units where patients infected with coronavirus or suspected of infection were followed in the university hospital where the research was conducted. The sampling acceptance criteria determined in the study are as follows: Being over the age of 18, volunteering to participate in the study, being a member of the physician or nursing profession, being responsible for patient care and treatment during the COVID-19 pandemic period, and working actively. The study's exclusion criterion was having less than three months of work experience. The required study sample size to be reached was calculated as 132, with the sample size formula used in cases where the number of individuals in the population is known in the prediction of the mass ratio.

$n= N\ t^2\ p\ q/d^2(N-1)+t^2\ p\ q$

n= Number of individuals to be sampled

N= Number of individuals in the population (200)

p= The estimated prevalence of the incident to be investigated in the population (0.5)

q= 1-p (0.5)

t= Theoretical value for the greatest degree of freedom in the z table at a given confidence level (1.96 for 95% confidence interval)

d= Standard error of the rate to be determined in the study (0.05 for 95% confidence interval)

n= 200x1.962x0.5x0.5/0.052x1499+1.962x0.5x0.5=132

Intervention

The physicians and nurses in the units where the patients infected with coronavirus or suspected of infection were followed up were invited to participate in the study by giving information about the study. The data collection tool link was then conveyed to the participants through the WhatsApp groups used by physicians and nurses working in these units for communication.

Outcome Measures and Data Collection

In the study, the job-related strain scale, and the literature form (12,13) were used by the researchers, and the data form created using the Google forms tool was used. The data form consists of seven parts. The first part had seven questions about descriptive characteristics. The second part had two questions regarding healthcare professionals' views on education needs and their information sources about COVID-19. The third part asked two questions regarding the difficulties of healthcare professionals during the management of coronavirus infection cases. The fourth part included one question regarding the technological tools that healthcare professionals needed within the scope of patient care. In the fifth part, one question asked about the level of self-sufficiency in providing health services during the COVID-19 pandemic period. One question was about the level of anxiety related to providing healthcare services. The data form's suitability regarding content was evaluated by four lecturers consisting of physicians and nurses.

Job-related strain scale: The scale was developed by Revicki et al. (17) in 1991. The validity and reliability of the scales conducted by Aslan et al. (18) in Turkey (1998) and the reliability coefficient were between 0.85 and 0.90, respectively. The Job-Related Strain Scale is a 4-point Likert-type scale with 18 items developed to determine job-related tension and stress in health workers. The items are evaluated as "totally suitable for me," "greatly suitable for me," "partially suitable for me," and "not suitable for me at all." Each item is scored between 4-1 points. Items 2, 4, 8, 9, 11, and 15 of the scale are graded reversely. The lowest score is 18, and the highest score is 72. Studies have shown that the 15th item decreases the item-test correlations of the scale. Therefore, article 15 was removed from the scale (18,19). In this study, the evaluation was made on 17 items, and the Cronbach alpha reliability coefficient was 0.67.

Statistical Analysis

Data analysis: SPSS 23 (Statistical Package of Social Sciences) program was used for data analysis. Qualitative data are shown in numbers and percentages (%) and analyzed by the chi-square test. The suitability of the quantitative data for normal distribution was evaluated with the Kolmogorov-Smirnov test. Parametric tests were used to analyze data that conform to a normal distribution, and non-parametric tests were used to analyze non-compliant data.

Ethical considerations: Ethical approval with the 24237859-272 document number was obtained from the Regional Local Ethics Committee for the study. Informed consent was obtained from participants after explaining the aim of the study. Also, an "I was informed about the study, and I agree to participate in the study" button was placed in the first part of the data collection tool. Clicking the button was mandated to answer the questions on the data collection form.

Results

The overall response rate was 73.5% in the study. The average age of the healthcare workers who participated in the study was 33.70±6.8 [minimum(min)=23, maximum (max)=54] years, and 46.9% were male, and 60.5% were physicians. The average working time of the participants in their professions was 10.0±7.0 (min=1, max=34) years. In the study, 4.1% of participants consisted of healthcare professionals who provided care only to patients diagnosed with COVID-19. While the rate of caregivers for suspicious patients was 43.5%, the rate of caregivers for both suspected and definitive patients was 52.4% (Table 1).

In the study, the psychological difficulties stated by most participants regarding the provision of health services during

Table 1. Participant characteristics

n		Nurse (n=58)		Physician (n=89)		Total (n=147)	
		%	n	%	n	%	
Gender	Female	50	86.2	28	31.5	78	53.1
	Male	8	13.8	61	68.5	69	46.9
Age (years)	23-30	24	41.4	35	39.3	59	40.1
	31-40	20	34.5	41	46.1	61	41.5
	>40	14	24.1	13	14.6	27	18.4
Working time in the profession	1-5 year	12	20.7	33	37.1	45	30.6
	6-10 year	14	24.1	32	36.0	46	31.3
	>10 year	32	55.2	24	27.0	56	38.1
Education status	High school/Associate degree	17	29.3	-	-	17	11.6
	Undergraduate	35	60.3	20	22.5	55	37.4
	Graduate	6	10.3	69	77.5	75	51.0
Chronic disease	Yes	17	29.3	14	15.7	31	21.1
	No	41	70.7	75	84.3	116	78.9
Working unit	Emergency Department	32	55.2	68	76.4	100	68.0
	Operating room	2	3.4	-	-	2	1.4
	Inpatient units	23	39.7	16	18.0	39	26.5
	Intensive care	1	1.7	5	5.6	6	4.1
Patient groups who were provided care by healthcare professionals	Diagnosed with COVID-19	2	3.4	4	4.5	6	4.1
	Suspicious	30	51.7	34	38.2	64	43.5
	Both	26	44.8	51	57.3	77	52.4

the COVID-19 pandemic were the anxiety (93.2%) of infecting the family/relatives. In the study, factors that make healthcare provision difficult for healthcare workers were asked. The discomfort caused using personal protective equipment was stated by the highest number of participants (85.0%) as a factor that makes it difficult to provide healthcare services. The frequency of staff insufficiency and overtime were considered factors that make healthcare provision difficult was significantly higher in the nurse group than the doctor group ($p<0.05$) (Table 2).

During the COVID-19 pandemic, the most needed training subject by healthcare workers was isolation methods (82.3%). The second was personal protective equipment (70.7%), and the third was the complications that could develop in COVID-19 case management and their prevention methods (69.4%). While the frequency of expressing that nurses needed training on respiratory system care was higher than physicians, physicians needed training about diagnostic methods was higher ($p<0.05$).

Most healthcare professionals used the official website of the Ministry of Health to get information on COVID-19 case management (87.8%). When sources of information on COVID-19 case management were analyzed by professional groups, most nurses (82.8%) received information from the Ministry of Health official webpage, and 79.3% of them from in-service training programs. The majority of doctors (87.8%) received information from the Ministry of Health official webpage, 66.7% of doctors from in-service training programs, and 59.9% of them from academic databases. Nurses had a significantly higher rate of receiving information from in-service training and television programs ($p<0.05$). Doctors used academic databases and search engines significantly more than nurses ($p<0.05$) (Table 3, 4).

As technological tools to facilitate the provision of health services during the COVID-19 pandemic, 58.5% of participants stated that sound systems provided a connection with other team members from the isolation room, 48.3% of them stated their utility as patient follow-up and early warning systems, and 37.4% of them stated their use as call systems. In the COVID-19 pandemic, there was no significant difference between occupational groups in terms of opinions regarding the technological tools required by healthcare professionals ($p>0.05$) (Table 4).

In the study, the average score of health workers on the job-related strain level was calculated as 37.51±5.80 (min=18, max=53). When the scale scores were examined according to the variables of the profession, age groups, gender, education level, and duration in the profession, there was no statistically significant difference between the groups ($p>0.05$) (Table 5).

In the study, 25.9% of healthcare professionals who participated stated that they considered themselves completely sufficient while providing care to patients who were followed up with suspicion

Table 2. Healthcare professionals' difficulties during the COVID-19 pandemic period (n=147)

	Nurse n (%)	Physician n (%)	Total n (%)	p
Psychological difficulties				
Anxiety about infecting family/relatives	53 (91.4)	84 (94.4)	137 (93.2)	0.516
Anxiety about getting infected	46 (79.3)	60 (67.4)	106 (72.1)	0.166
Unable to provide quality communication with patients	25 (43.1)	48 (53.9)	73 (49.7)	0.199
Losing the desire to go to work	28 (48.3)	34 (38.2)	62 (42.2)	0.299
Disruption of family processes due to work	25 (43.1)	32 (36.0)	57 (38.8)	0.486
Worries about death	20 (34.5)	13 (14.6)	33 (22.4)	0.009
Sense of inadequacy in intervention	14 (24.1)	17 (19.1)	31 (21.1)	0.600
Factors that make healthcare delivery difficult				
PPE use discomfort	52 (89.7)	73 (82.0)	125 (85.0)	0.302
Failure to provide adequate personal hygiene when leaving the workplace	33 (56.9)	46 (51.7)	79 (53.7)	0.536
Lack of staff	36 (62.1)	32 (36.0)	68 (46.3)	0.002
Insufficient information to ensure patient/employee safety	16 (27.6)	24 (27.0)	40 (27.2)	1.000
Mandatory quarantine, unable to go home	8 (13.8)	14 (15.7)	22 (15.0)	0.932
Overtime	17 (29.3)	12 (13.5)	29 (19.7)	0.032

COVID-19: Coronavirus disease-19

Table 3. Healthcare professionals' views on educational needs and their information sources about COVID-19

	Nurse (n=58) n (%)	Physician (n=89) n (%)	Total (n=147) n (%)	p
Educational subjects				
Insulation measures	48 (82.8)	73 (82.0)	121 (82.3)	1.000
Use of PPE*	41 (70.7)	63 (70.8)	104 (70.7)	1.000
Preventing complications	41 (70.7)	61 (68.5)	102 (69.4)	0.926
Respiratory care	46 (79.3)	52 (58.4)	98 (66.7)	0.014
Medical treatments	31 (53.4)	49 (55.1)	80 (54.4)	0.848
Diagnostic methods	17 (29.3)	49 (55.1)	66 (44.9)	0.002
Sources of information				
Official ministry website	48 (82.8)	81 (91.0)	129 (87.8)	0.217
In-house training	46 (79.3)	52 (58.4)	98 (66.7)	0.014
Academic databases	21 (36.2)	67 (75.3)	88 (59.9)	0.000
Social sharing sites	26 (44.8)	32 (36.0)	58 (39.5)	0.366
Internet search engines	14 (24.1)	37 (41.6)	51 (34.7)	0.046
Television programs	24 (41.4)	10 (11.2)	34 (23.1)	0.000
Newspapers	8 (13.8)	8 (9.0)	16 (10.9)	0.520

*PPE: Personal protective equipment, COVID-19: Coronavirus disease-19

of COVID-19 or who had a definitive diagnosis. While 70.1% of participants found themselves partially sufficient in this regard, 4.1% (n=6) stated that they did not consider themselves sufficient. During the COVID-19 pandemic, no significant difference was found regarding the self-sufficient qualifications of healthcare professionals while performing their duties (p>0.05).

The healthcare workers who participated in the study were asked if providing healthcare during the COVID-19 pandemic caused anxiety. While 2.0% of health workers stated that they did not experience anxiety, 33.3% (n=49) rated their level of anxiety due to providing health services in this period as "very" and 64.6% as "partially". When the level of anxiety caused by performing health services during the COVID-19 pandemic was analyzed according to healthcare professionals' descriptive characteristics, the average rank of women (81.13) was significantly higher than that of men (65.94) (U=2135.0, p=0.01). When the professions were compared, the average level of anxiety level of nurses

Table 4. Technological tools required by healthcare workers during the COVID-19 pandemic (n=147)

	Nurse n (%)	Physician n (%)	Total n (%)	p
Sound systems to connect with other team members from the isolation room	35 (60.3)	51 (57.3)	86 (58.5)	0.846
Patient monitoring and early warning systems	33 (56.9)	38 (42.7)	71 (48.3)	0.092
Hospital paging system	24 (41.4)	31 (34.8)	55 (37.4)	0.530
Video systems for communication with other team members from the isolation room	26 (44.8)	26 (29.2)	52 (35.4)	0.079
Mobile applications	21 (36.2)	30 (33.7)	51 (34.7)	0.894
Telehealth applications for communication with healthcare professionals at other institutions	21 (36.2)	22 (24.7)	43 (29.3)	0.190
Decision support systems	13 (22.4)	27 (30.3)	40 (27.2)	0.387
Emergency button	14 (24.1)	19 (21.3)	33 (22.4)	0.846

COVID-19: Coronavirus disease-19

Table 5. Distribution of Job-Related Strain scale scores by descriptive characteristics

		Median (min-max)	Test	p
Profession	Nurse	38.0 (27-49)	U=2359.5	0.379
	Physician	37.0 (18-53)		
Gender	Female	38.0 (18-49)	U=2532.5	0.538
	Male	37.0 (27-53)		
Education status	High School/Associate degree	37.0 (28-49)	H=0.564	0.754
	Undergraduate	37.0 (27-52)		
	Graduate	37.0 (18-53)		
Working time in profession*	1-5 years	37.68±5.97	F=0.460	0.632
	610 years	38.02±5.38		
	>10 years	36.94±6.05		
Age*	23-30	37.62±5.57	F=0.126	0.882
	31-40	37.62±5.85		
	>40	37.00±6.37		

*data are presented as, min: Minimum, max: Maximum

(85,76) was higher than doctors (66.34) (U=1899.0, p=0.001). When the anxiety level caused by providing healthcare services in the COVID-19 pandemic period was examined according to other introductory features, there was no statistically significant difference (p>0.05).

Discussion

As a consequence of its high virulence and genetic properties, COVID-19 has spread rapidly. The rapid expansion has turned into a pandemic that will shake the economic structure, social life, and health system of countries worldwide. In this process, various difficulties have arisen for all layers of society. Health workers, who are responsible for fighting the pandemic and maintaining health services, are among the most affected individuals in this process (12).

The study ascertained that the psychological difficulties healthcare professionals experienced the most during the COVID-19 pandemic were concerns about infecting their family/relatives and anxiety about getting infected. Similarly, in the SARS pandemic, healthcare workers expressed their fear and anxiety about infecting their families, friends, and colleagues (19). During the pandemic of COVID-19, 3387 healthcare workers were infected in Hubei Province in China until February 25, 2020, which caused increased concern among healthcare workers (20). In addition, COVID-19 infection is not only transmitted through symptomatic individuals, but asymptomatic individuals can become infectious and viral transmission from healthcare professionals to family members is common (11,21). During the COVID-19 pandemic, to prevent their family members from getting infected, healthcare professionals were not allowed to go home, and they were provided different accommodation services (22,23). Nevertheless, the study results emphasize the importance of early detection of psychological problems faced by healthcare workers during pandemics and the need to establish adequate support systems and develop solutions.

In the current study, in the process of the COVID-19 pandemic, most participants stated that the discomfort caused by the use of personal protective equipment made healthcare provision difficult. The use of personal protective equipment during the pandemic is vital to protect healthcare workers against the virus. It has been established that none of the healthcare professionals who performed the procedures that cause exposure to respiratory tract secretions of COVID-19 patients by using personal protective equipment were infected (24). However, various studies showed that the use of this equipment could lead to various problems. In the study of Oranges et al., due to personal protective equipment, skin problems in the nose and cheeks have generally been reported. In addition, symptoms such as burning, itching, or stinging could be observed due to the long stay of the masks on faces. This can lead healthcare professionals to perform behaviors that facilitate the spread of infection, such as adjusting and touching the equipment (25). Personal protective equipment can also cause dehydration, sweating, and fatigue; wearing personal protective equipment for a long time while working may cause isolation, claustrophobia, and anxiety (26). Healthcare workers' working hours can be shortened by providing personnel support to prevent these problems. In addition, by developing technological opportunities, producing personal protective equipment that healthcare professionals can use more easily is considered necessary.

Approximately half of the participants stated that staff shortage and overtime made healthcare provision difficult. The insufficient number of health professionals is a common problem for the whole world (27). However, healthcare workers being quarantined because they got infected or their family members were infected during the pandemic of COVID-19 further increased the need for healthcare workers (28,29). Especially at the beginning of the pandemic, unknown infectious factors, insufficient personal protective equipment, and the low level of awareness about the use of this equipment increased the risk in the role played by healthcare professionals. As a result, healthcare workers' workload and working time increased (20). It was also found that the frequency of staff shortage and overtime considered as factors that make healthcare provision difficult was higher in the nurse group than the physician group in the study. This may be related to the fact that nurses communicate more with patients than other healthcare professionals and are directly involved in the diagnosis, treatment, and care of patients. In addition, it is believed that since women constitute the majority of nurses, and overtime can cause women to experience anxiety of not being able to fulfill their domestic and social responsibilities. In addition, the anxiety in question may be higher in the nurse group than in the male gender-based physician group.

It was founded that most health professionals needed training on isolation measures. Because of the insufficient number of personnel employed in intensive care and infection services during pandemics, healthcare professionals working in different units can be assigned to these units (30). However, the extremely rapid progress of the process can make it difficult for healthcare professionals to devote enough time to training on the management of infected cases and new tasks. As a result, healthcare professionals may feel the need for training on various topics related to infected case management. In the study, the other topics that healthcare professionals needed training the most were the use of personal protective equipment, and complications that could occur in COVID-19 case management, and ways to prevent them. It is essential to organize the necessary training activities for healthcare professionals, prevent the spread of the infection in the hospital environment, and maintain the best patient care.

The official website of the Ministry of Health was the source of information that was used by healthcare professionals most frequently for gathering information on COVID-19 case management. In a study conducted during the H1N1 outbreak period, healthcare professionals often obtained the information they needed via radio and television. The rate of benefiting from the internet and medical journals was low (31). In our study, physicians used academic databases and search engines, and nurses used television programs to obtain information during the COVID-19 pandemic. Similar to our findings, it was found that nurses consulted specialists and colleagues rather than using the internet for professional information (32), whereas physicians preferred internet resources to obtain professional knowledge (33). Considering the resources preferred by healthcare professionals to obtain the information they need is important regarding reaching the target of personnel training activities during pandemics. In addition, distance in-service training programs may be useful for training and awareness-raising activities.

We found that that approximately half of the participants thought that various telemedicine applications, patient follow-up, and early warning systems could facilitate healthcare delivery during the COVID-19 pandemic. Due to its highly contagious nature, COVID-19 infection necessitated working under strict isolation measures. This situation can make communication between healthcare workers difficult and may cause disruptions in the bedside consultation process. In addition, the very rapid spread of COVID-19 infection has revealed the need to obtain accurate information about case management for healthcare professionals very quickly and to receive support from technological tools to meet the rapid increase in the need for treatment and care. Telemedicine is considered a groundbreaking technology that can provide online conversation and real-time clinical data exchange to tackle these challenges caused by the pandemic and combat outbreaks. Telemedicine was used for remote patient follow-up, multidisciplinary care organizations, and educational purposes in this period (34).

In our study, it was ascertained that healthcare workers received moderate scores from the job-related strain scale. The uncertainties brought about by the pandemic process can be a source of anxiety and tension. In addition, facing the infectious agent directly, trying to meet the complex care needs of patients both physiologically and psychologically, and managing to continue their treatment are factors that may affect healthcare workers'

job-related strain (35,36). The studies conducted determined that healthcare professionals experienced psychological distress during the COVID-19 pandemic and showed symptoms of anxiety, depression (37), and insomnia (38).

In the current study, nurses experienced more anxiety than physicians and women more than men while caring for COVID-19-infected or suspicious patients. Similar to our study, the anxiety level of nurses in the severe acute respiratory syndrome (2002-2004) outbreak was higher than in physicians (39). Nurses who continue to provide treatment and care services of COVID-19 patients are exposed to a high risk of infection because of their close, frequent contact with patients and prolonged time working during the pandemic. These stressful working conditions can result in anxiety and post-traumatic stress disorder (37,38).

Study Limitations

The study was carried out at a single center. This caused study limitations. Because of social distance rules and the outbreak situation, the study was not conducted face to face. This is another limitation of the study.

Conclusion

In the COVID-19 pandemic period, using personal protective equipment was a factor that made it difficult for healthcare workers to work. In contrast, anxiety about transmitting the disease to others was a major concern for healthcare workers. During the COVID-19 pandemic, health workers mostly used the official website of the Ministry of Health for information. According to healthcare professionals, various telemedicine applications are technological tools that can facilitate service delivery in this process.

Ethics

Ethics Committee Approval: Ethical approval with the 24237859-272 document number was obtained from the Regional Local Ethics Committee for the study.

Informed Consent: Informed consent was obtained from participants after explaining the aim of the study. Also, an "I was informed about the study, and I agree to participate in the study" button was placed in the first part of the data collection tool. Clicking the button was mandated to answer the questions on the data collection form.

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: Ö.T., P.Ş., Y.G., E.K.G., A.G., Design: Ö.T., P.Ş., Y.G., E.K.G., A.G., Data Collection or Processing: Ö.T., P.Ş., Y.G., E.K.G., E.K.G., Analysis or Interpretation: Ö.T., P.Ş., Y.G., Literature Search: Ö.T., P.Ş., Y.G., Writing: Ö.T., P.Ş., Y.G., E.K.G., E.K.G.

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Microbiological Diagnosis of COVID-19

COVİD-19'un Mikrobiyolojik Tanısı

Bilge SÜMBÜL, Mehmet Ziya DOYMAZ

Bezmialem Vakıf University Faculty of Medicine, Department of Medical Microbiology, İstanbul, Turkey

ABSTRACT

Various tests are used to detect the severe acute respiratory syndrome-coronirus-2 (SARS-CoV-2) virus causing Coronavirus disease-19 (COVID-19) disease. Today, the realtime (RT) -PCR test combined with the reverse-transcription reaction is the gold standard method used to diagnose SARS-CoV-2. This method is referred to as quantitative realtime PCR (RT-qPCR) because it determines not only the presence of SARS-CoV-2 but also the amount of virus in the specimen. Due to the use of virus-specific primers, the specificity of the tests is considered to be 100%. For this test, swab samples taken from the upper respiratory tract such as nasopharyngeal and throat, samples from the lower respiratory tract areas such as sputum and bronchoalveolar lavage fluid, rectal swab, feces, serum and urine samples are preferred. Correct use of personal protective equipment (PPE) by healthcare professionals during sampling and testing is important. Rapid antigen tests used in addition to RT-qPCR test for the diagnosis of SARS-CoV-2 are advantageous due to the theoretical rapid result time and low cost, but the sensitivity of this method is known to be very low. Virus detection in cell cultures can be used to detect SARS-CoV-2, but it is not for routine diagnostic because the results take a long time, require labor, and expertise. Serological tests are frequently used in the diagnosis and follow-up of this disease. These are mainly ELISA, CLIA, immunofluorescence test (IFA), western blot (WB), protein microarray (microarray) and neutralization. ELISA based immunoglobulin (Ig)M and IgG antibody tests have more than 95% specificity in the diagnosis of COVID-19.

Keywords: COVID-19, PCR, antibody, antigen

ÖZ

Koronavirüs hastalığı-19 (COVİD-19) hastalığına neden olan şiddetli akut solunum yolu enfeksiyonu CoV-2 (SARS-CoV-2) virüsünü tespit etmek amacıyla çeşitli testler kullanılmaktadır. Günümüzde revers-transkripsiyon tepkimesiyle birleştirilmiş Realtime (RT)-polimeraz zincir reaksiyonu (PZR) testi SARS-CoV-2'yi teşhis etmek için kullanılan altın standart yöntemdir. Bu yöntem, örnekte sadece SARS-CoV-2'nin varlığını değil aynı zamanda virüs miktarınıda belirlediği için kantitatif PZR (RT-qPZR) olarak anılmaktadır. Virüse özgül primerlerin kullanılması sebebiyle testlerin özgüllüğü %100 olarak kabul edilmektedir. Bu test için nazofarengeal ve boğaz gibi üst solunum yollarından alınan sürüntü örnekleri, balgam ve bronkoalveoler lavaj sıvısı gibi alt solunum yollarına ait alanlardan alınan örnekler, rektal sürüntü, dışkı, serum ve idrar örnekleri tercih edilmektedir. Örnek alma ve test çalışılması sırasında kişisel koruyucu ekipmanların sağlık çalışanları tarafından doğru kullanımı önemlidir. SARS-CoV-2 tanısı için RT-qPZR testine ilave olarak kullanılan hızlı antijen testleri teorik olarak hızlı sonuçlanma zamanı ve düşük maliyetli olmasından dolayı avantaj sağlar ancak bu yöntemin duyarlılığının oldukça düşük olduğu bilinmektedir. Hücre kültürü SARS-CoV-2 tespit etmek amacıyla kullanılabilir ancak sonuçların uzun zaman alması, emek gerektirmesi ve uzmanlık isteyen bir yöntem olması nedeniyle tanı amaçlı ve rutin olarak gerçekleştirilmez. Serolojk testler bu hastalığın tanısında ve takibinde sıklıkla kullanılmaktadır. Bunlar esas olarak ELISA, kemilüminesans testi (CLIA), immünofloresan testi (IFA), western blot (WB), protein microarray (mikrodizi) ve nötralizasyondur. ELISA bazlı immünoglobulin (Ig)M ve IgG antikor testlerinin, COVİD-19 tanısında %95'ten fazla özgüllüğe sahip olduğu belirtilmektedir. SARS-CoV-2 ile enfekte olan hastalarda en erken 7-11 gün sonra antikor cevabı geliştiği için hastalığın akut tanısında yararlı değildir. Virüs nötralizasyon testleri antikorların işlevselliğini ortaya koyması nedeniyle diğer serolojik testlere göre daha anlamlı sonuçlar ortaya koymaktadır.

Anahtar Sözcükler: COVİD-19, PZR, antikor, antijen

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Address for Correspondence: Bilge SÜMBÜL, Bezmialem Vakıf University Faculty of Medicine, Department of Medical Microbiology, İstanbul, Turkey
E-mail: bilgesumbul@hotmail.com **ORCID ID:** orcid.org/0000-0002-8768-3777

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Introduction

Coronaviruses (CoV) are a large family of viruses that can cause mild, self-limiting infections such as the common cold, common in the community, to more serious infections such as Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS). Based on the Latin meaning of these protrusions "corona" (crown), these viruses are named as CoV (crowned virus) (1).

This review summarizes all the laboratory diagnostic methods available in the management of COVID-19 and the latest scientific publications on this topic. Our aim includes the most up-to-date information showing the sample types taken in the tests performed for direct and indirect laboratory diagnosis of the virus, and the situations that need to be considered during the sample collection and transport phase.

Sample Types, Collection and Transport Media Alternatives

The rapid laboratory diagnosis of Coronavirus disease-19 (COVID-19) viral pneumonias caused by SARS-CoV-2 includes the application of correct test methods and the taking of the appropriate sample from the patient at the right time. SARS-CoV-2s can be detected from samples taken from both upper respiratory tract (URT) such as nasopharyngeal (NP) and throat, and lower respiratory tract (LRT) sites such as sputum and bronchoalveolar lavage fluid (BAL) (2). In addition, there are also publications stating that saliva taken from the URT can also be used in diagnosis (3). The collection of sputum, and especially BAL, by bronchoscopy creates an increased biological safety risk for healthcare workers through the generation of aerosol droplets. The correct use of personal protective equipment (PPE) by healthcare workers is important (4). Bronchoscopy is a highly technical procedure that requires well trained personnel. Upper respiratory specimens are easy to collect, facilitating access to testing for patients with mild symptoms and in resource-limited settings (4-6). Serum samples are another source for the detection of SARS-CoV-2. However, only 15% of patients hospitalized with viral pneumonia have detectable viral RNA in their serum (7). NP swab sample is most frequently preferred for the detection of SARS-CoV-2 by molecular methods [polymerase chain reaction (PCR)]. In addition, URT specimens such as oropharyngeal (OP), middle concha, or anterior nostrils may be accepted. Swabs with aluminum or plastic shafts are preferred. Swabs containing calcium alginate, wood or cotton are not recommended as they may contain ingredients that inhibit the PCR test (8). LRT samples such as sputum, endotracheal aspirates, and BAL have higher sensitivity than URT samples such as NP swabs. Even if the test result is negative in URT samples, the test must be repeated from the samples taken from the LRT especially in cases of severe progressive disease. Ideally, sputum or BAL are the recommended specimen types to demonstrate the highest viral load. In cases of severe pneumonia or ARDS, it is useful to take an LRT sample during intubation. Sputum and/or BAL samples can also be obtained after intubation. A high level of viral load was also found in the stool in cases with pneumonia. Serum and urine are usually negative for the presence of viral nucleic acid regardless of disease severity. (9,10).

SARS-CoV-2 has been shown in enterocytes and isolated from faecal cultures. For this reason, it will be beneficial to study real time (RT)-PCR in rectal samples as well as respiratory samples (11).

RNA positivity is at the highest level 7-10 days after the onset of symptoms from URT areas and it is recommended to take samples during this period for diagnosis. In patients with asymptomatic or mild symptoms, it is recommended to take both nasopharynx and oropharynx swabs together to increase sensitivity. These can be taken on the same viral transport medium (VTM). Since the RNA positivity continues for 3 weeks from the onset of the disease, it is recommended to take LRT samples from patients with severe symptoms, productive cough and intubated patients during this period. About two weeks after the onset of symptoms in the stool, the RNA is permanently detectable. Other samples such as urine and blood can be collected if necessary. Blood samples can be considered for serological investigations (3,12).

Samples collected for SARS-CoV-2 laboratory testing should be kept in a refrigerator (2-8 °C) for up to 72 hours; If it exceeds 72 hours, it should be stored frozen at –70 °C or below (3,13).

The Centers for Disease Control and Prevention (CDC) has published a procedure for laboratories to create their own viral transport media (VTM): other solutions that can be used in the absence of VTM are phosphate buffered saline, liquid Amies, and saline (14,15).

Sample packaging and in-house transport primary container must be closed with a screw cap. The container must be plastic. The outer surface of the primary container should be disinfected with 70% ethanol, placed in a sealed bag and placed in a secondary container prior to shipping. The secondary container must be leak proof and impact resistant and labeled as it contains infectious material. Pneumatic system should not be used for transportation (16-18). The triple packaging system should be used for transportation to the outer center (17-19). Aerosol generating processes must be carried out in a level II biosafety cabinet (BSC-II). Samples where nucleic acid extraction or inactivation has been performed in BSC can be processed outside of the BSC in accordance with standard precautions. Attention should be paid to cross contamination during nucleic acid extraction. If an automated nucleic acid extraction system is not used, procedures must be performed at Class II or higher BSC. After the processes are finished or when sample contamination occurs, the bench should be disinfected with appropriate disinfectants (70% ethanol, 2% glutaraldehyde, sodium hypochlorite [0.05%; 500 ppm] etc.) (19-22). The CDC recommends testing for 3 groups: inpatients with symptoms associated with COVID-19, symptomatic individuals at risk of poor prognosis of the clinical process, and individuals with a history of travel to the affected area or having contact with suspected/certain COVID-19 patients within 14 days. The CDC currently does not recommend testing for asymptomatic individuals (17).

Cell Culture

Isolation of SARS-CoV-2 in cell culture is not performed routinely for diagnostic purposes, as the results take a long time, requires effort and expertise. SARS-CoV-2 can primarily be produced in cell lines such as Vero monkey cells and LLC-MK2, but in suspected cases, cell culture-based diagnosis should not be performed in routine diagnostic laboratories for biosafety reasons. However, virus isolation in cell cultures is used to support the development of vaccines and therapeutic agents (23,24).

Rapid Antigen Tests

Rapid antigen tests are theoretically advantageous due to the rapid result time and low cost detection of SARS-CoV-2s, however, when the experiences with this method in influenza (Flu) viruses are evaluated, it can be stated that the sensitivity is quite low. Cases may be missed due to severe variation in viral load of patients (3,25). The development of an accurate, fast, early and simple fluorescence immunochromatographic method for the detection of the SARS-CoV-2 nucleocapsid protein in the NP swab for the diagnosis of COVID-19 has been reported (3). The inclusion of colloidal gold-based immunoglobulin G (IgG) as the detection reagent has been reported to be an approach that may increase the sensitivity of rapid antigen tests for respiratory viruses (26). The use of rapid bedside tests in suspicious cases will enable effective patient triage and lead to the correct use of limited quarantine facilities (3).

It can be expected that these tests will find wide use in small clinics or hospitals that do not have molecular methods or in screening before RT-PCR and become the recommended tests in guidelines.

Molecular Tests (Viral RNA Tests-Nucleic Amplification Tests)

Nucleic acid amplification tests (NAT) that detect viral RNA are used in the direct detection of SARS-CoV-2. The most important issue in these tests is that the viral RNA is present in the sample collected (27). Currently, the RT-PCR test combined with the reverse-transcription reaction is the gold standard method used to diagnose SARS-CoV-2. This method is referred to as quantitative-PCR (RT-qPCR) as it determines not only the presence of SARS-CoV-2 in the sample but also the amount of virus. Like almost all laboratory tests, the RT-qPCR method can give false positive or false negative results due to problems with sample collection and transport, RNA extraction and enzyme inhibitors (28). RT-PCR protocols used in the detection of SARS-CoV-2 RNA are provided on the CDC and website of World Health Organization (WHO) (29).

Target genes specific to SARS-CoV-2 can be investigated by RT-qPCR or sequencing (30). The most common preferred example for SARS-CoV-2 specific RT-qPCR is swab taken from the nasopharynx (NF) and/or oropharynx (OP). The swab is placed in a liquid transport medium (viral transport medium-VTM). In patients with pneumonia, LRT samples such as sputum and BAL should be tested in addition to NP and oral secretions. In detection of SARS-CoV-2, the probability of virus detection is different for each clinical sample. Virus detection rate may vary from patient to patient and during the course of the disease. For example, while nasal and OP samples are negative in pneumonia patients, LRT samples may be positive (8,31). A negative test result does not exclude the possibility of the person being infected. If the test result is positive, the result is probably correct. However, contaminating samples with viral RNA (by a laboratory worker infected with SARS-CoV-2 as a result of cross-contamination while collecting the sample) may lead to false positive results. Since viral RNA does not mean live virus, detection of viral RNA does not indicate that the patient is contagious. Considering that infectiousness may occur before symptoms begin or even without symptoms, screening asymptomatic patients may also be considered. Unfortunately, little is known about viral RNA detection in asymptomatic patients and such testing strategies are unrealistic to use available resources (32). Insufficient sample collection may cause false negativity. After sample is taken, RNA extraction is performed and then qualitative real time-PCR is applied for target detection (33). The panel developed by CDC is a real-time qPCR panel for the detection of all SARS-like betaCoV and SARS-CoV-2. Using three separate pairs of primers, the *N* gene is targeted. One primer/probe set detects all betacoronaviruses, while two sets are specific for SARS-CoV-2. If positivity is detected in all three sets, it can be reported positive for SARS-CoV-2. This panel received an emergency use authorizations (EUA) on February 4, 2020 (2,12). The most commonly used target gene regions are envelope (E), nucleocapsid (N), spike (S), RNA-dependent RNA polymerase (RdRp), and *ORF1* genes (34). Sensitivity and specificity are high in these tests. There is no cross reaction with other coronavirus strains. A cycle threshold value below 40 (Ct; "Cycle threshold") is used as the criterion for positivity (35). Ct is the minimum number of amplification cycles required to generate a fluorescent signal that can be detected in PCR. The low Ct value indicates the high amount of viral RNA in the sample. It has been stated that the Ct values obtained in cases with a generally severe course are lower than the Ct values of mild cases and that the virus release is long-term in severe cases (36). However, these data need to be supported by other additional studies. Generally, viral RNA can be detected in the NP swab of symptomatic cases on day 1 of symptoms and reaches a peak value in the first week. Positivity begins to wane towards the 3rd week and then drops to undetectable levels. However, Ct values obtained from seriously hospitalized patients are lower than the Ct values of mild cases, and PCR positivity may persist 3 weeks after the disease (36). It does not always indicate active virus presence. In some cases, viral RNA was detected even after 6 weeks after the first positive test. There are cases that are found to be positive after two consecutive negative PCR tests performed 24 hours apart. The most common mistakes include errors in the execution of the test, reinfection or reactivation. The PCR positivity process is different in samples except NP swab. PCR positivity in sputum samples can still persist even after NP samples become negative (37).

If the target gene and internal control amplification are invalid, the test should be repeated. In samples with low viral load, values close to Ct values may indicate false negative or false positive results. Therefore, if necessary, the test should be repeated from the same sample or from a new ordered sample (12). Due to the use of primers specific to the virus genome sequence, the specificity of the tests is accepted as 100%. False-negative results may occur due to unsuitableness of sampling timing (samples collected too early or too late) and inaccuracies in the sampling technique (especially inadequate sampling in NP samples). In addition, improperly processed or transported samples, the formation of viral genetic mutations, the presence of PCR inhibitors, and the application of antivirals before testing are other factors that cause false negative results. Possible false positive results are due to technical errors and reagent contamination (12,38,39). Appropriate positive, negative and inhibition controls should be used for extraction and amplification steps in order to ensure quality control of RT-PCR tests for the detection of SARS-CoV-2. Internal control primers specific for host genes such as the human *RNase P* gene should be used to avoid false negative results (40).

Serological Tests

Serological tests can be performed for diagnosis when nucleic acid tests (NAT) are not possible, or for serological investigations, including investigating an ongoing outbreak or retrospectively assessing the degree of an outbreak (41). There are various serological measurement methods for the detection of SARS-CoV and MERS-CoV. These are mainly enzyme-linked immunosorbent test (ELISA), chemiluminescence test (CLIA), immunofluorescence test (IFA), western blot (WB), protein microarray (microarray) and neutralization (39). It is stated that ELISA-based IgM and IgG antibody tests have a specificity of more than 95% in the diagnosis of COVID-19. Studying these tests when the first PCR test is performed and from two different serum samples taken 2 weeks later can further increase the diagnostic accuracy (42). Antibody response develops after 7-11 days in patients infected with SARS-CoV-2. Some patients may develop antibodies later. Therefore, antibody tests are not useful in the diagnosis of acute disease. It is not known whether individuals with SARS-CoV-2 infection are fully or partially protected from reinfection and how long protective immunity lasts (32). In monitoring SARS-CoV-2 serology from consecutive samples (in acute and recovery phase), the WHO recommends that the first serum sample be collected in the first week of the disease and the second after 3-4 weeks. If only a single serum sample is available, it is recommended that it be examined at least 3 weeks after the onset of symptoms (43). The use of serological tests in the diagnosis of acute infections is limited only when symptoms appear. Detection of the antibody response is possible after weeks. For this reason, negative results, especially in those who have been exposed to the virus recently, do not exclude SARS-CoV-2 infection. Other molecules such as rheumatoid factor, nonspecific IgM may cause a false positive result. The similarity of the N proteins of SARS-CoV-2 and SARS-CoV is approximately 91.2%. Therefore, a cross reaction between the N protein of SARS-CoV-2 and antibodies against other human CoV may occur (44). Tests that detect NC antibodies have the highest sensitivity, as the highest antibody response is against the virus's most abundant protein, nucleocapside (NC). Antibodies against the receptor binding region (RBD-S) of the spike protein are expected to be more specific and neutralizing. Therefore, the use of one or both antigens increases the detection sensitivity of immunoglobulin (Ig)G and IgM (9). The situations in which antibody tests are useful are listed below (32).

1. Contact tracking,

2. Serological surveillance at local, regional and national level,

3. Identification of individuals who develop an immune response against the virus,

4. Detection of the development of protective immunity,

5. Making the decision of returning to work for individuals who are at risk of being exposed to SARS-CoV-2 again, such as healthcare professionals,

6. Identification of individuals who can be donors for therapeutic and prophylactic neutralizing antibodies,

7. Do not detect the sensitivity of PCR tests,

8. Determining the true extent of the pandemic,

9. Calculation of statistics such as case mortality rate,

10. Diagnostic testing of viral RNA negative individuals presenting at the late stage of the disease.

Serological analysis, on the other hand, is important for understanding the epidemiology of asymptomatic infections and emerging SARS-CoV-2s (3).

Neutralizing Antibodies

Virus neutralization tests are tests aimed at detecting the highest serum titer in tissue culture that stops viral infection. Determination of serum titers can be made by Tissue Culture Infectious Dose 50 (TCID50) or plaque assays. These methods, which are serological tests, reveal more significant results than other serological tests that detect the binding of antibodies only to antigen, since they reveal the functionality of antibodies (45). Neutralizing antibodies are a subset of antibodies produced against a virus that independently block viral entry into host cells and consist primarily of the IgG isotype (32). It is not recommended for use as a routine test method.

As a result, timely and accurate laboratory diagnosis of COVID-19 has an important place in determining life-saving and infection control strategies by slowing down the pandemic, limiting the spread of the virus, starting from patient treatment management.

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Concept: B.S., M.Z.D., Design: B.S., M.Z.D., Data Collection or Processing: B.S., M.Z.D., Analysis or Interpretation: B.S., M.Z.D., Literature Search: B.S., M.Z.D., Writing: B.S., M.Z.D.

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Review

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COVID-19 Pandemic: Stress and Psychiatric Disorders

COVİD-19 Pandemisi: Stres ve Psikiyatrik Bozukluklar

İsmet KIRPINAR

Bezmialem Vakıf University Faculty of Medicine, Department of Psychiatry, İstanbul, Turkey

ABSTRACT

The epidemic, which first started as viral pneumonia in Wuhan, China at the end of 2019 and is now known as Coronavirus disease-19 (COVID-19), rapidly spread to almost every part of the world and named a pandemic in March 2020. It is well known that psychiatric symptoms and syndromes, especially posttraumatic stress disorder, major depression, anxiety, and sleep disorders reach high prevalence values in natural or man-made disasters. Especially in infectious disease epidemics where mortality rates are high, patients, those who are quarantined, and the whole society experience very intense mental stress and trauma. It is not easy to avoid psychological distress after facing highly fatal illnesses such as Ebola, severe acute respiratory syndrome (SARS), or COVID-19. When pandemics turn into a rapid and global disaster, the prevalence values of mental problems reach even higher levels. Combating mental disorders not only provides psychological well-being but also affects the course of the epidemic, as these disorders can delay efforts to fight epidemics.

Mental health complaints increase in healthcare workers as a result of the stress and trauma of working during the epidemic. Studies report that during the SARS epidemic, approximately one-fifth of healthcare workers experienced 'significant mental disorders'. Medical professionals who develop mental disorders will be less productive, which will weaken the fight against the epidemic. Therefore, it is very important to support healthcare professionals.

Since the COVID-19 outbreak is a relatively recent disaster, epidemiological study results have not yet been published sufficiently. However, the results of serious epidemics caused by viruses such as SARS and Ebola have previously been published. In this review, information about the psychiatric morbidity expected after COVID-19 is reviewed in the light of the results of studies conducted mainly in previous virus epidemics.

Keywords: Mental disorder, epidemic, anxiety, depression, post-traumatic stress disorder (PTSD), COVID-19, SARS

ÖZ

İlk olarak 2019 yılı sonunda Çin'in Wuhan şehrinde bir viral pnömoni olarak başlayan ve şimdi Covid-19 olarak bilinmekte olan salgın, hızlıca dünyanın hemen her tarafına yayılarak Mart 2020?de pandemi niteliği kazanmıştır. Doğal veya insan eliyle gerçekleştirilen afetlerde başta travma sonrası stres bozukluğu, majör depresyon, anksiyete ve uyku bozuklukları olmak üzere psikiyatrik belirti ve sendromların yüksek prevalans değerlerine ulaştığı iyi bilinmektedir. Özellikle mortalite oranlarının yüksek olduğu enfeksiyon hastalığı epidemilerinde hastalar, karantinaya alınanlar ve bütün toplum çok yoğun bir ruhsal stres ve travma yaşarlar. Ebola, şiddetli akut solunumsal sendrom (SARS) veya COVİD-19 gibi yüksek düzeyde ölümcül bir hastalıkla yüzyüze gelmek durumunda psikolojik distressten kaçınabilmeyi hayal etmek çok güçtür. Pandemiler hızlı ve global bir felakete dönüşürken, ruhsal sorunların prevalans değerleri daha da yüksek düzeylere ulaşmaktadır. Ruhsal bozukluklarla mücadele sadece psikolojik iyi oluşu sağlamakla kalmaz, bu bozukluklar salgın hastalıkla savaş çabalarını da geciktirebildiği için epideminin gidişini de etkiler. Salgın sırasında çalışmanın stres ve travmasının bir sonucu olarak sağlık çalışanlarında ruh sağlığı yakınmaları artar. Çalışmalar SARS salgını sırasında sağlık çalışanlarının yaklaşık beşte birinde "belirgin ruhsal bozukluklar" görüldüğünü bildirmektedir. Ruhsal bozukluk gelişen tıp profesyonelleri daha az üretken olacaklarından bu da epidemiyle mücadelenin zayıflamasına yol açacaktır. Bu yüzden özellikle sağlık çalışanlarının desteklenmesi önem arzetmektedir. COVİD-19 salgını görece yeni bir felaket olduğundan henüz epidemiyolojik çalışma sonuçları yeterince yayımlanmış değildir. Ancak SARS ve Ebola gibi virüslerin neden olduğu ciddi düzeydeki salgınlarla ilgili sonuçlar daha önce yayımlanmıştı. Bu derlemede, ağırlıklı olarak önceki virüs epidemilerinde yapılmış çalışma sonuçları ışığında COVİD-19 sonrası beklenen psikiyatrik morbidite ile ilgili bilgiler gözden geçirilmektedir.

Anahtar Sözcükler: Ruhsal bozukluk, salgın, anksiyete, depresyon, travma sonrası stres bozukluğu (TSSB), COVID-19, SARS

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Address for Correspondence: İsmet KIRPINAR, Bezmialem Vakıf University Faculty of Medicine, Department of Psychiatry, İstanbul, Turkey
E-mail: ikirpinar@bezmialem.edu.tr **ORCID ID:** orcid.org/0000-0002-7592-8036

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Introduction

A new virus severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) from the CoV family emerged in Wuhan, the largest metropolitan city of China's Hubei province, in the last months of 2019. This virus was first reported at the end of the year by the World Health Organization (WHO) China Country Office and is now known as coronavirus-19 (COVID-19). The COVID-19 outbreak, which started as viral pneumonia, quickly spread to almost every part of the world and became a pandemic in March 2020. Pandemic is the general name given to epidemic diseases that spread and affect a wide area in more than one country or continent in the world. The feature that distinguishes pandemics from natural disasters is the lack of time and space limit and high morbidity/mortality rates. The inability to predict the duration of the situation or even whether it is preventable means more uncertainty and anxiety than other disasters.

Infectious diseases continue to be one of the most threatening conditions for human well-being. Despite great advances in medicine, outbreaks of these diseases are still among the most important causes of morbidity and mortality in both developed and developing countries (1). According to WHO, viral diseases have become a serious threat to public health with emerging new viruses. Many viral epidemics have emerged in the last 20 years. SARS in 2003, influenza due to H1N1 (Swine flu) virus subtype in 2009, Middle East Respiratory Syndrome (MERS) in 2012, and Ebola virus disease in 2014 caused high morbidity and mortality rates. Each of these past outbreaks has led to the development of significant rates of psychiatric symptoms and disorders in those who are sick and in quarantine (2-4).

COVID-19 caused millions of people to become ill and hundreds of thousands of deaths around the world as of May 2020, when this review was prepared. With the spread of the virus, uncertainties and losses continue. It has created an unexpectedly large burden on the political, economic, and social security systems as well as the health systems as a result of its easy spread, the inability of the population to be immunized, the delay and insufficiencies in tests, the shortages of medical equipment and personnel, the delay and inadequacies in preventing contact with sick people (5). The severity of the disease, its unpredictable course and its consequences, the uncertainties, the need for distance and isolation, the failure of our conventional coping systems, and information pollution are at a level that may cause pessimism about the psychological effects of the emerging crisis. Initial observations suggest that the epidemic will leave a significant psychological sequel (6).

Since the COVID-19 outbreak is a relatively recent disaster, epidemiological study results have not yet been published sufficiently. However, results of serious outbreaks caused by associated coronaviruses, such as SARS and MERS, have previously been published (2,7,8). In addition, in the past epidemics, results showing an increased risk for mental problems in healthcare workers because of increased workload, the need for personal protection, and the psychological effects of the possibility of infection for themselves and their families were also reported. Although the worldwide COVID-19 threat is not consistent with the data we have gathered from our previous experiences, the information can be a guide to the current coronavirus pandemic.

Factors Related to the Psychological Dimensions of the Pandemics

It is well known that natural disasters cause mental disorders such as posttraumatic stress disorder (PTSD), major depression, anxiety disorders, and sleep disorders (9). As contagious diseases at a pandemic level spread rapidly and turn into a global disaster, the prevalence rates of mental problems also reach much higher levels.

Psychiatric morbidity in those infected with coronavirus seems to be due to the interaction of many factors. It is clear that a situation known to be fatal can have psychologically traumatizing effects. Biological factors include direct effects of viral infection (including brain infections), cerebrovascular diseases, degree of physiological threat (such as hypoxia), immunological response, and medical interventions. In non-infected individuals, the most consistent risk factor reported in studies is increased contact with affected patients. Among other risk factors, a previous history of psychiatric and/or general medical symptoms/disorders, long time in quarantine, perception of insufficient organizational support, and perceived social stigma are important (10). Finally, the role of stress/traumatic experience created by encountering an unexpected, sudden, and uncertain situation should not be overlooked.

Stress and Trauma

As in every living organism, there is a dynamic state of internal balance (homeostasis) based on the interaction of many factors in human beings. This balance, which is created by the interaction of various destructive and protective biological, psychological, and social factors induces a state of excitement called stress when faced with threatening situations (stress factors). This arousal has psychological symptoms such as tension, restlessness, anger, and cognitive symptoms such as memory and attention problems, which are briefly defined as "fight or flight reaction" and are largely due to autonomic hyperactivity, adrenaline discharge, and hypothalamo-pituitary-adrenal axis activation (11). Many experts add "freezing" as the third form of reaction.

Undoubtedly, the severity and duration of the arousal and symptoms that occur differ depending on the stress factor and many individual features. Individuals who encounter the stress factor may have different ways of perceiving and coping with the situation. The same event does not elicit the same reactions in every individual, while an individual finds the event quite stressful, it can be seen as a small problem for another individual (12). However, threats to physical or mental integrity cause stress in almost everyone. The severity and long duration of the stress factor lead to the persistence of the arousal and symptoms that occur.

Although "trauma" is generally used for events with a high stressor effect in colloquial language, the key concept is that it is

a severe event that exceeds the person's ability to cope. Although the difference between the concepts of stress and trauma is not very clear, trauma is generally understood as extreme helplessness and weakness and important situations that cause horror (13). These are experiences that threaten the life, body integrity, or mental health of the individual. A wide range of events that can shake the individual's basic beliefs about himself, the world, and others can be perceived as "traumatic". Processes that are deemed to have traumatic effects need not only be directed at the person but witnessing such an event experienced by someone else is also considered traumatic (14). The first reaction to this type of trauma is usually shocking; When a person is in shock, he both freezes and tends to deny the event as if it had not happened. Kübler-Ross (15) conceptualized a 5-stage trauma response that includes the stages of shock, (denial, anger, bargaining, depression, and acceptance) following a person is exposed to trauma. Kübler-Ross (15) stated that the last stage is not a "happy end", it involves various emotions, and this stage was defined by a patient as "the last rest before a long journey". Traumatic events or situations almost always play a triggering role for serious mental disorders and sometimes they directly cause mental disorders.

As with many events and situations that lead to psychological trauma, infectious disease outbreaks are sudden, overwhelming, and create feelings of helplessness, weakness, and guilt. People need to perceive the world as a safe place. This perception is important for people to feel safe and events are under control. Outbreaks are situations that shake people's perceptions, expectations, and the assumption that the world is reliable. In such cases, besides the loss of loved ones, relatives, or irreplaceable assets, the normal coping capacity of the person is destroyed, and a threat arises that compels emotional, cognitive, behavioral, and even religious/cultural beliefs. A study comparing SARS patients with healthy controls using the Perceived Stress scale found that stress rates were very high in patients, which was significantly associated with negative psychological effects. 25% of the patients later requested psychological follow-up (16). Again a study with SARS patients in 2003 found that even 1 year after the epidemic, patients continued to complain of high stress levels and psychological disturbances to be worried (17). In addition to anxiety, hopelessness, irritability, anger feelings, physical complaints such as fatigue, pain, and sleep disorders are common in people exposed to disasters (10). Depression and anxiety disorders are at least twice as common as usual crisis experiences (18).

Quarantine and Isolation

Quarantine is the separation and restriction of movement of people potentially exposed to an infectious disease to make sure they are well and to reduce their risk of infecting others. This definition is different from isolation, which means separating people diagnosed with an infectious disease from people who have not yet been diagnosed. However, these two definitions are often used interchangeably (5).

Separation from families and society with prolonged isolation has significant effects on individuals even if they do not get the disease and are only isolated. Similar effects were observed in healthcare workers working in isolation. Especially in epidemics where mortality rates are high, those who are quarantined as well as patients experience very intense mental tension. It is not easy to avoid psychological distress when faced with being infected with a highly fatal disease such as Ebola, SARS, or COVID-19.

The photo taken by Daniel Berehulak for The New York Times during the epidemic from the Ebola treatment center in Liberia which won the Pulitzer Prize highlights the situation more strongly than numerical data: "They meet and fear the officers wearing spacesuits they have never seen before. They are waiting for their test results, their next medical exam, their symptoms to appear or disappear. They are watching which ones in the canopy in the courtyard are getting better and which are sick. They are praying" (19).

Quarantine is almost always an uncomfortable experience. Separation from loved ones, loss of freedom, uncertainty about illness, and boredom can have dramatic effects. Suicides, serious anger attacks, and forensic events have been reported during quarantine in previous outbreaks (20,21). The anticipated potential benefits from quarantine against possible psychological costs should be carefully calculated (22). The success of quarantine which is a public health measure depends on keeping it as short as possible, taking into account its negative effects.

A study of healthcare workers who were quarantined due to the possibility of having contact with SARS showed a high risk for acute stress disorder (ASD) (23). Many quantitative studies reported higher rates of general psychological symptoms, depression, stress, low mood, post-traumatic stress symptoms, anger, burnout syndrome, anxiety, insomnia, irritability, and difficulty concentrating compared to those who were not quarantined. Another study reported that 29% of those quarantined for SARS showed signs of PTSD and 31% depression. In addition, staying in quarantine for a long time increases the probability to show PTSD symptoms (24). Similarly, a study conducted on people in quarantine in Toronto found the rate of depression at a very high level of 31.2% (25). A study examining depression symptoms in hospital workers found a high rate of depression symptoms in 9% of employees 3 years after the epidemic. About 60% of those with high depression symptoms remained in quarantine, while only 15% of those with low depression symptoms had a history of quarantine (7). Another study in China found that being quarantined in healthcare workers is a predictor of PTSD development even after 3 years (25).

Those who are quarantined continue to complain of many mental problems, even if they do not get sick and long after their quarantine ends. One study found that quarantine was a predictor for PTSD in hospital workers even after 3 years (25).

The Collapse of Social Support Systems

Medical professionals have long recognized the importance of strong social networks on mental health. Epidemics leave people feeling isolated and vulnerable by breaking down social support structures at a time when they are most needed. When faced

with an epidemic, many places where people receive social support, such as mosques, schools, and workplaces, can be closed to slow the rate of spread. Even minor social interactions, such as visiting a friend's home, may have been stopped for fear of encountering the disease.

In his book The Great Influenza, American historian John M. Barry explains the major breakdown in post-epidemic support systems as follows: "The fear began to destroy the sociality of the city. Trust was broken. Faced with public catastrophe, not only tension but anger, not just blaming someone or protecting their own interests, but signs of active selfishness began" (26). The destruction of social support can extend to the basic unit of the social structure, the family, which is the closest and most important bond of the individual. Manuel Fontaine, UNICEF Regional Director for West and Central Africa, observed that many families even abandoned their children due to fear and stigma during the Ebola epidemic in West Africa and said "Fear of Ebola exposure is stronger than family ties in some communities" (27).

Individuals obtain strength from social support systems as well as personal coping and defense mechanisms against psychological threats especially in times of stress and trauma. The perceived threat and the possibility of encountering its consequences are tried to be balanced with coping and support systems. A prospective longitudinal study conducted after an accident has shown that access to social support reduces subsequent post-traumatic symptomatology (28). During the SARS epidemic, it has been reported that coping behaviors that disperse negative emotions with open communication in a supportive environment caused people to accept the situation better and reduce psychological morbidity (29). On the other hand, if support systems are not successful and balance cannot be established, cognitive distortions such as insufficiency, helplessness, and uncertainty increase, and serious mental disorders are triggered. A study showed that social network changes after the earthquake continue to be a risk factor for psychiatric morbidity even after 1 year (30).

Stigmatization

Stigmatization is another mechanism of social isolation caused by epidemic diseases and has an important role in the formation of mental disorders. Especially in infectious diseases, people are stigmatized because of an association with the disease; Stereotypes circulate with unrealistic or distorted information, and targeted people are discriminated against. People and communities begin to exclude and perceive threats from each other due to feelings of fear, insecurity, and exclusion. This perception causes the stigmatized individual to become lonely and sometimes leads to symptoms of anxiety, social withdrawal, pessimism, hopelessness, inadequacy, helplessness, and the emergence of feelings such as anger, anxiety, and sadness. These feelings and thoughts are known to trigger mental disorders.

The most obvious target of stigmatization is sick people and those who are quarantined. But sometimes the entire population or community can be targeted, as were Asian Americans during SARS, West Africans during Ebola, Haitians and homosexuals in the early AIDS period. During the COVID-19 pandemic, especially the elderly, people from the Far East, people from abroad, and healthcare professionals were targeted. Healthcare professionals are among the most excluded and stigmatized groups, as it is known that they have close contact with patients. Health workers who are in close contact with patients can be excluded, people who send good messages from afar may display discriminatory behaviors when they see them shopping, in the apartment, at home even when necessary social distance and adequate precautions are taken. Common examples of exclusion include residents of neighborhood or their apartment avoiding contact and not inviting them to social environments.

Sometimes patients may escape from the healthcare system for fear of stigmatization. This has been a very important problem in HIV or AIDS patients who avoided tests and treatment due to stigma.

Epidemiology of Mental Disorders During the Pandemic

Infectious disease epidemics often affect body health and combat focuses on attempts to slow the rate of infection and heal those who are sick. However, even if the pathogenesis does not always involve the brain in these infections, pandemics generally cause mental illness. It is known that events that scare the person a lot, leave them in horror, and create feelings of helplessness, cause long-lasting mental problems. Therefore, epidemics are almost always accompanied by a silent epidemic of mental disorders. Several studies demonstrated that various psychiatric disorders, especially trauma and stress-related disorders, sleep disorders, alcohol-substance use disorders, depression, and anxiety disorders occur in pandemics. Rogers et al. (31) recently conducted a meta-analysis of 65 peer-reviewed articles which were selected among 1963 articles; the most common psychiatric problems observed in patients admitted due to SARS and MERS during the acute period were confusion (27.9%), depressive mood (32.6%), anxiety (35.7%), memory impairment (34.1%), and insomnia (41.9%). After the pandemic the prevalence of PTSD was 32.2%, depression was 14.9%, and anxiety disorders was 14.8% (31). Exacerbation of preexisting psychiatric disorders is also common (32). Children and adolescents may show regression, social isolation, and aggressive behavior due to misinterpretation of the "acting-out" defense. Several previous studies indicated that the relationship between catastrophic life events and event-related loss in resources is important. It is noted that the higher the number of casualties, the higher the risk of mental problems. Loss of resources is a key concept for protection as well as for mental problems (33,34). Fighting mental disorders during epidemics does not only provide psychological well-being; as these disorders may slow down the efforts to tackle pandemic, this may also affect the course of the pandemic.

Health Anxiety

Fear of COVID-19 or other illnesses can be considered as a special type of anxiety called health anxiety. Taylor and Asmundson (35) describe health anxiety as a beneficial response to physical illnesses to a certain extent. Normal levels of anxiety ensure that necessary measures are taken to prevent or alleviate

illness. However, when health anxiety is chronic and excessive or significantly greater than the severity of the health-related threat anxiety may be a problem (36). This type of anxiety leads to disability and is a common symptom in many psychiatric disorders such as hypochondriasis, OCD, panic disorder, and specific phobias. Patients with extreme health anxiety constantly seek assurances that they are not sick, but when this guarantee is given, they cannot be comfortable for a long time and their anxiety increases gradually (35). They often check their body and review medical resources frequently to confirm the illness. Excessive mental engagement with health anxiety leads to the development of bodily sensations and symptoms associated with anxiety, which leads to a further increase of anxiety in a vicious circle.

Obsessive-compulsive Disorder (OCD)

It is especially important during a pandemic. Anxiety symptoms can easily transform into fear of illness, and extreme-pathological avoidance can be developed to avoid contact with the disease. Contamination fears are the most common types of obsession in OCD (14,37). Also, a common obsessive-compulsive belief is an exaggeration of the threat. In contamination type OCD, this exaggeration leads a person to develop obsessions about being sick and contaminating others (38). Probably, after the COVID-19 pandemic, both new OCD cases will emerge and many of the old OCD patients will make this the main complaint. Exaggerated attempts, such as avoiding contact with the disease and testing for diagnosis, will keep clinicians busy during this period. Press is a determinant in the nature of this relationship.

It is important to remember that obsessive beliefs are not specific to OCD and can be seen in other anxiety disorders. Finally, pandemic-related fears are reported to be more common in individuals with disgust sensitivity (39).

Depression

Depression is one of the common disturbances after mental traumas. The most common symptoms of depression are loss of interest, fatigue, depressed mood, sleep and appetite disturbance, and inability to enjoy life. Depression can occur for the first time after a mental trauma, or a recurrence may occur in people who have had depression before. In a study conducted in a hospital structured for SARS in Taiwan, depression rates were found to be higher in nurses working in SARS units compared to nurses working in other units (38.5% vs. 6.7%). No significant difference was found between the nurses working in the normal SARS clinic and the intensive care SARS clinic (40).

Acute Stress Disorder and Posttraumatic Stress Disorder

Although the symptoms are the same in these disorders that arise in relation to the trauma, differential diagnosis is made on the basis of time. Conditions that occur and improve within 1 month after trauma are diagnosed as ASD, and symptoms lasting longer than 1 month are diagnosed as Post Traumatic Stress Disorder (PTSD). Generally, a relationship between the severity of the trauma and the quality and quantity of the symptom cluster is defined.

PTSD was initially named as a soldier's heart due to cardiac symptoms observed in soldiers during the American civil war. Later, it was used to define mostly traumatic reactions of soldiers as the irritable heart and Shell shock. Although similar symptoms were observed in Nazi concentration camp survivors after the Second World War and after the atomic bomb in Japan, this situation, which is generally ignored, was included as a diagnosis of PTSD in the third edition of DSM in 1978 after the Vietnam War. Later, in the revised form, the traumas that could lead to PTSD were defined as "The person has experienced an event that could be a source of distress for almost everyone, far beyond the usual human life" (14,41).

In DSM-5, the last edition of DSM published in 2013, the trauma required for the diagnosis of PTSD was described as "experiencing death, serious injury or sexual assault in a real or threatening way". For the diagnosis, other than directly experiencing traumatic events, seeing the events that happened to others directly, witnessing, learning that traumatic events have happened to a family relative or friend, and even repetitive or excessive encounters with disturbing details of traumatic events may be sufficient. This last point is particularly valid for healthcare professionals. For the diagnosis of PTSD, there should be symptoms in three main symptom clusters, which consist of somatic symptoms related to experiencing trauma day and night, avoiding stimuli reminding trauma, negative changes in cognition and mood, and increased responses of the autonomic nervous system (14).

It is reported that 60-80% of those with a lifetime diagnosis of PTSD develop at least one other psychiatric disorder throughout their life. The most common comorbid diagnoses in men are alcohol abuse and addiction, major depression, conduct disorder, and substance abuse. In women, the most common diagnoses are major depression, phobia, alcohol abuse, and addiction. People who have previously had a mental illness have a higher risk of recurrence of those diseases after trauma. If there is a second mental illness other than PTSD, both the distress experienced by the person and the loss of workforce increase, and it requires more intense and longer-term treatment (14).

Other Disorders

Confusion is the most common psychiatric finding in the acute phase of SARS and MERS, which suggests that delirium is common. Especially in intensive care patients, delirium syndromes, which are marked by impaired consciousness, orientation, and attention, are very common and make patient care difficult. Mania and acute psychosis have been reported in a small number of patients. Sleep disorders are very common conditions (31). A meta-analysis reported ongoing problems in more than 15% of patients after the recovery of infections, especially sleep disturbance, frequent recall of traumatic memories, emotional lability, concentration weakness, fatigue, and memory weakness (31).

Impacts on Healthcare Professionals and the Healthcare System

Epidemics have many negative effects on the mental health system as well as on the physical health system. Healthcare workers have the largest share of these negative effects. Psychiatric complaints of healthcare professionals increase significantly due to both being the occupational group with the most contact with patients and the severe working conditions during the epidemic. Healthcare workers dealing with the diagnosis and treatment of COVID-19 were faced more with additional stress sources such as limited protective equipment, lack of rest periods and sleep, physical isolation (even outside working hours), constant stimulation with infection control procedures, and disappearance of spontaneity. The conflict between the priorities of the health authority and the demands of patients and their families directly targets healthcare professionals. Also, serving traumatized people can itself be traumatic. This is called "secondary trauma". All healthcare professionals, from security personnel to cleaners, from doctors to administrative personnel, are at risk of secondary trauma during times of crisis and disaster. Secondary trauma is also known to increase the risk of burnout.

With the contribution of all risk factors, it is certain that working in the hospital or other health institutions during the epidemic creates stress and trauma in at least some of the healthcare workers. According to many studies, factors such as premorbid personality structure, traumatic events experienced in childhood, and presence of another mental disorder affect the behaviors of intense reaction to trauma and PTSD does not develop in 80-90% of people who are exposed to trauma (41). However, in outbreaks such as SARS and COVID, being in an intense struggle with a disease that spreads rapidly on a global scale and has a high mortality, regardless of these variables, poses a high enough risk. The prevalence of PTSD and other psychiatric disorders in healthcare workers increases significantly, especially when the agent is not fully recognized, the mode and cause of transition is not known, and the prognosis is uncertain (42). In addition, it is known that healthcare workers are exposed to more exclusion and stigmatization as they are thought to be more likely to be contagious than the general population, they also exhibit more avoidance behaviors from patients and crowded environments, experience more income loss, and all of these increase the risk.

In studies conducted during the SARS epidemic in Taiwan and Singapore, psychiatric morbidity rates in healthcare workers were found to vary between 20% to 75.3% (29,42-44). Although different rates are related to factors such as the severity of the epidemic, time to get it under control, or the difference in the scales used, there are very high rates compared to the general population. In studies conducted after the same epidemic in Hong Kong, Singapore, and Canada, emotional disturbances were found in 18% to 57% of healthcare workers during and immediately after the epidemic (43,45,46). The increase in psychiatric morbidity continues after the epidemic is brought under control. A study of Toronto hospital staff in Canada showed that depression attacks and new cases of PTSD were still occurring 1-2 years after the outbreak (32). A study comparing SARS patients with healthy controls found that patients who were healthcare workers reported more fatigue and health anxiety than others (16).

A very recent meta-analysis by Kisely et al. (47) reviewing 59 publications on healthcare workers involved in outbreaks such as SARS, MERS, and Ebola found that ASD, PTSD (odds ratio 1.71, 95% confidence interval 1.28), and psychological distress (1.74, 1.50-2.03) were at a high rate in healthcare workers exposed to infected patients. The most common risk factors for psychological distress were being young, female gender, lack of experience, having a dependent child, and having an infected family member. Also, a long duration of quarantine, lack of support, insufficient knowledge about the pandemic, and perception of stigmatizing attitudes towards healthcare personnel from neighbors and relatives are risk factors. History of psychological or physical illness in the periods before the epidemic was also important. Within professional groups, nurses were generally found to have a higher risk than doctors (47).

Many studies reviewed by Kisely et al. (47) demonstrated that open communication, access to appropriate personal protection, good education and adequate experience on infectious disease, appropriate rest periods, access to appropriate protective equipment, practical support, and psychological support from the family and the community helped reduce morbidity. Access to psychological interventions and the existence of protocols supporting staff had a very protective effect. Besides, frequent review and renewal of procedures to reduce the high risk of infection and keeping a low density at wards were shown to be effective. Keeping working hours short, resting during breaks, regular supply of food and daily living equipment, and opportunities to meet with families, albeit remotely, were defined as organizational supports that would reduce the risk.

Since medical professionals with mental disorders will be less productive, this will lead to a weakening of the fight against the pandemic. In fatal and easily transmitted infections, a large number of healthcare workers can get sick, die, and this can put the system into great difficulty. During times when the need for mental health services is greatest, the mental epidemic may reduce the health system's ability to cope with the epidemic. Healthcare professionals may be overly preoccupied with efforts to cope with pandemic while neglecting other medical conditions. In addition, patients may escape from healthcare facilities with fear of exposure to infection. Reduced access to mental health services may increase stress in health systems.

Especially in crisis situations, factors such as prolongation of working hours, excessive workload, the dangerous working environment can cause excessive consumption of energy and create a risk for burnout syndrome. Although it is not a defined disorder in systems such as DSM, Burnout syndrome, which is defined especially in professionals such as healthcare professionals, is a condition characterized by loss of motivation, interest, and desire, as well as a general loss of energy, negative feelings and thoughts about himself, inadequacy and a sense of failure. The COVID-19 outbreak poses a risk of burnout as it

creates a crisis in the health system. The WHO recommendations to the institutions to protect from burn-out syndrome includes good communication, multidisciplinary team meetings, implementation of a "partner" system which is based on the principle of matching employees who will take part in disasters or mass traumas, rotational work order and participatory techniques in which humor is widely used, discussing problems or experiences with colleagues, increasing the processes of supervision/consultation with colleagues.

Conclusion and Recommendations

Our previous experiences show that we will face an important risk of mental disorders after the pandemic. While efforts to organize the health system in a way to cope with the epidemic continue, it is also important to mature mental support and treatment programs. Especially healthcare professionals should be supported by organizational systems for their own mental health and quality of the service they will provide to people. Working and resting conditions should be improved, shortage of medical and protective equipment should be avoided, and they should have more opportunities to be with their families. In a crisis situation, additional financial problems should not be raised.

Similar improvements and measures are also recommended for the general population. People may lose their jobs, financial savings, or relatives during such disasters, and may have to stay in quarantine or isolation for long periods without friend or family support. In this case, the person feels helpless and hopeless, the distress levels gradually increase. Therefore, communication and correct information channels should be kept open. It is important for traumatized people to communicate with traumatized people like themselves, to talk about events, and to reveal their feelings, both to relieve their pain and to feel less alone. Different types of assistance and approaches to other affected persons can contribute to the traumatized person's recovery process. The benefits of written-visual media in terms of accurate information and social media in terms of support systems are certain. However, the media's sometimes exaggerated and intense news of uncertainty and despair can lead to an increase in feelings of anxiety and panic at the society level. Fears, worries, and false beliefs spread rapidly among individuals as well as in local communities and in public. Some authors believe that excessive exposure to the media increases distress levels and suggest to reduce the use of traditional and social media during these periods. It is very important to regulate sleep, nutrition, and rest functions during epidemic days to combat both infection and mental stress. It is recommended that every family should be encouraged to develop a family plan in order to access medical help in outbreaks and to cope with all aspects of the epidemic, as for other disasters. Seeking, forming and sharing new social support bonds, strengthening old bonds and seeking ways to help others are positive actions for mental health. It is recommended not to make sudden and major life changes during and immediately after the epidemic, and to avoid negative coping strategies such as alcohol-substance, or drug abuse. As with community-level planning, time should be planned for returning to normal life at a personal and family level. Finally, if the perceived stress and psychological problems last more than 2-3 weeks, ways to get mental help should be sought (18,47,48).

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Review

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Technological Innovations in New Type Coronavirus and Health System

Yeni Tip Koronavirüs ve Sağlık Sistemindeki Teknolojik Yenilikler

Yasemin GÜNER[1], Elif KILIÇ GÜNER[2], Dilek ÇİLİNGİR[3]

[1]Karadeniz Technical Univeristy, Faculty of Medical Science, Department of Medical Education, Trabzon, Turkey
[2]Karadeniz Technical University Farabi Hospital, Education Coordinator, Trabzon, Turkey
[3]Karadeniz Technical University Faculty of Health Sciences, Department of Surgical Nursing, Trabzon, Turkey

ABSTRACT

The new type of Coronavirus disease-19 (COVID-19) spreads rapidly as a global epidemic and affects health, economic and social systems. Increasing the number of patients in COVID-19 hospitals negatively affects the health system by causing insufficient materials and health workers to be exposed to the risk of infection. Ethical dilemmas regarding providing healthcare to all patients are more difficult due to uncertainties caused by the disease, change in social life, stress, emotional deterioration, having to work for a long time, insufficient intensive care conditions and mechanical ventilation during the pandemic period. In this process, new and creative approaches are needed in the health system to effectively meet the health needs of individuals. Telemedicine applications, mobile applications, web-based applications and psychological support applications are among these approaches. In this paper, a new type of COVID-19 pandemic in the world and Turkey was referred to the process of innovation in the health care system.

Keywords: Coronavirus, innovation, health system

ÖZ

Yeni tip koronavirüsün (COVİD-19), küresel bir pandemi olarak hızla yayılmakta olup sağlık, ekonomik ve sosyal sistemleri etkilediği görülmektedir. COVİD-19 hastanelerdeki hasta sayısının artması, malzeme yetersizliği ve sağlık çalışanlarının enfeksiyon riskine maruz kalmasına neden olarak sağlık sistemini olumsuz yönde etkilemektedir. Pandemi döneminde hastalığın neden olduğu belirsizlikler, sosyal yaşamdaki değişim, stres, duygusal çöküntü, uzun süre çalışmak zorunda kalma, yetersiz yoğun bakım şartları ve mekanik ventilatör nedeniyle tüm hastalara gereken sağlık hizmetini vermeye ilişkin etik ikilemler, bu süreci daha güç hale getirmektedir. Bu süreçte bireylerin sağlık bakım gereksinimlerinin etkin şekilde karşılanması için, sağlık bakım sisteminde yeni ve yaratıcı yaklaşımlara gereksinim duyulmaktadır. Teletıp uygulamaları, mobil uygulamalar, web tabanlı uygulamalar ve psikolojik destek uygulamaları bu yaklaşımlar arasında yer almaktadır. Bu derlemede, dünyada ve Türkiye'de COVİD-19 pandemi sürecinde sağlık sistemlerinde yapılan yeniliklere değinildi.

Anahtar Sözcükler: Koronavirüs, inovasyon, sağlık sistemi

Introduction

In December 2019, a new type of coronavirus, which is rapidly transmitted from person to person and has a high mortality, emerged in Wuhan, China. Today, there is no special antiviral treatment and vaccine to protect against the new type of Coronavirus disease-19 (COVID-19). This situation negatively affected the health systems of all countries in the world (1-5); the high numbers of patients experienced in hospitals caused disruption or postponement of outpatient, diagnostic and surgical procedures. At the same time, the new type of coronavirus pandemic process has led to changes and improvements in the health systems of countries (6). During the pandemic period, especially since the lack of some innovations in the health system, new and creative

**This work was supported by Gilead Sciences.*
Address for Correspondence: Yasemin GÜNER, Karadeniz Technical Univeristy, Faculty of Medical Science, Department of Medical Education, Trabzon, Turkey
E-mail: yasemin-kul@hotmail.com **ORCID ID:** orcid.org/0000-0003-4932-771X

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approaches were needed and it was revealed that innovation was critical in the health system (7-9). Therefore, countries have tried to face the pandemic by developing their digital infrastructure and engineering capabilities. In addition, the spread of COVID-19 has been tried to be mitigated by developing action plans with technologies that provide community-driven and communication tracking and by implementing some practices (10,11). In this review, we aimed to address the innovation made in the health care systems in the world and in Turkey during the new type of coronavirus pandemic period.

New Type of Coronavirus (COVID-19)

Coronaviruses are single-stranded RNA viruses that mostly infect birds and mammals and belong to the coronaviridae family. These viruses have been seen in humans as SARS (Severe Acute Respiratory Syndrome) and MERS (Middle East Respiratory Syndrome) disease (1,12,13). Today, a new coronavirus has been found that infects humans. The virus is expressed with the word "corona", which means crown in Latin, and named temporarily "2019-nCoV" and updated to COVID-19 as of February 12, 2020 (2,3). This virus can be transmitted rapidly from person to person through droplets and contact (1,14). Coronavirus causes symptoms such as fever, cough, dyspnea, fatigue, nausea, vomiting and diarrhea in humans. In severe cases, dyspnea, severe acute respiratory tract infection, kidney failure and pneumonia are seen. Death may occur depending on the progression of the disease (1,4).

Effect of COVID-19 on Health System

COVID-19 spread among people in a short period of time and affected the whole world and was classified as a pandemic by the World Health Organization (WHO). Until now, the total number of cases in the world has been reported as 8,349,972 and the total number of deaths as 448,962 (15). This indicates that the virus is rapidly transmitted and its mortality is high. Although there is no vaccine and specific treatment developed so far to prevent COVID-19, studies continue in many countries (1,4,5,16). The increase in patient numbers in hospitals due to COVID-19 has led to the disruption of the outpatient clinic services and other services provided to the patients and the delay of the surgeries (16). Countries have implemented emergency action plans by developing various strategies in order to solve the problems experienced in their health systems, to isolate suspicious cases and to prevent the spread of the disease (5,16). The precautions included in these action plans and these required to be implemented are non-pharmacological public health measures such as isolation, social distance and quarantine. Isolation includes segregation of symptomatic patients, and quarantine includes restriction of asymptomatic healthy individuals who have come into contact with confirmed or suspected cases. Quarantine can be applied on a voluntary basis or legally by the authorities at the individual, group or community level. These methods are known as the most effective way to respond to the pandemic (14,17). In addition, countries have followed the guidelines and recommendations put forward by global institutions (such as CDC, WHO) in health systems. Strict implementation of these measures is essential to reduce the spread of disease and prevent health system collapse. However, as there are serious gaps in developed economies and health systems, new and creative approaches in health services were required to learn, experience and able to connect during the pandemic (7,8,14). These new and creative approaches are listed below.

Telemedicine Applications

Telemedicine applications, which have a recent history in health care systems, started to be used more in the COVID-19 pandemic period. These web-based applications, in which electronic patient records are used to reduce the number of individuals applying for health services, are called "telemedicine". Telemedicine is a system that allows physicians and patients to communicate 24/7 using smart phones or computers and includes classification before they come to the emergency room. In addition, telemedicine is a system that was made available to all primary care patients in the healthcare system during the COVID-19 pandemic, and patients are guided according to whether they have symptoms of COVID-19. If the individual is asymptomatic, the presence of contact history with any known case is questioned and information is given about COVID-19 disease. If the individual is symptomatic, patients are divided into four categories (requiring urgent intervention, urgent, non-urgent or self-sufficient) and connected to the COVID-19 unit via telephone after planning. Respiratory symptoms that may be early signs of COVID-19, travel and contact histories of patients are among the most frequently evaluated conditions with this approach. Thus, the density in hospitals can be prevented, and the exposure of healthcare workers to COVID-19 is reduced. Another example of telemedicine applications is the "JeffConnect®" application. Patients can access this system with their user names and passwords via their mobile phone or computer system. In the system, the patient first fills in his personal information (location, phone number, nearest pharmacy, height, weight, etc.), and then information about his current illness (symptoms such as allergies, cough, constipation, diarrhea, etc.). Depending on the patient's complaint, the physician prescribes medication or gives information about the disease. With this system, physicians and healthcare professionals can provide consultancy services to patients who experience COVID-19 symptoms at any time via a mobile phone/tablet or a computer with a webcam. In addition, with this system, when patients with suspected COVID-19 need to be tested, central coordination can be achieved with healthcare personnel as well as local test institutions (18-21).

For telemedicine applications in our country, "ALO 184 Corona Information Line" (SABİM) has started to serve. With this application, individuals are guided by obtaining information from specialist physicians in case of COVID-19 symptoms (22). All of these applications have been developed to prevent unnecessary hospital applications during the pandemic by making the triage system more effective. These methods are patient-centered, convenient for individuals to self-quarantine and reduce the virus burden of healthcare workers.

Mobile Applications

Another technology developed during the COVID-19 pandemic is mobile applications. "TraceTogether" and "Coronavirus Pandemic Epidemiology (COPE)" are some of these applications. With these mobile applications, it provides many data such as demographic and clinical information of individuals, symptoms, test results, quarantine tracking of infected individuals and accessing the contact history of an infected individual and a healthy individual. In addition, applications provide guidelines for individuals regarding coronavirus disease, transmission routes, online screening tool, testing or situations requiring emergency intervention (23-27).

In Turkey, with the scope of COVID-19 combat, the Ministry of Health developed a mobile application named "Hayat Eve Sığar-HES", in which citizens can follow the risks and health conditions. In the HES application, individuals fill out the questionnaire regarding their own health status and can easily access the latest developments regarding the virus, the risk map of their location, the closest health institution, pharmacy, market chain, metro and stations. This practice aims to minimize the risks associated with the epidemic that may be experienced and to prevent its spread (28).

Another application developed by the Ministry of Health is the "Korona Önlem" application. With this application, the risk status of the individual is calculated as a result of inquiries about identity information, personal information, chronic diseases, travel history and complaints, and guidance is made (29).

Web-based Applications

Web-based maps were created to facilitate the tracking of the virus during the COVID-19 pandemic period. The map "Coronaviz.umiacs.io" is one of the web based maps. This application was developed in order to predict the emergence of the virus in new regions and to make countries more ready for the epidemic process (30). In this way, the regional spread of the virus can be seen in the world. In China, Lian Fei Technology has established a blockchain platform, providing up-to-date case numbers in the COVID-19 pandemic, ensuring the clarity of information, transparency and traceability of developments (31,32). In addition, the Global MediXchange platform, developed by the Alibaba cloud and Jack Ma Foundation, made available the studies on the subject using information and artificial intelligence technology and shared them with healthcare professionals around the world. In this way, online communication and cooperation between countries has been facilitated and experiences experienced during the pandemic process are shared with other countries in the world (33).

In our country, there are web-based applications within the scope of coronavirus studies. TUBITAK and Ministry of Industry and Technology together, in cooperation, implemented "COVID-19 Turkey Web Portal" and COVID-19 Pandemic Follow-up Display (TURCOVID19)", applications, which are among these web-based applications. In COVID-19 Turkey Web Portal, COVID-19 cases of instant availability and data are shared taht were gained by researchers engaged in research on the subject in Turkey and in the World, whereas in Turkey COVID-19 Pandemic Follow-Up Display (TURCOVID19) application, information about the cases of death and improving patient numbers, applied to the number of tests, the data in the case-fatality rate (VÖO), intensive care admission and intubated patient categories are shared with the public daily and visually (34,35).

Psychological Support Practices

Countries that anticipate that psychological side effects (fear, panic in the society) that develop due to isolation during the pandemic process may cause more harm than COVID-19 have attached importance to protecting the mental health of the society. Therefore, applications such as text messaging, chat, telephone, video conferencing, websites, mobile applications, online self-help platform and online group chat have been developed (36). With these practices, it was aimed to support societies by enabling individuals to cope more easily with feelings of fear, panic and helplessness in the face of uncertainty (37). In our country, "Corona Psychosocial Support Line" and "Corona Information and Counseling Line" have been put into practice to provide psychological counseling (38).

Other Developed Applications

In addition to the applications mentioned above, different applications have also come up. Home evaluation teams, virtual maintenance centers and 3D printers that produce equipment are some of them. The home evaluation team has been set up to provide real-time clinical assessments of patients who do not require emergency medical care or hospitalization. This model facilitated access to the COVID-19 test for patients, reducing complexity, and benefiting the health system by increasing safety and efficiency (39). In order to conduct a similar filiation/field examination in our country, an expert team has been formed to screen the relatives/contacts of positive cases. The filiation / field investigation team aimed to work on the determination of the source and the agent and to increase protection and control measures, including those who had contact with the virus (40). Another application is virtual care centers. This application includes an electronic intensive care unit monitoring program that allows nurses and physicians to remotely monitor the status of 60 to 100 patients hospitalized in the intensive care units of more than one hospital. This practice is an application that reduces the contact of healthcare professionals with infected patients in the intensive care unit (7). Another application is 3D printers that produce equipment. During the pandemic process, an innovative technology, three-dimensional (3D) printer, was used to ensure adequate production and distribution of medical products due to the limited number of N95 respirators, face shields, ventilator valves, test kits and other individual protective equipment (41,42). This new technology has enabled healthcare workers at the forefront of my pandemic to be provided with adequate equipment and vital products for patients.

As a result, it is seen that technology is used effectively in the COVID-19 pandemic process. Telemedicine, mobile and web applications are among the applications that enter our lives actively in this process. The use of technology has provided benefits in many aspects such as reducing the number of admissions in emergency services and the virus load of healthcare personnel, monitoring patients at home, protecting the mental health of the community, producing sufficient equipment and facilitating access to academic studies. It is thought that the innovations brought by technology to our lives during and after the COVID-19 process will be permanent. However, it is thought that these practices may have deficiencies such as the inability of health professionals to perform physical examinations, being based on the patient's statement, not necessarily using the applications, having difficulties in accessing technological infrastructure, and individuals not being able to use technology. Therefore, it is recommended to conduct studies evaluating the positive and negative aspects of these applications, and their effectiveness on patients and healthcare professionals.

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Review

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Coronavirus (COVID-19) and its Relationship with Ocular Surface

Koronavirüs (COVİD-19) ve Oküler Yüzey ile İlişkisi

Cansu EKİNCİ, Mehmet Hakan ÖZDEMİR

Bezmialem Vakıf University Faculty of Medicine, Department of Ophthalmology, İstanbul, Turkey

ABSTRACT

An outbreak in China's Wuhan city in December 2019, characterized by unidentified pneumonia, leading to severe acute respiratory distress syndrome has begun. The cause of the outbreak has been detected as Severe acute respiratory syndrome-related coronavirus-2 (SARS-CoV-2), which is a new coronavirus and due to its rapid spread in a short time, it has been announced as a pandemic in terms of public health by the World Health Organization. The virus is transmitted mainly by direct contact with the secretions of patients and inhalation of virus-containing micro-droplets. The transmission of the virus via the ocular route is a controversial issue and there are limited number of studies in the literature. Follicular conjunctivitis may be one of the ocular manifestations of the disease and even if there is no concomitant conjunctivitis, it is very important for the ophthalmologists and healthcare professionals to take preventive measures. In this review, the relationship of SARS-CoV-2 with ocular surface findings was evaluated in the light of the literature.

Keywords: Ocular surface, conjunctivitis, tear, COVID-19

ÖZ

Çin'in Wuhan şehrinde Aralık 2019'da nedeni belirlenemeyen pnömoni ile karakterize, ciddi akut solunum sıkıntıcı sendromuna yol açan bir salgın başlamıştır. Salgının etkeninin yeni bir koronavirüs olan şiddetli akut solunum yetersizliği sendromu-2 (SARS-CoV-2) olduğu saptanıp kısa bir süre içinde hızla yayılım göstermesiyle Dünya Sağlık Örgütü tarafından halk sağlığı açısından acil durum olan pandemi olarak ilan edilmiştir. Virüs başlıca hastaların sekresyonları ile doğrudan temas ile virüs içeren mikrodamlacıkların inhalasyonu ile bulaşmaktadır. Virüsün oküler yol ile bulaşması ise tartışmalı bir konu olup literatürde sınırlı sayıda çalışma mevcuttur. Foliküler konjonktivitin hastalığın oküler bulgularından biri olabileceği ve eşlik eden konjonktivit olmasa dahi özellikle oftalmologların ve sağlık çalışanlarının koruyucu önlemler almaları oldukça önem taşımaktadır. Bu derlemede SARS-CoV-2'nin oküler yüzey bulguları ile ilişkisi literatür eşliğinde değerlendirilmiştir.

Anahtar Sözcükler: Oküler yüzey, konjonktivit, gözyaşı, COVİD-19

General Information

Coronaviruses are enveloped, positive stranded RNA viruses and are members of the Coronavirinae subfamily within the Coronaviridae family. The name coronavirus comes from the Latin word "corona" which means "crown" because the characteristic spiny protrusions on its envelope create a crown-like appearance (1). It is known that coronaviruses infect various mammals and birds, and with the ability to mutate, they can acquire the characteristic of zoonotic pathogens that facilitate their transition from animal to human (2,3). Four types of coronaviruses known to infect humans have been identified (HCoV-229E, -NL63, -OC43, and -HKU1). The oldest information about the endemic human coronavirus goes back to the 1960s. severe acute respiratory distress (SARS) and Middle East respiratory syndrome (MERS) coronaviruses, which caused epidemics in 2003 and 2012, are of animal origin

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Address for Correspondence: Cansu EKİNCİ, Bezmialem Vakıf University Faculty of Medicine, Department of Ophtahalmology, İstanbul, Turkey
E-mail: cansuekinci@yahoo.com **ORCID ID:** orcid.org/0000-0002-5464-5627

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and can cause fatal respiratory failure in humans (4-7). Finally, a severe pneumonia of unknown cause, which started in Wuhan, China in December 2019, rapidly spread all over the world. In January 2020, it was reported that the cause of this epidemic was a new coronavirus (SARS-CoV-2) and was recognized as an international public health emergency by the World Health Organization (WHO). In February 2020, WHO named the new coronavirus disease (COVID-19) (8-10).

Coronaviruses bind to the respiratory or intestinal epithelium, causing changes and death in host cells. Its clinical outcomes are highly variable, and while the majority of cases show asymptomatic or mild symptoms, severe respiratory failure and death may result in those over 60 years of age and those with comorbid diseases such as hypertension, cardiovascular disease, chronic lung disease or cancer. The incubation period is 2-14 days, and typical signs and symptoms are high fever, dry cough, shortness of breath, myalgia, fatigue, and bilateral ground-glass appearance on chest computed tomography (CT) (11,12). Coronaviruses can also cause ocular and gastrointestinal system symptoms outside of the respiratory system. The main modes of transmission are by airborne microdroplets as a result of close contact with patients, direct contact with the patient or contaminated objects, and fecal-oral route. Micro-droplets that spread into the air by sneezing, coughing or exhaling can enter the body through the mouth, nasal mucosa or conjunctiva. Therefore, WHO stated that healthcare professionals who are in contact with suspected (COVID-19) patients should protect their mouth, nose and eyes with glasses, masks and visors (13).

COVID-19 and Ocular Surface Findings

It has been shown that respiratory tract viruses can cause ocular complications in infected patients and even cause respiratory tract infections later on. This situation creates serious concern especially for ophthalmologists. In 2004, HCoV-NL63 type CoV was detected for the first time in a 7-month-old baby who was found to have bronchiolitis and conjunctivitis in the SARS coronavirus epidemic (14). In a retrospective study conducted in France during the same epidemic period, when the data of children infected with HCoV-NL63 between 2000 and 2003 were examined, it was found that 17% of the patients had conjunctivitis (15). In 2004, Loon et al. (16) applied polymerase chain reaction (PCR) to early tear samples of 36 suspected SARS cases (eight of them were later confirmed by serology, the remaining patients were serologically negative) consisting of healthcare workers. In 3 of eight cases (37.5%), viruses were detected by PCR test of tears, in one of them, virus RNA could not be detected in feces and nasopharynx samples, but was detected only at eye tear. They stated that especially ophthalmologists and healthcare professionals work close to the eyes of patients, and because the virus is detected in the early period of the infection at the eye tear, and devices that are constantly used such as spectacle frames and applanation tonometers can be potential sources of contamination (16). On the contrary, in the study conducted by Chan et al. (17) in 2004, nasopharynx, feces, eye tear samples and conjunctival swabs were taken from 17 patients whose diagnosis was confirmed by serology. The nasopharynx and feces samples were PCR+ in 5 of them, but in eye tear and conjunctival swab samples, no virus genetic material detected by PCR. The authors explained this result for 3 possible reasons. The first is that the specificity of the PCR test is very high and the sensitivity is low, so the result may be false negative. It was stated that to increase sensitivity, more samples should be taken from more patients. Another reason is that since the virus is in body secretions for a limited time, negative results can be obtained due to sampling during the window period. Finally, they stated that the virus may not be present in eye tears (17).

Today, there is quite a limited amount of data regarding the relationship of COVID-19, which causes pandemic, with ocular involvement. In cases with symptoms, mild follicular conjunctivitis, hyperemia in the bulbar conjunctiva, epiphora, chemosis or mild eyelid edema are observed (13,18). In a report published in The Lancet, Guangfa Wang, who had studies on pneumonia, during his examination, in Wuhan, attributed himself to be infected because of not wearing protective glasses despite wearing an N95 mask. It has been reported that Wang developed pneumonia after conjunctivitis symptoms developed (19). In addition, ophthalmologist Dr. Li Wenliang infected and died as a result of contact with a patient. In a study, Xia et al. (20) took two samples from 30 COVID-19 patients, they examined eye tear, conjunctival swab and saliva samples and detected the virus by PCR only in 2 samples taken from a patient with conjunctivitis. The authors emphasized the importance of protecting with protective glasses from the patients with no signs of conjunctivitis, as they are at risk for transmission by droplets, although the virus is detected in very low levels at the eye tears, even if the virus is not present at ocular surface of the patients examined by ophthalmologists at close range (20). Similarly, in the study conducted by Seah et al. (21), a total of 64 eye tear samples were taken simultaneously with nasopharynx swab samples from 17 COVID-19 patients between the 3rd and 20th days from the onset of the findings, with an interval of one week, and evaluated with the viral culture and PCR, but no virus was shown in eye tears. Although the detection rates of the virus at eye tear are low in the literature, in one case reported, the virus was detected in the conjunctival swab on the 13th day from the onset of the findings, and the conjunctival swab sample was found to be PCR+ until the 19th day (18). In another case, conjunctivitis accompanying respiratory tract infection was present and the conjunctival swab PCR result was found to be positive until the 27th day of the disease, although the nasopharynx swab result was negative. This suggests that the virus can remain in the conjunctiva for a longer time (22).

Baig et al. (24) performed retinal examinations of 12 patients, whose diagnosis was confirmed by PCR or antibody detection, by using optical coherence tomography (OCT) device between 11 and 33 days after the onset of COVID-19 symptoms, and reported retinal changes associated with COVID-19 for the first time. They detected hyperreflective lesions in both eyes, ganglion cells and inner plexiform layer, particularly in the papillomacular nerve bundle in all patients. In addition, the presence of cotton wool spots and microhemorrhages at the level of the vascular

arcade in the fundus examination of four patients suggests that the disease may be a microvasculopathy.

Although there are concerns about COVID-19 infection acquired through ocular transmission, the underlying mechanism has not been fully clarified. It is emphasized that the virus infects host cells via angiotensin converting enzyme-2 (ACE-2) receptor and transmembrane protease serine-2 (TMPRSS-2), as in SARS (23,24). A study has shown that ACE-2 and TMPRSS-2 production is more dominant in corneal limbal cells rather than conjunctiva, but the contribution of this to the systemic circulation of the virus is to be discussed (13,25,26). In addition, due to the dynamism of the eye tear film, it is thought that the transition of eye tears to the nasal cavity by the canaliculi reduces the duration of the ocular surface and the risk of transmission. In patients with lacrimal drainage obstruction, on the contrary, it is stated that the duration of the virus on the ocular surface will be prolonged and may cause periocular skin contamination due to accompanying epiphora (27-29).

As a result, studies on ocular findings caused by SARS-CoV-2 in humans are increasing. As the ocular effects and details of SARS-CoV-2 are determined, possible prevention measures and treatment options will become clearer.

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Review

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Evaluation of Updated Therapeutic Options For COVID-19 in Pregnancy and Lactation

Gebelikte ve Emzirme Döneminde COVİD-19 Güncel Tedavi Seçeneklerinin Değerlendirilmesi

Zeynep TIRMIKÇIOĞLU

İzmir Atatürk Training and Research Hospital, Department of Clinical Pharmacology and Toxicology, İzmir, Turkey

ABSTRACT

A new respiratory tract infection caused by coronaviruses was identified in 2019 and called Coronavirus disease-19 (COVID-19). It has long been known that pregnant women are not more susceptible to viral illness. However, changes to their immune system in pregnancy can be associated with more severe symptoms. Pregnant women do not seem to be at higher risk than non-pregnant individuals of severe COVID-19 infection. There are currently no data suggesting an increased risk of miscarriage or malformations in relation to coronaviruses. There is no specific antiviral treatment for COVID-19. Therapeutic options for patients with confirmed COVID-19 have been recently updated as hydroxychloroquine and/or azithromycin, and favipiravir for severe pneumonia. According to updated national treatment guidelines for COVID-19, favipiravir is not recommended for use in pregnant or breastfeeding women, but lopinavir/ritonavir can be used as second-line therapy. Published experience with COVID-19 during breastfeeding is limited. The main risk of breastfeeding is the close contact between mother and baby. This paper presents a literature review regarding outcomes after use of hydroxychloroquine, azithromycin and lopinavir/ritonavir during pregnancy and lactation. Hydroxychloroquine and/or azithromycin use is not expected to increase the risk of birth defects and adverse effects in breastfed infants. Based on reports of human immunodeficiency virus- infected women, lopinavir/ritonavir use does not appear to increase the risk of adverse effects, and it may be chosen in life-threatening situations. It is important to pay special attention to the selection of drugs for COVID-19 and utilize the most up-to-date information to optimize outcomes for both infant and mother.

Keywords: COVID-19, drug, pregnancy, lactation

ÖZ

2019 yılında koronavirüslerin yol açtığı yeni tip bir viral solunum yolu enfeksiyonu tanımlanmış ve bu enfeksiyon Koronavirüs hastalığı-19 (COVİD-19) olarak isimlendirilmiştir. Gebe kadınların viral hastalıklara daha yatkın olmadıkları uzun zamandır bilinmektedir. Ancak gebelikte bağışıklık sisteminde meydana gelen değişiklikler, gebelerin bu hastalıkları daha ağır bulgularla geçirmelerine neden olabilir. Ağır COVİD-19 enfeksiyonu geçiren gebe olmayan kadınlarla karşılaştırıldıklarında gebe kadınlar, daha fazla risk altında gözükmemektedirler. Bugün için koronavirüslerin düşük, erken gebelik kaybı veya doğumsal defektlerle bir ilişkisi olduğuna dair kanıt yoktur. COVİD-19'un spesifik antiviral bir tedavisi bulunmamaktadır. COVİD-19 tanısı almış hastalarda tedavi seçenekleri son olarak, hidrosiklorokin ve/veya azitromisin, ağır pnömoni olgularında favipiravir olarak güncellenmiştir. Güncellenmiş COVİD-19 ulusal tedavi kılavuzuna göre, favipiravirin gebelerde ve emziren annelerde kullanımı önerilmemektedir. Lopinavir/ritonavir alternatif ya da kombine tedavi olarak diğer ilaçlara yanıt vermeyen gebelerde tercih edilebilir. Emzirme döneminde COVİD-19 ile ilgili yayınlanmış veriler sınırlıdır. Emzirmede esas risk, damlacık yoluyla hastalığı bulaştırabilecek anne ile bebeğin yakın temasıdır. COVİD-19 tedavisinde kullanılacak ilaçlar, fetus ve yenidoğana olası advers etkileri açısından dikkatle değerlendirilmelidir. Bu derleme gebelikte ve emzirme döneminde hidroksiklorokin, azitromisin ve lopinavir/ritonavir kullanımına ait literatür bilgisini sunmaktadır. Gebelikte ve emzirme döneminde hidroksiklorokin ve azitromisin kullanımının doğumsal kusur riskini artırması ya da yenidoğanda advers etkiye yol açması beklenmemektedir. Lopinavir/ritonavir tedavisi ile ilgili bilgilerimiz insan bağışıklık yetmezliği virüsü enfeksiyonu olan gebelere ait olmakla birlikte anne sağlığını tehdit eden durumlarda hem gebelikte hem emzirme döneminde bu ilaçlar kullanılabilir. Gebe veya emziren kadınlarda COVİD-19 enfeksiyonunu değerlendirmek zor olabilmekle birlikte ilaç seçimi konusunda özellikle dikkatli olunmalı ve hem anne hem bebek açısından ideal sonuçlar için en güncel bilgiler kullanılmalıdır.

Anahtar Sözcükler: COVİD-19, ilaç, gebelik, emzirme

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Address for Correspondence: Zeynep TIRMIKÇIOĞU, İzmir Atatürk Training and Research Hospital, Clinic of Clinical Pharmacology and Toxicology, İzmir, Turkey
E-mail: dr.zeynebfarma@gmail.com **ORCID ID:** orcid.org/0000-0002-5639-4665

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Introduction

Coronaviruses (CoV) are a family of viruses that can cause various degrees of respiratory, gastrointestinal, liver, kidney damage and neurological damage in humans and animals. They can cause different clinical outcomes from the common cold to more serious diseases such as Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS) (1).

The number of people infected by the new CoV, which has become a global problem in 2020, is today expressed in millions. Since it was first reported in 2019 in Wuhan, China, as a result of the examination of cases of pneumonia of unknown etiology, this virus-related disease defined as "2019-nCoV" is called Coronavirus disease-19 (COVID-19). COVID-19, an infection with respiratory symptoms, fever, cough and dyspnoea, can cause pneumonia, severe acute respiratory infection, kidney failure and even death in more severe cases.

It has long been known that pregnant women are not more prone to viral diseases. However, changes in the immune system during pregnancy may cause pregnant women to experience these diseases with more severe symptoms. However, to date, there is no evidence that pregnant women are more susceptible to COVID-19 infection, or that those with COVID-19 infection are more likely to develop more severe pneumonia (2).

No malformation has been reported in babies born to pregnant women with coronavirus infection. Although some neonatal complications have been reported that may be associated with SARS and MERS infections, data on COVID-19 infection are still limited. According to the reports of 9 pregnant women who gave birth at 29-36 weeks of gestation with COVID-19 infection, no health problem occurred in babies, and no coronavirus was detected in amniotic fluid and milk samples (3). Although all women have given birth by cesarean section, no reason has been presented for the need for a cesarean section except for the presence of COVID-19 infection. Three of the babies born weigh less than 2500 grams and this has been associated with prematurity and preeclampsia. In another case report, 10 babies born from 9 women with COVID-19 pneumonia were observed, and 6 babies, including twins, were born preterm and had respiratory symptoms (4). A 35-week-old baby died of multiple organ failure; The coronavirus tests of 9 babies tested were negative. Published information on COVID-19 and breastfeeding is very limited. Researchers who conducted systematic reviews reported that no virus was found in measurements made on the milk of 13 mothers with COVID-19 infection. However, it should be kept in mind that this number is not sufficient to interpret the results (5).

Currently, there is no specific treatment for COVID-19 with proven safety and effectiveness. In patients with a confirmed diagnosis of COVID-19, antibacterials other than azithromycin are discontinued unless there is clinical or laboratory evidence of the presence of an additional bacterial pathogen. Hydroxychloroquine is also added to the treatment in patients with suspected viral pneumonia (1). Although it was in the treatment plan in the first months when the infection started to spread, according to the treatment guideline of the Ministry of Health, oseltamivir is no longer used in treatment in patients whose diagnosis of influenza pneumonia has been ruled out (1,6). Favipiravir has been defined as an additional treatment option in patients with severe pneumonia who do not respond to the first treatment. According to the updated treatment options, use of hydroxychloroquine or lopinavir/ritonavir in pregnant women with a definite diagnosis of COVID-19 was deemed appropriate (Table 1). Although a treatment protocol for breastfeeding mothers has not been specified, it has been reported that favipiravir should not be used in pregnant women and nursing mothers (1).

The aim of this review is to re-evaluate the updated treatment options for COVID-19 and to provide detailed literature on the use of hydroxychloroquine, azithromycin, and lopinavir/ritonavir therapy in pregnancy and breastfeeding.

Use of Hydroxychloroquine in Pregnancy and Breastfeeding

The results of different studies and case reports about hydroxychloroquine are that the use of this drug during pregnancy does not increase the risk of congenital anomalies (7-9). Based on some experimental studies and case reports that hydroxychloroquine use during pregnancy may cause problems in vision and hearing functions in born babies, large-scale studies have been conducted on these defects (10). Children who were exposed to hydroxychloroquine in their mother's womb were followed up and no visual or hearing problems were found in their examinations (11,12). A 2011 systematic review concluded that there is no evidence that the use of chloroquine or hydroxychloroquine during pregnancy causes ocular toxicity (13).

In another study in which clinical studies conducted between 1980 and 2007 were compiled, it was reported that the use of hydroxychloroquine in pregnant women with autoimmune disease was not associated with congenital defects, miscarriage, stillbirth or preterm birth (14). Another meta-analysis published in 2015 reached similar conclusions; however, some increase in the risk of spontaneous abortion has been reported. The significant increase in the risk of miscarriage was thought to be due to the mother's autoimmune disease rather than hydroxychloroquine (15). The literature suggests that hydroxychloroquine should not be discontinued during and after pregnancy to prevent exacerbation of autoimmune diseases. In the European League Against Rheumatism (EULAR) report published on the use of antirheumatic drugs during pregnancy in 2016, it was stated that hydroxychloroquine treatment does not increase the risk of congenital malformations according to the available evidence; It has been recommended to continue using hydroxychloroquine in symptomatic patients during pregnancy (16).

Hydroxychloroquine is also recommended for malaria prophylaxis in pregnant women who have to travel to endemic areas. Since it is thought that malaria, which progresses badly

Table 1. COVID-19 Adult Patient Treatment Options *

Name of the drug	Daily dose/administration	Duration of medication (day)
Treatment in uncomplicated possible/definite diagnosed COVID-19 cases		
Hydroxychloroquine 200 mg tablet -/+ Azithromycin	2x200 mg tablet, oral First day, 500 mg tablet, oral Following 4 days 250mg/day	5 day 5 day
Treatment in possible/definite diagnosed COVID-19 cases with mild pneumonia (those without severe pneumonia)		
Hydroxychloroquine 200 mg tablet -/+ Azithromycin	2x400 mg loading dose, followed 2x200 mg, oral First day, 500 mg tablet, oral Following 4 days 250mg/day	5 day 5 day
Treatment in possible/definite diagnosed COVID-19 cases with with severe pneumonia		
Hydroxychloroquine 200 mg tablet AND/OR Favipiravir 200 mg tablet -/+ Azithromycin	2x400 mg loading dose, followed 2x200 mg, oral 2x1600 mg loading 2x600 mg maintenance First day, 500 mg tablet, oral Following 4 days 250mg/day	5 day 5 day 5 day
Treatment in patients whose clinical condition is aggravated or whose pneumonia symptoms progress while receiving hydroxychloroquine treatment		
Favipiravir 200 mg tablet (hydroxycoloquine treatment should be completed to 10 days and discontinued	2x1600 mg loading 2x600 mg maintenance	5 day
Treatment in pregnant women with covid-19 definite diagnosis		
Hydroxychloroquine 200 mg tablet or Lopinovir 200 mg/ritonavir 50 mg tablet	2x200 mg tablet, oral 2x2 tablet, oral	5 day 10-14 day

*https://covid19bilgi.saglik.gov.tr/depo/tedavi/COVID19-EriskinHastaTedavisi.pdf, COVID-19: Coronavirus disease-19

due to the decrease in cellular responses during pregnancy, will harm pregnancy much more, the use of hydroxychloroquine in mandatory situations has been accepted as safe (17).

Babies exposed to hydroxychloroquine during breastfeeding receive only a very small amount of the drug that passes into breast milk (18-20). It has been reported that babies of mothers who take hydroxychloroquine in doses of 200-400 mg per day may be exposed to 0.06-0.2 mg/kg drug with breast milk (21). No drug-related adverse effects in terms of growth, vision and hearing functions were found in babies whose development was followed up to the age of one (22-24). Hydroxychloroquine is considered to be acceptable for use during breastfeeding.

It has also been reported that the infants of mothers who took hydroxychloroquine once a week due to malaria prophylaxis, the amount of the drug in the milk that would not harm the baby, but did not protect the baby against malaria (25). Therefore, when malaria prophylaxis is required, breastfed babies should also take hydroxychloroquine at recommended doses.

Lopinavir/Ritonavir Use During Pregnancy and Breastfeeding

Exposure to protease inhibitors during pregnancy is not thought to cause an increased risk of congenital anomalies. Although adverse pregnancy outcomes were reported in the studies, they were observed in fewer and mostly premature babies.

In a study comparing the concentrations of protease inhibitors in maternal and cord blood, it was reported that these drugs did not exceed the placenta at term (26). In 2009, it was found that lopinavir was not in measurable concentrations in cord blood in samples taken from 26 human immunodeficiency virus (HIV)-infected pregnant women (27). As a result of the fact that some drug solutions contain propylene glycol and premature babies cannot eliminate this substance, kidney and respiratory problems have occurred in some premature babies. In a study reported from France in 2011, it was observed that adrenal dysfunction developed in babies of HIV-infected mothers who took lopinavir-ritonavir at birth and for an average of 30 days (28). All term babies born at term are asymptomatic; however, it was reported

that three of the preterm babies showed signs of dangerous adrenal insufficiency such as hyponatremia and hyperkalemia and cardiogenic shock developed in one premature baby. All adverse findings resolved after cessation of lopinavir-ritonavir exposure. Researchers also stated that these findings in premature babies may have occurred due to propylene glycol toxicity (28).

According to thousands of pregnancy data collected until 2019, the rate of congenital malformation in pregnant women who received lopinavir for HIV treatment is around 2.1%, which is similar to the general population (29). No increase in the risk of congenital defects was observed in pregnancies using lopinavir, 1333 of which were in the first trimester and 2371 in the second trimester (30). According to UK and Ireland national data, 134 babies with congenital defects were born out of 4864 pregnancies using lopinavir; the congenital anomaly rate is 2.9% (31). The defects reported by the researchers, who stated that there is no difference in anomaly rates between those who started the drug in the first trimester and afterwards, include limb deficiencies, heart defects, musculoskeletal defects, chromosomal abnormalities and urinary system defects. However, the rate of congenital anomalies reported in this study is not higher than the expected rate in the general population. Another study investigating the effects of lopinavir in different periods during pregnancy concluded that first trimester drug exposure may be associated with preterm delivery compared to late use (32).

Data on lopinavir and ritonavir treatment have been obtained from pregnant women and mothers with HIV infection. Accordingly, breastfeeding in HIV-infected mothers in many developed countries is restricted by the thought that the infection can be transmitted to the baby through milk. The World Health Organization (WHO) recommends that antiretroviral therapy be continued in a way that minimizes the risk of transmission of infection from mother to baby in countries where adequate and acceptable nutrition opportunities are not available instead of breast milk; However, there is no lopinavir-ritonavir among the treatment options recommended by WHO (33). Therefore, observational data on the use of lopinavir and ritonavir in lactation are very limited.

Lopinavir passes into breast milk in small amounts (34). In a study conducted with HIV-positive women, the average amount in breast milk was found to be 4263 mcg/L (35). In this study, 9 HIV-positive pregnant women received 3 doses of lopinavir (200 mg), ritonavir (150 mg), zidovudine (300 mg), lamivudine (50 mg) before cesarean section, 3 hours apart of each, and milk samples were collected at a mean postpartum 25th hour. Mean ritonavir levels measured in breast milk in the same study were 240 mcg/L. According to the results of an observational study conducted in breastfed infants, no adverse effects were observed at 1, 3 and 6 months in babies whose mothers received lopinavir (400 mg) and ritonavir (100 mg) twice daily as part of the HIV infection treatment (36).

Use of Azithromycin in Pregnancy and Breastfeeding

Based on experimental animal studies and human reports, the use of azithromycin during pregnancy is not expected to increase the risk of birth defects. In 21 human placentas where transplacental transmission was evaluated, it was reported that less than 3% of the maternal azithromycin dose passed to the fetal compartment (37).

In case reports and retrospective studies reporting the results of more than a thousand pregnant women who received azithromycin for the treatment of chlamydia infection, no risk of pregnancy complications and congenital defects was reported (38-40). According to the data of the Israel Teratogenicity Information Service published in 2012, no increase in the risk of major congenital malformation or cardiovascular defect was detected in 156 pregnant women exposed to azithromycin, 119 of which were in the first trimester (41). In a study examining 1459 children whose mothers used azithromycin during their pregnancy, no increase was identified in terms of congenital defects (42). In a study investigating the relationship between the use of antibiotics during pregnancy and spontaneous abortion in 2017, it was reported that azithromycin use may be associated with abortions (43).

Since azithromycin passes into milk in small amounts, it is not expected to have adverse effects in breastfed babies. Measurement and standardization of azithromycin levels in breast milk is difficult due to its slow clearance and accumulation. It has been reported that after 500 mg of oral azithromycin intake per day, breast milk concentrations increased to 1.3 mg/L 1 hour after the first dose and 2.8 mg/L 30 hours after the third dose (44). The amount that the baby can receive through breast milk has been calculated as approximately 0.5 mg/day.

If the mother is using azithromycin during the breastfeeding period, it should be monitored whether there are possible gastrointestinal findings such as candidiasis, vomiting, and diarrhea. Although there are studies reporting the risk of infantile hypertrophic pyloric stenosis in babies of mothers who used macrolides in the first two weeks of breastfeeding, the relation of this situation with drug use is highly doubtful (45,46). In a study conducted on babies whose mothers used macrolide and breastmilk, no relationship was found between pyloric stenosis and macrolide use (47). In this study, it was reported that the use of azithromycin during breastfeeding was present in 10 out of 55 mothers, and a comparison was made with the use of amoxicillin in terms of adverse effects. Accordingly, the rate of adverse reactions in infants exposed to macrolide was 12.7%, while this rate was similar to the adverse reaction rate seen in infants exposed to amoxicillin through breast milk. Reactions observed in infants include rash, diarrhea, decreased appetite, and tendency to sleep. It was reported that no adverse effects were observed in babies breastfed by eight mothers who were given 500 mg intravenous azithromycin at 15, 30 and 60 minutes prior to cesarean section (48). In two meta-analyzes reported in 2019, it was concluded that there was no relationship between macrolide use during breastfeeding and infantile hypertrophic pyloric stenosis (49,50).

Result

COVID-19 treatment options during pregnancy and breastfeeding should be carefully evaluated in terms of possible

risks and the patient should be informed. Following this evaluation and information, some medications administered to other adult individuals can also be used in the treatment of the pregnant patient in cases where medication is necessary. A risk assessment that is satisfactory for both the follow-up clinician and the patient, with detailed literature information, can also reduce anxiety related to the disease and possible drug use. The use of hydroxychloroquine and azithromycin during pregnancy and lactation is not expected to increase the risk of birth defects or cause adverse effects in the newborn. Although our information about lopinavir/ritonavir treatment belongs to pregnant women with HIV infection, these drugs can be used both during pregnancy and breastfeeding in situations that threaten maternal health. There is always a need for large-scale epidemiological studies to evaluate the effects of drugs used in the treatment of COVID-19 during pregnancy and lactation. Although COVID-19 is a disease full of unknowns for today, it is the duty of health professionals to provide treatment options to pregnant and breastfeeding mothers with an approach that takes into account both maternal health and baby's health in the light of current information.

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Review

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Precautions Prior to the Treatment in Oral and Maxillofacial Surgery in the Reopening Period during COVID-19 Pandemic

COVİD-19 Pandemisi Yeniden Açılma Döneminde Ağız Diş ve Çene Cerrahisinde Tedavi Öncesi Alınması Gereken Önlemler

Özge DOĞANAY, Doğan DOLANMAZ

Bezmialem Vakıf University Faculty of Dentistry, Department of Oral and Maxillofacial Surgery, İstanbul, Turkey

ABSTRACT

Oral and maxillofacial surgery is correlated with a high risk of severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) transmission. To assist our colleagues under physical and psychological burden by using the current literature data and considering the recommendations of the Ministry of Health Science board decisions, -The American Association of Oral and Maxillofacial Surgeons, American Dental Association and Centers for Disease Control and Prevention, this literature review has been prepared in order to organize elective surgeries. Interventions should be planned after evaluating both the logistic conditions of the institution and the situation during the pandemic before performing elective surgery. In order to save resources and to avoid unnecessary exposure to infected patients, there is the need to schedule interventions depending on their priority. In general, Emergency procedures do not allow any delay. In elective surgeries, risk assessments of both the patient and the surgical procedure is left to the surgeon. Inpatient and outpatient units have to be organized in such a way that the risk of cross-infection among patients is reduced to a minimum. Active Coronavirus disease-19 (COVID-19) patients should be treated in the operating room with negative pressure, and aerosol formation must be reduced to a minimum. During reopening period, treatments may be applied in cases where appropriate conditions are provided and recommendations for patient and physician safety are taken.

Keywords: COVID-19 pandemic, oral and maxillofacial surgery, personal protective equipment, reopening, elective treatments, protective measures

ÖZ

Ağız diş ve çene cerrahisi pratiği, şiddetli aku solunum yolu enfeksiyonu-2 (SARS-CoV-2) bulaştırıcılığı açısından yüksek riskli grupların arasında yer almaktadır. Sağlık Bakanlığı Bilim kurulu kararları, The American Association of Oral and Maxillofacial Surgeons, American Dental Association ve Centers for Disease Control and Prevention önerileri gözetilip, güncel literatür verileri kullanılarak, fiziksel ve psikolojik yük altındaki meslektaşlarımıza yardımcı olmak amacıyla elektif cerrahilerin planlanması ile ilgili bu literatür derlemesi hazırlanmıştır. Elektif cerrahiye geçmeden kurumun hem lojistik koşullarının, hem de pandemi içindeki durumunun değerlendirilmesinden sonra planlı cerrahinin/girişimlerin programlanması yapılmalıdır. Kişisel koruyucu ekipman gibi kaynakları tasarruflu kullanmak ve enfekte hastalara olan gereksiz maruziyeti ortadan kaldırmak için tedavilerin öncelik sırasına göre planlanması gereklidir. Genel kanı olarak, Koronavirüs hastalığı (COVİD-19) hastası acil cerrahi bir işlem için başvurduğunda gecikme yaşanmadan alınmaktadır. Elektif tedavilerde ise hastanın ve cerrahi işlemin risk durumu cerraha bırakılmaktadır. Servisler ve ayakta tedavi üniteleri, hastalar arasında çapraz enfeksiyon riskini en aza indirmek amacıyla yeniden düzenlenmelidir. Aktif COVİD-19 hastaları negatif basınçlı odalarda tedaviye alınmalı ve aerosolizasyon en aza indirilmelidir. COVİD-19 pandemisi "yeniden açılma" periyodunda, salgın nedeniyle tedavisi yarım kalan ya da müdahale edilmesi gereken olgular için, uygun koşullar sağlandığı ve hasta/hekim güvenliği için yapılan önerilerin dikkate alındığı durumlarda tedaviler yapılabilir.

Anahtar Sözcükler: COVİD-19 pandemisi, ağız diş ve çene cerrahisi, kişisel koruyucu ekipman, yeniden açılma, elektif tedaviler, koruyucu önlemler

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Address for Correspondence: Özge DOĞANAY, Bezmialem Vakıf University Faculty of Dentistry, Department of Oral and Maxillofacial Surgery, İstanbul, Turkey
E-mail: ozgedoganay87@gmail.com **ORCID ID:** orcid.org/0000-0001-5273-7774

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Introduction

Epidemic Coronavirus disease-19 (COVID-19) disease caused by the virus named severe acute respiratory syndrome-CoV-2 (SARS-Cov-2) spread worldwide in a very short time after emerging in Wuhan, Hubei, China in the last month of 2019. The disease was recognized as the "International Public Health Emergency" by the World Health Organization on January 30, 2020, and a global pandemic was declared on March 11, 2020. Turkey also has taken its place among the countries affected by the pandemic and described the first official event on March 11, 2020.

The Ministry of Health listed the measures to be taken to minimize the density in health institutions and to reduce the burden on health personnel with the circular number 14500235-403.99 dated 17/03/2020. Among these items, non-emergency elective surgical procedures; It was pointed out that under the extraordinary conditions caused by the pandemic, the efficient and rational use of health resources, planning a more appropriate date as possible in order to minimize the possibility of contamination between patients and strategically important healthcare professionals in this process.

On the other hand, sustainability of healthcare services and "necessary" initiatives other than COVID-19 has gained importance over the past 70 days. In this context, it has emerged that the patients who continue their active treatment and are interrupted due to the pandemic need to evaluate and plan the procedures to increase or protect the quality of life or function and pain treatments during the reopening process.

Representing the physician group who are active in the perioperative process, the decisions of the Ministry of Health Scientific Committee, The American Association of Oral and Maxillofacial Surgeons (AAOMS), American Dental Association (ADA) and Centers for Disease Control and Prevention (CDC) recommendations; using the current literature data, we review on the planning of elective surgeries has been prepared to help our colleagues under physical and psychological burden. Before implementing the directives in this review, regional factors should be considered first, and the decision should be made with the local health authority, taking into account the characteristics and possibilities of the institution in transition to elective operations.

Organization of the planned surgery/interventions should be done after evaluating both the logistic conditions of the institution and its situation in the pandemic before proceeding to elective surgery. Especially defining the concept of "elective surgery" very clearly and developing a common language among disciplines will be very useful in increasing harmony.

Clinical Findings of COVID-19 Infection

The incubation period of COVID-19 infection has been shown to be between 1-14 days, and asymptomatic individuals have been shown to play an important role in the spread of the virus. The possibility of transmission from asymptomatic carriers has increased today and therefore, measuring body temperature alone is not sufficient to screen these carriers (1-3).

In the prodromal phase, the primary symptoms of non-specific reported COVID-19 infection are malaise, fever, and dry cough. The most commonly reported signs and symptoms are fever (98%), cough (76%), shortness of breath (55%), myalgia or weakness (44%). Unlike other coronavirus infections (SARS-CoV), upper respiratory and intestinal symptoms such as sore throat, runny nose and diarrhea are less common in COVID-19 infection (1,4,5).

Case Selection during Pandemic Period

In this period, in order to safely perform interventions related to oral and maxillofacial surgery, the principles of simplifying the surgery were adopted by avoiding very complex and long-lasting surgical approaches (6). In cases where it cannot be determined whether the patient has COVID-19 (+) or not, strict precautions should be taken prior to elective practices to protect healthcare workers. Conducting the intervention in demarcated areas will ensure effective use of limited resources. For this purpose, a classification has been proposed according to the need for treatment related to maxillofacial surgery applications in the pandemic period (Table 1) (7).

Although no classification or algorithm has been proposed for oral and maxillofacial surgery in the re-opening period, it is recommended to plan elective surgeries taking into account certain criteria (Table 2) (8).

Things to Consider Before Elective Surgery

Before starting planned surgeries, in addition to evaluating the institutional facilities, cooperation and coordination with the local health authority should be ensured, the situation of the region in the pandemic should be evaluated together, and a period of continuous decrease in the rate of new COVID-19 cases should be ensured for at least 14 days in the relevant region (8).

Evaluation of COVID-19 Patients

Based on the available information, it is recommended to consider surgery in COVID-19 (+) cases only if life-threatening is in question, due to the high morbidity and mortality rates in early surgery (9).

In elective cases with COVID-19 (+), it is recommended to postpone elective therapy until the infection has resolved, symptoms have resolved and the patient has acquired COVID-19 (-) Antigen (Ag) for 28 days. Patients who do not show signs of COVID-19 can be considered as COVID-19 (+), and elective surgeries can be planned by taking necessary precautions (7-11).

COVID-19 Diagnostic Opportunities

As a rapid test for diagnosis, real-time reverse transcription polymerase reaction (PCR) tests are currently preferred, despite the high false negativity rate (approximately 30%) (12).

Table 1. Recommendations regarding the implementation of surgical procedures during the COVID-19 pandemic (Accepted: 31/03/2020) (7).

Procedures	Priority	Proposal
• Orbital decompression (visual acuity unaffected) • Orthognathic surgery • Primary and secondary surgery for cleft lip and palate malformations	Miscarriage (elective surgery) Systemically healthy patient	Postponing surgery until the COVID-19 pandemic period is resolved
• Secondary reconstructive procedures (free/pedicled flaps) • Surgery for temporomandibular pathologies causing limited pain • Treatment of craniofacial malformations without sleep apnea/high intracranial pressure	Miscarriage (Elective surgery) COVID-19 (+) Patient	Postponing surgery until the COVID-19 pandemic period is resolved
• Benign, slow-growing tumors • Closed fractures with limited dysfunction • Large cystic lesions	Middle Systemically healthy patient	Postponing surgery until the COVID-19 pandemic period is resolved as long as the risks associated with procrastination are under control
• Surgery for temporomandibular pathologies causing severe pain • Sleep apnea/treatment of craniofacial malformations with high intracranial pressure	Middle COVID-19 (+) Patient	Postponing surgery until the COVID-19 pandemic period is resolved as long as the risks associated with procrastination are under control; It must be confirmed that there is improvement!
• Deep head and neck infections without risk of airway obstruction • Malignant tumors with / without reconstructive procedures • Orbital decompression (decreased visual acuity)	Compulsory Systemically healthy patient	Surgical
• Open, fragmented broken • Tracheotomy (expected airway obstruction)	Compulsory COVID-19 (+) Patient	Surgical; It must be confirmed that there is improvement!
• Deep head and neck infections with risk of airway obstruction	Urgent Systemically healthy patient	Surgical
• Serious bleeding	Urgent COVID-19 (+) Patient	Surgical

COVID-19: Coronavirus disease-19

Table 2. Patient characteristics expected to be taken in the first place in the reopening period (8)

Re-opening period: patient characteristics for elective surgery
• Emergencies and mandatory treatments
• Required but delayed cases
• Individuals without concomitant illnesses
• Short-term local operations
• Outpatient procedures that do not require hospitalization, if possible
• If general anesthesia is required, the estimated operation time is less than 3 hours
• ASA 1-2 cases under 65 years of age
• Does not require blood transfusion
• Short-term transactions in a single session, if possible

In line with the information obtained so far, it has been stated that antibody testing has no role in perioperative screening and risk stratification (13). Antibodies develop in the second week of symptoms, and not all patients infected with SARS-CoV-2 develop detectable antibodies. In addition, antibody tests lead to false positive results due to their cross-reaction potential with other coronaviruses (14,15).

Surgical Team Screening

Before starting the study, staff and surgical team should be checked daily for temperature and verify that all COVID-19 screening questions documented daily with the initials of each employee should be negative. In the case of COVID-19 (+) Ag; with the antibody test, staff should be followed up regularly or until the antibody test is positive (9,16).

Clinical Conditions

The patient load should be reduced as much as possible to maintain social distance (>6 steps) between patients. Physical distancing measures should be taken in waiting rooms and other areas of the clinic to the extent possible. In clinics where practice is interrupted for a long time, the water lines of the units should

be disinfected in accordance with the manufacturer's instructions (9,17).

Removing all non-cleanable objects such as flowers, vases, boxes, bags, books, personal computers from the environment, simplifying the field, covering areas that cannot be cleaned with disinfectants such as keyboards, computers, reflectors with transparent films before each patient, and removing disposable films after each patient. The room should be cleaned in accordance with the disinfection protocols and covered with new films before each patient admission. After the patient leaves the room, depending on the size of the room, ventilation should be provided for at least 15 minutes, and the floor and surface of the room should be cleaned by wearing a mask, goggles and gloves. Areas with organic residues such as blood, saliva, and dental material should be wiped with water-soap/detergent before disinfection (9,18).

In all procedures likely to contain aerosols, spill-based measures should be applied according to the ministry of health guidelines for all personnel who will be closer to 6 steps. It is recommended to apply and use advanced high volume evacuation methods to remove aerosols generated during operation. Although these methods are not 100% effective, they can limit the degree of contamination of the surgical environment. It is recommended that emergency treatment of patients known to have COVID-19 (+) in dental faculty clinics should be performed in rooms with an appropriate ventilation system (negative pressure ventilation system) (9,19).

Personal Protective Equipment (PPE)

Maxillofacial surgeons are exposed to a high risk of viral transmission due to constant exposure to saliva, sputum and other body fluids. Therefore, it is recommended to use a mask, goggles and gloves during surgery or clinical examination (9,10).

Standard donning and doffing procedures for personal protective equipment (PPE) must be followed. Disposable shoe covers or special intraoperative shoes/slippers designed for in-clinic use only should be used, and civilian clothes should be replaced with surgical uniforms when entering and leaving the clinic. All personnel must wear a face mask at all times. In order for the patients to identify the treating team, it is recommended that the names of the team be affixed/written on the face protective visor or on the backs of the overalls. The order to wear protective equipment; Surgical overalls/gowns, surgical masks, goggles with closed sides, cap, face protective visor and gloves, and the order of removal should be in the form of gloves, protective visor, cap, goggles, apron and surgical mask. In addition to the use of proper PPE, frequent hand hygiene should always be practiced. PPE should be thrown into the medical waste bin after use, and hand hygiene should be applied before and after wearing PPE (16,18).

Antiseptic mouthwashes are thought to reduce viral load in the oral cavity (20,21). For this purpose, it is recommended to gargle with 1.5% hydrogen peroxide or 0.2% Betadine/povidone iodine for 60 seconds before the procedure. However, it should be noted that the iodine solution tastes bad, temporarily stains the mucosa and teeth, and may pose an increased risk of allergies. The use of peroxide products with a better taste can be considered for patient comfort and compliance (9).

PPE for Non-aerosol Generating Procedures (8)

• Eye protection; If not available, full face shields must be weared.

• High filtration or Type III (N99/FFP3) procedure mask.

• Re-washable or disposable surgical gown.

• Surgical gloves (double gloves may be considered to help limit contamination during doffing).

• If the procedure involves using an aerosol generating device unplanned, stop the procedure and go to the aerosol generator PPE protocol.

PPE for Aerosol Generating Procedures (Drill with Irrigation, Cautery, LASER, Ultrasonic Instrumentation, etc.) (9)

• The entire surgical team should follow the same level of PPE protocol.

• Face shield/visor

• OSHA Respiratory Protection Instructions, NIOSH or FDA certified, disposable N95 filter face mask or N99 face mask

• Surgical gloves (double gloves can be considered to help limit contamination during doffing)

• If possible, the use of smoke generating devices such as cautery should be limited, and rapid evacuation should be ensured by special intraoral and/or extraoral devices, High Volume Evacuation (HVE) and/or advanced aerosol evacuation methods.

• Reusable or disposable surgical gown

• Disposable or washable hair protection/surgical cap/bonnet.

Planning of Elective Surgery

In the case of COVID-19 infection, surgery is only recommended if vital. In the early period of the pandemic, it has been reported that the mortality in patients who were operated with insufficient evaluation increased up to 20-50% (22,23). Therefore, in cases where elective surgery is planned, the recommended approaches to minimize the risk of transmission are as follows (7,9,10,18).

Infection Control

i. For the elective surgery candidate, COVID-19-specific symptom, suspicious contact in the last 14 days, etc. A checklist questioning the situations should be completed.

ii. Information should be obtained about the use of antipyretic drugs including ibuprofen, acetaminophen or aspirin in the last 14 days.

iii. Non-contact infrared temperature meters measured on the forehead should be preferred and the temperature should be confirmed to be lower than 38 °C.

iv. Thoracic CT imaging is not recommended as a screening test in asymptomatic cases. In suspicious cases, in the presence of symptoms such as fever, cough, and respiratory distress, pre-operative thoracic CT imaging is recommended for further evaluation.

v. PCR testing is recommended for patients in non-urgent procedures that are planned with general anesthesia (7). Depending on the institution's test capacity and rapid conclusion, it is recommended that every patient should have 2 studied or 1 negative PCR result in the last 24 hours. In the follow-up of the test, the patient should be isolated at home.

vi. In general anesthesia procedures, the patient must be awakened in the operating room where the procedure is performed. During the recovery period, the patient should be monitored by placing a face shield instead of a surgical mask.

vii. Anesthesiology and transport personnel should be subject to the same level of infection control as surgical personnel.

viii. The postoperative service or intensive care bed of the patient to be taken under general anesthesia should be determined according to the PCR result.

ix. Considering the false negative rate of the PCR test, all elective surgery patients should be evaluated as suspected COVID-19 patients and should wear a surgical mask, and the approach in the operating room should be based on the same result.

x. The cases with positive PCR test but without any clinical and radiological findings except anosmia, gastroentistinal system findings, and generalized muscle pain; it is recommended to undergo elective surgery at the earliest 28 days after 2 negative PCR tests. Current information indicates that the risk of transmission will disappear after this time.

xi. There is not enough information in the literature about the recovery process of patients who have had COVID pneumonia (with PCR positive, respiratory symptoms and tomography findings). In this group, individual factors (age, comorbid diseases, etc.), characteristics of the surgery and respiratory functions during the recovery period can be evaluated and elective surgery can be planned by taking the opinion of the chest diseases specialist.

xii. In the advanced age group who is at high risk for COVID-19, the surgical requirement should be reconsidered, and a selective approach should be adopted for the near term in elective cases (7,9,18).

Appointment System/Patient Screening

In cases where an aerosolized procedure is to be performed, it is recommended that the number of people exposed to aerosols should be minimized and the day should be scheduled, and if possible, aerosolized procedures should be written for appointments at the last hours of the day.

Pre-appointment screening procedure should be applied to every patient. Using the patient follow-up form, symptoms associated with COVID-19 (fever, cough, shortness of breath, muscle-head-throat pain, weakness, flu-like symptoms, loss of taste-smell, history of contact with a person with or diagnosed COVID-19 symptoms, existence etc.) should be questioned.

For patients who are new to the health institution or who want to come for control, it is recommended to arrange the institutional facilities so that they can request an appointment by phone or using the web-appointment system. Patients should be contacted and their complaints related to dental treatments should be recorded and a record should be created for the priority order. The patient should stay in the clinic for as short a time as possible, and the necessary preparations should be completed beforehand. Patients in the high risk group for COVID-19 (over 65 and those with comorbid diseases) should not be written consecutively, and their appointments should be arranged as the first patient.

After the patients are pre-screened in the appointment system, an appointment should be made for the patients whose suspected COVID-19 (+) is excluded. In the meantime, it is important to provide preliminary information that they will be treated by screening again on the day of the procedure and signing an informed consent form if there is no doubt, in order to preserve the functionality of the new system.

Prior to the appointment, patients should be informed that if they show any symptoms that raise suspicion of possible COVID-19, they should reach out to the faculty or physician and request that their appointment be delayed. In this case, patients should be referred to the triage service for a detailed screening (7,9).

Precautions to be Taken in the Operating Room

There should be a minimum number of people in the operating room. If possible, only a doctor and a physician assistant should be present at the bedside, and the demand for supplies should be met by a waiting staff. The physician or assistant in charge of the patient should not leave the room before the procedure is completed by taking supplies or for another reason. If an outside staff needs to enter the operating room, they must follow the same PPE protocol as the surgical team. The operating room door should be kept closed at all times, and if there is a window, it should be left open.

An experienced team should carry out the surgery as much as possible. If the extraoral approach will be an alternative to the intraoral approach, it may be preferred to the intraoral approach to reduce aerosol formation. Using the water cooling system for hand motors, saws, ultrasonic and piezoelectric devices at maximum flow rate should be avoided. Instead of creating screw holes with rotary tools, self-piercing screws and bone cutters such as osteotomes may be considered. The use of electrocautery should be avoided or, if possible, used at the lowest power and with a smoke evacuation system (7,9).

Informed Consent Form

Although all necessary precautions have been taken with current information in patients undergoing elective surgery during the COVID-19 pandemic period, it is important to provide

additional information about the risk of transmission and to have the patient / patient's relative sign an informed consent form (9,10).

Postoperative Period

After the operation, the patient's epicrisis report should be recorded completely, including the entry-exit hours and the cleaning time of the operating room (9). There is controversy regarding the use of non-steroidal anti-inflammatory (NSAI) drugs such as ibuprofen in suspected and confirmed cases of COVID-19 when pharmacological management of pain is required. For pain control and antipyretic efficacy, it is recommended that paracetamol group drugs be the first choice, but the use of NSAI drugs should not be avoided when necessary (24,25). It is also stated that penicillin and clindamycin derivative antibiotics can be used safely in patients with known or suspected COVID-19 (26).

When appropriate, it may be recommended to make postoperative controls by teleconference method. The use of absorbable sutures can be considered in order not to increase the clinical density with repeated controls (9).

Patient Visit

Visitors should not be allowed, except for elderly and pediatric patients who cannot provide self-care. If the person / persons responsible for the care of the patient are required to enter the room of the patient with COVID-19 (+), they should be informed and supervised by a healthcare professional about putting on and removing PPE and hand hygiene practices before and after putting on PPE (9).

Discharge in Inpatients

1. Post-operative information should also include feedback from patients to their physician within the next 14 days in the presence of symptoms or signs of COVID-19. The paper-file transfer load should be reduced as much as possible. Active use of e-prescription system and e-report systems is important to reduce the risk of contamination. The patient should be discharged as soon as possible, if there is a drain, it should be emptied, and the patient should be educated about the care process such as simple dressings. In order to reduce the frequency of control, the patient should be given the care conditions in writing and the things to be done day by day should be explained (9,19,27).

Results

In elective surgery planning, each institution should create its own roadmap with a multidisciplinary team, taking into account its own geographical location, patient variety and number, supply of consumables and their sustainability, and the role they play in the pandemic. Depending on the severity of the outbreak and the availability of resources, the risks and benefits of performing elective surgical procedures should be carefully considered during this period. During the "reopening" period of the COVID-19 pandemic, treatments should be applied for cases whose treatment was unfinished due to the epidemic or in cases where appropriate conditions are provided and recommendations made for patient/physician safety are taken into account. It can be suggested that all physicians regarding the peak of COVID-19 cases, the return of implementation restrictions and social distancing measures, should create an emergency plan and make short-term patient planning considering the possibility of "re-closure".

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Case Report

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Clinical Course of COVID-19 in a Thalassemia Major Patient who Underwent Haematopoietic Stem Cell Transplantation

Hematopoetik Kök Hücre Nakli Yapılmış Bir Talasemi Majör Hastasında COVID-19'un Klinik Seyri

Aziz Ahmad HAMİDİ[1], Yıldız ULU[1], Habibullah AKTAŞ[2]

[1]Karabük Medical School, Infectious Diseases and Clinical Microbiology, Karabük, Turkey
[2]Karabük University Karabük Faculty of Medicine, Department of Dermatology, Karabük, Turkey

ABSTRACT

We herein reported the course of Coronavirus diasease-19 (COVID-19) in a 21-year-old patient with thalassemia majo rdisease. The patient who underwent haematopoietic stem cell transplantation in 2013 and developed alloimmunization, presented with high fever and weakness. His parents have been recently diagnosed with COVID-19. COVID-19 diagnosis was confirmed by real time-polymerase chain reaction (RT-PCR) method in the nasopharyngeal swab sample of the patient while his thorax computed tomography was not found in favor of pneumonia. The patient was treated with hydroxychloroquine 2x200mg and Favipravir 3x600mg. The temperature fell with in three days. The clinical condition of the patient improved rapidly. On the 20th day, he did not have any symptom with a recovery of anemia and lymphopenia, but the RT-PCR result was stil positive. In this case report, we wanted to point out that the course of the COVID-19 is unexpectedly mild in such a patient with thalassemia major.

Keywords: COVID-19, thalassemia major, beta-thalassemia

ÖZ

Talasemi major hastalığı olan 21 yaşındaki bir hastada Koronavirüs hastalığı-19'un (COVİD-19) klinik seyri sunulmuştur. 2013 yılında hematopoetik kök hücre nakli yapılmış ve alloimmunizasyon gelişmiş hasta, yüksek ateş ve halsizlik şikayeti ile başvurdu. Yakın zamanda anne ve babası COVİD-19 tanısı almıştı. Toraks tomografisinde pnömoni lehine bulgu saptanmayan hastanın COVİD-19 tanısı nazofarengeal sürüntü örneğinde gerçek zamanlı polimeraz zincir reaksiyonu (RT-PCR) yöntemiyle doğrulandı. Hastaya hidroksiklorokin 2x200 mg ve favipravir 3x600 mg tedavisi başlandı. Ateşi üç gün sonra düştü. Hastanın klinik durumu hızla iyileşti. Anemi ve lenfopenisi düzelen hastanın, tedavinin 20. gününde herhangi bir semptomu yoktu. Ancak RT-PCR sonucu hala pozitif idi. Bu olgu sunumuyla talasemi majörü olan bir hastada, COVID-19'un beklenmedik biçimde hafif seyrettiğine dikkati çekmek istedik.

Anahtar Sözcükler: COVID-19, talasemi majör, beta talasemi

Introduction

Novel coronavirus infection that occured in Wuhan, China in December 2019, has spread rapidly among people and caused pandemic. After isolation and identification of virus, the causative agent was named as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). The disease caused by the new pneumonia virus SARS- CoV-2 was defined Coronavirus disease-2019 (COVID-19) by World Health Organisation (1-3). In Turkey the first COVID-19 case was detected on March 10, 2020 and first death caused by SARS-CoV-2 was seen on March 15, 2020. Thalassemia is a common genetic disorder worldwide. In patients with homozygous thalassemia major, repeated transfusion and chelation treatments are required. Bone marrow transplantation offers cure oftenly when performed at first years of patient's life (4). The risk for the development

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Address for Correspondence: Aziz Ahmad HAMİDİ, Karabük Medical School, Infectious Diseases and Clinical Microbiology, Karabük, Turkey
E-mail: azizahmadhamidi@gmail.com **ORCID ID:** orcid.org/0000-0003-4108-0847

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of agranulocytosis and neutropenia is increased, especially in patients using chelation therapy. Accordingly, these patients may develop bacterial infections and sepsis. The risk for acute kidney injury, cardiac arrhythmias and cardiac failure increases during infections (5).

In this article, we present the course of COVID-19 disease in a thalassemia major patient who underwent haematopoietic stem cell transplantation and developed alloimmunisation.

Case Report

A 21-year-old man was admitted to the hospital with the complaint of fever and fatigue. It was learned that his parents who shared the same house, were hospitilized with a diagnosis of COVID-19 one day ago. The patient has a diagnosis of thalassemia major and he was performed haematopoietic stem cell transplantation and developed alloimmunisation in 2013. On admission, his body temperature was 39 degrees Celsius, systolic blood pressure 100 mm/Hg, diastolic blood pressure 60 mm/Hg and oxygen saturation of 97% while the patient was breathing ambient air. The chest auscultation findings defined no abnormal sound (crackles, rhonchi, orwheezing). Electrocardiography was normal. Blood routine tests were hemoglobin (hgb): 5.3 g/dL, white blood cell (WBC): 1.81/L, platelet (PLT): 103,000/L, lymphocyte: 980/L, aspartate aminotransferase (AST): 23 U/L, alanine aminotransferase (ALT): 10 U/L, creatinine: 0.37 mg/dL, C-reactive protein (CRP): 8.3 µg/mL, procalcitonin: 0.11 ng/mL, lactate dehydrogenase (LDH): 330 U/L, ferritin: 1,040 ng/mL, D-dimer: 0.31 µg/mL, total bilirubin: 6.6 mg/dL, directbilirubin: 0.5 mg/dL, total protein: 7.6 gr/dL, albumin: 5.0 g/dL. Computed tomography of the chest revealed no finding in favor of viral pneumonia. The patient's nasopharyngeal and oropharyngeal swab test for SARS-CoV-2 by real time-polymerase chain reaction (RT-PCR) assay was positive. He was hospitilized on April 26, 2020. The treatment started with hydroxychloroquine (HCQ) 400 mg bid loading dose for firstday, than 200 mg bid maintenance dose for other four days. On the third day of therapy, body temperature continued as 38.4 degrees Celsius. Control blood tests were hgb: 6.9 gr/dL, WBC: 1.45/L, PLT: 90,000/L, lymphocyte: 580/L, AST: 45 U/L, ALT: 25 U/L, creatinine: 0.35 mg/dL, CRP: 6.4 µg/mL, procalcitonin: 0.15 ng/mL, LDH: 297U/L, ferritin: 917 ng/mL, D-dimer: 0.19 µg/mL, total bilirubin: 4.3 mg/dL, direct bilirubin: 0.4 mg/dL. Then, favipravir 1,600mg q12h loading dose for the first day, than 600 mg q12h maitenence dose was added to the HCQ therapy. Because of low hgb level, 2 units of erythrocyte suspension with leucocyte fitler were transfused. On the fourth day of hospitalization, he maintained normal body temperature (37 degrees Celsius). The patient's symptoms improved, and his favipravir and HQL medications were completed in 5 days. On the tenth day of hospitalization, patient's nasopharyngeal andoropharyngeal swab test for SARS-CoV-2 by RT-PCR assay was stil positive while he has completely free of symptoms. On May 5, 2020, he was discharged, and taken home quarantine for at least 14 days. SARS-CoV-2 by nasopharyngeal and oropharyngeal swab RT-PCR assay remained positive in his follow- upcheck on 15 May. Control blood tests were hgb: 8.2 gr/dL, WBC: 3960 /L, PLT: 139,000/L, lymphocyte: 1,500/L, AST: 17U/L, ALT: 11U/L, CRP: 0.23 µg/mL, procalcitonin: 0.10 ng/mL, LDH: 231U/L, ferritin:1,476 ng/mL, D-dimer: 0.23 µg/mL, total bilirubin: 4.3 mg/dL, directbilirubin: 0.4 mg/dL. He was clinically wel. One week later, the RT-PCR assay was negative.

Discussion

COVID-19 causes coagulopathy, lymphopenia, thrombocytopenia and anemia with various mechanisms in the patients (2). Our patient had leukopenia, thrombocytopenia and anemia at the time of admission. This makes the patient at risk for the poor course of COVID-19. Fortunately there was no lung involvement. Iron accumulation due to frequent blood transfusion causes major complications in patients with thalassemia major. As a result of excessive irona ccumulation, complications such as growth retardation, sexual developmental delay, arrhythmia, cardiomyopathy, liver fibrosis, diabetes mellitus, hypogonadism, hypoparathyroidism and hypothyroidism (6). Our patient underwent two units of erythrocyte suspension transfusion. However, there was no need for PLT transfusion.

Ferritin is found in all cells in the body. It is especially found in macrophages and hepatocytes, which play a role in iron metabolism. In beta thalassemia cases, serum ferritin level is an indicator of iron load in the heart and liver (7). In addition, in COVID-19 cases, the high level of ferritin indicates the severity of the disease (8). The high ferritin level in our patient was thought to be due to beta thalassemia disease.

The development of alloimmunization after haematopoietic stem cell transplantation in this patient increases the tendency for both infections and thromboembolic events. However, COVID-19 was quite mild in our patient with no lung involvement. In addition, thromboembolic complications did not develop. Similarly, Motta et al. (9) presented the clinical features of 11 beta thalassemia patients who underwent COVID-19, while three patients were asymptomatic, six patients showed mild findings and one patient (accompanied by diffuse large B cell lymphoma) required non-invasive respiratory support. As a result, none of 11 patients showed death, severe acute respiratory syndrome and signs of cytokine storm (9).

SARS-CoV-2 infection has three major phases such as early infection, pulmonary involvement and systemic hyperinflammation phase (10). We observed that our patient was in the early phase of the disease (viral phase), due to the absence of pneumonia findings in the thorax CT and positivity of RT-PCR. In follow-up, the patient did not progress to the pulmonary involvment phase. The HCQ and favipravir administration may have had a positive effect in the patient. Yet in cases of thalassemia, it is necessary to identify host-related factors determinining the course of COVID-19 disease.

With this case report, we want a contribution regarding the progress of COVID-19 in thalassemia patients.

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Authorship Contributions

Surgical and Medical Practices: A.A.H., H.A., Concept: A.A.H., H.A., Design: A.A.H., Y.U., H.A., Data Collection or Processing: A.A.H., Y.U., H.A., Analysis or Interpretation: A.A.H., Y.U., H.A., Literature Search: A.A.H., Y.U., Writing: A.A.H., Y.U., H.A.

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Case Report

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Nursing Care of Patient with COVID-19: Case Report

COVİD-19 Hastasının Hemşirelik Bakımı: Olgu Sunumu

Seda Cansu YENİĞÜN[1], Tuğçe YEŞİLYAPRAK[2], Fatma DEMİR KORKMAZ[3]

[1]Uşak Training and Research Hospital, Clinic of Urology, Uşak, Turkey
[2]Pamukkale University, Health Services Vocational School, Denizli, Turkey
[3]Ege University, Faculty of Nursing, İzmir, Turkey

ABSTRACT

Coronavirus disease-19 (COVID-19) is a disease that emerged in Wuhan, China on January 7, 2020, and was declared as a pandemic by the World Health Organization. However, there is no specific treatment and management protocol for COVID-19, which has led to a high mortality and morbidity in our country and worldwide. This case report aimed to describe the nursing care of a patient who was admitted to the hospital with high fever, diarrhea, vomiting, and respiratory problems and diagnosed as COVID-19. The nursing diagnoses of the patient were made according to the 10th edition of NANDA and patient care was conducted in accordance with the Gordon Health Patterns Model.

Keywords: COVID-19, nursing care, functional health patterns

ÖZ

Koronavirüs hastalığı-19 (COVİD-19), ilk kez 29 Aralık 2019 tarihinde Çin'in Wuhan kentinde ortaya çıkmış, ilk tanı 7 Ocak 2020 tarihinde koyulmuştur. Bu nedenle COVİD-19 adını almıştır. 11 Mart 2020 tarihinde ise Dünya Sağlık Örgütü tarafından pandemi olarak ilan edilmiştir. Ancak dünyada olduğu gibi ülkemizde de yüksek morbidite ve mortalitiye yol açan COVİD-19 hastalığına yönelik spesifik bir tedavi ve bakım protokolü bulunmamaktadır. Bu olgu sunumunda yüksek ateş, ishal, kusma ve solunum problemleri ile hastaneye başvuran ve COVİD-19 tanısı konulan hastanın hemşirelik bakımına yönelik bilgi verilmesi amaçlanmıştır. Hastanın hemşirelik tanıları NANDA onuncu basıma göre belirlenmiş ve bakımı Gordon Sağlık Örüntüleri Modeli'ne göre gerçekleştirilmiştir.

Anahtar Sözcükler: COVİD-19, hemşirelik bakımı, fonksiyonel sağlık örüntüleri

Introduction

Coronavirus disease-19 (COVID-19) is known to be caused by a betacoronavirus belonging to the same species of pathogens that caused the severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome-coronavirus (MERS) outbreaks. COVID-19 first appeared in Wuhan, China on January 7, 2020, and was declared as a pandemic by the World Health Organization on March 11, 2020 (1). The treatment focuses on respiratory support; however, it seems that there is limited information about the nursing care of COVID-19 patients (2).

Case Report

D.K., aged 45 year, is a mother of 3 children, works in a factory, and lives with her family. She was diagnosed with type 1 diabetes mellitus five years ago and has no history of prior surgery. She is no known allergies to any medications or foods. She was admitted to the emergency room on 02.04.2020 with the complaints of diarrhea, vomiting, cough, fever (39.5 °C), shortness of breath, taste disturbance, myalgia, and fatigue. She stated that her complaints had started 2-3 days before the admission to the emergency room. Blood tests and radiological imaging were performed. CT scan revealed a ground glass image and she

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Address for Correspondence: Seda Cansu YENİĞÜN, Uşak Training and Research Hospital, Clinic of Urology, Uşak, Turkey
E-mail: seda.cansu.yenigun@gmail.com **ORCID ID:** orcid.org/0000-0002-9712-9171

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was hospitalized with suspicion of COVID-19. The patient's COVID-19 test was found to be positive on 04.04.2020.

Due to the low oxygen saturation (85%) of the patient, oxygen therapy was started via a nasal cannula (2 L/min). Fever, diarrhea, and vomiting continued during the first two days of hospitalization.

During the clinical monitoring, the patient was treated with anti-thrombotic, antiviral, antimalarial, antibacterial agents, analgesics when needed, and an antidiarrheal therapy for diarrhea. Her own anti-diabetic medications were also continued. Nursing care of the patient was performed according to Gordon's Functional Health Patterns Model (FHP). This model provides comprehensive nursing care by addressing the needs of individuals in 11 functional areas (3). The nursing diagnoses of the patient were made according to the tenth edition of NANDA (4), including risk of infection, nutritional imbalance (less than necessary), risk of electrolyte imbalance, risk of bleeding, anxiety, risk of fluid volume imbalance, hyperthermia, diarrhea, activity intolerance, ineffective breathing pattern, and acute pain. The patient's nursing care was performed in line with the established diagnoses.

Discussion

It is stated in the literature that the care of COVID-19 patients involves a multidisciplinary approach, including anesthesia and chest diseases specialist, frequent monitoring of hemodynamic and neurogenic parameters, and evaluation of the need for intensive care (5-8). Due to the respiratory distress and low oxygen saturation (85%) during the hospitalization, the patient was provided with intermittent nasal oxygen, and vital signs were monitored eight times daily. Consciousness status was assessed daily using the Glasgow Coma Scale (GCS). It was observed that D.K.'s GCS score was 15 during her stay in the hospital. It is necessary to prevent hypovolemia due to vomiting and diarrhea, monitor the albumin level in case of shock, and provide cardiac support (9,10). Due to vomiting and diarrhea during the first two days of hospitalization, she was provided with plenty of fluids. The medications requested by the physician were administered and the outcomes were monitored. In addition, personal protective equipment should be used to prevent infections and the restriction of visitors should be ensured. For the prevention of pressure wound, it is necessary to change the patient's position every two hours, provide skin care, and observe the skin in terms of pressure injury risk (6). Antiviral and antimicrobial treatments were applied based on the physicians' request. The patient was informed about airing the room during the day, washing her hands before and after checking vital signs, and ensuring hygiene with a hand antiseptic. The patient was kept in her room without any accompanying person, and her treatment and care was provided. Since the mobilization area for the pressure wound was limited, she was mobilized every two hours in the room. In addition, daily skin evaluation was done. Non-pharmacological methods to prevent deep vein thrombosis and bleeding should be applied to the patients and the medical treatment recommended by the physician should be administered. Agitation, anxiety, and delirium findings should be checked and pain assessment should be performed (6). Anti-thrombotic medication was applied carefully to D.K. and follow-up was performed for five days in terms of conditions such as ecchymosis on the patient's skin. She was told that her teeth should be brushed gently to prevent gingival bleeding. Each morning, the patient was visited in her room to relieve her anxiety, she was told to press the nurse call bell in case of emergency, and was encouraged to express herself. During the day, the patient was contacted by phone in order for her not to feel lonely. Daily pain assessment was done. When she had pain, non-pharmacological treatments were provided firstly, and analgesics were applied in accordance with the physician's request when the patient stated that the pain was not relieved.

Although the patients' health problems are partially eliminated with the nursing care provided according to Gordon's FHP and the NANDA nursing diagnoses, the needs of patients are evaluated more comprehensively and systematically in nursing models using comprehensive and standardized data collection methods. Furthermore, apparent and patient-specific nursing care and its use in a clinical setting also allow the nurse to evaluate each patient in an integrative manner. The patient's test result was COVID-19 negative 14 days after her discharge from the hospital.

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