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Investigation of SARS-CoV-2 Infection Rates and Contagion Status of Physicians and Nurses Working in the COVID-19 Intensive Care Unit

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ABSTRACT

Aim: The aim of this study was to examine the infection and infectiousness rates of physicians and nurses working in the COVID-19 intensive care unit with SARS-CoV-2. Method: This retrospective and cross-sectional study was conducted on a total of 90 healthcare professionals. The study included healthcare professionals who were infected between May 2020-January 2021. Research data were collected through the "Survey Form" created by the researchers by examining the literature. Results: 74.4% of participants were female, 82.2% were nurses and 17.8% were physicians. 66.7% of participants were infected with SARS-CoV-2, and 66.6% of those infected had COVID-19 symptoms within 14 days in their relatives. Rates of infection with SARS-CoV-2 were statistically significantly higher among health care workers (HCWs) who intervened with patients using personal protective equipment inappropriately. Conclusion: It has been determined that the HCWs, in intensive care units work longer hours and interact more closely with patients. In the early pandemic stages, these workers also had difficulties accessing personal protective equipment (PPE). These factors, together with the nature of duties performed by nurses and physicians, contribute to an increased rate of SARS-CoV-2 infection among this demographic.

Key words: COVID-19, Critical Care Unit, Infection Patient Care, Nurse, Physician.

COVID-19 Yoğun Bakım Hekim ve Hemşirelerinin SARS-CoV-2 ile Enfekte Olma Oranlarının ve Bulaştırıcılık Durumlarının İncelenmesi

ÖZ

Amaç: Bu çalışmada, COVID-19 yoğun bakım ünitesinde çalışan hekim ve hemşirelerin SARS-CoV-2 ile enfekte olma ve bulaştırıcılık oranlarının incelenmesi amaçlanmıştır. Yöntem: Bu retrospektif ve kesitsel çalışma, toplam 90 sağlık çalışanı üzerinde yürütülmüştür. Çalışmaya Mayıs 2020-0cak 2021 tarihleri arasında enfekte olan sağlık çalışanları dâhil edilmiştir. Araştırma verileri, araştırmacılar tarafından literatür incelenerek oluşturulan "Anket Formu" aracılığıyla toplanmıştır. Bulgular: Katılımcıların %74,4'ü kadın, %82,2'si hemşire, %17,8'i doktordu. Katılımcıların %66,7'si SARS-CoV-2 ile enfekte olmuş, enfekte olanların %66,6'sının yakınlarında 14 gün içinde COVID-19 semptomları görülmüştür. SARS-CoV-2 ile enfekte olma oranları, kişisel koruyucu ekipmanı uygunsuz kullanarak hastalara müdahale eden sağlık çalışanları arasında istatistiksel olarak anlamlı derecede yüksek bulunmuştur. Sonuç: Yoğun bakım ünitelerindeki sağlık çalışanlarının daha uzun saatler çalıştıkları ve hastalarla daha yakın etkileşim içinde oldukları tespit edilmiştir. Pandeminin erken dönemlerinde, bu çalışanlar kişisel koruyucu ekipmana erişimde de zorluklar yaşamıştır. Bu faktörler, hemşireler ve doktorlar tarafından yerine getirilen görevlerin doğasıyla birlikte, bu demografik grup arasında SARS-CoV-2 enfeksiyonu oranının artmasına katkıda bulunmaktadır.

Anahtar kelimeler: COVID-19, Doktor, Enfekte Hasta Bakımı, Hemşire, Yoğun Bakım Ünitesi.

INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), first surfaced in Wuhan, China in late December 2019 (Lu et al. 2020; WHO, 2020). This disease, later officially named "Coronavirus disease 2019" (COVID-19) by the World Health Organization (WHO), rapidly reached a high prevalence and transmission rate. Consequently, the WHO declared it a "pandemic" in March 2020.

Studies clarifying the transmission modes of the SARS-CoV-2 virus, specifically between droplet and aerosol, are yet to be conducted (WHO 2020; El Zowalaty and Järhult 2020; Jayaweera et al. 2020). COVID-19 is typically characterized by respiratory symptoms such as cough, fever, and joint pains. Gastrointestinal symptoms like nausea, vomiting, diarrhea, and impaired taste have also been reported (Auwaerter 2023; Pascarella et al. 2020).

As of March 30, 2023, the pandemic had infected approximately 697 million people globally, with approximately 6.93 million deaths due to the SARS-CoV-2 virus. The number of people vaccinated against the SARS-CoV-2 virus worldwide is approximately 5.63 trillion (Worldometers 2023). In our country, as per the Ministry of Health data as of January 30, 2023, approximately 17 million people were infected during the pandemic, with about 101 thousand succumbing to the disease (Ministry of Health of the Republic of Turkey 2023).

At the forefront of this global crisis are health care workers (HCWs), who have the important task of diagnosing and treating exponentially increasing numbers of acutely ill patients, often having to make critical decisions under physical and psychological pressure (Chen et al. 2020; Lai et al. 2020; Greenberg et al. 2020). WHO defines health workers as 'all people who take actions whose primary purpose is to promote health' (WHO 2020). HCWs include physicians, nurses, midwives, medical staff, hospital administrators and support staff, all of whom face occupational risk of infection with COVID-19 and even death.

In a vicious cycle, the shortage of health workers further increases the risk of transmission by forcing staff to continue working for days on end, even when fatigued or

when symptoms appear. Increased infection and mortality rates among health workers will paralyze a country's response to COVID-19 and have a significant and long-term impact on health care delivery, especially in health systems that, even before the pandemic period, are already facing labor shortages due to lack of trained personnel, skilled labor migration and geographical dispersion (WHO 2020; Liu et al. 2017; Sidibé and Campbell 2015; Global Health Workforce Alliance and WHO 2013).

Ensuring the protection of health workers is an essential element of any country's strategic response to the COVID-19 crisis, especially as governments seek to increase healthcare capacity to cope with the increase in patients requiring emergency care. WHO has published recommendations on the rational use of personal protective equipment (PPE) in hospital and community settings (WHO 2020). Various universities and specialized associations have formulated algorithms and guidelines to reduce the risk of COVID-19 transmission in their respective areas of practice. However, the protection of healthcare workers remains a challenge for most countries, where the lack of adequate PPE is a daily concern. Limited testing capacity brings in healthcare workers, asymptomatic COVID-19 patients and consequently unintended transmissions (COVIDSurg Collaborative 2020; Cook et al. 2020; Forrester et al. 2020; Razai et al. 2020).

The extended duration of the epidemic resulted in a rise in transmission to health workers (physicians, nurses, allied HCW), making disease control more challenging. COVID-19, now considered an occupational disease, has caused numerous deaths, with healthcare professionals accounting for 11% of the total (WHO, 2020). This has disrupted health services and strained resources (WHO 2020; Pan et al. 2020).

Whilemostvirus-infectedindividuals survive asymptomatically or with mild symptoms, severe respiratory tract involvement can occur. This can progress to acute respiratory distress syndrome (ARDS), requiring hospitalization in the COVID-19 ICU (Pascarella et al. 2020). The fatality rate in our country as of May 2, 2020, was 2.6%, compared to 3.8% reported by the WHO in the People's Republic of China (WHO 2020).

Respiratory support treatments like high-flow nasal oxygen

(HFNC), noninvasive mechanical ventilation (NIMV), and invasive mechanical ventilation increase the virus load in the working environment. This contributes to a rise in infection rates (Rochwerg et al. 2017). In the early stages of the epidemic, there was uncertainty regarding the appropriate personal protective equipment (PPE) to use and its effectiveness (Bartoszko et al. 2020).

Later studies demonstrated the superiority of FFP2/N95 respirators over simple medical masks in preventing respiratory tract virus transmission (lannone et al. 2020; CDC 2007). PPE is crucial for individual protection against health and safety risks. Adhering to the proper procedures when wearing and removing PPE can reduce the risk of healthcare workers contracting SARS-CoV-2 (CDC, 2023). Among frontline HCWs, reuse of PPE or inadequate PPE, which may indicate inadequate supply and/or quality, was associated with a 31-46% increased risk of COVID-19. While healthcare workers caring for COVID-19 patients who reported inadequate PPE had the highest risk, an increased susceptibility to infection was seen even among those who reported adequate PPE (Nguyen et al. 2020).

Based on experience with other viruses spread by respiratory droplets, consistent use of recommended PPE is critical to reduce hospital-acquired transmission (Verbeek et al. 2020). Recent guidelines from the United States (US) Centers for Disease Control and Prevention (CDC) recommend the use of respirators when caring for patients with suspected or confirmed COVID-19 and universal use of masks in the workplace (CDC 2023). Joint guidelines from health agencies in Europe, including the National Health Service in the United Kingdom (UK), have issued similarly graded PPE recommendations, determined by the intensity of clinical exposure and the likelihood of contact with bodily secretions (England 2020). However, global shortages of masks, face shields and gowns caused by increased demand and supply chain disruptions have been documented, leading to efforts to preserve PPE through prolonged use or reuse, and the recent development of disinfection protocols for which there is no peer-reviewed, scientific consensus on best practices (Fischer et al. 2020; Livingston et al. 2020; Schwartz et al. 2020).

Healthcare worker recommendations:

The CDC updated guidance for HCW (September 23, 2022), reflecting longer carriage in many with infectious virus beyond five days.

Quarantine: in most circumstances, regardless of vaccination status, asymptomatic workers and those who test negative do not need restrictions.

Isolation

HCW with mild to moderate disease (and not immunocompromised) may return to work if:

- At least 7 days have passed since symptoms first appeared if a negative viral test* is obtained within 48 hours before returning to work (or 10 days if testing is not performed or if a positive test at day 5–7), and
- At least 24 hours have passed since the last fever without the use of fever-reducing medications, and
- Symptoms (e.g., cough, shortness of breath) have improved.

HCW with severe/critical infection who are not immunocompromised may return to work if:

- At least 10 days and up to 20 days have passed since symptoms first appeared, and
- At least 24 hours have passed since the last fever without the use of fever-reducing medications, and
- Symptoms (e.g., cough, shortness of breath) have improved.
- The test-based strategy, as described below for moderately to severely immunocompromised HCWs, can inform the duration of work restriction (Auwaerter 2023).

Despite the significance of PPE in preventing transmission, literature lacks studies examining the accuracy of PPE use among healthcare professionals in the COVID-19 ICU. This study, therefore, aims to investigate the SARS-COV-2 infection rates and contagiousness among physicians and nurses in the COVID-19 ICU of a tertiary center.

MATERIAL AND METHOD

Study Design, Place and Time

This retrospective, cross-sectional study involved nurses and physicians working in a University of Health Sciences (UHS) Training and Research Hospital's Anesthesia Intensive Care Unit (COVID-19 ICU). The research period spanned from May 2020 to January 2021.

Material shortages have reduced the PPE ratio per person in the organization. 2 pieces of N95/FFP2 are provided per person in a 24-hour work shift.

Uniform washing services are not available at the institution. Healthcare workers clean uniforms by their own means.

Nurses do not leave the ICU where they provide bedside care (such as care of intubated patients, position changes every 2 hours, adjusting nutrition and treatment); they leave the area only during meals and short rest breaks during the 24-hour work shift. In addition, the time nurses spend caring for patients, especially those who are intubated and on respiratory support, increases their one-to-one contact with patients. Nurses, whose primary responsibility is the patient, are therefore more infected than physicians.

Physicians' consultation, preparation of treatment protocols and some other external responsibilities require them to leave the field more than nurses. In addition, physicians do not spend as much time in one-to-one contact with patients as nurses do during their care periods.

Sample

The study population consisted of 90 healthcare professionals. This included 74 nurses and 16 physicians who served in the Anesthesia Intensive Care Unit (COVID-19 ICU) of the University of Health Sciences Training and Research Hospital within the specified timeframe. All the professionals who volunteered to participate in the study were included, resulting in a sample size of 90, constituting 100.0% of the population.

Data Collection Tools

Data was gathered using a "Questionnaire Form," developed by the researchers following a thorough review of the literature. The form comprised 30 questions, of which 5 collected socio-demographic data. The remaining 20 assessed the rates of SARS-CoV-2 infection and transmission among the participants.

Data Collection

Before data collection began the participants were informed about the purpose of the study. The questionnaire took approximately ten minutes to complete for the healthcare professionals who volunteered to participate in the research.

Statistical Analysis

Data analysis employed descriptive statistics, presenting continuous results as mean \pm standard deviation and categorical results as number (n) and percentage (%). The Kolmogorov-Smirnov Test evaluated the data's normal distribution. Categorical variables were compared using the Chi-square and Fisher exact tests. The IBM SPSS 26.0 package program (IBM Corp., Armonk, NY, USA) performed statistical analysis, with a cutoff value of p<0.05 accepted as statistically significant.

Ethical Considerations

This study received ethical clearance from the Clinical Research Ethics Committee of a Training and Research Hospital (No: 2021-KAEK-15/2364, Decision Date: 09.11.2021). The Turkish Republic Ministry of Health General Directorate of Health Services provided written permission for the study (Date: 10.05.2020, Decision No: 2021-05-10T19-08-32). Additionally, verbal consent was obtained from the health professionals who agreed to participate in the study. The research was conducted in accordance with the Declaration of Helsinki of 1964.

RESULTS

Table I displays the socio-demographic characteristics of the participants. The mean age was 31.97±7.65. Female participants constituted 74.4 percent of the sample, 58.9 percent were married, and 70 percent held undergraduate degrees. Nurses made up 82.2 percent of the participants, and 61.1 percent reported living with their spouses and children.

Table 1. Distribution of the Demographic Characteristics of **Table 2.** Data on Working in the COVID-19 ICU (n=90) Participants (n=90)

Distribution of the demographic characteristics of participants	n=90	%
Sex Female Male	67 23	74.4 25.6
Marital Status Single Married	37 53	41.1 58.9
Education High School College Master's PhD Assistant Physician Specialist Physician	3 63 7 1 10 6	3.3 70 7.8 1.1 11.1 6.7
Who do you live with in your home? With Their Parents With Relatives With Wife/Husband and Children Alone	24 5 55 6	26.7 5.6 6 1.1 6.7
Job Physician Nurse	16 74	17.8 82.2

Table II presents the characteristics of the health professionals in the COVID-19 ICU regarding their training (about COVID-19), working, and living conditions. It was found that 66.7% of the participants received training on COVID-19 prevention, with 70.28% of these individuals reporting their training was conducted by a doctor or nurse. However, 58.9% stated that they did not have access to written documents related to COVID-19 in the hospital. Despite training, 83.34% of trainees revealed that their fears and worries did not decrease when attending to patients diagnosed with COVID-19.

Table 2. Data on Working in the Covid-19 1CO (11-90)				
Data on Working in the COVID-19 ICU	n=90	%		
Have you been infected with SARS-Cov-2?				
Yes	60	66.7		
Who was this training given by? (multiple options can be selected)				
Hospital Management	17	22.97		
Physician-Nurse	52	70.28		
Provincial Health Department	5	6.75		
Did you have the opportunity to find brochures, posters and information texts about COVID-19 in your hospital?				
No	53	58.9		
How was your approach to the patient diagnosed with COVID-19? (multiple options can be selected)				
Worried, Fearful	74	47.13		
Restless	50	31.84		
Uninformed	33	21.03		
Could the training you received reduce these situations?	60	66.7		
Did you have any difficulties in accessing personal protective equipment (N95, goggles, overalls, visors, surgical masks, etc.) in the hospital? Yes	48	53.3		
Did you use the provided equipment in accordance with the rules?	0/	07.7		
Yes	84	93.3		
With the patient diagnosed with COVID-19 have you been less than 1,5 m away without Personal Protective Equipment (PPE) due to situations such as Emergency situations etc,?				
Yes	58	64.4		
If yes, during which procedures? (multiple options can be selected)				
Aspiration, during oral care applications	29	21.32		
During CPAP, Helmet, High Flow applications	40	29.41		
During the general body care of the patient (wound care,	15	11.02		
catheter care, etc.) Emergency Intubation, cardiopulmonary arrest, during catheter procedures	52	38.23		
What are your weekly working hours in the ICU during the COVID-19 ICU?				
Less than 40 hours	3	3.3		
40 hours	5	5.6		
40-48 hours	60	66.7		
The number of patients you care for in the ICU during the COVID-19 period? (Nurses)				
2	74	100		

Regarding PPE, 53.3% reported difficulty accessing it, yet 93.3% stated that they used the available equipment correctly. On the other hand, 64.4% admitted to attending to patients in emergency situations without paying attention to the proper use of PPE. In emergency procedures such as intubation and catheter insertion, improper use of PPE occurred in 38.23% of cases, and in 29.41% of cases involving NIMV applications like CPAP and HFNC. It was found that 66.7% of the participants worked between 40-48 hours weekly, and the number of patients cared for by each nurse was 2.

Table III details the status of employees contracting SARS-CoV-2, how they experienced the COVID-19 disease process, and the incidence of COVID-19 symptoms in their close contacts within 14 days. It was found that 67.56% of nurses and 56.25% of physicians from the ICU contracted SARS-CoV-2. Among these, 64.4% admitted to not using PPE appropriately when attending to SARS-CoV-2 infected patients in emergency situations.

Nurses working in our COVID-19 ICU exhibited a higher infection rate (82.2%) than ICU physicians and other healthcare professionals. Of the 50 SARS-CoV-2 infected nurses in the COVID-19 ICU, 10% had more than 5 years of

professional experience, 30% had between 1-5 years, and 40% had less than 1 year. Among the infected physicians, 30% were specialists and 70% were assistant physicians.

All HCW infected with SARS-CoV-2 developed COVID-19 symptoms, with no asymptomatic cases detected. Among the 60 infected healthcare professionals, 66.6% developed COVID-19 symptoms within 14 days. Of these, 72.5% reported that at least 4-6 people in their close contacts contracted the virus during this period.

In this timeframe, 87.8% of HCW continued living with their families, and 62.2% of those living with their families needed isolation. Furthermore, it was revealed that they did not take additional measures, such as wearing masks, and 94.4% of them washed their work clothes at home.

DISCUSSION

Healthcare professionals across the globe have faced numerous SARS-CoV-2 cases during the pandemic and have been exposed to a significant viral load (Constantino et al. 2021). During the first wave of the pandemic, the WHO-China joint commission reported that 3387 healthcare professionals were infected with SARS-CoV-2 in 476 hospitals worldwide

Table 3. Data on Being Infected with SARS-CoV-2 and Transmitting SARS-CoV-2 to Others (n=90)

Data on being infected and transmitting SARS-CoV-2 to others	n=60	%
"Have you had any symptoms of COVID-19?" If your answer to the question is "Yes", did any of your relatives or colleagues experience		
any symptoms (fever, cough, headache, loss of taste and smell, etc,) within 14 days?		
Yes	40	66.6
If your answer is yes, how many people were seen?		
1-2 person	6	15
2-4 person	5	12.5
4-6 person	29	72.5
Have you ever had to share a house with someone close to you infected or in contact with COVID-19?		
Yes	45	50.6
Where were your uniforms washed while working in the ICU during the COVID-19 period?		
Home	85	94.4
Where did you stay while working in the ICU during COVID-19?		
With my family at home	79	87.8
If you stayed at home, did you take any additional precautions (isolation, mask, etc,) to prevent it from infecting your family?		
Yes	56	62.2

(Su 2020). The early phase of the pandemic, characterized by a lack of comprehensive understanding of the disease, unknown preventative methods, and low awareness regarding PPE usage, likely contributed to higher infection rates.

COVID-19 research suggests that human transmission primarily occurs through respiratory droplets and contact (Ferioli et al. 2020). The virus can also spread via aerosols formed during aerosolization processes and even during speech (CDC 2023). Our study supports this hypothesis. We found that 64.4% of ICU health professionals in our study neglected the one-meter social distancing rule during emergencies, thus potentially compromising their PPE usage. Emergency interventions, including aerosol-generating procedures such as CPAP, HFNC, and NIMV, accounted for 29.41% of cases, likely contributing to a higher rate of SARS-CoV-2 infection among healthcare professionals. The infection rate among nurses in our COVID-19 ICU was notably higher (82.2%) than among ICU physicians and other healthcare professionals, which might be attributed to the aerosol-generating respiratory treatments and personal care tasks that nurses perform in the ICU.

The majority (87.8%) of ICU health professionals reported sharing a house with their families during this period, and a significant portion admitted to not taking additional preventative measures such as isolation or mask usage (62.2%) or washing their ICU uniforms at home (94.4%). The occurrence of COVID-19 symptoms within 14 days in the close contacts of 66.6% of SARS-CoV-2-infected participants implies potential viral transmission outside the hospital by infected HCW. Our study findings are unique and contribute to the existing literature as no other national or international study corroborates these results.

Among 2,135,190 participants in the UK and US assessed between March and April 2020, it found that even after accounting for other risks, frontline healthcare workers had up to a 12-fold increased risk of reporting a positive COVID-19 test and predicting COVID-19 infection compared to members of the general population (Nguyen et al. 2020). Comparing the COVID-19 ICU with other departments revealed that the ICU had a higher percentage of infected nurses (37.87%) and physicians (13.69%). This demonstrates the increased workload and viral

exposure faced by critical care healthcare professionals compared to their counterparts in other departments. Among the 50 nurses working in the COVID-19 ICU and infected with SARS-CoV-2, 10% had professional experience of more than 5 years, 30% had between 1-5 years, and 40% had less than 1 year. Among the infected physicians, 30% were specialists and 70% were resident physicians. We found an inverse relationship between professional experience and SARS-CoV-2 infection rate, with infection rates declining as years of professional experience increased. Similarly, resident physicians were more infected than specialist physicians. A study conducted by Uzman and Ayazoğlu (2021) in a training and research hospital showed that only one person was infected with SARS-CoV-2 among 72 ICU staff treating 120 SARS-CoV-2 patients, highlighting the effectiveness of proper and appropriate PPE usage in protecting ICU healthcare professionals against SARS-CoV-2 transmission.

CONCLUSION AND SUGGESTIONS

Our study reveals that 66.7% of healthcare professionals reported receiving training from physicians and nurses on SARS-CoV-2 prevention. However, they could not access written materials, and the training provided did not alleviate the fear and anxiety of 83.34% of the HCW. Further, 53.3% of the participants experienced difficulties accessing PPE, and 64.4% did not use PPE appropriately during emergencies. In addition, longer working hours and the use of aerosolgenerating respiratory therapies contributed to 66.7% of the 90 healthcare professionals in our intensive care unit becoming infected with SARS-CoV-2, with 66.6% of these individuals subsequently transmitting the infection to their families. The surge in COVID-19 cases and the resulting increased workload for healthcare professionals has not only led to increased infection rates but has also disrupted healthcare systems due to the loss of healthcare workers to the disease.

COVID-19 infections and deaths among healthcare workers require the provision of adequate and appropriate PPE. Infection control training should be provided to those working on the front lines of the COVID-19 pandemic response, especially redeployed health workers who have little experience in the clinical management of infectious diseases.

To cope with this, healthcare professionals should be trained adequately on SARS-CoV-2 prevention and proper usage of PPE. These trainings should be regularly updated and repeated, with support sought from relevant units during the planning stages. Adherence to international guidelines on SARS-CoV-2 infection is crucial, and healthcare professionals should have access to updated information and written materials. Easy access to PPE must also be ensured. To prevent overexposure to the viral load, working hours should be reduced, and additional measures such as negative pressure ventilation systems should be implemented if aerosol-generating procedures are used. The health status of healthcare professionals should be closely monitored, and support should be provided for them to report any symptoms to their colleagues and family members, thus enabling swift implementation of necessary precautions.

LIMITATIONS

Our study does present a few limitations. Firstly, we observed exceptionally high infection rates in our country, which could be attributed to inadequate usage of Workplace Control Equipment (WCE) and a general lack of awareness. This might have skewed our findings and comparisons with regions having better infection control practices. Secondly, our study exclusively included participants from a single COVID-19 Intensive Care Unit in a tertiary hospital located in a densely populated district. Thus, our findings may not be representative of the experiences of healthcare professionals in different settings or locations with different population densities. These factors should be carefully considered when drawing comparisons with other hospitals and intensive care units.

AUTHOR CONTRIBUTION

Idea/Concept: EÖ, ND; Design: EÖ, ND; Data Collection and/ or Processing: EÖ; Analysis and/or Interpretation: EÖ, ND; Writing the Article: EÖ, ND, ÖK; Critical Review: EÖ, ND, ÖK.

CONFLICT OF INTEREST

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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ETHICAL STATEMENT

This study received ethical clearance from the Clinical Research Ethics Committee of a Training and Research Hospital (No: 2021-KAEK-15/2364, Decision Date: 09.11.2021). The Turkish Republic Ministry of Health General Directorate of Health Services provided written permission for the study (Date: 10.05.2020, Decision No: 2021-05-10T19-08-32).

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