Back to the First Days of the Pandemic: How Well Have We Done to Diagnose COVID-19 in Healthcare Workers?

Salgının İlk Günlerine Dönelim: Sağlık Çalışanlarında COVID-19'u Teşhis Etme Konusunda Ne Kadar Başarılı Olduk?

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ABSTRACT

Introduction: Healthcare workers (HCWs) are one of the most vulnerable groups for COVID-19. SARS-CoV-2 PCR was offered to HCWs who had symptoms compatible with COVID-19 or who had a close contact with COVID-19 patient. A rapid antibody test was used to identify the risk of exposure of the HCWs who worked at high-risk units in our hospital during the first month of the pandemic. Herein, we aimed to evaluate the usefulness of this approach.

Materials and Methods: The records of the HCWs from a university hospital who were tested by SARS-CoV-2 PCR or rapid antibody test between March 12, 2020 and April 04, 2020 were reviewed retrospectively. Demographic and clinical characteristics of HCWs were extracted from the electronic database. Wards or outpatient clinics that served COVID-19 patients were defined as high-risk units.

Results: A total of 599 HCWs were tested for SARS-CoV-2 by PCR and 409 by rapid antibody test. Thirty-seven (6.2%) were found to be PCR positive. Eleven (29.7%) out of 37 HCWs were asymptomatic when they were tested. There was no statistically significant relationship between PCR positivity and occupation or working unit. A positive PCR result was detected in 24 HCWs during the first admission. Eleven out of 114 HCWs who were tested by a second PCR were found to be positive and two out of 17 HCWs who were tested by a third test were reported as PCR positive. Median interval between the first and second PCR was seven days (IQR= 8.5 days) and median interval between second and third PCR test was 4.5 days for the HCWs who were reported as positive at repeated PCR tests. Rapid antibody test was positive in one HCW who did not have a history of COVID-19.

Conclusion: Approximately, one third of the SARS-CoV-2 PCR positive HCWs were asymptomatic. In case of increasing incidence of COVID-19 in the community, a regular screening policy for the HCWs regardless of their occupation and contact tracing might help to have a safe environment in hospitals. Screening policy should be based on well validated tests.

Key Words: Healthcare personnel; COVID-19; SaRS-CoV-2 antibody testing; COVID-19 nucleic acid testi; Contact tracing

ÖZ

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Giriş: Sağlık çalışanları Koronavirüs Hastalığı 2019 (COVID-19) için en duyarlı gruplardan biridir. COVID-19 ile uyumlu belirtileri olan ve COVID-19 hastalarıyla yakın temas öyküsü olan sağlık çalışanlarına SARS-CoV-2 polimeraz zincir reaksiyonu (PCR) testi yapılması önerilmektedir. Hastanemizde pandeminin ilk ayında yüksek riskli birimlerde çalışan sağlık çalışanlarına SARS-CoV-2'ye maruziyet riskini değerlendirmek amacı bir hızlı antikor testi uygulanmıştır. Bu araştırma bu yaklaşımın kullanışlı olup olmadığının değerlendirilmesi için yapılmıştır.

Materyal ve Metod: Ankara, Türkiye'den bir üniversite hastanesinde 12 Mart ve 04 Nisan 2020 tarihleri arasında SARS-CoV-2 PCR veya hızlı antikor testi ile test edilen sağlık çalışanlarının bilgileri geriye dönük olarak taranmıştır. Sağlık çalışanlarının demografik ve klinik özellikleri elektronik sistemden çekilmiştir. COVID-19 hastalarına hizmet veren poliklinik ve yatan hasta servisleri yüksek riskli birimler olarak sınıflandırılmıştır.

Bulgular: Sağlık çalışanlarının 599'una SARS-CoV-2 PCR ve 409'una hızlı antikor testi uygulandı. Otuz yedi (%6.2) sağlık çalışanı PCR pozitif olarak bulundu. Otuz yedi sağlık çalışanından 11'i (%29.7) test edildiği sırada belirtisizdi. PCR pozitifliği ile meslek ve çalışılan birim arasında istatistiksel olarak anlamlı bir ilişki saptanmadı. Yirmi dört sağlık çalışanının ilk başvurusu sırasında PCR testi pozitif sonuçlandı. İkinci kez PCR testi yapılan 114 sağlık çalışanının 11'i, üçüncü kez PCR testi yapılan 17 sağlık çalışanının ikisi pozitif olarak bildirildi. Tekrarlayan PCR testlerinde pozitiflik bildirilen sağlık çalışanlarında birinci ve ikinci PCR testi arasındaki ortanca süre yedi gün (ÇADA= 8.5 gün), ikinci ve üçüncü PCR testi arasındaki ortanca süre 4.5 gündü. Hızlı antikor testi COVID-19 öyküsü olmayan bir sağlık çalışanında pozitif sonuçlandı.

Sonuç: SARS-CoV-2 PCR pozitif sağlık çalışanlarının yaklaşık üçte biri asemptomatikti. Toplumda COVID-19 insidansının arttığı bir durumda sağlık çalışanları için mesleklerinden bağımsız olarak düzenli bir tarama politikası ve temaslı takibi hastanelerde güvenli bir ortam oluşturulmasında yardımcı olacaktır. Tarama politikası geçerliliği iyi gösterilmiş testlere dayanmalıdır.

Anahtar Kelimeler: Sağlık çalışanı; COVID-19; SaRS-CoV-2 antikor testi; COVID-19 nükleik asit testi; Temaslı izlemi

INTRODUCTION

The first confirmed Coronavirus disease 2019 (COVID-19) case was identified in Türkiye on March 10, 2020, one day before the World Health Organization (WHO) announced COVID-19 as a pandemic[1,2]. Healthcare workers (HCWs) are the most vulnerable group for COVID-19 as front-line fighters. The high rate of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infected HCWs is of concern. Turkish Minister of Health announced that 29.865 out of 273.000 patients diagnosed as COVID-19 were HCWs by September, 2020[3].

The first COVID-19 patients were two house-mate residents from the department of internal medicine in our hospital, diagnosed on March

20, 2020[4]. We decided to develop a strategy to detect COVID-19 in HCWs as early as possible. This strategy included polymerase-chain-reaction (PCR) based testing of HCWs with clinical symptoms consistent with COVID-19 or in case of close contact with a COVID-19 patient without appropriate use of personal protective equipment (PPE). A rapid antibody test was offered to HCWs without symptoms from high-risk units who took care of COVID-19 patients as a screening test to investigate SARS-CoV-2 exposure. In this study, it was aimed to the share the utility of this approach for the diagnosis of COVID-19 in HCWs during the first month of the pandemic in Türkiye.

MATERIALS and METHODS

Hacettepe University Hospital University Hospital is a tertiary care hospital in Ankara, Türkiye. HCWs with signs and symptoms of a respiratory infection were admitted to COVID-19 initial evaluation outpatient clinic (C1) organized by the department of infectious diseases, whereas those who had contact with a COVID-19 patient but did not have any symptoms were evaluated at the occupational health clinic (OHC) and then referred to C1 for PCR testing when necessary. A combined oropharyngeal and nasopharyngeal swab was taken from HCWs to detect SARS-CoV-2 by real-time reverse-transcriptase–polymerase-chain-reaction (RT-PCR). Viral nucleic acid isolation from the samples was achieved by using Bio-Speedy vNAT viral nucleic acid buffer (Bioeksen R&D Technologies Ltd, Türkiye). COVID-19 real-time PCR kit (Bioeksen R&D Technologies Ltd, Türkiye) was used for diagnosis in our hospital.

A CE (*Conformité Européenne*) certified immunochromatographic test named as Hotgen COVID-19 IgM/IgG Antibody Rapid Test (Beijing Hotgen Biotech Co, Ltd, China) was used to investigate the exposure of HCWs to SARS-CoV-2. Hotgen can detect both IgM and IgG against SARS-CoV-2 in human serum by using double antigen sandwich technology in 15 minutes according to the manufacturer's manual (http://www.hotgen.com.cn/ky/upt.html). This test kit was provided free of charge by the Turkish Ministry of Health. Priority for testing by Hotgen was given to the HCWs from high-risk units such as C1, intensive care units, wards caring for COVID-19 patients, as well as emergency ward.

All laboratory records were reviewed to identify the HCWs who were tested either by SARS-CoV-2 PCR or Hotgen between March 20, 2020 and April 09, 2020, retrospectively. Demographic and clinical characteristics of HCWs such as sex, age, occupation, presence of any symptom and history of contact with COVID-19 patient were extracted from the hospital database.

For descriptive statistics, continuous variables were given as mean ± standard deviation for normally distributed data, and as median and interquartile range (IQR) for data with the non-normal distribution. Categorical variables were reported as numbers and percentage distributions. Categorical variables were compared by Chi-Square test or Fischer's exact test, and continuous variables were compared by the independent-samples t test for normally distributed data or Mann-Whitney U test for non-normally distributed data. The odds ratios (OR) and their confidence interval (CI) 95% were calculated to give potential association as an effect size value. Type 1 error probabilities were accepted as 0.05 for all statistical tests. Statistical analyses were performed with Statistical Package for the Social Sciences (SPSS) version 23 software (IBM SPSS®, Armonk, New York, USA).

This study was approved by the Hacettepe University Non-interventional Clinical Researches Ethics Committee (Approval date: 22.05.2020, Number: 2020/10-40).

RESULTS

A total of 599 HCWs were tested for SARS-CoV-2 by PCR and 409 by Hotgen between March 12, 2020 and April 09, 2020. One hundred and forty-six HCWs were tested by both PCR and Hotgen at different time points.

Mean age of the HCWs tested by PCR was 34.5 ± 9.0 years. Three hundred and fifty-one (58.5%) were females. Physicians (n= 240, 40.1%) and nurses (n= 189, 31.6) were the most common HCWs who were tested by PCR.

Thirty-seven (6.2%) of 599 HCWs were found to be PCR positive. A positive PCR result was detected in 24 HCWs during the first admission. Eleven out of 114 HCWs who were tested by a second PCR were found to be positive, and two out of 17 HCWs who were tested by a third test were reported as PCR positive. Median interval between the first and second PCR was seven days (IQR= 8.5 days) and median interval between second and third PCR test was 4.5 days for the HCWs who were reported as positive at repeated PCR tests. Admission with any respiratory symptoms (OR= 8.26; p< 0.001), fever (OR= 6.13; p< 0.001), and pneumonia (OR= 7.16; p= 0.002) was more common in HCWs with a positive PCR. There was no statistically significant difference regarding the occupation and working unit (high vs low-risk) between PCR positive and PCR negative HCWs (Table 1). There were no deaths among HCWs during the study period.

Table 1. Descriptive characteristics of the healthcare workers tested by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) polymerase chain reaction (PCR)

	PCR Positive n (%)	PCR Negative n (%)	Odds Ratio (Confidence Interval 95%)	p
Female	24 (64.9)	327 (58.2)	1.32 (0.66-2.66)	0.42
Any symptom	26 (70.3)	125 (22.2)	8.26 (3.97-17.19)	<0.001
Fever	10 (27.0)	32 (5.7)	6.13 (2.73-13.77)	<0.001
Pneumonia	5 (13.5)	12 (2.1)	7.16 (2.38-21.57)	0.002
Contact history	32 (89.2)	461 (82.0)	1.81 (0.63-5.22)	0.26
Symptomatic + contact history	18 (48.6)	66 (11.7)	7.12 (3.56-14.25)	<0.001
Occupation				
Physicians (n= 240)	26 (70.3)	403 (71.7)		
Nurses (n= 189)				
The other healthcare workers				
• Housekeeping staff (n= 81)				
• Food servers (n= 44)			0.93 (0.45-1.93)	0.85
• Secretaries (n= 13)	11 (29.7)	159 (28.3)		
• Transport staffs (n= 17)				
• Technical staffs (n= 7)				
• The other workers (n= 8)				
Working Unit				
• High risk units	17 (45.9)	179 (33.6)	1.68 (0.86-3.28)	0.13
• Other units	20 (54.1)	353 (66.4)		
	Median (IQR)	Median (IQR)	z	p
Age (years) (n= 862)	31.0 (17)	33 (12)	0.12	0.99
Interval of the first and second PCR (days) (n= 114)	7 (8.5)	8 (12.5)	0.61	0.59
Interval of the second and third PCR (days) (n= 17)	4.5 (-)	5 (6)	0.58	0.88
Interval of the first symptoms and PCR (days) (n= 141)	2 (1)	0 (2)	2.37	0.01

IQR: Interquartile range, PCR: Polymerase chain reaction.

Mean age of the HCWs tested by rapid anti-body test was 34.2 ± 8.5 years and 228 (55.7) were female. Physicians (n= 127, 31.1%) and nurses (n= 153, 37.4%), and housekeeping staff (n= 96, 23.5%) were the most frequently tested HCWs by rapid antibody test. Two hundred and seventy-eight (73.0%) of 409 HCWs tested by rapid antibody test were working at high-risk units. Twenty (4.9%) of the healthcare workers tested with the rapid antibody test were symptomatic, and they were also tested with PCR. Two (0.5%) out of 409 HCWs were detected positive by rapid antibody test. One of these HCWs was diagnosed with COVID-19 pneumonia by PCR and positive chest scan, previously. SARS-CoV-2 PCR was performed just after the positive rapid antibody test result, and it was negative in the other HCW.

DISCUSSION

Approximately 5.600 HCWs work at Hacettepe University Hospitals. During the first 20 days of the pandemic in Türkiye, we tested nearly 10% of our HCWs. The testing strategy identified COVID-19 in 26 symptomatic HCWs, in 11 asymptomatic HCWs, and previous exposure to SARS-CoV-2 in one HCW. The rate of SARS-CoV-2 PCR positive HCWs in high-risk units and other clinics were similar in our study. While a study from Wuhan has reported that HCWs serving at high-risk clinics such as infectious diseases, respiratory diseases and intensive care units had 2.13-fold increased risk of getting COVID-19, a study from England has shown that COVID-19 rates were not different in hospital staff regarding the working unit or patient care[5,6]. Those findings underline the impact of a regular screening policy not only for the HCWs from high-risk units but also for the HCWs working at other services of the hospital particularly during high COVID-19 burden in the community.

Asymptomatic or pre-symptomatic HCWs can serve as an important source for the rapid spread of COVID-19 in the hospital setting. Approximately one-third (29.7%) of the PCR positive HCWs were asymptomatic in our analysis. A study from Saudi Arabia has reported that 62.8% of HCWs who were found to be seropositive for SARS-CoV-2 antibodies did not have any symptoms[7]. The rate of SARS-CoV-2 IgG positivity was 7.4% in 774 HCWs who were screened by Enzyme-Linked Immunosorbent Assay (ELISA) in our hospital, and only 3.5% of SARS-CoV-2 IgG positive HCWs were not previously diagnosed as COVID-19[8]. This finding shows that our policy as "low-threshold testing for HCWs with any respiratory symptom" seems to be successful. However, there were 16 HCWs with a positive SARS-CoV-2 PCR who were cumulated in three wards. Surgical mask became mandatory on March 30 at our hospital. In the absence of mandatory mask usage and low compliance to social distance until the detection of cumulation of SARS-CoV-2 infected HCWs, it is probable that the testing strategy that was based on symptoms and contact history did not allow to identify all infected HCWs immediately.

There is still a controversy about screening asymptomatic HCWs by PCR. Asymptomatic HCW ratio has been reported as 34% in a maternity and child hospital from London[9]. However, a proactive surveillance system for HCWs by summoning with text messages periodically has resulted in the diagnosis of 43 (0.9%) out of 4896 employees in Israel, and only five (11.6%) out of 43 were asymptomatic[10]. This situation can become more complex after the removal of mandatory mask use in vaccinated HCWs with mild symptoms. Thirty-nine of 62 HCWs diagnosed with COVID-19 infection were fully vaccinated by CoronaVac (Sinovac Life Sciences, Beijing, China) in a Turkish University Hospital[11], and all had mild symptoms. A decline in antibody levels has just been recently reported for HCWs who received two doses mRNA of BNT162b2 (Pfizer-BionTech) after three months[12]. In addition to immune waning, vaccine hesitancy is still of concern in HCWs[13,14]. Moreover, a recent study has shown that there was no difference between vaccinated and unvaccinated patients regarding secondary attack rates during the last COVID-19 wave by Omicron variant in Spain. The authors have reported that half of Omicron contagion events happened before symptom onset[15]. All of these problems underline the impact of a vigorous screening program for unvaccinated

HCWs, as well as healthcare providers who are at risk for immune waning after vaccination.

Limiting PCR testing in symptomatic patients or close contacts of COVID-19 patients during the surge of COVID-19 can result in the missing of asymptomatic HCWs with potential of transmission of SARS-CoV-2. However, there are several problems for regular screening by PCR. Obtaining a nasopharyngeal swab can be risky if proper PPE is not used or it is performed in a poorly ventilated area. It is not easy to arrange such an area and staff sampling for asymptomatic HCWs at hospital with a high number of COVID-19 admissions. Moreover, nasopharyngeal sampling can become a disturbing intervention when performed once or twice a week, so asymptomatic HCWs might avoid testing. Recent studies have shown that saliva is a promising sample to test for SARS-CoV-2 by PCR, and pooled analysis of saliva samples from nursing homes and schools resulted in decrease of COVID-19 infection ratio[16-18]. As another approach, self-collected gargle-samples were successfully used for PCR to screen asymptomatic 7513 HCWs with a sensitivity of 88.9% and a specificity of 99.8%[19].

During the early phase of the pandemic in Türkiye, ELISA based tests were not available. We detected only one HCW with positive antibody test who did not have any history of COVID-19. Since we did not have any comparative test, it was difficult to assess the performance of this test. Seven of 25 patients who had thoracic computed tomography findings compatible with COVID-19 had a positive test result with Hotgen that was performed 3-5 days after the second negative RT-PCR test results[20]. The consistency between Hotgen and Roche SARS-CoV-2 assay was reported as 70.3% for SARS-CoV-2 PCR positive patients (n= 31) and 100% for SARS-CoV-2 PCR negative patients[21]. Several limitations such as false negative or false positive results of rapid antibody tests in the early phase of the pandemic have been already reported[22]. The sensitivity of rapid antibody tests produced in China detecting both IgG and IgM varies between 11-100%. The performance of the tests is influenced by severity of the disease and testing days from disease onset[23]. More studies are needed to understand the performance of rapid antibody tests to investigate the risk of SARS-CoV-2 exposure in healthcare settings.

COVID-19 pandemic will not disappear in a short time. In case of increasing incidence of COVID-19 in the community, screening HCWs by a validated test regardless of occupation and contact history appears to be essential for a safe environment in hospitals. This might be particularly useful in settings where vaccination coverage and/or mask use compliance is limited with a high rate of COVID-19 in the community.

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ETHICS COMMITTEE APPROVAL

This study was approved Hacettepe University Non-invasive Clinical Research Ethics Committee (Decision no: 2020/10-05, Date: 20.05.2020).

CONFLICT of INTEREST

None of the authors had conflict of interest.

AUTHORSHIP CONTRIBUTIONS

Concept and Design: GM

Analysis/Interpretation: AS, GM, BC

Data Collection or Processing: DA, GM, GTD, AA, PZ, SÜ, ÖU, CŞ, DK

Writing: AS, GM, OU

Review and Correction: All of authors

Final Approval: All of authors

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