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Seroprevalence of SARS COV-2 anti-nucleocapsid antibodies in Turkish healthcare workers before vaccination schedule: January 2021

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Abstract

Objective: We aimed to assess the seroprevalence of SARS-CoV-2 infection and associated factors among Turkish HCWs, before the Covid-19 vaccination program in January 2021.

Material and methods: We performed antibody assessment against SARS-CoV-2 in blood samples from participants using the Elecsys® Anti-SARS-CoV-2 electrochemiluminescence immunoassay. Samples with a cut-off index (COI; signal sample/cut-off) <1.0 were considered negative, samples with ≥1.0 were deemed positive.

Results: 714 HCWs, 487 women (68.2%), were included in our study. The mean age of the participants was 35.9 ± 8.4 (min:18, max: 62). 370 (51.8%) HCWs's the antibody level was negative, and 344 (48.2%) was positive. While 47.1% (n=122) of the HCWs with positive RT-PCR were antibody positive, 48.8% (n=222) were negative. There was no statistically significant difference in mean age and age groups (p values 0.338 and 0.414, respectively). Also, there was no statistically significant difference in antibody levels by gender (p=0.236). There was no significant difference between antibody positivity according to the presence of comorbidity, and the risk area studied (p=0.556, p=0.335, respectively). There was a statistically significant difference between lung involvement and antibody positivity during Covid-19 infection (p= <0.001).

Conclusion: In our study, the seroprevalence of SARS-CoV-2 antibodies in HCWs was higher than the average population and approximately fifty percent. Multicenter studies with more HCWs would be helpful to determine overall seroprevalence rates.

Key words: COVID-19, SARS-CoV-2 antibody, healthcare worker

Introduction

The ongoing Covid-19 pandemic; According to the data of the World Health Organization, as of October 2021, it caused more than 240 million confirmed cases and over 4.8 million deaths [1]. This period reported 65 thousand deaths and 7 million patients in Turkey [2].

The diagnosis of SARS-CoV-2 infection is based on the presence of viral nucleic acid or antigen by nucleic acid amplification tests such as reverse transcription-polymerase chain reaction (RT-PCR) in the respiratory tract samples, mainly in the nasopharynx [3,4]. Especially in asymptomatic or subclinical infections, it is estimated that many patients could not be diagnosed with Covid-19 due to the lack of PCR testing. The best method in diagnosing cumulative incidence of infection in a population is the detection of anti-nucleocapsid antibodies [4]. Healthcare workers (HCWs) are particularly vulnerable as they care for patients with unknown COVID-19 status. Also, HCWs perform high-risk procedures for covid-19 transmissions, such as endotracheal intubation and cardiopulmonary resuscitation.

We aimed to evaluate the SARS-CoV-2 anti-nucleocapsid antibody level and affecting factors in Turkish HCWs before the Covid-19 vaccination program.

Material and methods

Study design and patients

We conducted this study in Kayseri City Training and Research Hospital on January 18, 2021. The study included all volunteered HCWs. Participants answered a questionnaire that included medical history, occupation, risk groups according to the study area, and their symptoms during the illness if they had COVID-19 recently. We defined risk groups as low, middle, and high according to the study area. The low-risk group included medical secretary, cleaning and support staff working standard wards, working office, store, or kitchen; the middle-risk group lab/radiology technicians, cleaning and support staff working COVID-19 ward. And doctors and nurses were in the high-risk group. All participants signed an informed consent form. The Bio-speedy SARS-CoV-2 (2019-nCoV) RT-qPCR detection kit (Bioeksen, Istanbul, Turkey) was used in the SARS-CoV-2 PCR test on nasopharyngeal swabs to determine the presence of SARS-CoV-2 infection.

Antibody assessment

Elecsys Anti-SARS-CoV-2 electrochemiluminescence immunoassay test used. This assay is intended for use on Cobas e analyzers (Roche Diagnostics International Ltd, Rotkreuz, Switzerland) for the in vitro qualitative detection of antibodies (both IgA and IgG) to SARS-CoV-2 in human serum and plasma. The Elecsys Anti-SARS-CoV-2 test uses the double antigen sandwich test principle and a recombinant protein representing the nucleocapsid antigen to detect antibodies to SARS-CoV-2. Anti-SARS-CoV-2 antibody per manufacturer's instructions: samples with a cut-off index (COI; signal sample/cut-off) <1.0 were considered negative, samples with ≥1.0 were deemed positive. A measured antibody level magnitude above the cut-off value is not considered an indicator of the sample's total amount of antibody present.

Sample size estimation

Based on the assumption that approximately 40% of healthcare professionals will have antibody positivity, we calculated the required sample size as 369 with a 95% confidence interval and 5% margin of error using the Statcalc calculator program in Epi Info (version 7.2.5.0).

Statistical analysis

Categorical data were summarized as frequency and percentage, continuous data with normal distribution as mean ± standard deviation, and data, not with normal distribution as median, 25%-75% interquartile range (IQR). We used the Shapiro Wilk test for normality controls of continuous measurements. We used independent sample t-tests to compare the regular and Mann-Whitney-U tests for the non-regular distributed two groups. And to compare categorical variables, the Chi-square test was used. The statistical significance level was 0.05.

Ethics approval

The Ethics Committee of the Kayseri City Hospital approved this study (Approval no: 59-11022022).

Results

A total of 714 HCWs, 487 women (68.2%), were included in our study. The mean age of the participants was 35.9±8.4 (min: 18, max: 62). Of the participants, 425 (59.5%) were nurses, 106 (14.8%) were medical secretaries, and 106 (14.8%) were physicians. When the participants were categorized in terms of SARS-CoV-2 transmission risk, 14.8% (n=106) low, 10.8% (n=77) moderate, 74.4% (n=531) high was in the risk group. At least one comorbid disease in 135 (18.9%) of the participants. The most common comorbid diseases were hypertension (3.5%), autoimmune diseases (3.5%), and diabetes (2.9%) (Table 1).

Two hundred and fifty-nine (36.2%) participants had previously been positive for SARS-CoV-2 RT-PCR, and lung involvement occurred in 11.2% (n=29).

Table 1 Demographic and Clinical Characteristics of HCWs

Age, mean (± SD), years	35.9 ± (8.4)	
Gender	n	**(%)**
Female	487	(68.2)
Male	227	(31.8)
Age Groups		
18-40	505	(70.7)
41-50	177	(24.8)
>51	32	(4.5)
Job groups		
Doctor	106	(14.8)
Nurse	425	(59.5)
Medical secretary	106	(14.8)
Lab/radiology technician	66	(9.2)
Cleaning and support staff	11	(1.5)
Risk groups according to the study area		
Low	106	(14.8)
Middl e	77	(10.8)
High	531	(74.4)
Comorbit diseases	**135**	**(18.9)**
Hypertension	25	(3.5)
Diabetes mellitus	21	(2.9)
Chronic obstructive pulmonary disease	19	(2.7)
Coronary artery disease	6	(0.8)
Autoimmune diseases	25	(3.5)
Malignancy	3	(0.4)
Hypothyroidism	15	(2.1)
Other	12	(1.7)
Antibody level		
COI <1.0	370	(51.8)
COI ≥1.0	344	(48.2)
RT-PCR history		
Negative	455	(63.8)
Positive	259	(36.2)
	Median	**IQRs 25-75% (min-max)**
Days from PCR positivity to the day of antibody testing	82	43-132 (2-314)
Symptoms of RT-PCR positive patients (n= 259)	n	%
Fever	34	(16.1)
Cough	56	(26.5)
Throat ache	32	(15.1)
Shortness of breath	21	(9.9)
Weakness	40	(18.9)
Myalgia	52	(24.6)
Headache	31	(14.6)
Diarrhea	6	(2.8)
Taste-smell loss	17	(8)
Asymptomatic	48	(18.5)
Presence of lung involvement in RT-PCR positive patients (n=259)	29	(11.2)

Table 2 Comparison of clinical characteristics and antibody levels of HCWs

	Elecsys® Anti-SARS-CoV-2 test		
	Negative	Positive	p value
	Mean (± SD)	**Mean (± SD)**	
Age, year	35.6 ± 8.3	36.2 ± 8.4	0.338*
	n (%)	**n (%)**	
Gender			
Female	245 (50.3)	242 (49.7)	0.236
Male	125 (55.1)	102 (44.9)	
Age Groups			
18-40	266 (52.7)	239 (47.3)	0.414
41-50	91 (51.4)	86 (48.6)	
>51	13 (40.6)	19 (59.4)	
Job groups			
Doctor	58 (54.7)	48 (45.3)	0.522
Nurse	212 (49.9)	213 (50.1)	
Medical secretary	60 (56.6)	46 (43.4)	
Laborant/Radiology technician	36 (54.5)	30 (45.5)	
Cleaning and support staff	4 (36.5)	7 (63.6)	
Risk groups according to the study area			
Low	60 (56.6)	46 (43.4)	0.556
Middle	40 (51.9)	37 (48.1)	
High	270 (50.8)	261 (49.2)	
At least one comorbid disease			
Absent	295 (50.9)	284 (49.1)	0.335
Presense	75 (55.6)	60 (44.4)	
RT-PCR history			
Negative	233 (51.2)	222 (48.8)	0.664
Positive	137 (52.9)	122 (47.1)	
Lung involvement during COVID-19			
Absent	137 (59.6)	93 (40.4)	< 0.001
Presense	0 (0)	29 (100)	
	Median (IQRs 25-75%)	**Median (IQRs 25-75%)**	
Days from PCR positivity to the day of antibody testing	101 (44- 131)	75.5 (43- 134)	0.426**

*p= Student's t-test
**p= Mann-Whitney U test
Other p values were calculated by the chi-square test.

The median value of the time elapsed between the date of RT-PCR positivity and antibody measurement of the participants was 82 days (IQRs: 43-132). The most common symptoms were cough (26.5%), myalgia (24.6%), weakness (18.9%), fever (16.1%), headache (14.6%) and asymptomatic (18.5%) (Table 1).

Table 1 shows the Demographic and clinical characteristics of the HCWs.

370 (51.8%) HCWs's the antibody level was negative, and 344 (48.2%) was positive. While 47.1% (n=122) of the HCWs with positive RT-PCR were antibody positive, 48.8% (n=222) were negative (Table 2).

The antibody levels of the participants in terms of mean age and age groups, there was no statistically significant difference (p values 0.338 and 0.414, respectively). Also, there was no statistically significant difference in antibody levels by gender (p=0.236). There was no significant difference between antibody positivity according to the presence of comorbidity and the risk groups (p=0.556, p=0.335, respectively) (Table 2).

According to job groups, although the highest seroprevalence was in cleaning and support personnel (63.6%), no significant correlation was found between antibody levels and occupation (p=0.522) (Table 2).

The history of RT-PCR positivity and the time elapsed since RT-PCR positivity was not significant by antibody positivity (p= 0.664, p=0.426, respectively). There was a statistically significant difference between lung involvement and antibody positivity during Covid-19 infection (p=<0.001). Antibody levels were positive in all HCWs (n=29) with lung involvement (Table 2).

Discussion

Covid-19 infection can manifest in different clinical pictures, including asymptomatic infection. Asymptomatic infection rates may vary in studies. In a systematic review, rates of asymptomatic infections ranged from 1.6% to 56.5% [5]. Approximately twenty percent of the HCWs had asymptomatic Covid-19 disease in our study.

A systematic review and meta-analysis study examined research published until August 2020, 47 studies covering 399265 people from 23 countries, SARS-CoV-2 seroprevalence in the general population ranges from 0.37% to 22.1%, with the pooled estimate reported as 3.38% [6]. In the study conducted in Boston in July 2020, there was a 5.5% IgG positivity, and 1.8% of people had mild Covid-19 symptoms, but they did not perform a test for diagnosis [7]. In the seroprevalence study conducted in the UK between May-June 2020 in HCWs, there was 31.6% antibody positivity [8]. In another survey conducted in April-May 2020, 1.6% SARS-CoV-2 seroprevalence was observed in 734 HCWs from 18 different centers [9]. In the study conducted in Belgium in April 2020, researchers measured IgG/IgM with the rapid test and found 6.4% IgG positivity in 3056 HCWs [10]. In our study, the seroprevalence of SARS-CoV-2 antibodies in HCWs was 48.2%. We can explain the high rate because our hospital serves as a tertiary level and the only pandemic hospital in the region.

The study at Hacettepe University between March and September 2020 showed a seropositivity rate of 7.4% of 774 HCWs. While seropositivity was 75.6% in HCWs diagnosed with COVID-19 by PCR or CT before the antibody test, this rate was 3.5% in HCWs not diagnosed with COVID-19 [11]. In a study conducted with 932 HCWs in three pandemic hospitals in Istanbul and Kocaeli in June 2020, seropositivity was 12.3%. The seropositivity HCWs who were previously diagnosed with PCR was 78.2%, while the rate was 2.7% in HCWs not diagnosed with COVID-19 [12]. Seroprevalence rates vary depending on factors such as the intensity of the pandemic region, working conditions of hospitals, date of the study. One reason for higher seroprevalence positivity than other studies is that our study was conducted later than others. The increased rate can be explained by the increase in HCWs encountering the Covid-19 infection.

Similar to other studies, we found no relationship between age, gender, and the presence of comorbidity in terms of SARS-CoV-2 antibody positivity [7,10,11].

When evaluated according to risk groups for the transmission of Covid-19 infection, in Mishra et al. [13], seropositivity was higher in the high-risk category. On the other hand, Hunter et al. [9] did not detect a difference between high and low contact risk groups. They attributed this to the effectiveness of personal protective equipment use. Alkurt et al. [12] found no difference between risk groups. In our study, there was no difference between risk groups, also.

Similar to our study, other studies have reported higher antibody seroprevalence rates in HCWs with lung involvement [11,12]. A higher rate suggests a positive correlation between disease severity and antibody positivity. Yan et al. [14], a positive correlation was observed between the severity of SARS-CoV-2 infection and IgG antibodies. The highest antibody levels were in the group of severe patients. Our study did not detect antibody positivity in 52.9% of HCWs with PCR positive, and 18.5% of those who had the disease were asymptomatic. Lower antibody formation may occur in HCWs with mild or asymptomatic infections.

The main limitation of our study was that we measured antibodies at one time period and did not assess the changes in antibody levels over time. Another limitation of our research, it was performed in a single center, and seroprevalence results can not generalize to the whole country.

Conclusion

Antibody tests can determine SARS-CoV-2 seroprevalence in the community or HCWs. We may explain the higher seroprevalence rate by 1) undiagnosed asymptomatic infections, 2) the rise in the number of people exposed to the virus as the pandemic continues, and 3) serious infections such as lung involvement. Multicenter studies with more participants would be helpful to determine overall seroprevalence rates.

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