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SARS-CoV-2 antibody seroprevalence in healthcare personnel during the pandemic's peak: The experience of single hospital

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Abstract

Serological severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibodies determination in healthcare personnels with a increased risk of infection is important for detecting asymptomatic coronavirus disease 2019 (COVID-19) and post-disease immunity. Purpose of study were to determine the seroprevelance of healthcare personnels with COVID-19 in university hospital. 439 healthcare personnels working at Biruni University Medical Faculty Hospital between March 2020 to January 2021 were included to the study. All participants were divided into groups based on the results of their immunoglobulin G (IgG) antibodies against novel coronavirus in blood test, collecting nasopharyngeal and oropharyngeal swabs reverse transcriptase–polymerase chain reaction (RT-PCR), and thorax computed tomography (CT). Group 1: Antibody positivity and RT- PCR negativity, Group 2: RT-PCR positivity without lung involvement, Group 3: RT-PCR positivity with lung involvement. The RT-PCR positivity was detected as 32.8 % (n=144) in all healthcare personnels, 68.8 % of RT-PCR positive healthcare personnels were symptomatic and 15.3 % of them had lung involvement. The IgG antibody positivity was detected as 41 % (n=180) in all healthcare personnels. The antibody positivity (p=0.353) and titers were similar in the healthcare personnels (p=0.361). Risk of COVID-19 and contagiousness is high in healthcare personnels under pandemic conditions. Additionally the antibody positivity and antibody titer are higher in those who have symptomatic disease compared to those who have asymptomatic.

Keywords: Healthcare personnels, COVID-19, seroconversion, antibody

Introduction

SARS-CoV-2 (acute respiratory syndrome coronavirus-2) caused COVID-19 (coronavirus disease), which was first identified in Wuhan, China, and quickly spread throughout the world, became a pandemic. As of 5 December 2021, the upward trend continued with four million new cases and 52.500 deaths per week [1]. Because of the epidemic's influence on patients' overall health, regional health systems, and worldwide economic activity, effective policies and trustworthy epidemiological statistics are required [2]. Rapid illness identification, isolation of patients, and prevention of transmission by adhering to social distancing guidelines are all critical public health strategies [3]. The virus is detected in respiratory tract samples using RT-PCR to validate a COVID-19 diagnosis [4]. High titres of SARS-CoV-2 IgG, which begin to rise in the second week following the beginning of disease-related symptoms, are the most sensitive and early serological indicators [5]. These serological tests are useful in the diagnosis of asymptomatic and suspected patients who have negative nucleic acid tests. Antibody response is an indicator of individual and social immunity, rather than active cases [2, 6].

COVID-19 first appeared in healthcare personnels at the end of January 2020 in Hubei, detected at a rate of 2.7%. The protection of healthcare workers from easily-transmitted diseases, such as COVID-19, is important for the implementation of infection control and precautions in the healthcare setting [7]. In pandemic conditions, health professionals should be monitored continuously to prevent the virus from spreading to staff, patients, friends and family. Furthermore, a rise in cases among healthcare professionals may lead to the destruction of the health system, exacerbating the pandemic [8]. The World Health Organization advises using personal protective equipment such as surgical mask, gowns, gloves, and eye protection [9]. Infection risks in healthcare personnels increases due to the use of improper equipment, long-term exposure to patients with COVID-19, and insufficient protective equipment. However, it is known that 50% of COVID-19 cases are asymptomatic [10], As a result, antibody

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surveillance in healthcare personnels at greater infection risks is critical for detecting asymptomatic and post-disease immunity. Unfortunately, there are insufficient data reporting both post-illness seroprevalence in healthcare personnels and the rate of asymptomatic cases.

The primary goal of this study was to evaluate the seroprevalence of COVID-19 among healthcare professionals. The secondary aim was assessing whether there is variability by unit of health workers

Materials and Methods

Study design

Study was planned a retrospective cross sectional. Patients from Biruni University Hospital's outpatient clinics were included in this study, which treated patients with potential or diagnosed SARS-CoV-2 infections.

Participants and case definition

Between March 2020 and January 2021, healthcare professionals who worked at University Medical Faculty Hospital as physicians, nurses, administrative personnel, healthcare assistants, porters or domestic employees, and medical clerks were investigated in the study. During the research period, COVID-19 RT-PCR tests were performed on all healthcare personnels with clinically suspicious symptoms of COVID-19 (fever, weakness, myalgia, dyspnea, nausea, loss of taste and smell). The test results of nucleic asid of SARS-CoV-2, the dates of nücleic asid test positivity, related symptoms, and the course of the disease were recorded. Whether the disease was symptomatic, the need for hospitalization due to the disease, and the presence of lung involvement as defined by positive chest computed tomography (CT) findings were examined in detail

Study protocol

The levels of antiviral immunoglobulin-G (IgG) of all healthcare workers were examined between 2 and 13 January 2021, before COVID-19 vaccination began on 14 January 2021. Hence, all data on the results of IgG antibodies performed in this period and RT-PCR tests performed prior to this period, between 11 March 2020 and 1 January 2021, were obtained from patient files.

After all data were obtained, parameters that could affect SARS-CoV-2 antibody levels were compared separately. All patients were grouped according to SARS-CoV-2 IgG, SARS-CoV-2 nucleic acid test, and chest CT findings. Group 1: patients whose SARS-CoV-2 IgG antibody positivity and negative SARS-CoV-2; Group 2: patients whose SARS-CoV-2 IgG positivity without pneumonic infilrations; and Group 3: patients whose SARS-CoV-2 IgG positivity and pneumonic infilrations. Group 2 and group 3 SARS-CoV-2 PCR positive but group 2 was not have pneumonic infiltrations and group 3 was have pneumonic infiltrations.

All research participants had nasopharyngeal specimens were collected for the SARS-CoV-2 nucleic acid assay. Both mouth and nose swab samples were placed in VNAB (viral nucleic acid buffer) fluid. VNAB fluid provides viral nucleic acid extraction. VNAB liquid was added to the prepared PCR mix and it was worked on Biorad CFX96 Realtime PCR device. As a result of real time pcr device operation, 200 RFU value was taken as threshold value in each channel. HEX channel was studied as an internal control. And in this channel, sigmoidal curves with Ct value <= 32 were accepted. Sigmoidal curves with a Ct value of <= 38 in the FAM channel were accepted as positive. Samples with ct values> 38 in the FAM channel or with no peaks were considered negative provided that internal controls were run. To determine IgG positivity against SARS-CoV-2, blood samples were collected from each participating healthcare personnels in January 2021. Blood samples were analyzed in two hours after they were collected at 24.5 centigred degree. Immunofluorescence assay (IFA) was performed using COVID-19 IgG antibody IFA rapid test kits (IF2084 for Getein 1600, Getein Biotech, Inc. Nanjing, China) to assess the presence of serum SARS-CoV-2 IgG. SARS-CoV-2 nucleocapsid protein (N protein) and spike protein (S protein) were used in combination by IFA. These test findings were shown quantitatively in terms of the cut-off index (COI) value. Those with a COI test result lower than 1.0 were considered negative. Novel coronavirus(2019-nCoV) IgM/IgG antibody has been determined and validated using 500 samples confirmed as negative and 88 samples confirmed as positive. The test IgM sensitivity 56,7% (17/30) %95 confidence interval (39,2%; 72.6%) and IgM specifity was shown 98.8% (79/80). IgM was not used to evaluate immune response due to low sensitivity and because it is more specific to acute infection. Because of we used the test IgG sensitivity 73.3% (22/30) %95 confidence ınterval (55.6%; 85.8%) and IgG specificity was shown 100% (80/80) (95.4%; 100%) [11]

Ethics

The research was accepted by ethics committee and the Ministry of Health, and was performed in accordance with the Helsinki declaration. The patients were fully informed about the information to be used in the study before receiving written agreement. Study was approved by Biruni University Ethics Committee and ethic approval number was (2021/47-42).

Statistical analysis

The Kolmogorov-Smirnov test was used to assess the fit of all data to a normal distribution. Continuous variables are provided as mean standard deviation, whereas categorical variables are presented as percentages. Chi-square test and t-test were used to analyze variables. An analysis of variance was performed to review different group means. The Bonferroni technique was used to perform the following post-hoc analysis. Pearson's correlation was applied to numeric values. SPSS 20.0 (SPSS, Chicago, IL, USA) software was used to analyze all data, and $p<0.05$ was tested for significance.

Results

Demographic characteristics, comorbidities, COVID-19 RT-PCR test results, and SARS-CoV-2 IgG levels of the healthcare personnels are shown in Table 1. Physicians were considerably older (p 0.001). Females was higher in medical clerks ($p <0.001$). The smoking behaviors of the groups were not differ. High blood pressure, hyperglycemia, chronic bronchitis, coronary artery disease, and hyperlipidemia were markedly higher among physicians and porters or domestic workers. The number of swab test screenings for COVID-19-like symptoms prior to positive

was considerably higher in medical clerks (p = 0.001). RT-PCR positivity was detected at 32.8% (n = 144) in all healthcare workers, 68.8% (n = 99) of RT-PCR-positive healthcare workers were symptomatic, and 15.3% (n = 22) of RT-PCR-positive healthcare workers had lung involvement. Hospitalization was significantly higher in physicians and porter or domestic workers (p = 0.026). Antibody positivity was detected at 41% (n = 180) in all healthcare workers. Additionally, the antibody positivity and titres were similar in healthcare workers (p = 0.353 and p = 0.361, respectively). The presence of previous COVID-19 positivity (RT-PCR or antibody) was detected at 45.8% (n = 201) in all healthcare workers.

Demographic characteristics, IgG antibody positivity to SARS-CoV-2, and antibody titres of healthcare workers who were grouped according to negativity or positivity of RT-PCR with or without lung involvement are shown in Table 2. Age was higher in the test positive group with lung involvement (p = 0.005). SARS-CoV-2 IgG titres were considerably lower in the antibody-positive nucleic asid test negative group (p 0.001). The prevalence of IgG antibody positivity was greater in the swab test positive group with lung involvement than in the swab test positive group without lung involvement (p 0.001).

The subgroup analysis of healthcare workers for antibody titre is shown in Table 3. The antibody titre was significantly higher in healthcare workers with RT-PCR positivity, symptomatic disease, lung involvement, and hospitalization. The titre of SARS-CoV-2 IgG was found to be considerably positively associated with age (r = 0.149 and p = 0.048).

Table 1. The demographic characteristics, comorbidities, RT- PCR Testing and Immunglobulin G antibodies to SARS-CoV-2 in the healthcare workers

	Overall(n=439)	Nurse(n=173)	Physician (n=37)	Administrative staff (n=86)	Health care assistant (n=52)	Porter or domestic worker (n=13)	Medical clerk (n=78)	p
Age (years)	30.5±9.6	29.1±9.3	42.8±10.5	32.6±8.7	28.4± .5	38.2±9.4	25.7±4.8	<0.001
Gender (female)	280(63.8)	120(69.4)	11(29.7)	45(52.3)	30(57.7)	3(23.1)	71(91)	<0.001
Smoking	136(30.9)	55(31.8)	10(27.1)	25(29.1)	16(30.8)	4(30.7)	26(33.3)	0.221
Comorbidities								
Hypertension	15(3.4)	1 (0.6)	5(13.5)	3(3.5)	1(1.9)	2(15.4)	3(3.8)	<0.001
Diabetes mellitus	4(0.9)	0	1(2.7)	1(1.2)	1(1.9)	1(7.7)	0	0.026
COPD/Asthma	4(0.9)	0	2(5.4)	1(1.2)	0	1(7.7)	0	0.019
Coronary artery disease	3(0.7)	0	1(2.7)	1(1.2)	0	1(7.7)	0	0.016
Hyperlipidemia	2(0.5)	0	1(2.7)	0	0	1(7.7)	0	0.001
Count of RT-PCR screening for symptoms resembling COVID-19 until positivity	2.2±2.7	1.8±2.7	1.6±2.1	2.8±2.9	1.6±2.2	2.5±3.1	3.1±3.3	0.001
RT-PCR positivity	144(32.8)	68(39.3)	12(32.4)	19(22.1)	15(28.8)	5(38.5)	25(32.1)	0.137
Symptomatic	99(22.6)	43(24.9)	10(27)	12(14)	8(15.4)	4(30.8)	22(28.2)	0.154
Lung involvement	22 (5)	6(3.5)	6(16.2)	4(4.7)	1(1.9)	1(7.7)	4(5.1)	0.036
Hospitalization	24 (5.5)	6(3.5)	6(16.2)	5(5.8)	2(3.8)	2(15.4)	3(3.8)	0.026
Antibody positivity	180(41)	80(46.2)	16(43.2)	28(32.6)	18(34.6)	5(38.5)	33(42.3)	0.353
Antibody titer	38.1±21.1	38.4±20.9	41.2±25.1	35.6±20.4	43.8±20.9	48.2±22.3	32.9±16.3	0.361
COVID-19 positivity (RT-PCR or antibody)	201 (45.8)	91(52.6)	18(48.6)	28(32.6)	22(42.3)	5(38.5)	37(47.4)	0.074

Immunglobulin G (Ig G); COPD, chronic obstructive pulmonary disease; RT-PCR, reverse transcriptase–polymerase chain reaction

Table 2. Age, gender, immunoglobulin G antibody positivity, and SARS-CoV-2 titers among healthcare workers with RT-PCR negativity or positivity

	RT-PCR negativity with antibody positivity (n=57)	RT-PCR positivity without lung involvment(n=122)	RT-PCR positivity with lung involvement (n=22)	P
Age (years)	29.4±9.5	29.4±9.2	35.7±13.6	0.005
Gender (female)	34(59.6)	77(63.1)	12(54.5)	0.203
Antibody positivity	57(100)	103(84.4)	20 (90.9)	<0.001
Antibody titer	25.1±18.1	42.9±17.1	46.7±24.9	<0.001

Immunglobulin G (Ig G)

Table 3. The subgroups analysis of healthcare workers for Immunglobulin G antibodies titers to SARS-CoV-2.

		N	Antibody titer	p
Smoking	No	131	40.2±18.4	0.935
	Yes	80	39.9±20.7	
Gender	Female	123	37.1±18.9	0.458
	Male	78	39.4±22.9	
RT-PCR positivity	No	57	25.1±18.1	<0.001
	Yes	144	43.8±18.9	
Symptomatic	No	102	33.1±19.9	0.001
	Yes	99	43.5±19.9	
Lung involvement	No	179	36.1±19.4	0.001
	Yes	22	52.6±23.7	
Hospitalization	No	177	36.9±19.2	0.028
	Yes	24	48.4 ± 28.9	

Discussion

In our study, regardless of the duties of healthcare personnels, it was observed that SARS-CoV-2 nucleic asid swab test and SARS-CoV-2 IgG antibody positivity were similar. Additionally, SARS-CoV-2 IgG antibody titre and antibody positivity were higher in patients who were SARS-CoV-2 nucleic asid test positive, symptomatic, with lung involvement, and hospitalized. Age and antibody titre were shown to have a positive correlation. SARS-CoV-2 mean time of incubating is 72-120 hours, shows rapid transmission from person to person, and continues to cause serious mortality and morbidity (12). It is quite common in healthcare workers worldwide. Although many antiviral (avifavir, favipravir, remdesivir), anti-inflammatory (corticosteroids, colchicine, tocilizumab), and antimalarial (klorokin ve hydroxychloroquine) drugs have been used to treat the disease, the vaccine is seen as the best hope (13). Large-scale vaccination studies and rapid vaccination programs are ongoing at present to end the pandemic all over the world. Community immunization is being vigorously pursued both to protect the physical and mental health of society and to reduce the pandemic's negative impact on the world's economies (14). In studies conducted among healthcare professionals, a wide range of seroprevalence has been detected—from 1.6% to 44.7%; virus prevalence affects seroprevalence in the hospital and the community [15]. While seropositivity was 2.9% among healthcare personnels case hospitals in Saudi Arabia where patients were followed, it was 0.8% in control hospitals where COVID-19 was not followed [16]. In an observational cohort study in Denmark, Iversen et al. found a seroprevalence of 4% in 29,000 healthcare workers [17]. Zawadzki et al. showed that the prevalence was 1.13% in their study of 2,924 patients in California, and attributed the low prevalence to a low overall prevalence in the geographic region, precautions, effective testing, and a patient triage strategy [18]. Shields et al. showed that seroconversion was 24% in their study conducted on 516 healthcare workers in England [22]. Moscola et al. found that the PCR positivity rate was 36%, seropositivity was 13%, antibody positivity was 93% in PCR-positive patients, and antibody positivity was 9% in PCR-negative patients in a large-scale study conducted on 40,000 volunteer healthcare workers who were provided protective equipment in New York [21]. Venogoupal et al.'s study, which included 468 healthcare workers in a community hospital severely affected by the pandemic in New York, found that the seroprevalence rate was 27% and that 53% of the patients were asymptomatic. In the same study, 167 antibody-positive patients were 44% symptomatic and 13% asymptomatic. It was shown that symptomatic group had increased antibody titres, and that seropositivity increased in those with loss of taste and smell [19]. Our study showed that nucleic asid test positivity was 32.8%, antibody positivity was 41%, and nucleic asid test or antibody positivity was 45.8% among in-hospital healthcare personnel. The reason for the high seroprevalence in our study, similar to the pandemic hospital in New York, is the increase in social exposure due to the pandemic in Istanbul and the increase in the number of COVID-19 patients in outpatient clinics and services in our hospital.

In our study, in PCR-positive healthcare workers who had symptoms and lung involvement, similar to other studies [19, 20, 21], antibody titre was found to be higher compared to PCR-negative patients with no symptoms and antibody positivity. Recent research suggests that CD4+ and CD8+ T lymphocytes play a role in antibody production [26]. Grifoni et al. found a connection between IgG titres for SARS-CoV-2 and CD4+ T cell response to spike protein in a research comparing PCR-positive patients with PCR-negative individuals who had not been exposed to the virus [22].

The average age of patients with increased antibody titres in healthcare staff has been found to be higher. Similar to our study, Gudbartjson et al. detected higher antibody titres in elderly hospitalized patients, and Liu et al. found higher antibody titres in patients over 65 years of age in the intensive care unit [23, 24]. Our mortality rate among healthcare workers was 0%. In a study conducted by Levene et al. in England, mortality in healthcare

professionals due to COVID-19 was found to be 0.15 per 1000 people and lower than in the general population—0.75 per 1000 people.Safety equipment, low mean age, and lower comorbidities of healthcare personnels decrease mortality [25].

There are several limitations for this research. First, this is a single-centre cross-sectional study that recruited healthcare professionals working in a pandemic hospital in a community with a high case density. Second, it cannot be generalized to the whole society because the average age of the study is low compared to the population, and comorbid diseases are less common in healthcare workers. Third, the number of patients over the age of 65 and the number of people tested for antibodies after 6 months are both low. In addition, ongoing virus exposure is higher than in society, and the neutralizing antibody type with high protection was not considered separately. Finally, our study was unable to offer data on the connection between antibody titres or seroconversion rate and re-infection or current illness.

Conclusion

As a result, we recommend antibody screening of groups with socially intensive virus exposure, especially healthcare workers, in order to determine the continuity of immunity and to identify groups in need of vaccination during the pandemic process, where coronavirus mutations and adequate vaccine supply may be a problem. Serological tests can be used to differentiate asymptomatic cases that cannot be diagnosed.

Conflict of interests
The authors declare that they have no competing interests.

Financial Disclosure
All authors declare no financial support.

Ethical approval
Study was approved by Biruni University Ethics Committee and ethic approval number was (2021/47-42)

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