Original Article

Iranian Journal of Immunology
https://iji.sums.ac.ir

Prevalence of Anti-SARS-CoV-2 Specific Antibodies in Health-Care Workers Compared to General Population, Tehran-Iran

Sahar Mortezagholi[1], Davood Rostamzadeh[2], Maedeh Alinejad[3], Vahid Younesi[3], Payam Tabarsi[4], Mahdi Shabani[1]*

[1]Department of Immunology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran; [2]Medicinal Plants Research Center, Yasuj University of Medical Sciences, Yasuj, Iran; [3]Synapse IVD Accelerator, Tehran, Iran; [4]Clinical Tuberculosis and Epidemiology Research Center, National Research Institute of Tuberculosis and Lung Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran

ABSTRACT

Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) rapidly transmit in general population, mainly between health-care workers (HCWs) who are in close contact with patients. **Objective:** To study the seropositivity of HCWs as a high-risk group compared to general population.

Methods: 72 samples were obtained from HCWs working in Masih Daneshvari hospital as one of the main COVID-19 admission centers in Tehran, during April 4 to 6, 2020. Also we collected 2021 blood samples from general population. The SARS-CoV-2 specific IgM, and IgG antibodies in the collected serum specimens were measured by commercial ELISA kits.

Results: Based on the clinical manifestations, 25.0%, 47.2%, and 27.8% of HCWs were categorized as symptomatic with typical symptoms, symptomatic with atypical symptoms, and asymptomatic, respectively. Symptomatic individuals with typical and atypical symptoms were 63.2% and 36.8% positive in RT-PCR test, respectively. Anti-SARS-CoV-2 IgM and IgG antibodies were detected in 15.3% and 27.8% of HCWs samples, respectively. Antibody testing in the general population indicated that SARS-CoV-2 specific IgM and IgG were found in (162/2021) 8%, and (290/2021) 14.4%, respectively. The frequency of positive cases of IgM and IgG were significantly increased in HCWs compared to general population (p= 0.028 for IgM and p= 0.002 for IgG).

Conclusion: The frequency of SARS-CoV-2 specific antibodies in HCWs was higher than general population indicating a higher viral transmission via close exposure with COVID-19 patients.

Keywords: COVID-19, ELISA, General Population, Health-Care Workers, SARS-CoV-2, Seroprevalence

*Corresponding author:
Mahdi Shabani, PhD;
Department of Immunology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
Tel/Fax: +98 21 22439970
Email: msshabani@sbmu.ac.ir

Cite this article as:
Mortezagholi S, Rostamzadeh D, Alinejad M, Younesi V, Tabarsi P, Shabani M. Prevalence of Anti-SARS-CoV-2 Specific Antibodies in Health-Care Workers Compared to General Population, Tehran-Iran. *Iran J Immunol.* 2021; 18(1):82-92, doi: 10.22034/iji.2021.88168.1851.

Received: 2020-09-18
Revised: 2020-12-29
Accepted: 2021-01-10

INTRODUCTION

Since the occurrence of the coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in Wuhan, China, in December 2019, it has quickly spread around the world (1, 2). SARS-CoV-2 is a RNA virus in the Coronaviridae family which classified as a new beta-coronavirus (3). COVID-19 considered third coronavirus pandemic after severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) in 2002 and 2012, respectively (4).

The most common presenting symptoms in COVID-19 patients are cough, fever, dyspnea, myalgia, diarrhea, and nausea and vomiting (5, 6). The manifestations of COVID-19 can be varied ranging from asymptomatic, or mild disease to severe pneumonia or multi-organ failure (6-8). COVID-19 diagnosis is mostly based on the clinical manifestation, physical examination, CT scan and laboratory tests including real-time reverse transcriptase polymerase chain reaction (RT-PCR) (9, 10). Immune-based assesses including lateral flow immunoassay test, enzyme-linked immunosorbent assay (ELISA) and chemiluminescent immunoassay could also be used as diagnostic aids in COVID-19 accompany with clinical, CT, and molecular findings (2, 10-12).

One of the key characters of SARS-CoV-2 is the extremely contagious rate of virus that is mainly spread via respiratory droplets or direct contacts. In this context, the transmission of SARS-CoV-2 can rapidly occur human-to-human, mainly between family members and health-care workers (HCWs) in the hospital setting who are in close contact with symptomatic patients (5). Therefore, HCWs are one of the major high-risk population for infection with SARS-CoV-2. As mentioned earlier, infection with SARS-CoV-2 could be asymptomatic, suggesting the potential for virus transmission regardless of symptoms (13). In another word, asymptomatic patients have been proven to be contagious and accordingly pose a substantial challenge in infection control (7). Hence, the prevalence of SARS-CoV-2 infection in this population may be ignored or underestimated, which demands to focus on the epidemiological investigation of asymptomatic cases. To find the prevalence of the infected persons, RT-PCR is not beneficial to detect past infection, however, serological assays can detect both active and past infections if apply in the accurate time after symptoms onset (14, 15). Serological testing in a large population provides better insight into the COVID-19 epidemiology and helps the policy-decision makers have better strategy to fight against SARS-CoV-2 silent transmission in the community. Therefore, we persuade to estimate the seropositivity of HCWs as a high-risk group compared to the general population as a low-risk group.

MATERIALS AND METHODS

Sample Collection

In this cross-sectional study, 72 whole blood were collected from HCWs (doctors, nurses, allied health professionals, administrators and others; 37.5% male) who have been working in Masih Daneshvari hospital as one of the main COVID-19 admission centers in Tehran, during April 4 to 6, 2020. All HCWs completed a questionnaire regarding general descriptions and current and previous COVID-19 symptoms, date of corresponding symptoms onset, chest CT scan findings, and real-time RT-PCR results. According to the clinical presentation on the day of sampling or during the preceding 2 months, the HCWs were categorized into three groups. The HCWs who had two or more symptoms of fever (greater than 37.8°C), cough, shortness of breath and loss of the senses of smell and taste were classified as symptomatic with typical symptoms groups. The individuals were considered as symptomatic with atypical symptoms if they had symptoms included chills, weakness, malaise, rhinorrhea, hyperhidrosis, fatigue, sore throat, myalgia, headache, nausea, and diarrhea. And subjects with no

symptoms classified as asymptomatic group (16, 17). Besides, 2021 whole blood samples were obtained from low risk general population (74.5% male) who has been working in private sectors and governmental organizations outside of the health system. Sera were separated using centrifugation and stored at -20 ℃ until use in the serology assay. This study was approved by Medical Ethical Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.RETECH.REC.1399.055). Written informed consent was obtained from all HCWs participants. Data records for general population were anonymous, so informed consent was waived for this group.

SARS-CoV-2 Specific IgM, and IgG Antibodies Detection Using ELISA

IgM, and IgG antibodies specific to SARS-CoV-2 nucleocapsid antigen were detected in serum specimens using corresponding ELISA kits (Pishtaz Teb Diagnostics, Tehran, Iran; cat. numbers: PT-CoV2 IgM-96, and PT-CoV2 IgG-96) according to manufacturer's instructions. Briefly, the serum samples were diluted 1:100 in assay buffer (and incubated for 20 min at room temperature in case of IgM detection) before adding into appropriate wells. One hundred microliters of each positive and negative control sera and 1:100 diluted serum specimens were added into appropriate wells. After 30 min incubation at 37 °C, the well contents were flicked and washed 5 times using working wash buffer. Next, 100 µl of appropriate conjugates (anti-human IgM-HRP, or anti-human IgG-HRP) were applied into the wells and incubated for 30 min at 37 °C. After washing the wells for 5 times, 100 µl of chromogenic substrate was dispensed into the wells. All plates were incubated at room temperature and darkness for 15 min in order to develop the color. The reaction was then stopped by adding 100 µl stop solution, and the optical densities of the wells were measured at 450 nm as well as 630 nm as the reference filter using ELISA reader (BioTek Instrument Inc., Winooski, VT, USA). Both negative and positive controls were included in all assays. Test values were calculated as sample ODs divided by cut-off index as instructed by the manufacturer. Those test values above 1.1 and below 0.9 were considered positive and negative, respectively, while those values between 0.9 and 1.1 considered to be borderline.

Statistical Analysis

The data was analyzed using SPSS 22.0 software (SPSS Inc., Chicago, IL, USA) and GraphPad Prism software version 8.0 (GraphPad Software, Inc., San Diego, USA). Continuous variables were displayed as mean±standard deviation (mean±SD) and categorical variables were reported as counts and percentages. All groups were tested for normal distribution using the Shapiro–Wilk test. Data are reported as the median and mean ± standard deviation for each group. Mann–Whitney U test was used for non-parametric comparisons. A p-value less than 0.05 was considered to be statistically significant. Asterisks *, **, and *** were used in order to show those p-values between 0.01–0.05, 0.001–0.01, and 0.0001–0.001, respectively.

RESULTS

Of 72 HCWs enrolled in the study, 62.5% were female and mean of age was 39.7 years (95% CI, 37.9-41.6) (Table 1). Based on the clinical manifestations, 25.0% (18/72), 47.2% (34/72), and 27.8% (20/72) of HCWs were categorized as symptomatic with typical symptoms, symptomatic with atypical symptoms, and asymptomatic, respectively. The median time of symptom onset to blood sampling was 29 days (95% CI, 25-36) with range of 5-49 days. Chest CT patterns in the favor of COVID-19 and SARS-CoV-2 RNAs were found in 26.3% (10/38) and 38.8% (19/49) of HCWs, respectively (Table 1). Symptomatic individuals with typical and atypical symptoms were 63.2% and 36.8% positive in RT-PCR test, respectively.

Anti-SARS-CoV-2 IgM and IgG antibodies

Table 1. Demographic and clinical characteristics of 72 enrolled health-care workers

Characteristic	Results
Age (years), Mean±SD	39.7±7.53, (95% CI, 37.9-41.6) Range of 23-66
Male	37.5% (27/72)
Female	62.5% (45/72)
SARS-CoV-2 RT-PCR	
Positive	38.8% (19/49)
Negative	61.2% (30/49)
Lung CT scan finding	
Positive	26.3% (10/38)
Negative	73.7% (28/38)

Table 2. Serological detection of anti-SARS-CoV-2 antibodies in health-care workers and general population

	Ab (s)	Positive
Health-care workers	IgM	15.3% (11/72)
	IgG	27.8% (20/72)
	IgM and/or IgG	31.9% (23/72)
	IgM and/IgG	12.5% (9/72)
General population	IgM	8% (162/2021)
	IgG	14.4% (290/2021)
	IgM and/or IgG	17.8% (359/2021)
	IgM and/IgG	IgM and/IgG

Table 3. SARS-CoV-2 viral RNA and antibody in the three categorized groups of health-care workers

Test	Symptomatic with typical symptoms	Symptomatic with atypical symptoms	Asymptomatic
RT-PCR	63.2% (12/19)	36.8% (7/19)	0.0% (0/10)
IgM	22.2% (4/18)	17.6% (6/34)	5% (1/20)
IgG	61.1% (11/18)	23.5% (8/34)	5% (1/20)
IgM/IgG	61.1% (11/18)	32.4% (11/34)	5% (1/20)

were detected in 15.3% (11/72) and 27.8% (20/72) of HCWs samples, respectively (Table 2). In the symptomatic persons with typical symptoms, IgM, and IgG were positive in 22.2% and 61.1%, respectively. However, in lower frequency IgM, and IgG were found in 17.6% and 23.5%, in symptomatic HCWs with atypical symptoms, respectively (Table 3 and supplementary Table 1). Anti-SARS-CoV-2 IgM were detectable in 26.3% and 13.3% of HCWs with positive and negative RT-PCR, respectively. In addition, anti-SARS-CoV-2 IgM was identified in 33.3% of HCWs with typical symptoms and positive RT-PCR (Supplementary Table 1). Analysis of IgG antibody indicated that 68.4%, and 10% of HCWs with positive and negative RT-PCR had correspondingly anti-SARS-CoV-2 IgG. Most of IgG positive HCWs (75%; 9/12) were belong to subjects with typical symptoms.

Antibody testing in the general population indicated that SARS-CoV-2 specific IgM and IgG were found in (162/2021) 8%, and (290/2021) 14.4%, respectively (Table 2). Combination of SARS-CoV-2 IgM and/or IgG could slightly increase the frequency

of virus exposure subjects to 17.8%. The frequency of positive cases of IgM and IgG were significantly increased in HCWs compared to the general population (P=0.028 for IgM and P=0.002 for IgG). Additionally, the mean of sample to cut off value of IgM and IgG showed that both SARS-CoV-2 IgM (mean±SD: 1.03±2.75) (P=0.002) and IgG (mean±SD: 2.31±4.42) (P=0.001) in HCWs were significantly higher than those in the general population (Figure 1).

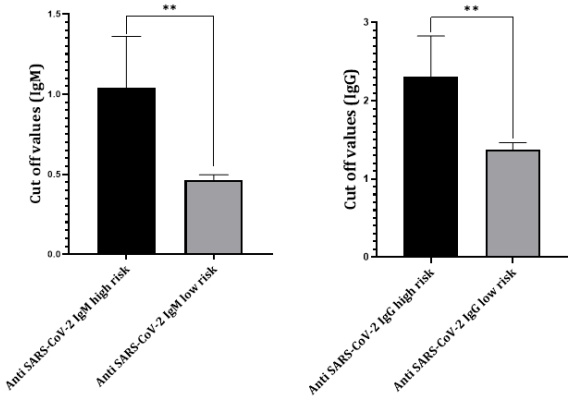

Figure 1. Comparison of SARS-CoV-2 specific IgM, and IgG antibodies in high risk health-care workers and low risk general population

DISCUSSION

Today, the COVID-19 pandemic is the major challenge for public health systems globally (18). It is well-known that SARS-CoV-2 has ability to transmit through respiratory tract by infected droplets between people via close contact. The highest viral load is seen in COVID-19 patients near symptoms presentation, which could be an explanation for the fast-spreading nature of this pandemic (19). Like MERS-CoV and SARS-CoV, transmission of SARS-CoV-2 can mainly occur between HCWs employed in the hospital setting who are in close contact with patients (6, 20). Therefore, HCWs are a major high-risk population for infection with SARS-CoV-2. On the other hand, infection with SARS-CoV-2 could be asymptomatic or cause mild and nonspecific symptoms, which intensify the spread of COVID-19 in the community and accordingly pose a substantial challenge in infection control. Hence, focusing on the epidemiological investigation of asymptomatic cases as well as HCWs in terms of active and past exposure to SARS-CoV-2 could be important in understanding real situation of virus transmission in the society. Obviously, early and accurate screening of infected persons with SARS-CoV-2 or asymptomatic carriers could be crucial in preventing the virus spreading.

In the current study, the majority of enrolled HCWs (72.2%) manifested COVID-19 typical and atypical symptoms. In this regard, COVID-19 was confirmed in 38.8% of HCWs by SARS-COV-2 specific RT-PCR. Serological findings revealed that 31.9% of HCWs had detectable IgM and/or IgG to SARS-CoV-2 in their serum. Interestingly, the proportion of infected HCWs reached 68.4% whenever the combination of RT-PCR along with serology results used for analysis of active or past exposure to the SARS-CoV-2. In 16.7% (5/30) of individuals with undetectable viral RNA, IgM/IgG were positive that indicated the importance of both molecular and serological testing for more efficient case finding approaches as mentioned in other studies (15, 21-23). In one case, following IgM positivity for SARS-CoV-2, the COVID-19 was confirmed by RT-PCR. In a study conducted by Delgado and colleagues, the rate of SARS-CoV-2 infection was investigated in HCWs and personnel of a large public hospital in Madrid, Spain during March 2020 (24). The SARS-CoV-2 infection was confirmed in 38% of enrolled HCWs using RT-PCR method. There were no significant differences in the frequency of positive subjects who had close contact with COVID-19 patients and clerical, administrative or laboratory personnel without direct contact with patients (24). The reported percentage of the infection rate in HCWs is in line with our findings with 38.8% of PCR confirmed HCWs cases. In another study in two Dutch hospitals, March 2020, 6% of HCWs were confirmed for SARS-CoV-2 infection using RT-PCR specific to the E-gene of the virus. Fever and/or coughing

and/or shortness of breath were reported in 92% HCWs (25). Hunter et al. studied SARS-CoV-2 incidence in 1654 staff (mainly hospital employees and local general practitioners) in an English hospital. They pointed out that RdRp gene of SARS-CoV-2 was detected in 14% of HCWs (26). Interestingly, nonclinical staff had similar positivity rates compared to frontline staff and thus isolation protocols and personal protective equipment appear sufficient to prevent high levels of nosocomial transmission to frontline staff (26). The applied methodology in these works was different from WHO recommendation for detection of at least two different targets on the COVID-19 virus genome in RT-PCR (27). In addition, Corman et al. suggested confirmatory testing with the RdRp gene after the first-line screening using E gene of SARS-CoV-2 (7). Thus, it might lead to a lower sensitivity of RT-PCR in finding infected individuals. In addition, the sampling method of oropharyngeal swabbing with 32% sensitivity is not the optimum sample for the molecular testing in COVID-19 (28). Thus, the lower frequency of SARS-CoV-2 infected HCWs in these studies might be due to major false negative results. To the best of our knowledge there is no published work on serology assay on HCWs, thus, we could not compare our findings with others.

Antibody testing in the general population as a low risk group indicated that SARS-CoV-2 specific IgM, and IgG were found in 8%, and 14.4%, respectively. Cumulative frequency of virus exposure in general population was 17.8% if the presence of IgM and/or IgG would be considered for analysis. It is noteworthy to note that sensitivity and specificity of SARS-CoV-2 ELISA kits were 79.4%, 97.3% in case of IgM and 98.3% and 94.1% for IgG, respectively. The positive predictive value and negative predicated value basically affected by the disease prevalence. Based on recently published work, the prevalence of COVID-19 in Tehran was 16.3% during April 17 and June 2, 2020 that showed overall agreement with our findings in HCWs and GPs (29). Thus, the positive predictive value and negative predicated value were 47% and 54% for IgM and 53% and 48% for IgG, respectively. In one published data, Shakiba et al. reported seroprevalence of COVID-19 in 196 household from Guilan province, one of the SARS-CoV-2 epicenters in Iran (30). The authors used VivaDiag rapid test to detect IgM/IgG against COVID-19 (VivaChek Biotech, Hangzhou, China) and showed that the prevalence of seropositivity was 22% and test performance adjusted prevalence was 33% (30). The higher reported prevalence in Guilan during April 2020 is compatible with the higher identified infected cases at that time compared to our enrolled general population from Tehran during April 2020. In this regard, Bendavid et al. reported that the frequency of anti-SARS-CoV-2 antibodies was 2.8% using a lateral flow immunoassay in the community of Los Angeles County which was substantially greater than the cumulative number of confirmed cases in the county at the same time (31). The author declared that the reported prevalence could change with new information on the accuracy of the applied test kits. In a cross-sectional study during the outbreak of COVID-19 in Milan, the presence of anti-SARS-CoV-2 IgM/IgG antibodies to nucleocapsid protein was assessed by a lateral flow immunoassay (32). SARS-CoV-2 seroprevalence was found in 4.4-10.8% of healthy adults by the end of April in Mialn, Italy (32). Overall, the observed differences in the seroprevalence of SARS-CoV-2 in different studies around the word could be originated by the assay features (type of assay, sensitivity and specificity, and applied virus antigen in those assays) and the infection rates in the time of sampling. Additionally, our results indicated that titer of SARS-CoV-2 specific IgM and IgG in HCWs were significantly higher than those in the general population (Figure 1) that implied on higher risk of infection in this group due to different causes such as close contact with patients. HCWs are encountering some pressure and facing challenges including

a high risk of infection, and shortage of equipment for emergency situation.

This study has limitations. Small sample size of HCWs which needs to be studied in larger sample in a multicentric study. In addition, self-reporting of clinical manifestation by HCWs could decrease precision of our study. Regards to general population, selection bias should be considered because symptomatic and asymptomatic cases were not excluded by an examination. This bias could increase the seropositivity in the studied population.

In conclusion, although RT-PCR diagnostics will still be vital for identifying acute infection, serological assays could be very essential for identifying the asymptomatic SARS-CoV-2 infected persons, as well as fast screening of HCWs who are at risk of virus infection via their directly and close contact exposure. In addition, combination of serology and molecular techniques could improve the efficiency of case finding approaches in COVID-19 epidemiological studies, which is critical for public health policies for management of the COVID-19. Serological testing in large population provide better insight into the COVID-19 epidemiology and helps the policy-decision makers have better approach for fighting against SARS-CoV-2 spread in the community.

ACKNOWLEDGMENTS

This study financially supported by Shahid Beheshti University of Medical Sciences (grant number 23103). In addition, we would like especially thanks to Pishtaz Teb diagnostics for providing us with the SARS-CoV-2 ELISA kits.

AUTHORSHIP CONTRIBUTION STATEMENT

Sahar Mortezagholi: data collection, analysis, and writing original draft, Davood Rostamzadeh: data analysis, and writing original draft, Reza Jooya: performing the tests, Maryam Eskandarian: performing the tests, Alireza Metvaei: performing the tests, Maedeh Alinejad: blood sampling, filling questioners, data importing, and performing the tests, Sedigheh Vafaei: filling questioners, and performing the tests, Afshin Moniri: data collection, Majid Marjani: data collection, Vahid Younesi: methodology consult, Payam Tabarsi: investigation, methodology, project administration, supervision, validation, writing and editing, and Mahdi Shabani: conceptualization, data curation, formal analysis, investigation, methodology, project administration, supervision, validation, writing and editing.

Conflicts of Interest: None declared.

REFERENCES

1. Guo Y-R, Cao Q-D, Hong Z-S, Tan Y-Y, Chen S-D, Jin H-J, et al. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak–an update on the status. Mil Med Res. 2020; 7:1-10.
2. Xie X, Zhong Z, Zhao W, Zheng C, Wang F, Liu J. Chest CT for Typical Coronavirus Disease 2019 (COVID-19) Pneumonia: Relationship to Negative RT-PCR Testing. Radiology. 2020; 296:E41-E45.
3. Su S, Wong G, Shi W, Liu J, Lai ACK, Zhou J, et al. Epidemiology, Genetic Recombination, and Pathogenesis of Coronaviruses. Trends Microbiol. 2016; 24:490-502.
4. Chen J. Pathogenicity and transmissibility of 2019-nCoV—a quick overview and comparison with other emerging viruses. Microbes Infect. 2020; 22:69-71.
5. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020; 382:1708-1720.
6. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020; 395:497-506.
7. Corman VM, Landt O, Kaiser M, Molenkamp R, Meijer A, Chu DK, et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Euro Surveill. 2020; 25.

8. Wrapp D, Wang N, Corbett KS, Goldsmith JA, Hsieh CL, Abiona O, et al. Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. Science. 2020; 367:1260-1263.
9. Li X, Geng M, Peng Y, Meng L, Lu S. Molecular immune pathogenesis and diagnosis of COVID-19. J Pharm Anal. 2020; 10:102-108.
10. Vashist SK. In Vitro Diagnostic Assays for COVID-19: Recent Advances and Emerging Trends. Diagnostics (Basel). 2020; 10.
11. Zhao J, Yuan Q, Wang H, Liu W, Liao X, Su Y, et al. Antibody Responses to SARS-CoV-2 in Patients With Novel Coronavirus Disease 2019. Clin Infect Dis. 2020; 71:2027-2034.
12. Lou B, Li TD, Zheng SF, Su YY, Li ZY, Liu W, et al. Serology characteristics of SARS-CoV-2 infection after exposure and post-symptom onset. Eur Respir J. 2020; 56.
13. Kimball A, Hatfield KM, Arons M, James A, Taylor J, Spicer K, et al. Asymptomatic and Presymptomatic SARS-CoV-2 Infections in Residents of a Long-Term Care Skilled Nursing Facility - King County, Washington, March 2020. MMWR Morb Mortal Wkly Rep. 2020; 69:377-381.
14. Haveri A, Smura T, Kuivanen S, Osterlund P, Hepojoki J, Ikonen N, et al. Serological and molecular findings during SARS-CoV-2 infection: the first case study in Finland, January to February 2020. Euro Surveill. 2020; 25:2000266.
15. Winter AK, Hegde ST. The important role of serology for COVID-19 control. Lancet Infect Dis. 2020; 20:758-759.
16. Arons MM, Hatfield KM, Reddy SC, Kimball A, James A, Jacobs JR, et al. Presymptomatic SARS-CoV-2 Infections and Transmission in a Skilled Nursing Facility. N Engl J Med. 2020; 382:2081-2090.
17. Dixon BE, Wools-Kaloustian K, Fadel WF, Duszynski TJ, Yiannoutsos C, Halverson PK, et al. Symptoms and symptom clusters associated with SARS-CoV-2 infection in community-based populations: Results from a statewide epidemiological study. medRxiv. 2020.
18. Cao M, Zhang D, Wang Y, Lu Y, Zhu X, Li Y, et al. Clinical Features of Patients Infected with the 2019 Novel Coronavirus (COVID-19) in Shanghai, China. medRxiv. 2020.
19. To KK, Tsang OT, Leung WS, Tam AR, Wu TC, Lung DC, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. Lancet Infect Dis. 2020; 20:565-574.
20. Liu S, Chan T-C, Chu Y-T, Wu JT-S, Geng X, Zhao N, et al. Comparative epidemiology of human infections with Middle East respiratory syndrome and severe acute respiratory syndrome coronaviruses among healthcare personnel. PloS one. 2016; 11:e0149988.
21. Long QX, Liu BZ, Deng HJ, Wu GC, Deng K, Chen YK, et al. Antibody responses to SARS-CoV-2 in patients with COVID-19. Nat Med. 2020; 26:845-848.
22. Yongchen Z, Shen H, Wang X, Shi X, Li Y, Yan J, et al. Different longitudinal patterns of nucleic acid and serology testing results based on disease severity of COVID-19 patients. Emerg Microbes Infect. 2020; 9:833-836.
23. Stowell SR, Guarner J. Role of Serology in the Coronavirus Disease 2019 Pandemic. Clin Infect Dis. 2020; 71:1935-1936.
24. Folgueira MD, Munoz-Ruiperez C, Alonso-Lopez MA, Delgado R. SARS-CoV-2 infection in Health Care Workers in a large public hospital in Madrid, Spain, during March 2020. J Hosp Infect. 2020; 106:357–363.
25. Kluytmans-van den Bergh MFQ, Buiting AGM, Pas SD, Bentvelsen RG, van den Bijllaardt W, van Oudheusden AJG, et al. Prevalence and Clinical Presentation of Health Care Workers With Symptoms of Coronavirus Disease 2019 in 2 Dutch Hospitals During an Early Phase of the Pandemic. JAMA Netw Open. 2020; 3:e209673.
26. Hunter E, Price DA, Murphy E, van der Loeff IS, Baker KF, Lendrem D, et al. First experience of COVID-19 screening of health-care workers in England. Lancet. 2020; 395:e77-e78.
27. WHO. Coronavirus disease (COVID-19) technical guidance: Laboratory testing for 2019-nCoV in humans 2020 [Available from: https://www.who.int/publications/i/item/assessment-tool-for-laboratories-implementing-covid-19-virus-testing.
28. Wang W, Xu Y, Gao R, Lu R, Han K, Wu G, et al. Detection of SARS-CoV-2 in Different Types of Clinical Specimens. JAMA. 2020; 323:1843-1844.
29. Poustchi H, Darvishian M, Mohammadi Z, Shayanrad A, Delavari A, Bahadorimonfared A, et al. SARS-CoV-2 antibody seroprevalence in the general population and high-risk occupational groups across 18 cities in Iran: a population-based cross-sectional study. Lancet Infect Dis. 2020.
30. Shakiba M, Nazemipour M, Salari A, Mehrabian F, Nazari SSH, Rezvani SM, et al. Seroprevalence of SARS-CoV-2 in Guilan Province, Iran, April 2020. Emerg Infect Dis. 2020; 27.
31. Bendavid E, Mulaney B, Sood N, Shah S, Ling E, Bromley-Dulfano R, et al. COVID-19 Antibody Seroprevalence in Santa Clara County, California. MedRxiv. 2020.
32. Valenti L, Bergna A, Pelusi S, Facciotti F, Lai A, Tarkowski M, et al. SARS-CoV-2 seroprevalence trends in healthy blood donors during the COVID-19 Milan outbreak. medRxiv. 2020.

Supplementary Table 1. SARS-CoV-2 related lab findings in health-care workers groups' divided based on clinical symptoms

Code	Age (Year)	SEX	SARS-CoV-2 PCR	Anti-SARS-CoV2 IgM*	Anti-SARS-CoV-2 IgG*	Groups based on symptoms
1	40	Female	NA	0.16	0.04	Symptomatic with typical symptoms
2	36	Female	Negative	0.09	0.05	Symptomatic with typical symptoms
3	43	Female	NA	0.04	0.01	Asymptomatic
4	41	Male	Negative	0.32	0.03	Symptomatic with typical symptoms
5	42	Male	Negative	0.18	0.07	Symptomatic with typical symptoms
6	48	Female	Positive	4.4	19.41	Symptomatic with typical symptoms
7	43	Female	Positive	0.51	9.22	Symptomatic with typical symptoms
8	NA	Female	Positive	11	12.24	Symptomatic with typical symptoms
9	45	Female	Positive	0.23	6.83	Symptomatic with typical symptoms
10	44	Male	Positive	14.82	19.5	Symptomatic with typical symptoms
11	33	Female	NA	6.09	14.22	Symptomatic with typical symptoms
12	37	Female	Positive	0.3	5.23	Symptomatic with typical symptoms
13	24	Female	Positive	0.04	0.03	Symptomatic with typical symptoms
14	23	Female	Positive	0.36	0.05	Symptomatic with typical symptoms
15	32	Female	Negative	0.07	0.07	Symptomatic with typical symptoms
16	31	Female	Negative	0.44	0.06	Symptomatic with typical symptoms
17	50	Female	Positive	0.04	14.1	Symptomatic with typical symptoms
18	36	Female	Positive	1.77	0.66	Symptomatic with typical symptoms
19	49	Male	Negative	0.05	0.23	Symptomatic with typical symptoms
20	47	Male	Negative	0.04	0.05	Asymptomatic
21	37	Female	Negative	4.11	0.04	Symptomatic with typical symptoms
22	30	Female	Positive	2.66	14.5	Symptomatic with typical symptoms
23	44	Female	NA	2.74	15.15	Symptomatic with typical symptoms
24	32	Female	Positive	0.12	0.16	Symptomatic with typical symptoms
25	47	Female	Negative	0.04	0.09	Asymptomatic
26	45	Female	Negative	0.43	0.03	Symptomatic with typical symptoms

27	35	Female	Positive	0.18	2.06	Symptomatic with typical symptoms
28	45	Male	NA	0.06	0.03	Asymptomatic
29	52	Male	Negative	0.04	0.03	Symptomatic with typical symptoms
30	33	Male	NA	0.03	0.05	Symptomatic with typical symptoms
31	33	Male	NA	0.03	0.07	Symptomatic with typical symptoms
32	44	Female	Negative	0.05	0.05	Symptomatic with typical symptoms
33	38	Female	Negative	0.2	0.04	Asymptomatic
34	34	Male	Negative	0.04	0.05	Asymptomatic
35	35	Male	NA	0.06	0.03	Symptomatic with typical symptoms
36	43	Female	NA	0.32	0.06	Asymptomatic
37	45	Female	Negative	0.32	0.03	Asymptomatic
38	44	Female	Negative	0.05	0.03	Asymptomatic
39	42	Male	Positive	0.85	0.89	Symptomatic with typical symptoms
40	45	Female	NA	0.05	0.09	Symptomatic with typical symptoms
41	33	Female	Negative	15.23	11.32	Symptomatic with typical symptoms
42	43	Female	NA	0.07	0.03	Symptomatic with typical symptoms
43	36	Male	Negative	0.12	0.06	Asymptomatic
44	36	Male	Negative	0.04	0.43	Symptomatic with typical symptoms
45	33	Male	Positive	0.05	0.06	Symptomatic with typical symptoms
46	48	Male	Negative	0.24	0.31	Asymptomatic
47	NA	Male	Positive	3.36	15.61	Symptomatic with typical symptoms
48	46	Female	Negative	0.45	0.03	Symptomatic with typical symptoms
49	48	Female	Negative	0.04	0.02	Asymptomatic
50	37	Male	Negative	0.15	0.05	Symptomatic with typical symptoms
51	40	Female	Negative	0.17	0.05	Symptomatic with typical symptoms
52	36	Male	Negative	0.12	0.05	Symptomatic with typical symptoms
53	38	Female	Negative	0.03	0.05	Symptomatic with typical symptoms
54	49	Male	NA	0.06	0.03	Asymptomatic
55	42	Female	Negative	0.3	0.27	Symptomatic with typical symptoms
56	41	Female	Negative	2.02	4.69	Asymptomatic
57	37	Female	NA	0.06	0.03	Asymptomatic
58	28	Female	NA	0.11	0.02	Asymptomatic
59	50	Female	Negative	0.24	2.94	Symptomatic with typical symptoms
60	27	Male	Negative	0.256	0.077	Symptomatic with typical symptoms

61	NA	Female	Positive	0.388	3.91	Symptomatic with typical symptoms
62	46	Female	Positive	0.655	25.577	Symptomatic with typical symptoms
63	29	Male	Negative	0.202	0.346	Symptomatic with typical symptoms
64	31	Female	NA	0.186	0.109	Asymptomatic
65	66	Female	Positive	0.713	2.378	Symptomatic with typical symptoms
66	41	Male	NA	0.547	0.679	Asymptomatic
67	NA	Male	NA	0.24	0.122	Asymptomatic
68	NA	Male	NA	0.229	0.09	Asymptomatic
69	NA	Male	NA	0.36	13.333	Symptomatic with typical symptoms
70	37	Female	Positive	0.213	0.615	Symptomatic with typical symptoms
71	NA	Male	NA	0.826	10.474	Symptomatic with typical symptoms
72	35	Female	NA	0.248	7.801	Symptomatic with typical symptoms

NA: not available; *Test values were calculated as sample ODs divided by cut-off index. Those test values above 1.1 and below 0.9 were considered positive and negative, respectively, while those values between 0.9 and 1.1 considered to be borderline.