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Original Article

코로나19 병동의 의료기관 종사자들의 SARS-CoV-2의 항체 양성률

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Severe Acute Respiratory Syndrome Coronavirus-2 Antibody Seropositivity among Healthcare Workers Working in Coronavirus Disease Wards

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Background: Healthcare workers (HCWs) involved in the care of patients with coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are at risk of being infected. This study aimed to investigate the seropositivity of SARS-CoV-2 among the HCWs.

Methods: From June to July 2020, 151 serum samples of HCWs involved in the care of COVID-19 patients from two hospitals in South Gyeongsang Province, South Korea, were collected to test for the presence of SARS-CoV-2 immunoglobulin G (IgG) antibodies. Epidemiologic data were collected using a questionnaire.

Results: Among the 151 HCWs, 3 (2.0%) had detectable SARS-CoV-2 IgG. Two of them were nurses working in the COVID-19 ward of the first hospital and had no direct contact with confirmed COVID-19 patients without personal protective equipment (PPE). The other HCW worked at the infection prevention office and was 6 weeks pregnant at the time of the study. In this study, 19 participants self-reported 33 episodes of contamination during PPE removal, but none of them tested positive.

Conclusion: This study reported a seropositivity rate of 2.0% for SARS-CoV-2 IgG among HCWs. Following the exclusion of an HCW with a suspected false-positive result, the adjusted rate was 1.3%, which was higher than that reported at approximately the same time in the community (0.07%). However, there was no evidence of viral transmission among the colleagues of that HCW in this study. Standard precautions, proper monitoring, and PPE use could help prevent the spread of COVID-19 in hospital settings.

Key Words: COVID-19, HCWs, SARS-CoV-2, Seropositivity

Introduction

Healthcare workers (HCWs) involved in the treatment of patients with coronavirus disease (COVID-19) are at a high risk of infection. However, the identification of asymptomatic severe acute respiratory syndrome coronavi-

rus-2 (SARS-CoV-2) infections remains challenging [1]. Therefore, it is essential to compare the antibody-positive rate of HCWs with that of the community members. A research conducted from April to June 2020 in Seoul (Korea) showed 0.07% anti-SARS-CoV-2 antibody seropositivity among 1,500 outpatients from university hospitals [2]. In a previous report of June 2020, the number of confirmed COVID-19 cases per 1 million people in Seoul and South Gyeongsang Province was 102.4 and 35.7, respectively [3].

Since November 2020, the incidence of COVID-19 in South Korea has been increasing rapidly. In January 2021, the number of confirmed cases per 1 million people was 1324.3 in Korea, 2068.2 in Seoul, and 418.6 in South Gyeongsang Province.

The positivity rate of SARS-CoV-2 antibodies in the community is expected to change drastically within few months, owing to the rapidly increasing incidence of COVID-19 in Korea. Therefore, assessing the prevalence of SARS-CoV-2 antibodies among the hospital staff working in COVID-19 wards can help evaluate the risk of contracting SARS-CoV-2 infection in this group as compared to the community members. Moreover, it would be useful to accumulate data on whether standard precautions, such as the use of masks and effective hand hygiene protocols, are effective in preventing the spread of the disease in cases of asymptomatic infection among the hospital staff. Furthermore, it would be relevant to determine the effectiveness of the use of personal protective equipment (PPE) and the protocols of donning and doffing PPE in preventing SARS-CoV-2 infection.

Therefore, this study aimed to identify the seropositivity rate among HCWs in two hospitals in South Gyeongsang Province: a COVID-19-dedicated hospital and a tertiary hospital treating patients with severe clinical manifestations transferred from the COVID-19-dedicated hospital. Furthermore, we evaluated the correlation between the self-reported history of unintended contamination and the SARS-CoV-2 antibody seropositivity rate among the HCWs.

Materials and Methods

1. Study subjects

This study was performed at the Masan Medical Center (Hospital 1) and Yangsan Pusan University Hospital (Hospital 2) in the Republic of Korea. Hospital 1 is a public hospital located in South Gyeongsang Province and the primary COVID-19-dedicated hospital for asymptomatic and mild COVID-19 cases. Hospital 2 is a tertiary hospital that treats severe-to-critical COVID-19 patients.

The inclusion criteria for the HCWs were as follows: participation in treatment, transfer management, cleaning, waste disposal, and specimen processing of COVID-19 patients from January 20 to July 10, 2020; never been diagnosed with COVID-19; not in quarantine at the time of blood collection; no COVID-19-related symptoms such as fever, cough, and sore throat at the time of the study; and voluntary participation. By the time of blood collection, Hospital 1 had treated approximately 70 COVID-19 patients, while Hospital 2 had provided medical services to 16 such patients since January 2020. Individuals with positive antibody results were subjected to reverse-transcriptase polymerase chain reaction (PCR) test for SARS-CoV-2 to rule out an active infection.

2. Measurements

From June to July 2020, we collected 5 mL of blood from each participant, and the serum was preserved at 4℃ after centrifugation. Anti-SARS-CoV-2 immunoglobulin G (IgG) antibodies were detected in the sera using semi-quantitative enzyme-linked immunosorbent assay (Euroimmun Medizinische Labordiagnostika, Lübeck, Germany) according to the manufacturer's instructions. A self-reported questionnaire was used to collect information on age, sex, history of SARS-CoV-2 PCR testing, history of COVID-19-related symptoms during work at the COVID-19 isolation wards, unintentional exposure, type of PPE used, and type of procedure involved (applicable to doctors and nurses only). The SARS-CoV-2

PCR test was performed for the samples of individuals with a positive SARS-CoV-2 antibody test to rule out an active infection, regardless of the presence or absence of symptoms. Moreover, the epidemiological data of all subjects was subjected to descriptive analysis, wherein the data of participants with positive test results were reviewed in detail. Statistical analyses were performed using Statistical Product and Service Solutions, version 26.0 (IBM Corp., Armonk, NY, USA). In order to compare the characteristics of the HCW groups of the two hospitals, categorical variables were analyzed using Pearson's chi-squared test or Fisher's exact test and continuous variables using student's t-test.

Results

The number of medical staff members of Hospital 1 and Hospital 2 involved in the treatment of confirmed COVID-19 patients was 110 and 100, respectively. Among them, 103 (93.6%) from Hospital 1 and 48 (48%) from Hospital 2 were enrolled in this study, comprising 10 physicians, 101 nurses, and 40 staff members of other occupations (Table 1). Three nurses tested positive for the SARS-CoV-2 antibody test, but their colleagues working in the same department tested negative.

Among these three nurses, two had worked in the COVID-19 ward for 84 and 62 days, respectively (Table 2); the third nurse had worked at the infection prevention office and had not participated directly in the treatment of any COVID-19 patients. She managed patient transfers, i.e., the guidance of ambulances on separate access and management of the transfer so that no additional people would be exposed during patient transfers. She mainly worked while wearing PPE and retained a distance of more than 2 m from the COVID-19 patients. Since she was 6 weeks pregnant at the time of blood collection, the antibody test result was likely to be false positive [4,5].

The two nurses working in the COVID-19 ward did not experience flu-like symptoms nor did they self-report any contamination while doffing the PPE until the blood collection in this study. Moreover, they had no direct contact with any HCWs with COVID-19 before the start of this study. They underwent one PCR test for SARS-CoV-2 while conducting a full-scale examination of the medical

Table 1. Characteristics of participants in hospitals 1 and 2

	Hospital 1	Hospital 2	Total	*P* value
Total (n)	103	48	151	
SARS-CoV-2 IgG (n, (%))	2 (1.9)	1 (2.1)	3 (2.0)	0.954
Age (mean, 2SD)	35.41±12.10	32.85±7.42	34.60±10.88	0.180
Sex				
Female	100 (97.1)	41 (85.4)	141 (93.4)	0.012
Male	3 (2.9)	7 (14.6)	10 (6.6)	
Occupation (n, (%))				
Doctor	4 (3.9)	6 (12.5)	10 (6.6)	0.074
Nurse	72 (69.9)	29 (60.4)	101 (66.9)	0.249
Laboratory technologist	0	5 (10.4)	5 (3.3)	0.004
Radiology technologist	0	4 (8.3)	4 (2.6)	0.009
Nurse assistant	27 (26.2)	3 (6.3)	30 (19.9)	0.011
Hospital office worker	0	1 (2.1)	1 (0.7)	1.000
Work experience (years)	6.94±7.022	7.77±5.104	7.21±6.469	0.414
Participants with symptoms* (n, (%))	15 (14.6)	9 (18.8)	24 (15.9)	0.512
Working period related to COVID-19 (days)	82.28±25.624	63.94±20.71	76.45±25.28	<0.0001
Self-reported contamination during doffing of PPE† (times/person)	0.13±0.518	0.42±0.846	0.22±0.625	0.010
Self-reported contamination during doffing of PPE (n, (%))	6 (5.8)	13 (27.1)	19 (12.6)	0.001
Number of participants in self-quarantine*	6	1	7	0.432
Number of times SARS-CoV-2 PCR‡ was performed (mean, 2SD)	1.53±0.623	0.79±0.939	1.28±0.826	<0.0001

*Symptoms: cough, sputum, sore throat, febrile sensation, myalgia, headache.
†Personal protective equipment.
‡Polymerase chain reaction.

Table 2. Characteristics of three participants with SARS-CoV-2 seropositive antibody test results

	Case 1	Case 2	Case 3
Affiliated hospital	Hospital 1	Hospital 1	Hospital 2
Sex	Female	Female	Female
Age (years)	25	26	31
Occupation	Nurse	Nurse	Nurse in the infection prevention office
Working period as a health care worker (years)	4	6	8
Working period in COVID-19 wards (days)	84	62	0
Working arrangement	3 shifts	3 shifts	8 hours during daytime and additional on-call
Presence of symptoms	None	None	None
Contact history with patients with COVID-19 without PPE	None	None	None
Type of PPE	Level D	Level D	Level D or 5-piece set*
Self-reported contamination during doffing of PPE	None	None	None
Number of times COVID-19 PCR was performed before blood collection	2	1	0
COVID-19 PCR at the time of blood collection	Negative	Negative	Negative
Possible interpretation of the test results	Asymptomatic infection	Asymptomatic infection	False-positive result or possible asymptomatic infection

*5-piece set; includes hat, N95 mask, gloves, gown, and overshoes.

staff in COVID-19 wards in Hospital 1, and one nurse was retested to confirm the negative result just before returning to another department. The members of the medical staff in Hospital 1 were thoroughly tested before this study started because that hospital had a confirmed COVID-19 case of a nurse, who was excluded from this study. Since the HCW was confirmed to have COVID-19, PCR test for SARS-CoV-2 was performed for all medical staff members involved in the treatment of COVID-19 patients in Hospital 1. No additional positive cases were reported. All HCWs who were in close contact with her during the infectious period (from 2 days before the onset of symptoms) were self-quarantined for 14 days. HCWs working in COVID-19 wards had limited contact with others, because they did not use the staff cafeteria. Thus, six members of the medical staff who were in self-quarantine were included in the study. Notably, this study included all six employees who had direct contact with the nurse infected with SARS-CoV-2, and their antibody test results were negative.

The two nurses who tested positive had never worked with the nurse confirmed with COVID-19 at the same time or same zone during the period of possible transmission. Furthermore, the two nurses hardly ever worked or ate together according to their recollection. Therefore, there is a limited correlation between previous infection in the other medical staff members and the positive results of the two nurses in this study.

Unintended exposure events during doffing of PPE through self-reporting were frequent in Hospital 2. However, there were no cases of SARS-CoV-2 seropositivity due to such exposure events. Hospital 1 was responsible for the treatment of patients with mild COVID-19, whereas Hospital 2 contributed to the clinical care of patients with severe or critical COVID-19. Consequently, most high-risk procedures, such as tracheal intubation, endotracheal aspiration, and nebulization, were performed in Hospital 2. The high rate of self-reported unintended contamination in Hospital 2 could be attributed to the pressure involved in performing high-risk procedures, resulting in a more sensitive reaction and a heightened memory of unintended contamination. However, these contamination events would probably not be associated with infection transmission if they were followed by appropriate disinfection.

Discussion

In this study, the seropositivity rate of SARS-CoV-2 antibodies in HCWs from the two hospitals was 2.0%.

However, following the exclusion of a case with suspected false-positive result, the adjusted rate was 1.3%. The prevalence of SARS-CoV-2 antibodies among HCWs was found to be higher than that among the community members (0.07%) at approximately the same time of this study [2].

By mid-2020, the incidence of SARS-CoV-2 infection in South Korea varied by region, and reports of sudden outbreaks in Daegu were estimated at 2,837 cases per 1 million people in June 2020 [3]. In a recent study, the estimated seroprevalence in Daegu was 7.6% [6]. In contrast, the number of confirmed COVID-19 cases per 1 million people was 235.5 in Korea, 102.4 in Seoul, and 35.7 in South Gyeongsang Province. Thus, this suggests that the 1-2% positive rate of SARS-CoV-2 antibodies of the HCWs is higher than that of the community members. Given the lack of specimens and the limited number of tests, our cohort might not be representative of the medical staff members working in COVID-19 wards. Therefore, our results should be interpreted cautiously.

Because the SARS-CoV-2 IgG test is not completely accurate, its results should be interpreted with caution. The performance of the Euroimmun assay has been evaluated in some studies, showing an IgG sensitivity of 85-95% and specificity of 95-100% more than 14 days after symptom onset [7,8]. In this study, we examined the presence of antibodies induced by a previously unrecognized infection rather than by acute infection; hence, we used the Euroimmun assay based on previously reported results [7,8]. It is necessary to recognize the limitations of the low positive predicted value, because this study was conducted at a time when the prevalence rate in the community was low. Nevertheless, it is important that the medical staff participating in the care of confirmed COVID-19 patients showed a higher positive antibody rate than that reported by the previous SARS-CoV-2 antibody study on community members. This could translate to a greater probability of exposure to SARS-CoV-2 for HCWs.

As mentioned earlier, 2 months before the initiation of the study, one nurse was infected with SARS-CoV-2 in Hospital 1. However, this incident did not cause an infection outbreak in the hospital. Our study confirmed negative results for SARS-CoV-2 antibodies in the colleagues who had close contact with the infected HCW. Self-reported unintentional COVID-19 contact history during the doffing of PPE was not associated with positivity of SARS-CoV-2 antibodies. Thus, if contamination during the doffing of PPE is detected immediately and proper disinfection is performed, the risk of SARS-CoV-2 infection may be reduced. However, the risk of infection could be more closely related to unrecognized viral contamination than to recognized unintentional contamination. More meticulous self-monitoring and, if possible, monitoring by colleagues to prevent infection during donning or doffing of PPE should be conducted.

Following the exclusion of one suspected false-positive result, two participants might have had asymptomatic infections. Several studies have reported that the viral loads detected in asymptomatic populations are similar to those in symptomatic patients, indicating that asymptomatic infection has transmission potential [1,8]. Hence, it is not only important to wear appropriate PPE when treating confirmed or suspected COVID-19 patients, but also to maintain standard precautions to prevent transmission through asymptomatic cases [9]. Both hospitals strongly recommended effective hand hygiene and the use of masks in all departments. This study shows that these policies can contribute to the prevention of SARS-CoV-2 outbreaks in hospital settings. The HCWs who participated in this study wore level D PPE or other PPE in line with the Korean SARS-CoV-2 treatment guidelines, and appropriate monitoring of the process and self-reporting of contamination during doffing of PPE were conducted in both hospitals.

A report from Germany demonstrated that the seropositive rate of HCWs with daily contact with known or suspected SARS-CoV-2-positive patients was 1.6% [10], which was similar to that in our study. Furthermore, HCWs in high-risk departments, where hand hygiene and protective equipment are well maintained, had a lower antibody positive rate than those in the intermediate-risk group [10]. In the United States, the SARS-CoV-2 infection rate among HCWs was reported to be lower than that

of the general population [11]. Researchers have suggested that proper PPE use is the reason for HCWs having a lower SARS-CoV-2 antibody positivity rate than that of the community members [10]. Based on these findings and those of our study, it seems that the use of masks and proper PPE and maintaining hand hygiene in all areas of the hospital are effective ways of preventing SARS-CoV-2 transmission.

This study has several limitations. First, it included a limited number of participants. Since enrollment in the study was voluntary, it was not possible to examine all medical staff members suspected of exposure. Second, SARS-CoV-2 seroprevalence data of the community of South Gyeongsang Province, Korea were not available. However, during the study period, the incidence of COVID-19 in South Gyeongsang Province was lower than that in Seoul; hence, the seroprevalence of SARS-CoV-2 antibodies in South Gyeongsang Province was expected to be lower than 0.07%. Third, the survey was based on self-reporting of the participants; hence, there may have been some recall bias. However, it was necessary to rely on participant self-reports to investigate the association between SARS-CoV-2 seropositivity and unexpected exposure to SARS-CoV-2 while using appropriate PPE. Consequently, we assume that the positivity rate of SARS-CoV-2 antibodies among HCWs in this study may be significantly higher than that of the community. Third, possible false-positive and false-negative results are known limitations of serological tests for SARS-CoV-2. Finally, family members of HCWs could not be tested to identify the asymptomatic individuals among them.

Nevertheless, this study is important for several reasons. First, it included HCWs from two hospitals who participated in the clinical care of patients with confirmed COVID-19 in Korea. Second, we demonstrated that the use of masks and appropriate hand hygiene could be beneficial in preventing SARS-CoV-2 transmission among HCWs. Third, recognizing unintentional contact with SARS-CoV-2 and taking appropriate disinfection measures may reduce the risk of infection, whereas unrecognized contamination could be more closely related to infection transmission. Monitoring and self-reporting systems regarding the donning or doffing of PPE can contribute to the prevention of SARS-CoV-2 infection among HCWs.

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Disclosure of conflict of interest

The authors declare no competing interests.

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Conceptualization: Seungjin Lim, Su Jin Lim
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Ethics statement

The study protocol was reviewed and approved by the Institutional Review Board of Yangsan Pusan University Hospital (Approval No. 05-2020-121).

References

1. Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, et al. SARS-CoV-2 viral load in upper respiratory specimens of infected patients. N Engl J Med 2020;382:1177-9.
2. Noh JY, Seo YB, Yoon JG, Seong H, Hyun H, Lee J, et al. Seroprevalence of anti-SARS-CoV-2 antibodies among outpatients in southwestern Seoul, Korea. J Korean Med Sci 2020;35:e311.
3. Center for Infection Prevention and Control (CIPAC). Number of confirmed COVID-19 cases million people. Commun Dis Wkly Update 2020;5:234.
4. Emmerich P, Murawski C, Ehmen C, von Possel R, Pe-

karek N, Oestereich L, et al. Limited specificity of commercially available SARS-CoV-2 IgG ELISAs in serum samples of African origin. Trop Med Int Health 2021;26:621-31.
5. Dörschug A, Schwanbeck J, Hahn A, Hillebrecht A, Blaschke S, Mese K, et al. Comparison of five serological assays for the detection of SARS-CoV-2 antibodies. Diagnostics (Basel) 2021;11:78.
6. Song SK, Lee DH, Nam JH, Kim KT, Do JS, Kang DW, et al. IgG seroprevalence of COVID-19 among individuals without a history of the coronavirus disease infection in Daegu, Korea. J Korean Med Sci 2020;35:e269.
7. Nicol T, Lefeuvre C, Serri O, Pivert A, Joubaud F, Dubée V, et al. Assessment of SARS-CoV-2 serological tests for the diagnosis of COVID-19 through the evaluation of three immunoassays: two automated immunoassays (Euroimmun and Abbott) and one rapid lateral flow immunoassay (NG Biotech). J Clin Virol 2020;129:104511.
8. Hanssen DAT, Slaats M, Mulder M, Savelkoul PHM, van Loo IHM. Evaluation of 18 commercial serological assays for the detection of antibodies against SARS-CoV-2 in paired serum samples. Eur J Clin Microbiol Infect Dis, in press 2021.
9. Walsh KA, Jordan K, Clyne B, Rohde D, Drummond L, Byrne P, et al. SARS-CoV-2 detection, viral load and infectivity over the course of an infection. J Infect 2020;81:357-71.
10. Heinzerling A, Stuckey MJ, Scheuer T, Xu K, Perkins KM, Resseger H, et al. Transmission of COVID-19 to health care personnel during exposures to a hospitalized patient - Solano County, California, February 2020. MMWR Morb Mortal Wkly Rep 2020;69:472-6.
11. Korth J, Wilde B, Dolff S, Anastasiou OE, Krawczyk A, Jahn M, et al. SARS-CoV-2-specific antibody detection in healthcare workers in Germany with direct contact to COVID-19 patients. J Clin Virol 2020;128:104437.