Note

Evaluation of Seroprevalence of SARS-CoV-2 IgG in Healthcare Workers in a Tertiary Hospital in Seoul

Minjeong Nam, Hee-Won Moon, Hanah Kim, Mina Hur, Yeo-Min Yun
Department of Laboratory Medicine, Konkuk University School of Medicine, Seoul, Korea

서울의 3차 의료기관 의료인에서 SARS-CoV-2 IgG 혈청 유병률 평가

남민정, 문희원, 김한아, 허미나, 윤여민
건국대학교병원 진단검사의학과

ABSTRACT

Healthcare workers (HCWs) may be at high risk for exposure to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) because of their frequent contact with patients or the direct handling of respiratory samples. We investigated the seroprevalence of SARS-CoV-2 IgG in HCWs in Seoul compared to those in coronavirus disease (COVID-19) patients and community-based individuals to evaluate the antibody response. A total of 358 samples from 348 individuals (155 HCWs, 7 COVID-19 patients, and 186 community-based individuals) were collected from April to November 2020. SARS-CoV-2 IgG was detected in 1 of 155 HCWs (1 of 46 HCWs with direct contact), 7 of 7 COVID-19 patients, and none of the 186 community-based individuals (95% CI: 0.6%, 0.1 - 3.6%; 100%, 64.5 - 100%; 0.0%, 0.0 - 2.0%, respectively). The single HCW with a positive result showed 2.32 signal-to-cutoff (S/C) and 2.31 S/C at a 3-week interval. Therefore, it was assumed to be a false positive due to autoantibody or medication. The positive samples from 7 patients had a median of 3.79 S/C (range 1.72 - 6.54). The seroprevalence of SARS-CoV-2 IgG in HCWs was very low. The current infection control standard seems to be effective in protecting HCWs from COVID-19.

Keywords: Healthcare workers, SARS-CoV-2 IgG, Seroprevalence

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Corresponding author
Hee-Won Moon
E-mail: hannasis@hanmail.net
Tel: +82-2-2030-5587
Fax: +82-2-2030-5587

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The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a pandemic causative agent of coronavirus disease (COVID-19). The clinical features of COVID-19, which is spread predominantly from person to person, are varied, ranging from asymptomatic to critical and deceased [1]. According to the World Health Organization (WHO), by October 15, 2020, SARS-CoV-2 had spread to 180 countries with approximately 31 million confirmed patients and 1.0 million deaths [2]. At the same time in South Korea, a total of 20,182 confirmed cases were reported, of which the majority were from Seoul (3,961, 19.6%) and Gyeonggi-do (near Seoul, 3,323, 16.5%) [3]. The confirmatory test for SARS-CoV-2 is nucleic acid amplification (NAT), but the interest in serologic assays, used to detect antibodies against SAR-CoV-2, is increasing. The determination of seroprevalence among community-based individuals and

specific groups will allow us to identify true COVID-19 patients and accurately calculate the mortality rate. It will also provide better insight into the pandemic nature and may help us estimate how far we are from reaching the herd immunity threshold [4]. Healthcare workers (HCWs) are a vulnerable group since they are highly exposed to SARS-CoV-2 owing to their frequent contact with patients or direct handling of respiratory samples. In South Korea, the Korea Disease Control and Prevention Agency (KDCA) has released official personal protective equipment (PPE) guidelines for HCWs. According to these guidelines, HCWs should routinely wear a dental mask and use KF94 equivalent filtering respirator protector or powdered air-purified respirators with whole-body protective clothing and safety glasses, depending on the situation [5]. As the pandemic crisis progresses, it is becoming increasingly difficult to accurately predict the seroprevalence of HCWs as there is a wide variation in official PPE guidelines by country, sample size, and methodology [6]. This study aimed to investigate the seroprevalence of HCWs in a tertiary hospital in Seoul in comparison with community-based individuals and COVID-19 patients. This cross-sectional cohort study was performed from April to November 2020 at the Konkuk University Medical Center (KUMC). During the study period, approximately 20 COVID-19 patients were treated in the KUMC, a 900-beds tertiary-care hospital (3 bed for COVID-19 patients) located in the Middle East of Seoul. Among the total of 2,547 HCWs, this study included 155 HCWs (doctors, 29/155, 18.7%; nurses, 36/155, 23.2%; laboratory personnel, 26/155, 16.8%; radiographers, 31/155, 20.0%; and administrative staff, 33/155, 21.3%). All HCWs used appropriate PPE under the national guidelines [5]. Almost all HCWs were vaccinated against the influenza virus, due to an annual infection control policy from October 12 to October 14, 2020. Among all HCWs, 46 HCWs (29.7%) treated and nursed COVID-19 patients, collected samples, or performed laboratory tests or radiography. Samples of 155 HCWs were collected from October 15 to October 16, samples of 7 COVID-19 (16 samples) patients from April to October, and 186 community-based individuals, who visited for general examination from October to November. The median age (years) of each group was 40 years (range: 21 - 66 years), 73 years (range: 23 - 82 years), and 39 years (range: 20 - 78 years), and the ratio of females was 72.3% (112/155), 57.1% (4/7), and 68.8% (128/186), respectively. Except COVID-19 confirmed patients, the participants did not have fever or respiratory symptoms during a period of 14 days before blood sampling. Demographic and clinical information of HCWs were collected using a structured questionnaire. Seven patients with SARS-CoV-2 were confirmed positive by RT-PCR assay for SARS-CoV-2 (Seegene Inc., Seoul, Korea). The 186 community-based individuals were selected based on gender and age criteria to match the 155 HCWs. This study was approved by the Institutional Review Board of KUMC (IRB No. 2020-08-031-003). For the SARS-CoV-2 IgG assay, informed consent was obtained from HCWs but not from the COVID-19 patients and individuals undergoing general examination since we used samples leftover after performing all the requested tests. SARS-CoV-2 IgG was tested in a qualitative manner with a cutoff of 1.4 signal-to-cutoff (S/C) using SARS-CoV-2 chemiluminescent microparticle immunoassay (CMIA) kit (nucleocapsid protein-based assay; Abbott, Sligo, Ireland) and the Alinity i system (Abbott Laboratories, Abbott Park, Illinois, USA) according to the manufacturer's recommendation. SARS-CoV-2 IgG was detected in 1 of 155 (0.6%, 95% CI, 0.1 - 3.6%) HCWs, 7 of 7 (100%, 95% CI, 64.5 - 100%) COVID-19

patients (from 9 out of 16 samples from 7 patients depending on collection time), and was not detected in the community-based population (0.0%, 95% CI, 0.0 - 2.0%). The SARS-CoV-2 IgG in an HCW with positive results showed 2.32 and 2.31 S/C when tested three weeks apart, and 9 of 16 samples from the COVID-19 patients showed a median S/C of 3.79 (range: 1.72 - 6.54 S/C) (Table 1). The median seroconversion for SARS-CoV-2 IgG was 12.5 days (range: 8 - 14 days) after diagnosis by RT-PCR in all COVID-19 patients except one, diagnosed in another hospital and then transferred to this institution (Table 2). To date, a lot of point-of-care or fully automated methods have been developed to detect SARS-CoV-2 antibodies, and it is essential to evaluate their performance and usefulness in clinical laboratories before implementing them for patient management and pandemic control. According to previous reports, the Abbott SARS-CoV-2 IgG assay has high sensitivity (80.5 - 94.6%) and specificity (95.1 - 100%), and low cross-reactivity [7-9]. Chen et al. [9] demonstrated that the Abbott SARS-CoV-2 IgG assay cross-reacts with anti-CMV IgM (1.61 and 1.98 S/C) and autoimmune antibodies (2.17 S/C). According to the ELISA manufacturer, the percentage of false positives for SARS-CoV-2 IgG was 2.5% in sera containing autoantibodies and 3.4% in sera obtained from influenza vaccine recipients [4]. Although all HCWs were vaccinated against influenza immediately before the samples were obtained, the period between vaccination and sample collection was short of forming influenza antibodies. Thus, it was not considered a false positive from vaccination. The HCW had ever been in contact with COVID-19 patients with doing radiography, but the RT-PCR for SARS-CoV-2 was negative. He has ankylosing spondylitis (AS) and has undergone treatment for AS with infliximab for several years, which is a DNA-derived chimeric IgG monoclonal antibody used to block tumor necrosis factor alpha [10]. The result of fluorescent antinuclear antibody (FANA) was positive (1:80, homogenous pattern). The S/C values of the HCWs (2.32 and 2.31) were similar to the 2.17 S/C of sera containing autoantibodies which are reportedly cross-reactive with the Abbott SARS-CoV-2 assay [7]. Hence, the positive result of the HCW could be a false positive due to autoantibody or medication. These findings indicate that the seroprevalence (0.6%) of HCWs in this institution was very low. In disagreement with these findings, a more recently published meta-analysis that included 49 studies involving 127,480 HCWs, showed a higher overall seroprevalence of 8.7% (95% CI, 6.7 - 10.9%) [6]. A previous study reported that seroprevalence in North America was higher (12.7%, 95% CI, 8.6 - 17.5%) than that in Europe (8.5%, 95% CI, 5.8 - 11.6%), Africa (8.2%, 95% CI, 0.8 - 22.3%), and Asia (4%, 95% CI, 1.8 - 7.1%) [6]. The seroprevalence in Seoul, Korea, was reported to be about 0.07% among 1,500 outpatients [11], although this previous study was conducted during the period when the number of confirmed COVID-19 patients was half of the time of the present study. Low prevalence in South Korea could be accredited to the various control measures taken by the government since the beginning of the pandemic crisis including promptly updated official PPE guidelines, social distancing, rapid tracing, and intensive mass tests to isolate the patients [12,13]. In this study, the low seroprevalence of HCWs indicated that the current infection control standard, such as routinely wearing a face mask and selecting higher grad PPE in specific situations, effectively protects vulnerable HCWs from COVID-19. SARS-CoV-2 IgG antibody was detected at a median of 12.5 days (range: 8 - 14 days). The observed median S/C in asymptomatic patients with SARS-CoV-2 was 3.72 (range: 1.72 - 6.54), and that in samples from a

symptomatic patient was 6.09 (range: 5.72 – 6.45). In close agreement with the present study, Naaber et al. and Elslande et al. [14,15]. demonstrated that the Abbott SARS-CoV-2 IgG assay targeting the nucleocapsid protein shows faster conversion (7 – 14 days) and low median S/C (Asymptomatic: 3.02, range: 1.99 – 5.21; Symptomatic: 5.61, range: 2.01 – 7.65) than the SARS-CoV-2 IgG assay targeting spike protein. This indicates that different analytical sensitivities and target proteins may result in earlier antibody conversion and decreased antibody levels. This study has several limitations. Firstly, we tested only the Abbott SARS-CoV-2 IgG assay, and hence, could not compare other test kits targeting different viral proteins. Secondly, this study included a small number of symptomatic COVID-19 patients. It is difficult to conclude the SARS-CoV-2 antibody response from the limited number of samples. Therefore, a large-scale study will have to be undertaken in the near future. In conclusion, the seroprevalence of SARS-CoV-2 IgG in HCWs was very low in a tertiary hospital in Seoul and comparable to that of community-based individuals. This might resulted in relative low cumulative prevalence and well controlled SARS-CoV-2 infection in South Korea. In addition, the current infection control standard, including appropriate PPE, seems to be effective in protecting HCWs from COVID-19 patients.

Table 1. Seroprevalence of SARS-CoV-2 IgG in healthcare workers, COVID-19 patients, and community-based population

Variable	Healthcare worker	Patients	Community
Number	155	7	186
Positive, n (%, 95% CI)	1 (0.6%, 0.1 - 3.6)	7 (100%, 64.5 - 100)	0 (0.0%, 0.0 - 2.0)
S/C*	2.32, 2.31	3.79 (1.72 - 6.54)	-

*The values indicate two positive results of an HCW and median (ranges) for positive results of COVID-19 patients.

Abbreviations: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; IgG, immunoglobulin G; COVID, coronavirus disease; n, number; CI, confidence interval; S/C, signal-to-cutoff.

Table 2. Comparison of IgG S/C values in 7 COVID-19 patients

Patient	Clinical features	Test	Gender	Age	Tested days since Dx	S/C	Interpretation
1	Pneumonia	1	F	82	0	0.02	Negative
		2			5	0.43	Negative
		3			11	6.45	Positive
		4			22	5.72	Positive
2	Asymptomatic	1	M	74	0	0.02	Negative
		2			6	0.03	Negative
		3			14	2.64	Positive
3	Asymptomatic	1	M	74	0	0.03	Negative
		2			4	0.02	Negative
		3			13	5.95	Positive
4	Asymptomatic	1	M	73	13	3.72	Positive
5	Asymptomatic	1	F	68	Unknown*	6.54	Positive
6	Asymptomatic	1	F	23	12	3.65	Positive
		2			20	3.79	Positive
7	Asymptomatic	1	F	43	3	0.12	Negative
		2			8	1.72	Positive

*Patient 5 was transferred to our institution after being diagnosed by a confirmatory test at another hospital.

Abbreviations: IgG, immunoglobulin G; S/C, signal-to-cutoff; COVID-19, coronavirus disease; Dx, diagnosis; F, female; M, male.

요약

의료종사자는 환자와 자주 접촉하거나 호흡기 검체를 직접 다룸으로써 중증급성호흡기증후군 코로나바이러스 2 (the severe acute respiratory syndrome coronavirus 2, SARS-CoV-2)에 노출될 위험이 높다. 본 연구는 의료종사자와 코로나바이러스감염증-19 (COVID-19) 환자 및 지역사회 기반의 일반인과 혈청 유병률을 비교하여 항체 반응을 평가하고자 한다. 348명(의료종사자 155명, COVID-19 환자 7명, 지역사회 기반의 일반인 186명)에서 총 358개의 검체를 수집하였다. SARS-CoV-2 IgG 항체는 155명의 의료종사자 중 1명(0.5%, 95% CI: 0.1 - 3.6%), 7명의 COVID-19 환자 중 7명(100%, 95% CI: 64.5 - 100%)에서 검출되고 지역사회 기반의 일반인에서는 검출되지 않았다 (0.0%, 95% CI: 0.0 - 2.0%). 양성 결과를 보인 한 명의 의료종사자는 2.32 signal to-cutoff (S/C)와 3주 후 2.31 S/C를 보였고, 9명의 양성 환자 검체는 중앙값 3.79 S/C (범위 1.72 - 6.54)를 보였다. 결론적으로 의료종사자는 SARS-CoV-2 IgG 혈청 유병률은 매우 낮았다. 현재 감염 통제 기준은 의료종사자를 COVID-19로부터 보호하는데 효과적인 것으로 보인다.

CONFLICTS OF INTEREST

No potential conflicts of interest relevant to this article were reported

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