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LETTER

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Seroprevalence of antibodies against SARS-CoV-2 among workers in a national research institute and hospital in Central Japan

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Abstract: To achieve effective prevention and control strategies for COVID-19, regular survey of seroprevalence of antibodies against severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is essential. Using four serological tests, we examined the residual sera collected in an annual medical checkup of the staff members of the National Center for Geriatrics and Gerontology in Aichi Prefecture, Central Japan in June 2020. Of the 631 samples, two were positive for anti-SARS-CoV-2 antibodies in at least two tests, showing a seroprevalence of 0.32%. Four subjects showed positive results in only one test. All individuals were asymptomatic and had not been in close contact with patients diagnosed with COVID-19. Multiple antibody tests could be used to assess the prevalence of SARS-CoV-2 infection including individuals without COVID-19 symptoms.

***Keywords*:** SARS-CoV-2, COVID-19, seroprevalence

The spread of SARS-CoV-2 had various impacts on social activities. Since the first case of coronavirus disease 2019 (COVID-19) was identified in January 2019, more than 813000 cases and 15000 deaths have occurred in Japan so far. Just before the opening of the Olympics, the number of new cases has been again increasing in Tokyo. Although the vaccination rollout started in mid-February, only 29.6% of the population has completed at least once in Japan and the pandemic has still not ended. As a considerable number of individuals have only mild or no symptoms, the extent of infection has been evaluated by seroepidemiological studies (*1*). The seroprevalence in the Japanese general populations was 0.03-0.17 in June 2020 and 0.14–0.91 in December 2020 (*2,3*). To achieve effective prevention and control strategies for COVID-19, regular survey of seroprevalence is essential.

The National Center for Geriatrics and Gerontology (NCGG), which comprises a hospital and research institute, is one of the national centers for advanced and specialized medicine located in Aichi Prefecture, a central region of Japan. To investigate the seroprevalence of SARS-CoV-2 among NCGG workers over time, we designed a repeated cross-sectional study and reported the results of the first survey using the sera collected at annual health checkups in June 2020.

Of the 743 NCGG employees invited, 632 agreed to participate in the survey (participation rate: 85.0%). However, one was excluded because of insufficient serum volume. Thus, 631 samples were tested for anti-SARS-CoV-2 antibody levels. In January 2021, the participants were asked to answer an electronic questionnaire on sociographic and COVID-19-related factors. All participants provided written informed consent, and the Institutional Review Board of the ethics and conflicts of interest committee approved this study (No: 1481).

At the inhouse laboratory, serum anti-SARS-CoV-2 antibodies were measured using clinical diagnostic systems manufactured by Sysmex, Abbott, and Roche. We performed Sysmex SARS-CoV-2 N-IgG and SARS-CoV-2 S-IgG assays that detect immunoglobulin G against viral nucleoprotein and spike protein antigens, respectively. In addition, we performed Abbott SARS-CoV-2 assay that detects IgG against nucleocapsid protein. Further, we performed the Roche Elecsys Anti-SARS-CoV-2 RUO assay that detects total antibodies, including IgG against nucleocapsid protein. Samples with positive results in two or more tests were considered antibody positive. To compare the distribution of values,

Table 1. Individual index values of each test in samples that were tested positive in at least one test

Participants	Age Range	Gender	Tests (positive threshold value)			
			Abbott (1.4)	Sysmex-S (10)	Sysmex-N (10)	Roche (1.0)
A	≥ 50	female	**2.58**	**13.9**	**43.8**	**2.220**
B	30-39	male	**1.61**	0.0	**22.8**	0.071
C	40-49	male	**1.52**	0.0	0.2	0.204
D	30-39	female	0.01	0.0	0.6	**1.340**
E	40-49	female	0.01	0.0	0.8	**1.500**
F	≥ 50	female	**1.56**	0.0	0.0	0.070

Positive values are indicated in bold letters.

logarithmic transformation of the index value +1 was used.

Table S1 (*https://www.ghmopen.com/site/supplementaldata.html?ID=25*) summarizes the participant characteristics. The proportions of participants in their 20s, 30s, 40s, and older than 50 years were 22.1%, 23.1%, 31.5%, and 23.3%, respectively, and 63.6% were female. The healthcare workers including doctors, nurses, and allied healthcare professionals accounted for 65.0%, whereas the others were engaged in basic research and investigation, general office duties, and other nonclinical work. A total of 104 (16.5%) participants were reported to have engaged in work activities with high infection risks.

As shown in Table 1, among 631 participants, only two were positive in two or more tests, indicating a seroprevalence of 0.32% (95% confidence interval: 0.04–1.14). One participant was positive in all tests, with indices of 2.58, 13.9, 43.8, and 2.220 in the Abbott, Sysmex-N, Sysmex-S, and Roche tests, respectively. Another participant was positive in Abbott test (index: 1.61) and Sysmex-N test (index: 22.8). Both individuals were nonclinical workers. Meanwhile, four participants were positive in one of the tests, two in the Abbott test (indices: 1.52 and 1.56) and two in the Roche test (indices: 1.340 and 1.500). No participant had a history of PCR testing or close contact with patients diagnosed with SARS-CoV-2. In addition, they claimed absence of any symptom implying infection between January and June 2020.

The Ministry of Health, Labor, and Welfare of Japan conducted a survey of the general population; the results showed that the seroprevalences in Tokyo, Osaka, and Miyagi were 0.10%, 0.17%, and 0.03%, respectively, in June 2020 (*2*). During the same period, SoftBank Group Corp. reported that 0.20% of their employees in Aichi Prefecture, where NCGG is located, were positive in the anti-SARS-CoV-2 antibody test (*4*). Furthermore, 2.1% of the healthcare workers in Kanagawa Prefecture (near Tokyo) (*5*) and 0.16% of those in the National Center for Global Medicine in Tokyo were antibody positive (*6*). The antibody prevalence in the present study is similar to that reported in these surveys, suggesting that the residual serum of medical examinations can be used for the rough estimation of seroprevalence.

In this study, discordant assay results were obtained in five cases. Such discrepancies were observed in samples presumably with low antibody levels (*7,8*). When the normalized values were compared between assays, the Sysmex tests (both S and N) showed a clear distinction between positive and negative values (Figure S1, *https://www.ghmopen.com/site/supplementaldata.html?ID=25*). The discordance among the tests may have resulted from the difference in assay characteristics. Antibodies reportedly cross-react with some SARS-CoV-2 epitopes detected in the serum from individuals without SARS-CoV-2 infection or those with seasonally spreading human coronaviruses (HCoV), possibly because the cross-reactivity persisted from earlier HCoV infection (*9*). Cross-immunity is possible in cases that show positivity in a single assay. Therefore, multiple assays are needed to identify individuals with prior SARS-CoV-2 infection.

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