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Letter to the Editor

Seroprevalence of antibodies against SARS-CoV-2 in a large national hospital and affiliated facility in Tokyo, Japan



We read with interest Jones et al.'s report of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) seroprevalence among health-care workers (HCWs) and support staff at North Bristol NHS Trust.¹ The authors reported 9.3% seroprevalence and its variation by ethnicity, with higher rate observed among non-White including Asian (14.6%) than White (8.2%). A large geographical variation of seroprevalence among HCW has been reported: higher in North America and Europe than Asia.² In Japan, which has relatively high number of Covid-19 cases in Asia, data are limited on the seroprevalence among HCW.^{3,4}

National Center for Global Health and Medicine (NCGM), due to its special role in the control of infectious diseases in Japan, has been taking a leading role in combatting Covid-19 since the early phase of its epidemic, and many NCGM staff have been involved in various missions with potential exposure to SARS-CoV-2, including health check of returnees on charter flights from Hubei, China⁵ and infection control on the Diamond Princess cruise ship.⁶ We designed a study comprising repeated cross-sectional surveys among staff of NCGM. Here, we report the results of the first survey on July 2020 (after the first wave of epidemic in Japan), which was mainly targeted for those who had worked in Covid-19 related department or was engaged in any Covid-19 related task, or nurses of inpatient ward. Of 1579 employees invited, 1228 (77.8%) agreed to participate in the survey. Written informed consent was obtained from each participant. This study was approved by the ethics committee of NCGM.

We asked participants to complete an electronic questionnaire and donate venous blood. Serum separated was measured for SARS-CoV-2 antibodies by using test systems manufactured by Abbott and Roche at in-house laboratory. We run the Abbott Architect[®] instrument using the SARS-CoV-2 IgG assay, based on the chemiluminescent microparticle immunoassay to detect IgG against the SARS-CoV-2 nucleoprotein, and Roche cobas[®] e602 analyzer using the Elecsys[®] Anti-SARS-CoV-2 based on the electrochemiluminescence immunoassay to detect total antibodies including IgG to the SARS-CoV-2 nucleoprotein. For the sample with positive on either test, we quantified IgG with Anti-SARS-CoV-2 [anti-S1] ELISA (EUROIMMUN AG, Luebeck, Germany) and neutralizing antibody titer by using live virus (**Supplement**).

We defined antibody positive if either test shows positive (sensitivity priority). We calculated the proportion of those with antibody positive and its 95% confidence interval (Clopper-Pearson), and compared the seroprevalence with that of the general population survey in Tokyo,⁷ which used the same assays as the current study. We also defined antibody positive if both tests are positive (specificity priority).

Table

Characteristics of study participants.

	No.	%
Total	1228	100
Male sex	353	28.7
Age, years		
<30	465	37.9
30–39	335	27.3
40–49	257	20.9
≥50	171	13.9
Affiliation		
Hospital	1095	89.2
Others	133	10.8
Job		
Doctor	237	19.3
Nurse	601	48.9
Allied health care professional	169	13.8
Clerical and administrative staff	128	10.4
Other	93	7.6
Occupational risk of SARS-CoV-2 infection¹		
Low	408	33.2
Middle	478	38.9
High	342	27.9
Engagement in Covid-19 related work		
Screening of returnees of the charter flight from Wuhan	135	11.0
Infection control on the cruise ship	55	4.5
Covid-19 testing center, fever consultation clinic	119	9.7
Care facility for Covid-19 patients with mild symptom	26	2.1
Works done within 1 m of Covid-19 patient	526	42.8
Works done at 1 m or more of Covid-19 patient	315	25.7
SARS-CoV-2 laboratory testing	74	6.0
Handling SARS-CoV-2 other than testing	122	9.9
Cleaning, laundry, sterilization, waste disposal	222	18.1
Fever screening of outpatient and visitors	126	10.3
Others	141	11.5
Any of the above	850	69.2
Symptom indicative of Covid-19		
Common cold-like symptom lasting 4 days or longer	153	12.5
High fever	53	4.3
Severe fatigue	98	8.0
Dyspnea	30	2.4
Loss of sense of taste or smell	10	0.8
Close contact with Covid-19 patient²	57	4.6
History of PCR testing for SARS-CoV-2	91	7.4
History of Covid-19	1	0.1

¹ Categorized according to the type of Covid-19 related work engaged.

² Contact with Covid-19 patient within 1 m without personal protective equipment, having lived with Covid-19 patient, etc.

The mean (SD) age of study participants was 36 (11) years and 71% were female. As shown in **Table**, major occupational categories were nurses (49%), doctor (19%), other allied health care professional (14%), and clerical and administrative staff (10%). A total of 850 participants (69%) reported having being engaged in any work associated with Covid-19; of these, 343 (40%) were engaged in work with high infection risk.

Of study participants, only two were positive on either antibody test; one on Abbott test (index: 2.24) and another on Roche test (index: 7.64), giving a seroprevalence of 0.16% (95% confidence interval: 0.02 to 0.59). The observed SARS-CoV-2 seropositivity is no greater than that of the general population survey in Tokyo on June 2020 (0.41%, recalculated according to the definition of the present study).³ The participants with positive test result were both female nurses aged 20's, and reported having no symptoms indicative of Covid-19, no engagement in Covid-19 related work, and no close contact with infected patient without personal protecting device. Another nurse who was previously diagnosed as Covid-19 showed negative on the present antibody tests. The two positive samples on either test were proved to be negative on both EUROIMMUN IgG quantitative test and neutralizing antibody test. If we adopt specificity priority-definition of antibody positive (positive on both tests), the seroprevalence is zero.

A systematic review of seroprevalence studies suggested high risk of SARS-CoV-2 infection among HCW.² In contrast, we observed a very low seropositive rate in the staff of NCGM as of July 2020, which was even lower than that among the general population in Tokyo. In a tertile hospital in the US, the rate of SARS-CoV-2 infection among HCW was lower than that among the general public in the surrounding region.⁸

The observed low seroprevalence may reflect effective infection control in the hospital. While having accepted a large number of inpatients and being involved in various Covid-19 related work since early phase of this epidemic, NCGM have introduced comprehensive measures to protect staff against the infection. These include sufficient provision with personal protective equipment for HCW depending on their infection risk, intensive and frequent hand washing/alcohol sanitation practice, universal masking, limiting visitors, checking body temperature at hospital entrance, notification of fever from staff on daily basis, SARS-CoV-2 PCR test for staff who reported fever or close contact with infected patient and for pre-operative patients, partitioning dining table with acrylic board, and periodic advisory e-mail message to the staff, all of which might have collectively contributed to minimizing infection risk in hospital. These measures have been strengthened according to the epidemic of the time.

The staff face high infection risk in their daily life outside hospital, which is located in the central Tokyo, an epicenter. NCGM has taken measures to address this issue. For instance, the infection control department delivers an e-mail on every Friday to all the staff to raise the awareness of preventive behaviors that should be taken during the weekend. Such advisory message might have contributed to high compliance of staff with preventive practice and lowering risk of community-acquired infection.

In conclusion, this seroepidemiological study in a large hospital in Tokyo adds evidence to support that comprehensive infection control measures in hospital can decrease risk of SARS-CoV-2 infection among HCW combatting Covid-19 to the levels comparable to or even lower than that of the general population. Repeated testing of antibody among HCW is warranted to monitor the spread of infection and assess control measures in hospital.

Declaration of Competing Interest

Antibody test reagents were provided from Abbott and Roche Diagnostic to the present study.

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Supplementary materials

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