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Note

Effectiveness of personal protective equipment in preventing severe acute respiratory syndrome coronavirus 2 infection among healthcare workers $\overset{\star}{\sim}$



Infection and Chemotherapy



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ABSTRACT

Introduction: Information on the effectiveness of personal protective equipment (PPE) for preventing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection among healthcare workers (HCWs), especially among HCWs with frequent contact with patients with SARS-CoV-2, is limited. *Methods:* We conducted a prospective cohort study on 49 HCWs who worked in close contact with patients with SARS-CoV-2 infection. HCWs had blood samples taken every 2 weeks to test for SARS-CoV-

2 antibodies using two different types of assay. *Results:* Forty-nine participants (31 nurses, 15 doctors, 3 other workers) were enrolled. In total, 112 blood samples are obtained from participants. The median work days in 2 weeks was 9 (interquartile range (IQR): 5–10) days. In a single work day, 30 of the 49 participants (61.5%) had contact with patients with suspected or conformed SARS-CoV-2 at least 8 times, and approximately 60% of participants had more than 10 min of contact with a single patient. The median self-reported compliance to PPE was 90% (IQR: 80–100%). Seven participants tested positive for SARS-CoV-2 antibody using enzyme-linked immuno-sorbent assay (ELISA); however, none were seropositive for SARS-CoV-2 neutralizing antibody, so the positive ELISA results were assumed to be false-positive.

Conclusions: The study provides evidence that appropriate PPE is sufficient to prevent infection amongHCWs. It is necessary to establish a system that provides a stable supply of PPE for HCWs to perform their duties.

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Abbreviations: CDC, US Centers for Disease Control and Prevention; COVID-19, coronavirus disease 2019; ELISA, enzyme-linked immunosorbent assay; HCW, health care worker; ICU, intensive care unit; Ig, immunoglobulin; IQR, interquartile range; PPE, personal protective equipment; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; WHO, World Health Organization.

* All authors meet the ICMJE authorship criteria. TS and KH organized this study and drafted the manuscript. AA, NI, KS, NN and TS was responsible for antibody analysis. YW, YA, YM, KN, SI, HN, TN, MO, YM, YS, SS, SM, MI, NK and SK supervised the study design and manuscript. NO was responsible for the study. All authors read and approved the final manuscript.

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Since the first cases were reported in December 2019, coronavirus disease (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become pandemic [1]. In Japan, the first case was reported in mid-January 2020, and more than 16.000 cases had been reported as of May 31, 2020 [2]. The World Health Organization (WHO) and the US Centers for Disease Control and Prevention (CDC) guidelines on prevention of SARS-CoV-2 infection in healthcare settings [3,4] recommend wearing personal protective equipment (PPE) including masks, gowns, gloves, and eye protection, when providing direct care to COVID-19 patients. Many healthcare workers (HCWs) have been infected with SARS-CoV-2 [5], including almost 10,000 HCWs in the US [6]. In HCWs with SARS-CoV-2 infection, it is difficult to determine HCWs whether they acquired the infection at work or in the community. Information on the effectiveness of PPE at preventing infection among HCWs is limited. In Japan, there were only 528 cases of COVID-19 reported in Tokyo by the end of March 2020, and the risk of community-acquired infection during this period was limited [7]. Our hospital is a designated infectious disease hospital and we have been promoting infection control since before COVID-19 endemic, so compliance with PPE use is likely to be high. For patient care, airborne precautions (N95 mask) and contact precautions (gloves, gown, cap) are used. Eye shields are also used according to WHO and CDC recommendations [2,3]. Alcohol hand sanitizers are available for hand hygiene. During aerosol-producing procedures (e.g., intubation, extubation, and bronchoscopy), a powered air-purifying respirator and coverall are used.

Under these circumstances, it was possible to evaluate the effectiveness of PPE against acquiring SARS-CoV-2 infection at work. We conducted an observational study of HCWs to determine the effectiveness of PPE at preventing SARS-CoV-2 infection.

This single-center prospective cohort study was conducted in National Center for Global Health and Medicine. We recruited participants and collected blood samples between February 14 and April 3, 2020. This study was approved by the Ethics Committee of the Center Hospital of the National Center for Global Health and Medicine. Written informed consent was obtained from all participants.

HCWs with close contact with COVID-19 patients were recruited for the study. Close contact was defined as either talking with patients at close range (within 1 m), touching patients for examination and/or care, or taking samples such as nasopharyngeal swabs or blood. Blood samples of HCWs were obtained at enrolment and every 2 weeks after enrolment until April 3, 2020.

At enrolment, participants answered a web-based self-reported questionnaire about their compliance with PPE use. The questionnaire included questions about participants' PPE use during the previous 2 weeks, their compliance, and details of their exposures at enrolment and at every blood sampling.

In order to minimize the possibility of false-negative results, serum SARS-CoV-2 antibody titres were measured using an enzyme-linked immunosorbent assay (ELISA) and a neutralization assay.

For ELISA, SARS-CoV-2-infected and SARS-CoV-2-uninfected Vero 9013 cells were lysed with phosphate-buffered saline (PBS) containing 1% Nonidet-P40. After centrifugation, the supernatant was collected as a positive or negative antigen. Half of the wells in microtiter plate were coated with SARS-CoV-2-positive antigen, and the other half were coated with mock antigen. Sera collected from HCWs were heat-inactivated at 56 °C for 30 min and then 50 μ L of serum diluted 100-fold with 5% skim milk in PBS containing 0.05% Tween-20 (M-PBST) was added to each well for reaction at 37 °C for 1 h. After washing, 50 μ L of HRP-labeled goat

anti-human immunoglobulin G (IgG) antibody (Thermo Fisher Scientific, Waltham, MA) diluted 1000 times with M – PBST was added to each well, and incubated at 37 °C for 1 h. After washing, 50 μ L of ABTS chromogenic substrate solution (Roche, Basel, Switzerland) was added to each well for the reaction at room temperature for 30 min. Absorbance of 405 nm was measured using iMark Microplate Reader (BIO-RAD, Hercules, CA). The optical density (OD) value of SARS-CoV-2-specific antibodies was obtained by subtracting OD value against negative antigen from that against positive antigen.

VeroE6/TMPRSS2 cells [8] were used for the neutralization assay. The cells were cultured as monolayers in Dullbecco's modified Eagle medium supplemented with 5% fetal calf serum, 50 IU/ml penicillin G, and 50 µg/ml streptomycin. SARS-CoV-2 strain 2019-nCoVJPN/TY/WK-521/2020 used as challenge virus was originally isolated with VeroE6/TMPRSS2 cells from a patient. Serial 2-fold dilution of the test serum (from 1:20 to 1:320) and equal amounts of the challenge virus (100 TCID50) were mixed at 37 °C for one hour, followed by the addition of 100 µL of VeroE6/TMPRSS2 cells (2×10^4 cells). After 5 days of incubation at 37 °C, the presence or absence of cytopathic effect in each well was observed using an inverted microscope. After formalin fixation, staining with crystal violet solution was performed for the final evaluation.

The first patient with COVID-19 was admitted to our hospital on January 26, 2020. As of April 3, 50 laboratory-confirmed COVID-19 patients had been admitted to our hospital and over 25 laboratoryconfirmed COVID-19 patients had visited our outpatient department. Forty-nine participants (31 nurses, 15 doctors, 3 other workers) were enrolled. Among the nurses, 15 worked in the COVID-19 ward, 9 worked in the intensive care unit (ICU) where severe COVID-19 cases were treated, and 7 worked in the outpatient clinic where patients with suspected COVID-19 were examined and nasopharyngeal swabs were collected. All physicians had close contact with patients with confirmed and suspected SARS-CoV-2 infection in the inpatients ward, ICU, and outpatient clinic.

The questionnaire completion rate was 96/112 (85.7%) based on the number of samples collected and 47/49 (95.9%) based on the number of participants. The participant characteristics and SARS-CoV-2 contact history are summarized in Tables 1 and 2.

In total, 112 blood samples were obtained from the participants. Thirty participants (62.5%) provided their first blood sample between February 23 and February 29. Over 80% in this group provided 3 blood samples at 2-week intervals. Of the participants, 8 (16.3%), 18 (36.7%), and 23 (46.9%) provided 1, 2, and 3 samples, respectively. Seven samples tested positive for SARS-CoV-2 using ELISA; but all the samples were negative using the neutralizing antibody. Thus, all the participants were considered seronegative.

Table 1

Participant characteristics ($N = 49$).	
Characteristic	n (%)
Female	34 (69.4)
Occupation	
Nurse	31 (63.3)
Doctor	15 (30.6)
Other ^a	3 (6.1)
Age category (years)	
20-29	5 (10.6)
30-39	25 (53.2)
40-49	11 (23.4)
50-59	4 (8.5)
>60	2(4.3)

^a The other workers were 1 pharmacist, 1 medical translator, and 1 clerk.

Table 2

Contact with patients during the 2 weeks preceding the blood sampling.

Contact characteristic	Value
Work days, median (IQR)	9 (5–10)
Maximum number of contacts with patients per day, n (%)	
≤3	17 (17.7)
4-7	20 (20.8)
≥8	59 (61.5)
Maximum duration of contact per patient, n (%)	
≤5 min	11 (11.5)
5–10 min	28 (29.2)
\geq 10 min	57 (59.4)
Compliance ^a of PPE, median % (IQR/range)	90 (80-100/60-100)

^a Self-reported. Compliance with each item of PPE (e.g. mask, glove, gown) was not collected.

There is limited evidence of the effectiveness of the PPE against SARS-CoV-2. Wang et al. [9] recently reported the potential role of PPE use in the protection against COVID-19 using the cohort of HCWs who were dispatched to work in Wuhan. They found that none of the HCWs were infected with COVID-19 using throat swab samples for SARS-CoV-2 real-time reverse transcription polymerase chain reaction as well as specific antibody levels measured with immunoglobulin M, immunoglobulin G, and immunoglobulin A by chemiluminescent kits. We used more sensitive laboratory tests and included HCWs with greater exposure to SARS-CoV-2.

The accuracy of screening of the serostatus of a population with low infection prevalence is uncertain. To minimize the falsenegative and false-positive results, we used two different antibody tests: ELISA using SARS-CoV-2 antigen to enhance sensitivity and neutralizing antibody to enhance specificity. The 7 samples that were seropositive on ELISA tested negative with the neutralization assay, and hence, were considered to be false positives.

A previous study revealed that the sensitivity of antibody tests in COVID-19 patients in 15–39 days after onset is 100% [10]. Our hospital started admitting COVID-19 patients in January 26, 2020, and so participants had sufficient time to develop antibodies if they had been infected. Most patients were admitted to our hospital as soon as they were diagnosed with COVID-19 and are likely to have been infectious during their hospitalization [11].

SARS-CoV-2 infections among HCWs can occur due to lack of PPE, improper use of PPE, or infection in the community [5]. Our findings suggest that the proper use of airborne and contact precautions can prevent SARS-CoV-2 infection among exposed HCWs. Nevertheless, it is important to avoid unnecessary contact with COVID-19 patients. In conclusion, the study provides evidence that appropriate PPE is sufficient to prevent infection among health care workers. It is necessary to establish a system that provides a stable supply of PPE for HCWs to perform their duties. To improve compliance to PPE, it is important to promote further research on PPE innovation.

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Declaration of competing interest

None.

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References

- Kutsuna S. Coronavirus disease 2019 (COVID-19): research progress and clinical practice. Global Health & Medicine 2020;2:78–88.
- [2] World Health Organization. Coronavirus disease (COVID-2019) situation reports. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/ situation-reports/. [Accessed 6 June 2020].
- [3] World Health Organization. Rational use of personal protective equipment (PPE) for coronavirus disease (COVID-19): interim guidance. 2020. https:// apps.who.int/iris/handle/10665/331498. [Accessed 18 May 2020].
- [4] Centers for Disease Control and Prevention. Interim infection prevention and control recommendations for patients with suspected or confirmed coronavirus disease 2019 (COVID-19) in healthcare settings. https://www.cdc.gov/ coronavirus/2019-ncov/hcp/infection-control-recommendations.html. [Accessed 18 May 2020].
- [5] Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med 2020;382:1199–207. https://doi.org/10.1056/NEJMoa2001316.
- [6] CDC COVID-19 Response Team. Characteristics of health care personnel with COVID-19 — United States, February 12-April 9, 2020. MMWR Morb Mortal Wkly Rep 2020;69:477–81. https://doi.org/10.15585/mmwr.mm6915e6.
- [7] Nippon Hoso Kyokai (NHK). Featured Website: novel coronavirus disease. https://www3.nhk.or.jp/news/special/coronavirus/data/. [Accessed 18 May 2020].
- [8] Matsuyama S, Nao N, Shirato K, Kawase M, Saito S, Takayama I, et al. Enhanced isolation of SARS-CoV-2 by TMPRSS2-expressing cells. P Natl Acad Sci USA 2020;117:7001–3. https://doi.org/10.1073/pnas.2002589117.
- [9] Wang W, Min Y-Z, Yang C-M, Hong H-O, Xue T, Gao Y, et al. Association of personal protective equipment use with successful protection against COVID-19 infection among health care workers. medRxiv 2020. https://doi.org/ 10.1101/2020.04.24.20070169.
- [10] Zhao J, Yuan Q, Wang H, Liu W, Liao X, Su Y, et al. Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019. Clin Infect Dis 2020. https://doi.org/10.1093/cid/ciaa344.
- [11] Wölfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Müller MA, et al. Virological assessment of hospitalized patients with COVID-2019. Nature 2020. https://doi.org/10.1038/s41586-020-2196-x.