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Original Article

A cross-sectional seroprevalence for COVID-19 among healthcare workers in a tertially care hospital in Taiwan

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Background: Healthcare workers (HCWs) are at the frontline during the pandemic of COVID-19 globally. According to the WHO situation report at April 17, there were 22,073 HCWs contracted the infection. Whether the infection control policy and practice in the hospital setting can protect the HCWs is an important issue.
Methods: We performed a cross-sectional serology study in a tertiary care hospital in Taiwan to explore the sero-prevalence rate among HCWs. The participants are enrolled on a voluntary basis. A structured questionnaire was collected to gather the epidemiology character and risk factors for potential exposure. ELISA tests as Architect SARS-CoV-2 IgG (Abbott) and Elecsys Anti-SARS-CoV-2 assay (Roche) were used to detect antibody responses. If any of the tests was positive, a western blot assay was used for confirmation.
Results: There were 194 HCWs participated during July 1 to Aug. 31, 2020. The mean age was 36.3 ± 10.4. More than half of the participants had possible hospital associated risk for COVID-19 exposure (110/192, 57.3%) and 64 had possible community risk for COVID-19 exposure (64/194, 33.0%). There was only one participant had positive test by Architect IgG test and confirmed to be negative for seasonal coronavirus and SARS-CoV-2 antibody. (Mikrogen Diagnostik, Germany).
Conclusion: The cross-sectional serology study in a tertiary care hospital in Taiwan revealed no HCWs had positive serology response to SARS-CoV-2. We believe that the infection control

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Introduction

Since the pandemic of coronavirus disease 2019 (COVID-19) in late 2019, healthcare workers (HCWs) have been on the frontline to fight against the menace. According to the WHO situation report at April 17, there were 22, 073 HCWs contracted the infection.[1] Since the data are coming from 52 countries only, this could be an underestimated number of infected HCWs globally. In the hospital settings, logistic, personnel, and environmental control measures have been build up to protect the HCWs and also aim to prevent disease transmission among the healthcare facilities.[2]

However, the HCWs can also get infection from the community level. Globally, each government have developed different strategies to contain the COVID-19 pandemic. In Taiwan, the main infection control policies include quarantine, rolling definition for case reporting and detection, contact tracing, wearing mask, social distancing, and isolation of every COVID-19 patients, etc.[3]

Up to August, 31, 2020, there were 488 confirmed COVID-19 patients in Taiwan and the last local case was reported at April 9, 2020.[4] Thus the main possible exposure to COVID-19 patients among HCWs should mainly come from hospital exposure. Benton R. Hunter et al. recently reported the prevalence of SARS-CoV-2 antibodies among HCWs was 1.6% in Indiana University Health, USA.[5] Since the seroprevalence rate had no major difference among groups with different exposure level to COVID-19 patients, they believe their personal protective equipment (PPE) policy is effective to prevent the disease transmission. Thus, we aim to conduct a cross sectional seroprevalence study among HCWs in a tertiary care hospital in Taiwan to evaluate the effect of infection control policy and practice in the hospital setting in Taiwan.

Materials and methods

Setting

National Taiwan University Hospital (NTUH) is a university affiliated, 2200 beds tertiary care hospital in northern part of Taiwan and there were 10,372 HCWs in the hospital in August, 2020.

Up to August 31, 2020, there were 488 confirmed COVID-19 patients in Taiwan and 18 of them were hospitalized at NTUH. The first COVID-19 patient was admitted on January 21, 2020 and the last patient was admitted on August 7 and remained hospitalized up to August 31, 2020. A 19-bed ward was used as the COVID-19 designated ward since January 22, 2020 and another 19-beds ward was used as COVID-19 quarantee ward for hospitalization and isolation of

suspected COVID-19 patients during March 17 to May 7, 2020. None of the HCWs of NTUH had been diagnosed as confirmed COVID-19 infection.

The PPE regulations at NTUH are universal wearing surgical mask in clinical setting of whole hospital and wearing N95 mask, face shield, hair cover, isolation gowns, and gloves while taking care of or performing oropharyngeal/nasopharygeal swab for confirmed or suspected COVID-19 patients, according to the suggestions from Centers for Disease Control, Taiwan (TW, CDC).[6]

Participants

HCWs of NTUH who have been working at the COVID-19 ward, providing care for suspected and/or confirmed COVID-19 patients, or HCWs who regards himself/herself had risk for COVID-19 exposure were encouraged to participate the study. Open e-mail invitation was sent to each setting. The study protocol has been reviewed and approved by the Research Ethics Committee of the hospital (202003003RINC).

Study design

This is a cross-sectional study performed during July 1 to August 31, 2020. After participants signed the informed consent, a self-administered structured questionnaire were collected, including age, sex, underlying diseases, possible hospital associated risk factors, community associated risk factors, travel history, possible COVID-19 associated symptoms (fever, cough, taste or olfactory change).[7,8] The hospital associated risk factors were defined as working at COVID-19 ward, or short distance taking care of COVID-19 patients (defined as <1.5 m), or perform oropharyngeal/nasopharyngeal swab sampling for suspected or confirmed COVID-19 patients. The community associated risk factors were defined as recent clinic visit within 3 months, family/friends with possible COVID-19 associated symptoms (fever, cough, taste or olfactory change) within 3 months, or family with international travel history.

The blood sample were collected. Two enzyme-linked immunosorbent assay (ELISA) as Architect SARS-CoV-2 IgG (Abbott) and Elecsys Anti-SARS-CoV-2 assay (Roche) were used to detect antibody responses against SARS-CoV-2 nucleocapsid protein.[9,10] If any of the ELISA test was positive, a western blot (WB) assay was performed (recomLine SARS-CoV-2 IgG [Aviditaet] (REF 7374) Mikrogen Diagnostik, Germany) to detect antibody against SARS-CoV-2 antigen. The definition for seropositive for SARS-CoV-2 infection is the participants has either one or more positive ELISA test and confirmed by positive WB assay.

According to the Abbott's instructions, the cutoff value as positive IgG response was the index value > 1.4. The Elecsys assay is a modified double-antigen sandwich immunoassay, which can be used to detect antibody independent of the subclass. According to the manufacture's instruction, the positive value was defined as a cutoff index (COI)$\geqq$1.0.[10]

If any of the ELISA test was positive, a WB assay was performed. The antigens of the test panel include seasonal human coronaviruses HCoV (229E, NL63, OC43, HKU1) nucleocapsid protein, SARS-CoV-2 nucleocapsid protein (NP SARS-2), SARS-CoV-2 receptor binding domain protein (RBD SARS-2) and SARS-CoV-2 spike surface protein (S1 SARS-2).[11] According to the manufacturer's instruction, SARS-CoV-2 IgG positive was defined if one or more SARS-CoV-2-specific antigen bands (NP, RBD and/or S1) are positive, that is, they react with the same or a stronger intensity than the cutoff band. The laboratory test was performed in a single laboratory of NTUH during July 1 to August 31, 2020.

Statistical analysis

The continuous variables were presented as mean ± SD, or median with range if not normally distributed. All analyses were performed using STATA version 11 (Texas, USA).

Results

There were 194 HCWs participated in the cross-sectional survey. The mean age was 36.3 ± 10.4. Seventy of the participants were male (70/190, 36.8%, 4 missing data). Most of the participants had no underlying diseases. There were 8 participants reported as having hypertension, 4 diabetes mellitus, 2 chronic kidney disease, 5 autoimmune diseases, and 2 cancer history.

More than half of them had possible hospital associated risk for SARS-CoV-2 exposure (110/192, 57.3%, 2 missing data), including 109 working at the COVID-19 ward (109/193, 56.5%, 1 missing data), 71 had performed oropharyngeal/nasopharyngeal swab for possible or confirmed COVID-10 patients (71/192, 37.0%, 2 missing data), and 52 participants had short distance contact with COVID-19 patients (52/193, 26.9%, 1 missing data).

Sixty-four of the participants have possible community risk for COVID-19 exposure (64/194, 33.0%). Many of them were due to family/friends had possible COVID-19 symptoms (29/194, 15.0%), followed by the HCWs had visited clinic in recent 3 months (27/194, 13.9%), and family member had international travel history (23/194, 11.9%).

Thirty-seven of the participants had ever had possible COVID-19 symptoms in past three months (37/193, 19.2%, 1 missing data). Twenty-two of them had international travel since January 1, 2020 (22/194, 11.3%).

Both Architect SARS-CoV-2 IgG (Abbott) and Elecsys Anti-SARS-CoV-2 assay (Roche) were performed for all participants. There was only one participant had a positive result in Architect SARS-CoV-2 IgG test (index value 1.49) (The COI was 0.1 by Elecsys assay, negative). Confirmatory WB assay revealed both negative for HCoV and SARS-CoV-2 antibody (Supplement figure S1).

Discussions

In this cross-sectional seroprevalence study, we noted the seropositive rate was 0% among the participated HCWs from a tertiary care hospital in Taiwan. Based on the relatively low disease burden (488 confirmed cases, 2.07/100,000 populations) in Taiwan up to August 31, 2020, the result may come from the successful infection control policy and practice in the hospital, and also from the low disease burden in the community and in the hospital.

While reverse transcription polymerase chain reaction (RT-PCR) is the main tool for diagnosis of SARS CoV-2 infection, serology study is believed to provide further evidence for late presenters, past infection or immune response.[12] There are currently around 353 and merging serology tests available globally.[13] However, using serology as a surveillance tool in general population should be cautious since the specificity in asymptomatic population is not yet well evaluated.[14] For asymptomatic patient who had been confirmed by RT-PCR, Long et al. reported that the asymptomatic patients with SARS-CoV-2 infection had lower antibody titer and earlier decay of antibody, comparing with symptomatic patients.[15] Another study at Korea reported that only 71% of asymptomatic SARS CoV-2 infected patients had positive SARS-CoV-2 IgG result at 8 weeks post infection (n = 7), and the titer is also lower than symptomatic infected patients (n = 17).[16]

There are some studies target specifically for high risk population, eg: HCWs. Hunter et al. reported the prevalence of SARS-CoV-2 antibodies among HCWs was 1.6% in Indiana University Health, USA[5] and there was no major difference among groups with different exposure level to COVID-19 patients. Thus they believe their PPE policy is effective to prevent the disease transmission. Another preliminary result from a serial follow-up by RT-PCR and serology among HCWs in Centre Hospitalier Universitaire Saint-Pierre in Brussels revealed 41 cases of SARS-CoV-2 infection in a 14 days follow up (41/326, 12.6%).[17] The hospital had adopted the infection control policy according to European Centre for Disease Prevention and Control. They also noted there was no difference of infection rate among the staff working in COVID-19 ward, COVID-19 intensive care unit or emergency department in the univariate analysis. On the other hand, the presence of co-morbidity was a risk factor for SARS-CoV-2 infection. In our study, we also did not noted a difference of the seropositive rate between HCWs who had healthcare associated risk factors or not. However, none of our participated HCWs had positive sero-response, we could not explore the effect of underlying diseases in this study. Our study result is in line with another study among HCWs in Taiwan. Chan MC et al. reported that 195 HCWs had receive virological surveillance due to fever or any respiratory symptoms. All of the tested HCWs was negative for SARS-CoV-2.[18] Our studies support that current infection control policy and PPE regulation in the hospital setting in Taiwan is adequate to protest HCWs against the SARS CoV-2.

Bryan et al. have evaluated the sensitivity and specificity of Architect SARS-CoV-2 IgG. They utilized serum specimens collected before SARS-CoV-2 circulation at USA to test the specificity of the IgG test as 99.00%.[9] They also noted the

consistent seroconversion among RT-PCR confirmed COVID-19 patients up to 28 days after RT-PCR positive or symptoms onset. By taking the WB as gold standard, the specificity of Architect SARS-CoV-2 IgG test in our study is 99.48%, which is parallel to Bryan et al.'s report.

The limitation of the study is mainly due to the voluntary participation nature. The participants who want to join the study may due to the personal judgment as higher risk for COVID-19 infection. Thus, the study tend to include high risk population and may have the possibility of overestimation of the seroprevalence among the HCWs in the institution. In addition, the positive predictive value of the anti-SARS-CoV-2 antibodies will be low since the prevalence of COVID-19 in Taiwan was low during the study result. However, even with this possibilities for overestimation, we still did not detect any seropositive HCWs.

On the other hand, if the duration of SARS-CoV-2 IgG is short, then the sero-prevalence would be underestimated. He L., et al. had performed serology study among HCWs in Renmin Hospital of Wuhan University in two time point.[19] They noted that the duration of IgM is relatively short while 59.5% of the HCWs turn to be seronegative after one month and the duration of IgG lasted longer and 71.8% were still seropositive in the second test. A recent meta-analysis revealed that sensitivity of ELISA test was higher while 3 weeks after symptoms onset than within first week, as 82.1% and 23.7% respectively.[20] But there is not yet specific study target at asymptomatic COVID-19 infected population.[12] Further studies are needed to clarify the average duration of IgG persistence and the sensitivity issue in asymptomatic infected patients.

In conclusion, the cross-sectional serology study in a tertiary care hospital in Taiwan revealed no HCWs had positive serology response to SARS CoV-2. We believe that the infection control policy and practice in the hospital and in the community are both important to prevent the disease transmission.

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Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jfma.2021.01.002.

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