

Seroconversion of COVID-19 in Frontline Healthcare Workers in a Tertiary Care Hospital in Oman

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ARTICLE INFO

Article history:

Received: 16 February 2021

Accepted: 3 February 2022

Online:

DOI 10.5001/omj.2022.74

Keywords:

Health Personnel;

Seroconversion;

Seroepidemiologic Studies;

SARS-CoV-2; COVID-19;

Oman.

ABSTRACT

Objectives: This research aimed to study the seroconversion among frontline staff at the highest risk of exposure to SARS-CoV-2 infections, including emergency department, critical care, and COVID-19 isolation wards in all healthcare job categories. **Methods:** We conducted a prospective cohort study on the incidence of seroconversion among frontline health care workers (HCWs) at the Royal Hospital, Muscat, Oman. Two sera were collected 12 weeks apart to look for seroconversion. We used proportions with 95% confidence interval (CI) for categorical data and mean/median as appropriate for continuous data. **Results:** Fourteen out of 328 HCWs seroconverted in this study accounting for an incidence rate of 3.6%, excluding four HCWs that were positive at baseline. The median age was 43.5 (range = 28–57). About 75.0% of HCWs were between 31–49 years old, with a seroconversion rate of 4.9% (95% CI: 2.7–8.1). Females accounted for most seroconverted HCWs (14/257) at a rate of 5.4% (95% CI: 3.1–8.8). Omanis seroconverted with a rate of 6.4% (95% CI 2.6–12.8), whereas non-Omanis seroconverted at a rate 4.3% (95% CI: 2.2–7.5). Ninety-two percent (302/328) of the staff lived in the capital area, and a minority lived outside the capital (3/26). Thirteen Muscat citizens seroconverted at a rate of 4.3% (95% CI: 2.4–7.1). Nurses comprised the majority (accounting for about 81%) followed by doctors (19%) at rates of 5.6% (95% CI: 3.2–9.2) and 4.2% (95% CI: 1.07–10.9), respectively. Staff covering COVID-19 isolation wards and intensive care unit comprised over 60% (n = 10) of those who seroconverted with a rate of 5.4% (95% CI: 2.8–9.5) followed by infectious diseases doctors and adult emergency at 19.0% (n = 3) and 12.5% (n = 1), respectively. Approximately 81.3% (n = 13) of HCWs performed aerosol-generating procedures at a seroconversion rate of 4.3% (95% CI: 2.4–7.1). About 50.0% of those who seroconverted had a positive polymerase chain reaction (PCR) before seroconversion, 25.0% had a negative PCR before second serology testing, and 25.0% were not tested with PCR. Approximately 20.0% of seroconverted staff had no reported symptoms compared to 80.0% who reported symptoms such as sore throat (70.0%), fever (50.0%), myalgia (20.0%), and a less frequency (15.0%) runny nose, loss of smell, and headache. **Conclusions:** Detection of infection among HCWs is important to prevent further transmission, especially asymptomatic carriers. A combined screening strategy of symptoms, serology, and PCR might help detect potential infections and asymptomatic carriage.

Worldwide, there is an increasing demand for frontline healthcare workers (HCWs) to manage the various challenges of the SARS-CoV-2 pandemic. Frontline workers are at high risk

of exposure to SARS-CoV-2 and other emerging infections compared to the general population due to several reasons.^{1,2} Shortage of personal protective equipment (PPE) and lack of appropriate infection prevention and control mitigation measures increase

the risk of SARS-CoV-2 infection in hospital settings.^{3,4}

The World Health Organization (WHO) reported that over 35 000 frontline HCWs had SARS-CoV-2 infection by 21 April 2020, an underestimated figure.⁴ China's National Health Commission said that as of early March 2020, > 3300 HCWs contracted SARS-CoV-2 infection, and 22 had died by the end of February. Similarly, almost one-fifth of frontline hospital staff were infected in Italy, with some reported deaths.⁵

Transmission of SARS-CoV-2 infection by asymptomatic carriers has been reported.^{6,7} There is an increased risk of transmission and seroconversion among frontline HCWs. Undiagnosed infection in HCWs is common and can have catastrophic consequences, including staff absenteeism and transmission within healthcare facilities.⁸ The risk posed by asymptomatic infected individuals to others may be variable. The extent of seroconversion in the healthcare population may play a vital role in containing SARS-CoV-2 infection spread. This research aimed to study seroconversion incidence among frontline staff at the highest risk of exposure to SARS-CoV-2 respiratory infections, including emergency department, critical care, COVID-19 isolation wards, and all healthcare job categories, including infectious diseases specialists and infection prevention. The first two cases of SARS-CoV-2 were diagnosed on 24 February 2020 in the community and the first case diagnosed at our hospital was on 10 March 2020. Since this date, the hospital has continued to have further cases.

METHODS

The Royal Hospital is a tertiary care hospital with 800 beds. During the pandemic, bed occupancy decreased significantly. Four wards were assigned for admission of SARS-CoV-2 infected patients, two for general medical patients requiring hospitalization and two for critically ill ventilated patients. An additional ward consisting of 16 single rooms (multi-specialty ward) utilized mainly for isolation of patients with infectious diseases was dedicated to patients with suspected SARS-CoV-2 infection who were admitted transiently until confirmation was ready. Critically ill patients with suspected SARS-CoV-2 infection were admitted transiently into single negative pressure rooms in

the general intensive care unit (ICU) and then were shifted to COVID-19 ICU once SARS-CoV-2 test was positive.

The population studied were frontline HCWs, who were likely to be continuously exposed to suspected/confirmed cases of SARS-CoV-2. This included the emergency department (adult and pediatric), adult critical care, COVID-19 isolation wards, infectious diseases specialists, and infection control staff. All job categories were included in the study. During the initial stage of the pandemic, COVID-19 isolation wards were cared for by ICU doctors and nurses. Later in the pandemic, HCWs were recruited from other departments, such as medicine and surgery, to provide ICU care. However, the same staff recruited in the study were included and followed up.

This prospective cohort study was on the seroconversion rate among the frontline HCWs at the highest risk of exposure to SARS-CoV-2 infection. This was conducted between May and August 2020 when the country experienced the highest rates of community spread. Demographic characteristics of participants were collected on enrollment to the study, included age, gender, comorbidities, HCW category, location of work, and type of exposure using a questionnaire that was filled through an interview after taking consent from participating staff.

We planned to include all HCWs working in the proposed locations. Enrollment was based on consent to participate on the study and there were no exclusion criteria.

Two serum samples were collected as a baseline in May 2020, and a second sample was collected after 12 weeks. Three to five milliliters of blood samples were collected in serum separator tubes and saved at -80 °C until testing was performed. Samples were tested for SARS-CoV-2 immunoglobulin G (IgG) with Euroimmun ELISA kit. This is an enzyme-linked immunosorbent assay intended for the qualitative detection of IgG class antibodies to SARS-CoV-2 in human serum or plasma (K+-EDTA, Li+-heparin, and Na+-citrate). Results were evaluated by calculating an odds ratio (OR) of the control or patient sample over the OR of the calibrator. Results were interpreted as follows: OR < 0.8 as negative and a ratio ≥ 1.1 was considered positive. SARS-CoV-2 infection was diagnosed by testing nasopharyngeal swabs with SARS-CoV-2

Table 1: Characteristics of seropositive healthcare workers.

Characteristics	Total n (%)	1st SARS-CoV-2 IgG reactive	2nd SARS-CoV-2 IgG reactive	Positivity rate n (%)	95% CI
Age, years					
< 30	56 (17.1)	0	2	2 (3.6)	0.6–11.3
31–49	246 (75.0)	3	9	12 (4.9)	2.7–8.1
≥ 50	26 (7.9)	1	1	2 (7.7)	1.3–23.2
Total	328	4	12	16 (4.9)	2.9–7.6
Nationality					
Omani	94 (28.7)	1	5	6 (6.4)	2.6–12.8
Non-Omani	234 (71.3)	3	7	10 (4.3)	2.2–7.5
Indian	136 (41.5)	3	4	7 (5.1)	2.3–9.9
Filipino	67 (20.4)	0	2	2 (3.0)	0.5–9.5
Others	31 (9.5)	0	1	1 (3.0)	0.16–14.9
Gender					
Male	71 (21.6)	2	0	2 (2.8)	0.5–9.0
Female	257 (78.4)	3	11	14 (5.4)	3.1–8.8
Wilayat (city)					
Muscat governorate	302 (92.1)	3	10	13 (4.3)	2.4–7.1
Bowshar	191 (58.2)	2	8	10 (5.2)	2.7–9.1
Seeb	43 (13.1)	0	2	2 (4.6)	0.8–14.5
Matrah	45 (13.7)	1	0	1 (2.2)	0.1–10.5
Muscat	23 (7.0)	0	0	0	
Outside Muscat	26 (7.9)	1	2	3 (11.5)	3.0–28.3
Work location					
COVI-19 area and ICU	184 (56.1)	2	8	10 (5.4)	2.8–9.5
Emergency	116 (35.4)	1	1	2 (1.7)	0.3–5.6
MSPW	17 (5.2)		1	1 (11.7)	2.0–33.7
Infectious disease	6 (1.5)	1	2	3 (50.0)	14.7–85.3
IP&C	5 (1.5)				
Job category					
Doctor	72 (22.0)	1	2	3 (4.2)	1.07–10.9
Nurse	230 (70.1)	3	10	13 (5.6)	3.2–9.2
Medical orderly	2 (0.6)	-	-	-	-
Cleaner	5 (1.5)	-	-	-	-
Physiotherapist	5 (1.5)	-	-	-	-
Radiographer	10 (3.0)	-	-	-	-
Infection preventionist	4 (1.2)	-	-	-	-
Comorbidities					
Yes	75 (22.9)	1	5	6 (8.0)	3.3–15.9
DM	10 (3.0)	-	1	-	-
HTN	16 (4.9)	-	1	-	-
Obesity	17 (5.2)	-	1	-	-
Dyslipidemia	1 (0.6)	-	1	-	-
Pregnancy	4 (1.2)	-	1	-	-
Immunosuppressant	2 (0.6)	1	-	-	-
Others	25 (7.6)	-	-	-	-
No	252 (76.8)	3	6	10 (4.0)	2.0–7.0
AGPs					
Yes	301 (91.8)	3	10	13 (4.3)	2.4–7.1
No	27 (8.2)	1	2	3 (11.0)	2.9–27.0

IgG: immunoglobulin G; CI: confidence interval; ICU: intensive care unit; MSPW: male specialist ward; IP&C: infection prevention and control; DM: diabetes mellitus; HTN: hypertension; AGPs: aerosol-generating procedures.

Table 2: Characteristics of seroconverted healthcare workers (PCR and symptoms).

Characteristics	1st IgG reactive n = 4	2nd IgG reactive n = 12	Total n (%)
PCR			
Positive	1	7	8 (50.0)
Negative	1	3	4 (25.0)
Not done	2	2	4 (25.0)
Presence of symptoms			
Symptomatic	2	11	13 (81.3)
Asymptomatic	2	1	3 (18.8)
Acquisition			
Hospital-acquired	1	1	2 (12.5)
Community acquired	0	5	5 (31.3)
Unknown source	3	6	9 (56.3)

PCR: polymerase chain reaction; IgG: immunoglobulin G.

polymerase chain reaction (PCR) using GeneXpert system. Testing by PCR was done for those who showed symptoms suggestive of SARS-CoV-2 infection. This study was approved by the hospital ethics and research committee (reference number SRC#33/2020).

We used proportions with 95% confidence interval (CI) for categorical data and mean/median as appropriate for continuous data. Statistical inference was drawn using the chi-square test wherever needed. The statistical significance level was fixed at 0.05.

RESULTS

A total of 364 HCWs were enrolled in the study initially. Only 328 HCWs provided the second sample for seroconversion; hence, the remaining 36 were excluded. Table 1 shows the demographic characteristics of the enrolled HCWs.

Table 1 shows the characteristics of seroconverted HCWs. Fourteen out of 328 HCWs seroconverted in this study giving an incidence rate of 3.6%, excluding four HCWs that were positive at baseline. The median age was 43.5 (range = 28–57). About 75.0% of HCWs were aged between 31–49 years with a seroconversion rate of 4.9% (95% CI: 2.7–8.1). Females accounted for the majority of seroconverted HCWs (14/257) at a rate of 5.4% (95% CI: 3.1–8.8). Omanis seroconverted with a rate of 6.4% (95% CI 2.6–12.8), whereas non-Omanis seroconverted at a rate of 4.3% (95% CI: 2.2–7.5). Ninety-two percent

(302/328) of the staff lived in the capital area, and a minority lived outside the capital (3/26). Thirteen Muscat citizens seroconverted at a 4.3% rate (95% CI: 2.4–7.1).

Nurses comprised the majority accounting for about 81% followed by doctors (19%) at rates of 5.6% (95% CI: 3.2–9.2) and 4.2% (95% CI: 1.07–10.9), respectively. Staff covering COVID-19 isolation wards and ICU comprised over 60% (n = 10) of those who seroconverted with a rate of 5.4% (95% CI: 2.8–9.5) followed by infectious diseases doctors and adult emergency doctors at 19% (n = 3) and 12.5% (n = 1), respectively. Approximately 81.3% (n = 13) of HCWs performed aerosol-generating procedures (AGPs) at a seroconversion rate of 4.3% (95% CI: 2.4–7.1). Risk factors were reported in just below half of the cases, including obesity, hypertension, diabetes mellitus, and pregnancy.

Table 2 shows the characteristics of seroconverted HCWs (PCR and symptoms). Only four HCWs were positive for SARS-CoV-2 IgG at baseline, around 1.0% of the cohort, while 4.0% converted later. About 50.0% of those who seroconverted had evidence of infection with a positive PCR before seroconversion, 25.0% had a negative PCR before second serology testing, and 25.0% did not have any evidence of infection and were not tested with PCR. One ICU doctor had a significant contact exposure with a COVID-19 case and was asymptomatic, but tested positive by PCR; however, he did not seroconvert. Approximately 20.0% of seroconverted staff had no reported symptoms compared to 80.0% who reported symptoms such as sore throat (70%), fever (50.0%), myalgia (20.0%), and to a lesser frequency (15.0%), runny nose, loss of smell, and headache. None of the tested staff had pneumonia or required hospitalization.

DISCUSSION

In our cohort, the incidence rate was 3.6%. The majority of the HCWs were between 31–49 years old. Expatriate citizens, mainly Indians and Filipinos, comprised the majority at a rate of 4.3% compared to Omanis, and this might be due to the low number of Omanis in the recruited population (28.7%). Moreover, from a report that was published about COVID-19 infections in Muscat Governorate, Omanis constituted 25.9% compared to 74.1% of expatriates in the period from February to May 2020.⁹

Female HCWs constituted the majority with a positivity rate of 5.4%. The majority was from the capital city, mainly from Bowshar, at 4.3%. This might be due to the location of the hospital in Bawshar and the staff residing in proximity. In addition, reports from the community showed that this region had one of the highest rates of SARS-CoV-2 infection (23%) in Muscat.⁹ Only doctors and nurses seroconverted compared to other tested job categories at 4.2% and 5.6%, respectively. About 62.5% worked in the COVID-19 wards with seroconversion rate of 5.4%.

The seroconversion rate in our study was similar to the overall infectivity rate at the Royal Hospital staff that was reported previously.¹⁰ Similarly, a US study reported a lower seroconversion rate at 1.6%.¹¹ Our rate was low compared to previous reports from other countries such as the UK (44%), Italy (16.8%), Australia (19.4%), and China (17.1%).¹²⁻¹⁴ In the UK study, 25% of the cohort was seropositive at enrollment compared to only 1.0% in this study. The high infection rate reported in some of these countries might have been associated with failure of healthcare system at the peak of the pandemic,¹⁵ unlike the situation in Oman that had a successful response plan in the initial phases.¹⁶

There was a higher tendency of infection among the middle age group (31–49 years), contrary to what was reported by Catherine et al,¹² as more frequent infections were reported in lower age groups (< 30 years). Females accounted for the majority of seropositive cases, similar to the overall COVID-19 infections among HCWs at Royal Hospital in one report. This is contrary to community reports that showed 80% of infections were in males.^{10,17}

The highest seropositivity was seen in the staff covering ICU and COVID-19 isolation wards comprising about 60.0% of infections, more in nurses than doctors. This is different from what was reported in a preprint report from Turkey, with high seropositivity rates among cleaning staff 6% and radiology technicians 1%, in addition to doctors and nurses.¹⁸ The majority of infected staff performed AGPs (81.3%) with a seroconversion rate of 4.3%. A high infection rate was reported among frontline HCWs in the US and the UK compared to the community and other HCWs who are not involved with direct care of COVID-19 patients. They also identified inadequate PPE supply and reuse of PPEs as a significant risk for SARS-CoV-2

infection.¹⁹ Al Lawati et al,²⁰ reported an outbreak related to unprotected exposure of 38 HCWs to a patient who was on non-invasive ventilation for 48 hours that showed 86.9% tested positive for SARS-CoV-2 PCR.²⁰

In our study, the lower rates of infections among frontline workers might be due to the stringent infection prevention and control practices that were implemented with confirmed and suspected cases. These practices included a designated area for PPE donning and doffing and changing uniforms before and after work. Moreover, an area was dedicated to eating and resting while maintaining social distancing. Continuous education and training of all staff working in frontline areas were established to improve the infection control practices led by a dedicated team. However, adequate PPE supply was a challenge in our setting earlier in the pandemic, especially N95, that needed to be extendedly used or reused in some instances and may explain a higher seroconversion among those staff. Extended use was used among nurses caring for non-critical patients and reused for doctors and those not involved with direct patient care. In addition, frequent cleaning and disinfection of high touch surfaces was emphasized using disinfectant wipes and chlorine-based solutions as per hospital disinfection guidelines.

Half of the seroconverted HCWs had evidence of acute infection as proven by PCR test. Also, 25.0% of those with reactive SARS-CoV-2 IgG had a prior PCR but showed negative results that might indicate failure of detection at early stage. One systematic review that analyzed five studies revealed that false negativity of PCR was between 2 and 29%.²¹

There was no PCR test for 25.0% ($n = 4$) of those who had positive IgG because they had no symptoms or had very mild symptoms that did not necessitate seeking medical advice. Furthermore, three patients seroconverted without showing symptoms suggestive of SARS-CoV-2 infection. One study reported that 48% of those who seroconverted had symptoms as per COVID-19 case definition and 38% had asymptomatic carriage.¹² Asymptomatic carriage of the virus might lead to silent transmission of the infection among healthcare workers. This may suggest that screening of HCWs by symptoms alone is not enough to detect potential carriers. Hence, an intensified screening protocol for frontline HCWs with continuous exposure to SARS-CoV-2 patients

is needed as was recommended by Julia et al.²² This must include active or self-screening for symptoms that warrant immediate testing with PCR. Periodic testing for asymptomatic staff might not be feasible in our setting due to shortage of PCR kits and considered not cost effective as the performance of PCR depends on the pretest probability and might give false negative results in such population.²³ If the pretest probability is high, repeat testing is recommended to rule out infection. Serology testing is not useful to rule out acute infections, however, it could be utilized as a periodic screening tool for staff to evaluate the effectiveness of mitigation measures at the peak of pandemic and detect asymptomatic carriage that might be missed by PCR.

About 5 (31.3%) of the seroconverted HCWs had confirmed community source for their infections. Two acquired it from hospital due to contact with a positive colleague (12.5%) and 9 (56.3%) had no identified source for their infections. Another study reported the most common acquisition of COVID-19 among HCWs was from the community (61.3%), followed by hospital acquisition (25.5%); no source was identified in 13.2% of cases.¹⁰ In contrast, Al-Siyabi and colleagues showed that hospital acquisition was the most common source of infection.²⁴

Our study has a few limitations that need to be addressed. First, despite the good sample size in our study, it was single centered which makes it difficult to draw generalizable conclusions. Second, the HCWs were not screened periodically with symptoms, serology, and PCR tests instantly. However, serum samples were collected at the beginning and at the end of the study. PCR was done only if there was an indication for testing those who met the case definition for SARS-CoV-2 infection by self-monitoring. Third, asymptomatic carriers could have been missed during the study period with this methodology. In addition, the duration between the first and the second test was long due to delay in submission of the samples especially from critical care unit staff. This led to difficulty in identification of the exact time of seroconversion in these HCWs. Moreover, the vast majority of HCWs categories that were included in the study were nurses and doctors and less paramedical staff and contractors were included, which might not give the real prevalence of COVID-19 infections in these categories.

CONCLUSION

Detection of COVID-19 infection among HCWs is important to prevent further transmission especially asymptomatic carriers. Combined screening strategy by symptoms, serology, and PCR might help in the detection of potential infections and asymptomatic carriage. However, implementation of such protocols is challenging due to limited resources. Stringent infection prevention and control practices in the workplace and adequate supply of PPEs are important in protecting frontline HCWs.

Disclosure

All authors declared no conflicts of interests. No funding was received for the study.

Acknowledgments

We thank all participants in this study. We also thank all staff in microbiology department, infection prevention and control, and staff clinic which helped in the data and sample collection.

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