# Seroconversion Of COVID-19 In Frontline Healthcare Workers In A Tertiary Care Hospital In Oman

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## ABSTRACT

***Objectives:*** This research aimed to study the seroconversion among frontline staff who were at highest risk of exposure to SARS-CoV-2 infections including emergency department, critical care, COVID-19 isolation wards in all healthcare job categories. ***Methods:*** This was a prospective cohort study on the incidence of seroconversion among frontline HCWs at the Royal hospital. 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 healthcare workers that were positive at baseline. The median age was 43.5 ranging between 28 and 57. About 75% of HCWs were between 31-49 with a seroconversion rate of 4.9% (95% CI 2.7-8.1). Females accounted to the majority of seroconverted HCWs in this cohort (14/257) at a rate of 5.5% (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 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 at 19 % (n=3) and 12.5% (n=1) respectively. Approximately 81% (n=13) of HCWs performed aerosol-generating procedures (AGPs) at a seroconversion rate of 4.3%(95% CI 2.4-7.1). About 50% of those who seroconverted had a positive PCR before seroconversion, 25% had a negative PCR prior to second serology testing and 25% were not tested with PCR. Approximately 20% of seroconverted staff had no reported symptoms compared to 80% who reported symptoms such as sore throat (70%), fever (50%), myalgia (20%), and to a less frequency (15%) runny nose, loss of smell and headache.
***Conclusion:*** Detection of infection among healthcare workers 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.

Worldwide, there is an increasing demand upon the frontline healthcare workers (HCWs) to manage the various challenges of the Severe Acute Respiratory Syndrome Corona Virus 2 (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]

World Health Organization (WHO) reported that over 35,000 frontline healthcare workers had SARS-CoV-2 infection by 21 April 2020, which is an underestimated figure.[4] China's National Health Commission reported that as of early March 2020 more than 3300 health-care workers contracted SARS-CoV-2 infection, and at least 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 healthcare workers. Undiagnosed infection in healthcare workers is common[8] and can have catastrophic consequences including staff absenteeism and transmission within healthcare facilities. The risk posed by asymptomatic infected individuals to others may be variable. The extent of seroconversion in health care population may play a vital role in containing SARS-CoV-2 infection spread. This research aimed to study the incidence of seroconversion among frontline staff who are at highest risk of exposure to SARS-CoV-2 respiratory infections including emergency department, critical care, COVID-19 isolation wards and in all healthcare job categories including infectious diseases specialists and infection preventionist. The first two cases of SARS-CoV-2 were diagnosed on 24th February 2020 in the community and the first case diagnosed at our hospital was on the 10th of March 2020. Since this date, the hospital continued to have further cases.

## METHODS

The Royal hospital is a tertiary care hospital with almost 800 beds occupancy. During the pandemic, bed occupancy was decreased significantly and 4 wards were assigned for admission of SARS-CoV-2 infected patients, 2 for general medical patients requiring hospitalization and 2 for critically ill ventilated patients. An additional ward consists of 16 single rooms (Multi-specialty ward, MSPW), that was utilized mainly for isolation of patients with infectious diseases, was dedicated for patients with suspected SARS-CoV-2 infection whom were admitted transiently until confirmation is ready. Critically ill patients with suspected SARS-CoV-2 infection were admitted transiently into single negative pressure rooms in the general ICU and then were shifted to COVID-19 ICU once SARS-CoV-2 test was positive.

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

This was a prospective cohort study on the seroconversion rate among the frontline HCWs who were at the highest risk of exposure to SARS-CoV-2 infection. This study was conducted between May and August 2020 where 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 through a questionnaire that was filled through an interview after taking a consent from participating staff.
It was planned to include all HCWs working in the proposed locations; however, the enrollment was based on consenting 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 -80C until testing was performed. Samples were tested for SARS-CoV-2 IgG with Euroimmune ELISA kit that was validated in the lab. 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, Na+-citrate). Results were evaluated by calculating a ratio of the OD of the control or patient sample over the OD of the calibrator. Results were interpreted as follows: OD Ratio <0.8 as negative, and Ratio ≥1.1 was considered positive. SARS-CoV-2 infection was diagnosed by testing nasopharyngeal swabs with SARS-CoV-2 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 with a 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 Chi square test wherever needed. The statistical significance level was fixed at 0.05.

**RESULTS:**

*Baseline characteristics:*

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.

**Table1. Characteristics of seropositive healthcare workers**

| | Total number (%) | 1st SARS-CoV-2 IgG reactive | 2nd SARS-CoV-2 IgG reactive | Positivity rate (%) | 95% CI |
|---|---|---|---|---|---|
| **Age, years** | | | | | |
| <30 | 56 (17) | 0 | 2 | 2 (3.6) | 0.6- 11.3 |
| 31-49 | 246 (75) | 3 | 9 | 12 (4.9) | 2.7-8.1 |
| >= 50 | 26 (8) | 1 | 1 | 2 (7.7) | 1.3-23.2 |
| Total | 328 | 4 | 12 | 16 (4.9) | 2.9-7.6 |
| **Nationality** | | | | | |
| *Omani* | 94 (29) | 1 | 5 | 6 (6.4) | 2.6-12.8 |
| *Non-Omani* | 234 (71) | 3 | 7 | 10 (4.3) | 2.2-7.5 |
| Indian | 136 (41) | 3 | 4 | 7 (5.1) | 2.3-9.9 |
| Filipino | 67 (20) | 0 | 2 | 2 (3.0) | 0.5-9.5 |
| Others | 31 (10) | 0 | 1 | 1 (3.0) | 0.16-14.9 |
| **Gender** | | | | | |
| Male | 71 (22) | 2 | 0 | 2 (2.8) | 0.5-9.0 |
| Female | 257 (78) | 3 | 11 | 14 (5.5) | 3.1-8.8 |
| **Wilayat (City)** | | | | | |
| *Muscat governorate* | 302 (92) | 3 | 10 | 13 (4.3) | 2.4-7.1 |
| Bowshar | 191 (58) | 2 | 8 | 10 (5.2) | 2.7-9.1 |
| Seeb | 43 (13) | 0 | 2 | 2 (4.6) | 0.8-14.5 |
| Matrah | 45 (14) | 1 | 0 | 1 (2.2) | 0.1-10.5 |
| Muscat Wilayat | 23 (7) | 0 | 0 | 0 | |
| *Outside Muscat* | 26 (8) | 1 | 2 | 3 (11.5) | 3.0-28.3 |
| **Work Location** | | | | | |
| COVID 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) | 14.7-85.3) |
| IP&C | 5 (1.5) | | | | |
| **Job category** | | | | | |
| Doctor | 72 (22) | 1 | 2 | 3 (4.2) | 1.07-10.9 |
| Nurse | 230 (70) | 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) | | | | |
| Infection preventionist | 4 (1) | | | | |
| **Comorbidities** | | | | | |
| *Yes* | 75 (23) | 1 | 5 | 6 (8.0) | 3.3-15.9 |
| DM | 10 (3) | | 1 | | |
| HTN | 16 (5) | | 1 | | |
| Obesity | 17 (5) | | 1 | | |
| Dyslipidemia | 1 (0.6) | | 1 | | |
| Pregnancy | 4 (1) | | 1 | | |
| Immunosuppressant | 2 (0.6) | 1 | | | |
| Others | 25 (8) | | | | |
| *No* | 252(77) | 3 | 6 | 10(4.0) | 2.0-7.0 |
| **AGPs** | | | | | |
| Yes | 301 (92) | 3 | 10 | 13 (4.3) | 2.4-7.1 |
| No | 27 (8) | 1 | 2 | 3 (11.0) | 2.9-27.0 |

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

| | | 1st IgG reactive N=4 | 2nd IgG reactive N=12 | Total (%) |
|---|---|---|---|---|
| PCR | Positive | 1 | 7 | 8 (50) |
| | Negative | 1 | 3 | 4 (25) |
| | Not done | 2 | 2 | 4 (25) |
| Symptomatic | | 2 | 11 | 13 (81) |
| Asymptomatic | | 2 | 1 | 3 (19) |
| Hospital acquired | | 1 | 1 | 2 (12.5) |
| Community acquired | | 0 | 5 | 5 (31.25) |
| Unknown source | | 3 | 6 | 9 (56.25) |

*Baseline characteristics of seroconverted healthcare workers:*

Table 1 shows the characteristics of seroconverted healthcare workers. Fourteen out of 328 HCWs seroconverted in this study accounting for an incidence rate of 3.6% excluding four healthcare workers that were positive at baseline. The median age was 43.5 ranging between 28 and 57. About 75% of HCWs had an age between 31-49 with a seroconversion rate of 4.9% (95% CI 2.7-8.1). Females accounted to the majority of seroconverted HCWs in this cohort (14/257) at a rate of 5.5% (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 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 at 19 % (n=3) and 12.5% (n=1) respectively. Approximately 81% (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, pregnancy and others.

*Seroconversion:*
Only 4 HCWs were positive for SARS-CoV-2 IgG at baseline, which is around 1% of the cohort while 4% converted later. About 50% of those who seroconverted had an evidence of infection with a positive PCR before seroconversion, 25% had a negative PCR prior to second serology testing and 25% did not have an evidence of infection and were not tested with PCR. One ICU doctor had a significant contact exposure with COVID-19 case and was asymptomatic, tested positive by PCR, however he did not seroconvert. Approximately 20% of seroconverted staff had no reported symptoms compared to 80% who reported symptoms such as sore throat (70%), fever (50%), myalgia (20%), and to a less frequency (15%) runny nose, loss of smell and headache. None of the tested staff had pneumonia or required hospitalization.

**DISCUSSION:**
In our cohort, the incidence rate after excluding those was 3.6%. The majority of the HCWs were between 31 to 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 (27%). Moreover, from the report that was published by Lamya et al. about COVID-19 infections in Muscat Governorate, Omanis constituted 25.9% compared to 74.1% in expatriates in the period from February to May 2020. [9]

Female healthcare workers constituted the majority with a positivity rate of 5.5%. The majority was from the capital Muscat mainly from Wilayat of Bowshar at a rate of 4.3%. This might be due to the location of the hospital in Bawshar and 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 rates of 4.2% and 5.6% respectively. About 62.5% worked in the COVID 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 by Zaina et al at about 4.3%. [10] Similarly, a US study reported a lower rate of seroconversion 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%. [12,13,14] In the UK study, 25% of the cohort was seropositive at enrollment compared to only 1% 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 between 31-49 in contrary to what was reported by Catherine et al. as more frequent infections were reported in lower age groups of <30 years[12]. Females accounted for the majority of seropositive cases similar to the overall COVID-19 infections among HCWs at Royal hospital in the report by Zaina et al and in contrary to the community reports by Faryal et al that showed 80% of infections were in males. [10, 17]
The highest seropositvity was seen in the staff covering ICU and COVID-19 isolation wards comprising about 60% 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%) with a seroconversion rate of 4.3%. High rate of infection was reported among frontline healthcare workers in US and the UK compared to the community and other healthcare workers 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] Adil et al 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 designated area for PPE donning and doffing and changing uniforms before and after work. Moreover an area was dedicated for eating and resting with maintenance of social distancing. Continuous education and training of all staff working in frontline areas was established to improve the infection control practices that were led by a dedicated team of infection control department. However, adequate supply of PPEs was a challenge in our setting earlier in the pandemic especially N95 that needed to be extendedly used or reused in some instances which may explain a higher seroconversion among those staff. Extended use was used among nurses caring for non-critical patients and reuse for doctors and those who are 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 an evidence of acute infection as proven by PCR test. Also, 25% 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%(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, 3 patients seroconverted without showing symptoms suggestive of SARS-CoV2 infection. Catherine et al. 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 healthcare workers by symptoms alone is not enough to detect potential carriers. Hence, an intensified screening protocol for frontline health care workers 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%) of the seroconverted HCWs 5 had confirmed community source for their infections. Two only acquired it from hospital due to contact with a positive colleague (12.5%) and 9 (56.25%) had no identified source for their infections compared to the report by Zaina et al. who 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, Nada and colleagues showed that hospital acquisition was the most common source of infection.[24]

In the present study, there are few limitations that need to be addressed. Firstly, despite the good sample size in our study, it was single centered that makes it difficult to draw generalizable conclusions. Secondly, the healthcare workers were not screened periodically with symptoms, serology and PCR tests instantly. However, serum samples were collected at the beginning and the end of the study. PCR was done only if there was an indication for testing with HCWs who met the case definition for SARS-CoV-2 infection by self-monitoring. Thirdly, 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 healthcare workers categories that were included in the study were nurses and doctors and less numbers of paramedical staff and contractors were included that might not give the real prevalence of COVID-19 infections in these categories.

**CONCLUSION:**

Detection of infection among healthcare workers 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 healthcare workers in high-risk areas.

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