



# SARS-CoV-2 Antibodies in the Public Hospital Staff: The Second Report of a Seroprevalence Cohort Study from Iran

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## Abstract

**Background:** SARS-CoV-2 is a novel virus that caused the recent global pandemic. Health care workers (HCWs), especially hospital staff, are at a higher risk of infection by this virus than the general population. In this study, anti-SARS-CoV-2 IgG antibodies were assessed in hospital workers.

**Methods:** This prospective seroconversion-based cohort study assessed chronic immunity against covid-19 in the staff of two hospitals, the main referral hospital and a general hospital in Shiraz, south of Iran. A valid and reliable checklist was filled out for each available staff member willing to participate in this study through a face-to-face interview. Furthermore, the titer of anti-covid-19 IgG was measured by ELISA twice; in July 2020 after the second wave of COVID-19 and in February 2021 after the third wave in IRAN.

**Results:** One hundred forty (65%) of the 214 members who participated in both stages of this consideration were from the COVID-19 referral healing center, and 74 (35%) were from the common clinic. Twelve (5.6%) of staff members had anti-SARS-CoV-2 IgG antibodies, including 10 (7.1%) from the referral healing center and 2 (2.7%) from the common healing center ( $P = 0.23$ ). In the second measurement (second overview), 79 (36.9%) of members had IgG antibodies; 58 (41.4%) from the primary hospital and 21 (28.3%) from the second healing center ( $P = 0.039$ ). Crude of the IgG titer within the first study and the referral clinic was  $0.8 \pm 0.3$  compared to  $0.15 \pm 0.42$  within the common clinic ( $P = 0.001$ ). These figures were  $3.05 \pm 4.58$  and  $1.74 \pm 3.53$  in both clinics and within the second overview separately ( $P = 0.003$ ). IgG levels were significantly higher in the second overview compared to the first ( $P < 0.0001$ ).

**Conclusions:** During the third wave of COVID-19, a significant proportion of hospital staff developed COVID-19 IgG, especially in the referral hospitals for COVID-19. As a result of their higher and chronic exposure to COVID-19 patients than the general hospital staff, the titer of IgG in the referral hospital staff was also higher. However, the seroconversion rate between the two waves was 1.8 times in the general hospital staff compared to the referral hospital, possibly due to less conservative precautions against covid-19 among them. Even after receiving the anti-covid-19 vaccination, it is important to monitor the immunity of hospital staff to covid-19 and to adhere strictly to standard precautions.

**Keywords:** Hospital, Staff, Health Care Worker, COVID-19, SARS-CoV-2, Chronic Immunity, IgG

## 1. Background

SARS-CoV-2 may be a novel respiratory crown infection that causes a global widespread (1). As one of the primary nations included, Iran's case was detailed on February 20, 2020 (2). As of November 28, 2021, there had been 61,33839 confirmed cases of COVID-19 and 13,376 deaths reported across the country (3). Despite worldwide continuance and handfuls of inquiries, there is no clear known cure for this

infection (4). The location of patients remains one of the most significant challenges for wellbeing systems considering the wide variety of clinical indications, from asymptomatic and mellow respiratory indicators to COVID-19 and passing other than a shifted hatching period of 2 - 14 days (5-7). Researchers are trying to introduce novel methods of overcoming this problem, but these methods are only being studied in clinical settings (8). There is also the question of post-infection immunity, whether it exists, how

long it lasts, and whether it can prevent or decrease symptomatic reinfection. Recent studies suggest that neutralizing antibodies against the spike protein receptor-binding domain of SARS-CoV-2 may provide some post-infection immunity. However, the association between antibody titers and plasma neutralizing activity is assay-dependent and time-dependent (9-11). It has been demonstrated in a large cohort study of 12,541 health care workers (HCWs) that anti-spike and anti-nucleocapsid IgG antibodies are associated with a reduced risk of COVID-19 reinfection within six months of infection (12). HCWs are among high-risk groups for getting coronavirus (13), and they are accounted for a significant proportion of COVID-19 worldwide due to multiple sources of COVID-19 transmission from patients, colleagues, and the community (14). Screening HCWs for COVID-19 symptoms is a standard prevention protocol for the early detection of the disease and restriction of its spreading among them. However, studies demonstrate that many incubated asymptomatic patients may spread the virus (15-18). Numerous studies have examined the risk of SARS-CoV-2 infection in the health care workplace, but the findings have been contradictory (19-24). As a result, we could help implement surveillance of SARS-CoV-2 sero-immunity and protective protocols among HCWs by determining the seroconversion of IgG antibodies in this prospective study. According to the first report of this cohort study that was conducted on the staff of two hospitals in Shiraz, Iran, in 2020, anti-SARS-CoV-2 IgG was positive in 5.9% of HCWs (25).

## 2. Methods

### 2.1. Study Design, Participants, and Data Collection

The cohort study, which measured SARS-CoV-2 IgG seroconversion in HCWs of two fundamental clinics in Shiraz City, the capital city of Fars Area in the south of Iran, was conducted between July 13, 2020, and February 25, 2021. Two chosen clinics included one as the COVID-19 referral clinic (Ali-Asghar healing center) and another one as a non-referral typical clinic (Dastgheib clinic). Choosing the moment healing center was to reveal any plausible differences between the two healing centers, one of which was committed to COVID-19 cases, and the other was not. The 214 hospital staff from different segments eager to take part without thinking about it were inspected helpfully after two weeks of declaration in these healing centers. The participants did not receive covid vaccines at the time. Once the overview had been clarified, a checklist comprising socio-demographic and occupational characteristics was compiled using a face-to-face interview with each interviewee independently and privately in clinics.

### 2.2. Serologic Measurement

A recent systematic review concluded that RT-PCR is the most accurate test for diagnosing SARS-CoV-2. Although the technique is complex and expensive, inappropriate sampling can give false results. Therefore, alternative serological methods could be useful in addition to RT-PCR (26). Many new methods are emerging with appropriate specificity and sensitivity, such as serological monoclonal IgG antibody detection against the S1 protein of SARS-CoV-2, although additional evidence is required in clinical practice (27). Following the first serosurvey, which was in July 2020 and after the second wave of COVID-19 in IRAN, the second measurement was conducted in February 2021, after the third wave of COVID-19. Approximately three milliliters of blood were taken from each member. A centrifuge was then used to separate the sera, which were stored at -80°C until they were tested. According to World Health Organization (WHO) guidelines, we measured IgG levels using the anti-SARS-CoV-2-enzyme-linked-immunosorbent (Pishtaz Co. ®), a qualitative ELISA kit with a sensitivity of 94.1% and specificity of 98.3. The recombinant nucleoprotein was coated (100 ng/well) overnight onto 96-well plates (22). At that point, it was hatched with weak serum tests at 1:101. The Optical density (OD) (450 nm - 630 nm) was measured. Then, the OD of the test was calculated to decide the cutoff file. The cutoff records higher than 1.1 were considered positive tests.

The cutoff files below 0.9 were considered negative tests (19, 23). For lists inside the dim zone (0.9 - 1.1), testing was rehashed to realize a clear value. A random recheck of selected tests was conducted in another laboratory as a means of quality assurance.

### 2.3. Statistical Analysis

Factual examinations were performed using SPSS 20.0. Additionally, the standard deviation was applied to show persistent factors, while categorical factors appeared as recurrence and rate. The univariate investigation was done utilizing a t-test and chi-squared test, considering P-values < 0.05 as the implication level.

### 2.4. Ethical Approval

At all stages of this process, intentional interest and security maintenance were considered. Each subject provided a marked educated assent frame. The result of counteracting agent titer was sent to each member by the short message service (SMS) based on their demands. As endorsed by the Shiraz College of Restorative Sciences (Entireties), this thought adhered to the moral rules of the 1975 announcement of Helsinki. An enrollment number

of IR.SUMS.REC.1400.203 has been assigned to the Morals Committee.

#### 4. Results

It was found that the average age of 214 study participants was  $38.1 \pm 8.8$  years, while the majority of them (145; 67.7%) were females, and 162 (75.7%) were married. The majority of interviewees worked in admission wards (35; 16.3%), operating rooms (33; 15.4%), intensive care units (20; 9.3%), laboratories (18; 8.4%), administrative sections (18; 8.4%) and emergency departments (12; 5.6%). A total of 140 participants (65.4%) were from the COVID-19 referral hospital and 74 (34.6%) from the general hospital. In the first survey, 12 (5.6%) participants were positive for the anti-SARS-CoV-2 IgG antibodies, including 10 (7.1%) of the reference hospital due to COVID-19 and 2 (2.7%) of the general hospital ( $P = 0.23$ ). In the second survey, 79 (36.9%) participants were positive, with 58 (41.4%) from the reference hospital and 21 (28.3%) from the general hospital ( $P = 0.039$ ). Nine (4.2%) participants were positive for the first and second surveys, and 128 (59.8%) were negative for the first and second surveys. Sixty-nine (32.2%) were positive only for the second survey, while three (1.4%) were positive only for the first survey. Additionally, the mean titer of IgG in the referral hospital was  $0.8 \pm 0.3$  compared to  $0.15 \pm 0.42$  in the non-referral hospital ( $P = 0.001$ ), while in the second measurement, the figures were  $3.05 \pm 4.58$  and  $1.74 \pm 3.53$ , respectively ( $P = 0.003$ ). The increase in IgG level in the second investigation over the first for each hospital was also significant ( $P < 0.0001$ ). In the second measurement, 52 (65.8%) of the IgG-positive participants reported a positive PCR test compared to 4 (33.3%) in the first. IgG negative tests with positive PCR were also observed at 33 (15.4%) in the second measurement, compared to 83 (38.7%) in the first measurement. In the second survey, 20 (9.3%) participants reported they had positive CT scans according to lungs' covid-19 related signs while they were negative for IgG compared to 54 (25.2%) participants with similar conditions in the first measurement. Out of 146 participants (68.2%) who reported exposure to COVID-19 patients, 9 (6.1%) and 62 (42.4%) had positive seroimmunity in the first and second surveys, respectively. As a result of the first and second surveys, COVID-19 hospitals constituted a significantly higher percentage (7.6%, 49%) than general hospitals (2.4%, 29%). The ratio of IgG positivity in the covid-referral hospital (7/95; 7.4%) was not significantly higher than in the general hospital (2/45; 4.4%) in the first survey ( $P = 0.48$ ). In the second survey, the figures for both hospitals were 45/92 (48.9%) and 18/45 (40%) ( $P = 0.7$ ).

#### 5. Discussion

A prospective longitudinal survey of hospital staff was conducted as part of the first cohort study in Shiraz, Iran, aimed to detect anti-SARS-CoV-2 IgG in staff. Nearly one-third of them were found to be positive. In addition, the positivity rate in the second survey (36.9%) was six times that in the first (5.9%). In addition, a higher prevalence and mean titer of SARS-CoV-2 IgG in HCWs in the covid-19-referral hospital remarked that they are at a greater rate of exposure and getting this infection than non-referral general hospitals' staff. Additionally, the study revealed that many HCWs were capable of developing COVID-19 antibodies without developing clinical symptoms. There is a significant risk associated with COVID-19 for healthcare workers (28). Within the first measurement, approximately one-third of HCWs had positive anti-SARS-CoV-2 IgG responses, and no significant difference was found between most referral and general clinics in terms of COVID-19 IgG responses. However, within the moment overview, the contrast was relatively higher in the reference clinic, likely due to higher presentation to infection and higher viral stack. This study also showed that many HCWs might develop antibodies over time without showing clinical signs and symptoms. According to the results of RT-PCR tests performed in 2020 on 4854 health care workers in 44 hospitals across Fars Province, Iran, 5.62% were positive (28). They also revealed that most infected cases were nurses (51.3%), while physicians showed a higher infection rate (3.2%). Emergency rooms had the highest infection rate among different departments (30.6%).

Additionally, about a third of the patients were asymptomatic, and myalgia (46%) and cough (45.5%) were the most frequent clinical features among those who were symptomatic (28). In the study mentioned above, the positivity rate (5.6%) was similar to ours (5.9%); however, the methods were different. According to the results of our study, a study in Saudi Arabia found higher seroconversion of SARS-CoV-2 antibodies in hospitals than in control hospitals (19). In addition, in health care workers with the post-covide syndrome (PCS), one study found no significant relationship between RT-PCR and antibody level. The results showed that although some health care workers developed a severe and prolonged infection, the antibodies were not produced after infection (29). Thus, the front-line HCWs are at a higher risk of severe disease and mortality. Therefore, commitment and compliance with standard precautions are necessary and effective in preventing virus transmission from patient to staff (30). An assessment conducted in Belgium found no differences in the presentation of COVID-19, but healthcare workers had a lower mortality rate (31). One explanation for these outcomes could

be that a higher level of exposure can cause a higher level of antibodies in HCWs, leading to milder clinical symptoms and lower mortality rates. According to another study conducted in Italy, non-severe SARS-CoV-2 infection can cause rapid declines in antibody titers and pro-inflammatory cytokines, suggesting that protection against reinfection may be temporary and only last for a short time. Therefore, serological testing is prudent to estimate the prevalence of SARS-CoV-2 infection with caution (32).

### 5.1. Strengths and Limitations

This study was conducted in the context of two centers (a COVID-19 primary referral clinic and a common healing center), making a comparison between them possible. In any case, this consideration was hindered by a few obstacles. As a result of a lack of budget, we were unable to conduct PCR and CT tests for health care workers, and we relied on self-reports from patients. There was also the issue that we might not be able to take tests in irregular intervals, and clinic staff from different segments interested in the study in a helpful manner.

### 5.2. Conclusions

According to this study, by the third wave of COVID-19, a significant proportion of hospital staff had developed COVID-19 IgG, particularly in the COVID-referral hospital. The titer of IgG in referral hospital staff was also higher than in general hospitals, which may be explained by their higher and chronic exposure to COVID-19 patients. Despite this, the seroconversion rate between the two waves in the general hospital staff was 1.8 times greater than in the referral hospital staff, possibly since they took less conservative precautions against covid-19. Continual monitoring of hospital staff immunity towards covid-19 and strict adherence to standard precautions are recommended even following anti-covid-19 vaccination.

### Footnotes

**Authors' Contribution:** Study concept and design: K. B. L, N. O. and B. H.; Acquisition of data: M. B. A. G., F. R., S. A. D., F. I. Analysis and interpretation of data: B. H., N. O., and M. S. Drafting of the manuscript: A. A, B. H. Critical revision of the manuscript for important intellectual content: B. H., N. O., A. A. Statistical analysis: N. A., A. A. and B. H..

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**Data Reproducibility:** The authors did not declare it.

**Ethical Approval:** IR.SUMS.REC.1400.203.

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**Informed Consent:** During all stages of the study, including interviews, data collection, recording, analysis, and reporting, the participants' privacy was assured. Each participant received the results of the antibody titers via SMS based on their request. All subjects provided written informed consent during all stages of this study, and their voluntary participation was respected at all times.

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