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Research Paper

# Seroprevalence of Anti-SARS-CoV-2 IgG Antibody in Healthcare Workers: A Report From Rafsanjan City

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## ABSTRACT

**Background:** Healthcare workers (HCWs) have a high risk of catching SARS-CoV-2 infection. Seroprevalence studies can provide related data on HCWs with a history of infections. Despite numerous seroepidemiological reports of COVID-19 in different groups, there are no such reports for HCWs working in Rafsanjan City, Iran. This study aimed to determine the SARS-CoV-2 seroprevalence among HCWs.

**Methods:** Blood samples were obtained from 295 participants, including healthcare personnel and administrative staff. The SARS-CoV-2 IgG antibody was measured by the ELISA method, and the obtained data were analyzed with the Chi-square test and logistic regression. A P<0.05 was considered statistically significant.

**Results:** The previous exposure to COVID-19 was higher in HCWs than in administrative department staff. Fifteen out of 130 (11.5%) participants had experienced SARS-CoV-2 infection without any symptoms. The results of logistic regression indicated that traveling (OR: 018, 95% CI: 0.08–0.74, P=0.001), occupation (OR: 0.2, 95% CI: 0.01–0.94, P<0.05), history of respiratory problems (OR: 0.15, 95% CI: 0.01–1.94, P<0.05), and major clinical signs (OR: 8.09, 95% CI: 3.7-17.66, P<0.001) are important factors which affect SARS-CoV-2 IgG antibodies.

**Conclusion:** Our results indicated an occupational risk for SARS-CoV-2 infection among HCWs. Because some HCWs are asymptomatic, their communication, such as traveling, must be controlled, and it is necessary to ensure the safety of HCWs and reduce their transfer to the community and patients.

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## 1. Introduction

The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), the cause of coronavirus disease 2019 (COVID-19), was first identified in Wuhan, China, in December 2019. COVID-19 spread rapidly worldwide, and World Health Organization (WHO) declared COVID-19 a pandemic on March 11, 2020 [1]. In Iran, the first confirmed case of COVID-19 was reported on February 19, 2020 [2]. SARS-CoV-2 causes symptoms ranging from mild symptoms to acute respiratory distress syndrome, severe pneumonia, and death [3]. Nevertheless, studies have shown that many individuals might be carriers of the virus without presenting symptoms for several days. So, the exact number of individuals infected by SARS-CoV-2 is unknown [4].

Healthcare workers (HCWs) have the highest risk of infection because they have close and direct contact with COVID-19 patients. They are more exposed to infection compared with the general population and, if infected, pose a risk to other HCWs and patients [5]. HCWs with a positive test need to be isolated or should be quarantined and self-isolated. In the peak of coronavirus infection, the supply of front-line HCWs may decrease and therefore be insufficient to respond to the HCW demand. To overcome this event, several policies, such as weekly shifts and periodic screenings, are implemented in patient care units [6-8].

Seroprevalence studies can provide related data on individuals who have experienced past or recent infections [9]. In this regard, screening for specific antibodies against SARS-CoV-2 is performed. immunoglobulin G (IgG) antibodies are secreted against pathogens and show evidence of recent or past infection [10]. Seroprevalence determination could provide a snapshot of the burden of infection among HCWs, and is beneficial for identifying risky units and assessing the levels of infection risk among hospital or non-hospital personnel [11, 12]. According to the Health Department of RUMS (Rafsanjan University of Medical Sciences), the first definitive case of this disease in HCWs was reported on March 12, 2020, while the first definitive diagnosis of COVID-19 was registered in the city on March 3, 2020. The total number of definitive patients in this group until the end of March 2020 was 127, a relatively significant number (Data unpublished).

Serological tests can determine the prevalence and incidence of SARS-CoV-2 infection [9]. Determining the number of infected HCWs and identifying the proportion of undetected infected people are important to inform infection control and prevention measures during the peak of the pandemic [6-8, 11, 12]. Despite the numerous seroepidemiological reports of this disease in different groups [5, 6, 11, 13-15], there are no such reports in health personnel under the supervision of RUMS. Thus, we aimed to determine the baseline seroprevalence of SARS-CoV-2 IgG antibody among this group and assessed the occupational and clinical signs for seropositivity. This research is one of the largest seroprevalence studies focusing on HCWs under the Deputy Minister of Health in Rafsanjan, Iran. Finally, we report the prevalence of asymptomatic carriers of COVID-19 among HCWs in Rafsanjan City and suggest some guidelines to reduce transmission of the disease.

## 2. Materials and Methods

### Study design, population, setting, and procedures

The present seroepidemiological study was conducted to measure SARS-CoV-2 IgG antibodies in employees working at RUMS, Rafsanjan, Iran, in the third quarter of 2021. After obtaining written informed consent, all participants completed a questionnaire containing sociodemographic data (i.e. age, sex, height, weight), clinical information such as exposure to confirmed COVID-19 cases, professional information (i.e. shift, hospital department, and occupation), self-report of COVID-19 related symptoms (i.e. fever, dry cough, fatigue and weakness, sore throat, impaired sense of smell and taste), and history of reverse-transcription polymerase chain reaction (RT-PCR) testing. In this seroepidemiological study, 5-mL blood samples were obtained from 295 individuals, including administrative staff (ADSs) and HCWs personnel. The exclusion criteria were taking immunosuppressive medication, autoimmune disease, and a history of cancer. All collected specimens were transferred to the laboratory for serum isolation and storage.

### Ethical approval

This study was approved by the Ethics Committee of RUMS, Rafsanjan, Iran (Ethical code: IR.RUMS.REC.1400.024). This trial procedure was conducted under the ethical standards of the Iranian Ministry of Health and Medical Education on human experimentation and in accordance with the Helsinki Declaration. Finally, all participants signed a consent form.

### Quantification of IgG against SARS-CoV-2

We used the ELISA kit (Pishtazteb Co., Iran) to measure serum-IgG antibody against SARS-CoV-2, according to the manufacturer's instructions. In this regard, 0.9-1.1, 1.1, and 0.9 cut-off values were considered borderline, positive, and negative, respectively. The ELISA diagnostic kit sensitivity and specificity for IgG were 94.1% and 98.3%, respectively.

### Classification of previous exposure to COVID-19

Before the determination of seroprevalence of COVID-19 among the individuals, previous exposure to COVID-19 was estimated, according to clinical signs. For this aim, based on self-report of clinical signs, two clinical criteria (minor and major) were considered. Then the individuals were divided into four subgroups according to clinical criteria, and the possibility of previous exposure to SARS-CoV-2 was estimated (Table 1).

### Statistical analysis

The IBM® SPSS software version 20 was used for data analysis and management. The obtained data were analyzed using the Chi-squared and logistic regression tests. P<0.05 was considered statistically significant.

## 3. Results

### Demographic data

A total of 295 HCWs were enrolled in this study (184 [62.3%] women and 111 [37.7%] men, with a mean age of 38.7±9.00 years). The results of IgG titers by age, sex, and other demographic data are shown in Table 2. Also, 223 (75.5%) of the individuals were HCWs in medical centers, and the others (24.5%) worked in the administrative departments. The SARS-CoV-2 IgG showed that the previous exposure to COVID-19 in HCWs was higher compared to ADS (24.2% vs 13.8%, respectively; Table 2), maybe this positive SARS-CoV-2 IgG titer was due to close contact with COVID-19 patients. However, the statistical analysis showed no significant relationship between the two groups (P=0.5). Also, our results indicated that a history of respiratory problems and COVID-19 were associated with positive SARS-CoV-2 IgG (P=0.001; Table 2).

### Previous exposure to COVID-19 and SARS-CoV-2 IgG titer

The SARS-CoV-2 IgG titers indicated that the individuals in the high possibility subgroup had a positive past disease (43.6%). Also, 15 out of 130 (11.5%) asymptomatic participants were positive for SARS-CoV-2 IgG antibodies (Figure 1 and Table 3). The statistical analysis showed a significant relationship between four subgroups (P=0.001, Table 3). Major signs, especially fever, dry cough, and fatigue, are common symptoms of SARS-CoV-2 infection among HCWs, and they should be considered infected if they have such symptoms.

### The role of travelling during COVID-19 pandemic on positive results

The results of traveling out of town during the COVID-19 pandemic among participants showed that suburban relocation could cause high exposure to COVID-19 (99 out of 143 [70%]) or spread the disease (Table 3). The statistical analysis showed a significant relationship between the traveler and no traveler groups (P=0.049, Table 3).

**Table 1.** Categories of individuals to the classification of previous exposure to COVID-19 based on the presence of clinical criteria

| Clinical Criteria | |
|---|---|
| **Major Signs** | **Minor Signs** |
| - Close contact with a COVID-19 patient<br>- Dry cough or shortness of breath<br>- Fatigue and weakness<br>- Fever or chills | - Body aches or headaches<br>- Gastrointestinal symptoms<br>- Sore throat<br>- The impaired sense of smell and taste |

| Categories of Participants | | | |
|---|---|---|---|
| **High Possibility** | **Medium Possibility** | **Low Possibility** | **Asymptomatic** |
| ≥3 major signs or<br>≥2 major signs and ≥1 minor sign | ≥2 major signs or<br>≥1 major sign and ≥2 minor signs | 0 major signs or<br>≥1 major sign and 1-2 minor signs | 0 major signs or<br>0 minor signs |

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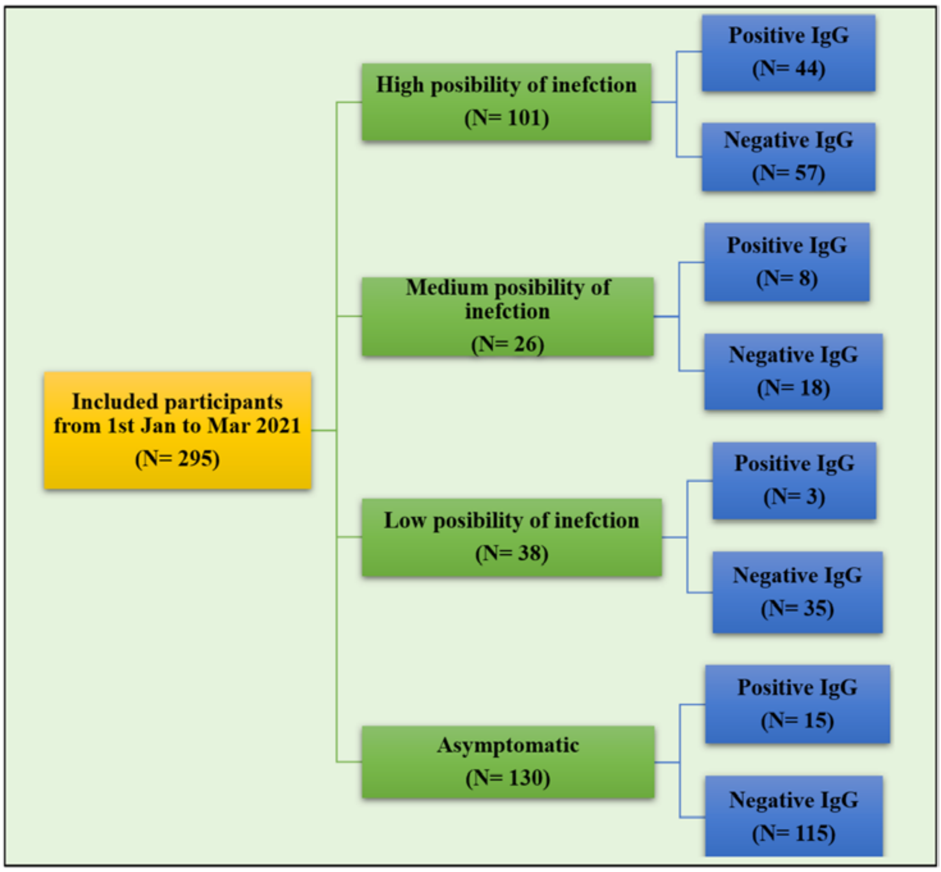


**Figure 1.** Flow diagram of study selection and outcomes



**Table 2.** Demographic data of participants

| Variables Positive | | No. (%)/Mean±SD | | | P |
|---|---|---|---|---|---|
| | | IgG Antibody | | Total | |
| | | Positive | Negative | | |
| Age (y) | >25 | 6(42.9) | 8(57.1) | 38.7±9.00* | 0.026 |
| | 25-34 | 12(12.9) | 81(87.1) | | |
| | 35-44 | 23(24.2) | 72(75.8) | | |
| | 45-54 | 23(28.7) | 57(71.3) | | |
| | <54 | 4(36.4) | 7(63.6) | | |
| Sex | Women | 41(22.3%) | 143(77.7) | 184(62.4) | 0.48 |
| | Men | 29(26.1%) | 82(73.9) | 111(37.6 ) | |
| Occupation | HCWs** | 54(24.2%) | 169(75.8) | 223(75.5) | 0.050 |
| | ADSs*** | 10(13.8%) | 62(86.2) | 72(24.5) | |
| Close contact with a COVID-19 patient | Yes | 53(23.1%) | 176(76.9) | 229(77.7) | 0.49 |
| | No | 17(25.7%) | 49(74.3) | 66(22.3) | |
| History of respiratory problems and COVID-19 | Yes | 39(42.4%) | 53(57.6) | 92(31.2) | 0.001**** |
| | No | 31(15.3%) | 172(84.7) | 203(68.8) | |

*** Administrative department staff; **** Significant relationship.

**Table 3.** SARS-CoV-2 Igg titer categories of participants to the classification of previous exposure to COVID-19 according to the presence of clinical criteria

| Categories Positive | | No. (%) IgG Antibody Positive | Negative | Borderline | Total | P |
|---|---|---|---|---|---|---|
| Categories of participants based on clinical criteria | High possibility | 44(43.6) | 57(56.4) | 0 | 101(34.2) | 0.001* |
| | Medium possibility | 8(30.8) | 18(69.2) | 0 | 26(8.8) | |
| | Low possibility | 3(7.9) | 35(92.1) | 0 | 38(12.9) | |
| | Asymptomatic | 15(11.5) | 115(88.5) | 0 | 130(44.1) | |
| Traveling out of town during the COVID-19 pandemic | Yes | 99(70) | 44(30) | 0 | 143(48.5) | 0.049* |
| | No | 29(19.1) | 123(80.9) | 0 | 152(51.5) | |

* Significant relationship.



**Table 4.** Logistic regression modeling to assess the effect of confounding variables on positive results

| Confounding Variables | Groups | OR (95% CI) | P |
|---|---|---|---|
| Traveling out of town during the COVID-19 pandemic | No | References group | |
| | Yes | 0.18(0.08-0.74) | 0.001*** |
| Occupation | HCWs* | References group | |
| | ADSs** | 0.2(0.01-0.94) | <0.05*** |
| Sex | Women | References group | |
| | Men | 0.81(0.41-1.58) | 0.529 |
| Close contact with a COVID-19 patient | No | References group | |
| | Yes | 0.54(0.2-1.42) | 0.211 |
| History of respiratory problems and COVID-19 | No | References group | |
| | Yes | 0.15(0.01-1.94) | <0.05*** |
| Possibility | Asymptomatic | References group | |
| | Low possibility | 0.71(0.19-2.71) | 0.616 |
| | Medium possibility | 4.83(1.6-14.56) | 0.005 |
| | High possibility | 8.09(3.7-17.66) | <0.001 |
| Age (y) | 25< | References group | |
| | 25-34 | 0.16(0.04-0.64) | 0.009*** |
| | 35-44 | 0.35(0.09-1.33) | 0.125 |
| | 45-54 | 0.56(0.14-2.15) | 0.394 |
| | 54> | 0.67(0.1-4.36) | 0.675 |

* Healthcare workers; ** Administrative department staff; *** Significant relationship.

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### Assessment of logistic regression of confounding variables on positive results

The logistic regression modeling was conducted to assess the effect of confounding variables, including travel, occupation, sex, age, clinical signs, etc., on positive results. The results of logistic regression modeling indicated that traveling (OR: 018, 95% CI: 0.08–0.74, P=0.001), occupation (OR: 0.2, 95% CI: 0.01–0.94, P<0.05), history of respiratory problems (OR: 0.15, 95% CI: 0.01–1.94, P<0.05), major clinical signs (OR: 8.09, 95% CI: 3.7-17.66, P<0.001), and age (OR: 0.16, 95% CI: 0.04–0.64, P=0.009) are important factors influencing SARS-CoV-2 IgG antibody positivity (Table 4).

## 4. Discussion

In the present study, 15 out of 130 (11.5%) HCWs had been infected with SARS-CoV-2 without any symptoms. It was found that HCWs are a high-risk group to be exposed to SARS-CoV-2 infection, and a significant number of them may be asymptomatic but spread the infection. Also, major signs, especially fever, dry cough, and fatigue, are common symptoms of SARS-CoV-2 infection among HCWs, and they should be considered infected if they show such symptoms. The infection rates among HCWs are 14% and 7.1% in symptomatic and asymptomatic forms, respectively. These numbers are higher than the general population and suggest an occupational risk [16, 17].

In the current study, 54 out of 223 (24.2%) HCWs had previous exposure to COVID-19, nearly double that of the non-medical staff (24.2% vs 13.8%). It seems that essential factors in increased HCWs exposure may include close contact with COVID-19 patients, HCW to HCW transmission, and travel during the COVID-19 pandemic [18]. Most concerns are about HCW to HCW transmission because space limitations in many medical centers prevent compliance with social distance. In addition to evidence of nosocomial transmission, this factor has caused recent changes to the Rafsanjan health center's policy on using masks.

Several studies have assessed the seroprevalence of SARS-CoV-2 antibodies in HCWs of medical centers in Iran. These reports revealed that seroprevalence varies widely, with rates as high as 23% and as low as 5% [13, 14, 19], and this range may reflect the difference in COVID-19 burden in different cities of Iran. In comparison with other countries, the prevalence of COVID-19 among the HCWs in Dutch hospitals [20], British teaching hospitals [21], and Denmark [15] revealed that the seroprevalence rates of SARS-CoV-2 are 6%, 3%, and 4%, respectively. The results of the present study showed that the seroprevalence of SARS-CoV-2 antibodies in HCWs in a small city like Rafsanjan is very high.

In our study, both symptomatic and asymptomatic HCWs were screened, and it was found that 15 out of 130 (11.5%) asymptomatic HCWs had been infected with SARS-CoV-2. Several studies have revealed the prevalence of asymptomatic COVID-19 among HCWs, ranging from 0% to 100% [21-26]. In this regard, Fakhim H. et al. reported that 66% of HCWs with the confirmed disease had no symptoms [22]. A systematic review and meta-analysis by Ma, Qiuyue, et al. evaluated the global percentage of asymptomatic SARS-CoV-2 infections among the tested population and individuals with confirmed COVID-19 diagnosis and revealed that 40.50% of the confirmed-COVID-19 population are asymptomatic [27]. Also, Subramanian, R. et al., by computational modeling (with observed cases, serology tests, and testing capacity), showed a 50% COVID-19 transmission rate among asymptomatic individuals [28]. Overall, this large number may be due to a systemic problem, which must be addressed. Since front-line HCWs have close contact with COVID-19 patients, they might carry the virus without presenting any symptoms for several weeks. So, HCWs' communication, such as travelling, must be controlled, and they should be checked regularly for possible infections [29]. Iran has passed five peaks of COVID-19 since the beginning of the COVID-19 pandemic. HCWs were involved in the same periods in our city. So, there is a justifiable high seroprevalence of COVID-19 among the HCWs in this region.

Finally, travel increases the chances of spreading and getting COVID-19 infection. Centers for Disease Control and Prevention (CDC) and the Minnesota Department of Health (MDH) recommend that high-exposure groups like HCWs do not travel at COVID-19 peaks [30]. Our results indicated that the travel of HCWs during the COVID-19 pandemic was associated with positive SARS-CoV-2 IgG antibodies.

The limitation of this report is that we did not check SARS-CoV-2 IgG antibodies among HCWs before they traveled. Other limitations of the current study were issues with sample and selection, the insufficient sample size for statistical measurement, lack of previous research studies in Rafsanjan City, and confounding factors that have not been identified and their effects have not been justified.

## 5. Conclusion

The main findings indicated an occupational risk for SARS-CoV-2 infection among HCWs, and major signs, especially fever, dry cough, and fatigue, are common symptoms of SARS-CoV-2 infection among HCWs, and they should be considered infected if they showed such symptoms. Also, some HCWs (11.5%) are asymptomatic. Their communication, such as traveling, must be controlled, and they should be checked regularly for infections. Also, it is necessary to ensure the safety of HCWs and reduce their transfer to the community and patients, and these actions may reduce the ongoing SARS-CoV-2 pandemic.

## Ethical Considerations

### Compliance with ethical guidelines

This study was approved by the Ethics Committee of RUMS, Rafsanjan, Iran (Ethical code: IR.RUMS.REC.1400.024). This trial procedure was conducted under the ethical standards of the Iranian Ministry of Health and Medical Education on human experimentation and in accordance with the Helsinki Declaration. Finally, all participants signed a consent form.

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### Authors' contributions

Mahnaz Tashakori contributed to the design and implementation of the research and the writing of the manuscript. Ahmad Jamalizadeh and Mohsen Nejad-Ghaderi contributed to organized sampling from participants. Moghadam and Athareh Soresrafil contributed to the sampling. Maryam Hadavi and Aliakbar Yousefi-Ahmadipour contributed to the analysis of the results. Fatemeh Mohseni Kazem Mashayekhi contributed to the final version of the manuscript, analyzed the data, and supervised the project. All authors approved the final version of the manuscript for submission.

### Conflict of interest

The authors declared no conflicts of interest in the research, authorship, and publication of this article.

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