

## Original Article

# Seroprevalence of SARS-CoV-2 among ICU Healthcare Workers

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Received: September 5, 2021; Accepted: September 29, 2021

## Abstract

**Background and Aim:** Coronavirus disease-2019 (COVID-19) has affected most countries in the world. The Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) was first reported in late December 2019 in Wuhan, China, and then spread around the world. In Iran, the first case with a definitive test was reported on February 20 in Qom province and a month later in March, the first case was reported in Mashhad. Hospital staff is among the most susceptible groups who are more likely to be infected due to direct contact with patients. The aim of this study was to evaluate the serum prevalence of antibodies against COVID-19 in patients with or without clinical symptoms working in the Intensive Care Unit (ICU) of hospitals affiliated with Mashhad University of Medical Sciences.

**Methods:** The present study is a cross-sectional study of sero-epidemiological type that was conducted to investigate the serological prevalence of COVID-19 in the period from August 25 to September 30, 2020, in Mashhad. A total of 300 serum samples were collected from the ICU staff of the hospitals affiliated with Mashhad University of Medical Sciences. Sero-prevalence and 95% confidence interval (CI) were calculated for all individuals who were stratified by job title, COVID-19 risk of exposure, direct contact with patients, hospitals, and intensity of care. The significance level was set generally at  $p < 0.05$ . Data were analyzed using SPSS V.25.

**Results:** The total sero-prevalence of IgG N antibody was 30.67% in COVID-19 ICU healthcare workers. The most prevalence (35.21 %) was recorded in nurse assistances who have the most contact with patients. Among asymptomatic individuals, 17.1% showed to be positive without any symptoms which emphasize the risk of the virus spread from this population who are not aware of their infection. Odds ratios and 95% confidence intervals were reported in the results. The significant difference indicates a statistically significant association with a p-value less than 0.05 (P-value=0.001).

**Conclusion:** Our study showed that less contact with patients with COVID-19 results in a lower risk of infection. Also, there is a high percentage of positive people among the staff who did not show any symptoms of the disease.

**Keywords:** Seroprevalence; SARS-CoV-2; Mashhad, Iran; ICU Healthcare Workers.

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**Please cite this article as:** Jafari M, Bamdad T, Asli S, Moghbeli F, Amel Jamedar S. Seroprevalence of SARS-CoV-2 among ICU Healthcare Workers. Arch Med Lab Sci. 2022;8:1-7 (e2). <https://doi.org/10.22037/amls.v8.36039>

## Introduction

Coronaviruses are a group of viruses that cause mild to severe respiratory and gastrointestinal infections in animals and humans (1). Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) are two highly pathogenic viruses that emerged in humans at the

beginning of the 21st century and led to fatal respiratory diseases (2). Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is a highly transmissible and pathogenic coronavirus that emerged in late 2019 and caused an acute respiratory pandemic called Coronavirus disease 2019(COVID-19) that threatens human health and public safety. In terms of the number of infected

people and the extent of infected areas in the world, it has almost surpassed SARS and MERS (3, 4).

Fever, cough, fatigue, and gastrointestinal symptoms are among the most common clinical signs of COVID-19 disease. Due to the unknown behavior of the virus, in addition to the known clinical symptoms of the disease, it may cause other mild or severe symptoms (5).

Along with vaccination, an effective strategy for controlling COVID-19 is to develop highly accurate methods for rapid identification and isolation of patients infected with SARS-CoV-2 (6).

There are two main ways to identify people who are infected with the virus:

1) Laboratory tests that detect SARS-CoV-2 (its RNA or protein) in clinical specimens (usually nasopharyngeal swabs) of infected individuals.

2) Serological tests detect evidence of a host immune response to the virus, such as the evaluation of various serum antibodies like IgG, IgM, and IgA in an infected person (7).

It should be noted that serological tests detecting IgM and especially IgG is more reliable due to persistence for a long time after the disease in symptomatic and asymptomatic individuals (8-11).

N-protein and S-glycoprotein are usually tested for antibodies to the SARS-CoV-2. N protein is a very strong immunogen and is usually produced in high amounts in patients, while the S antibody is produced in smaller amounts and to some extent indicates the immunity to the virus. Therefore, the N antibody is more suitable for assessing the percentage of infected people in the community (12-14).

In epidemic conditions, assessing changes in disease prevalence over time is an important tool for predicting disease spread and deciding on required health care (9).

The rate of disease spread is affected by the number of infected people, the ability to transmit the virus, and the number of susceptible individuals, so in addition to treating the disease, one of the important needs to prevent the spread of the disease is to know the epidemiology of the infection (15).

Hospital health care workers, especially those in the intensive care unit (ICU) of COVID-19, are more likely to be at risk of infection. The aim of our

study was to evaluate the serum prevalence of IgG N antibody against SARS-CoV-2 in the staff of the COVID-19 ICU unit in Mashhad.

## Methods

**Study design:** In this cross-sectional study, 300 physicians, nurses, and other staff working in the ICU of hospitals affiliated to Mashhad University of Medical Sciences (Imam Reza, Dr. Shariati, and Akbar Children's Hospitals) in the period from August 25 to September 30, 2020, were randomly selected without screening in terms of the presence or absence of symptoms and criteria of age, gender, and race. Simultaneously with serum sampling, information such as age, gender, job title, direct contact with patients with COVID-19, hospitals, underlying disease, PCR test result, the severity of symptoms, duration of symptoms, and days from the symptoms to sampling were collected if performed. IgG antibody titers against N-protein of SARS-CoV-2 were then measured for them.

The inclusion and exclusion criteria of this study are as follows: These people are selected from all age groups and are not required for mandatory residence in a city or travel during the study period. No screening is done for race, gender, or age. Samples were collected voluntarily from personnel working in the ICU department.

**Assay of specific IgG antibodies against SARS-CoV-2 by ELISA:** To detect IgG N antibody, the enzyme immunoassay method was used. The SARS-CoV-2 (anti-N IgG) ELISA kit (Pishtaz Tab, Iran) was applied to qualitatively detect the presence of IgG antibodies against the N protein of SARS-CoV-2 virus in human serum. In this kit, the plate wells are coated with SARS-CoV-2 N antigens. During the test, diluted samples are added to the wells. In the presence of antibodies against SARS-CoV-2 N antigen, the antibodies bind to the coated antigen and IgG-labeled anti-human IgG binds to them. After washing, a dye solution is added into the wells, the intensity of the blue color is proportional to the immune complex formed in the wells. Adding the stopper solution turns the blue to yellow, which has the best light absorption at a wavelength of 450 nm. The results are obtained by comparing the OD of samples with negative control

and considering the cut-off. The sensitivity and specificity of the assay were 94.1 and 98.3 as reported by the company.

**Statistical analysis:** Descriptive statistical analyses were conducted separately for the results. The frequency and percentages (%), mean and standard deviations (SD), or median and interquartile range (IQR) were reported for categorical and continuous variables.

To compare associations between test positivity and variables, chi-squared/Fisher's test or Student's t-test/non-parametric test was performed.

The seroprevalence 95% confidence intervals (95% CI) were also calculated for all participants and separately for the job title, the COVID-19 risk exposure, and direct contact with patients, hospitals, and intensity of care when data were available.

To evaluate which covariates were associated with high seroprevalence, logistic models and estimated odds ratios (ORs) and 95% CIs were performed.

In detail, to avoid the problem of sparse data, we aggregated some categories with few participants. The final multivariable model was obtained using a backward procedure with a threshold of 0.10, including age and gender independently from their statistical significance as they were considered of clinical interest.

The significance level was set generally at  $p < 0.05$ . Data were analyzed using SPSS V.25.

## Results

In this study, 300 ICU staff members of three hospitals affiliated to Mashhad University of Medical Sciences participated as follows: Imam Reza Hospital (186 patients, 62%), Dr. Shariati Hospital (63 patients, 21%) and specialized hospital Akbar children (51 people, 17%).

To evaluate which covariates were associated with high seroprevalence, logistic models and estimated odds ratios (ORs) and 95% CIs were performed. Moreover, to avoid the problem of sparse data, some categories with few participants were aggregated.

In addition, in order to evaluate the presence of multicollinearity, the LASSO (least absolute shrinkage and selection operator regression) model was performed and removed regression coefficients that were co-dependent.

Then, different invariable models and each variable with a p-value less than 0.10 was conducted and considered for the multivariable model. The final multivariable model was obtained using a backward procedure with a threshold of 0.10, including age and gender independently from their statistical significance as they were considered of clinical interest.

The mean age of the participants was 34.1 with a standard deviation of 7.294 years, of which 39% were men and 61% were women. In terms of job title distribution, 205 (68.33%) participants were nurses, 71 (23.67%) were health and nurse assistants, 17 (5.67%) were cleaning staff and 7 (2.33%) were physicians. Forty-six (15.33%) participants had severe symptoms, 52 (17.33%) had moderate symptoms, 56 (18.67%) had very mild and general symptoms, and 146 (48.67%) had no symptoms.

A total of 30.67% had IgG antibodies against N-protein SARS-CoV-2 that of them, 34.9% from Imam Reza Hospital, 28.6% of Shariati Hospital and 17.6% of Akbar hospital were seropositive.

The highest seroprevalence was reported in people over 60 years of age. Regarding job distributions, 35.21% of healthcare and nurse assistants, 29.76% of nurses, 28.57% of physicians and 23.53% of hospital cleaning staff were seropositive.

In the seropositive population, 25% had severe symptoms, 25% moderate symptoms, 22.83% mild symptoms and 27.17% of people had no disease symptoms (Figure 1).

As expected, 90.22% of the total seropositive participants were those who were in direct contact with patients with Covid-19. The results in the study population are summarized in Table 1.

**Table 1.** Demographic and serologic results of precipitants in regards to job, disease status, underlying disease and PCR test.

Variable		Number (%)	Positive (%) <sup>a</sup> , (%) <sup>b</sup>	Negative (%) <sup>a</sup> , (%) <sup>b</sup>	Borderline (%) <sup>a</sup> , (%) <sup>b</sup>	Seroprevalence <sup>c</sup>
Gender	Men (%)	117 (39.0)	37 (40.22), (12.33)	79 (39.11), (26.33)	1 (16.67), (0.34)	31.6
	Women (%)	183 (61.0)	55 (59.78), (18.33)	123 (60.89), (41)	5 (83.33), (1.67)	30.1
Age (years)	20-30	1 (0.34)	0	1 (0.49), (0.34)	0	0
	31-40	142 (47.33)	43 (46.74), (14.33)	96 (47.53), (32)	3 (50.0), (1)	30.2
	41-50	109 (36.33)	29 (31.52), (9.67)	77 (38.12), (25.67)	3 (50.0), (1)	26.6
	51-60	45 (15.0)	18 (19.57), (6)	27 (13.37), (9)	0	40.0
	+60	3 (1.0)	2 (2.17), (0.67)	1 (0.49), (0.34)	0	66.7
Job title	Doctor	7 (2.33)	2 (2.17), (0.67)	4 (1.98), (1.33)	1 (16.67), (0.34)	28.6
	Nurse	205 (68.33)	61 (66.4), (20.33)	139 (68.81), (46.33)	5 (83.33), (1.67)	29.8
	Healthcare and Nurse Assistants	71 (23.67)	25 (27.17), (8.33)	46 (22.77), (15.33)	0	35.21
	Cleaning staff	17 (5.67)	4 (4.35), (1.33)	13 (6.44), (4.33)	0	23.5
Contact with COVID-19	Yes	248 (82.67)	83 (90.22), (27.67)	162 (80.2), (54)	3 (50.0), (1)	33.5
	No	52 (17.33)	9 (9.78), (3)	40 (19.8), (13.33)	3 (50.0), (1)	17.3
Hospital	Emam Reza	186 (62.0)	65 (70.65), (21.67)	118 (58.42), (39.33)	3 (50.0), (1)	34.9
	Shariati	63 (21.0)	18 (19.57), (6)	44 (21.78), (14.67)	1 (16.67), (0.34)	28.6
	Akbar	51 (17.0)	9 (9.78), (3)	40 (19.8), (13.33)	2 (33.33), (0.67)	17.6
Underlying disease	Yes	45 (15.0)	18 (19.57), (6)	27 (13.37), (9)	0	40.0
	No	255 (85.0)	74 (80.43), (24.67)	175 (86.63), (58.33)	6 (100.0), (2)	29.02
PCR result	Positive	45 (15.0)	29 (31.52), (9.67)	16 (7.92), (5.33)	0	64.4
	Negative	20 (6.67)	2 (2.18), (0.67)	18 (8.91), (6)	0	10.0
	No test	235 (78.33)	61 (66.3), (20.33)	168 (83.17), (56)	6 (100.0), (2)	25.9
Symptoms	Severe	46 (15.33)	23 (25.0), (7.67)	23 (11.39), (7.67)	0	50.0
	Moderate	52 (17.33)	23 (25.0), (7.67)	29 (14.36), (9.67)	0	44.2
	Mild	56 (18.67)	21 (22.83), (7)	32 (15.84), (10.66)	3 (50.0), (1)	37.5
	Asymptomatic	146 (48.67)	25 (27.17), (8.33)	118 (58.41), (39.33)	3 (50.0), (1)	17.1

<sup>a</sup> Percent in the related category<sup>b</sup> Percent in the total population<sup>c</sup> Percent in the seropositive population

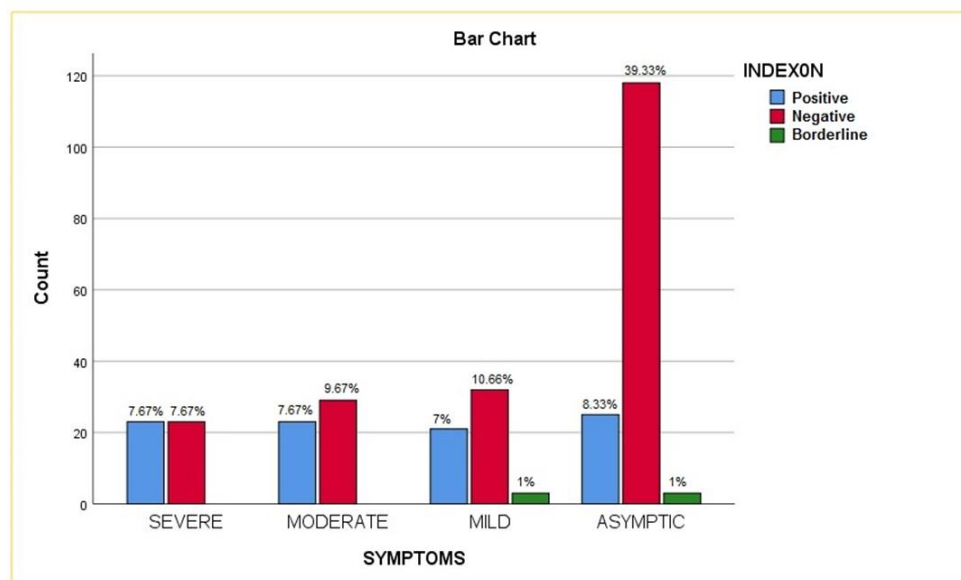
**Table 1.** Demographic and serologic results of precipitants in regards to job, disease status, underlying disease and PCR test. (Continued from previous page)

Variable		Number (%)	Positive (%) <sup>a</sup> , (%) <sup>b</sup>	Negative (%) <sup>a</sup> , (%) <sup>b</sup>	Borderline (%) <sup>a</sup> , (%) <sup>b</sup>	Seroprevalence <sup>c</sup>
Duration of symptoms	1-7 days	88 (29.33)	30 (32.61), (10)	56 (27.72) (18.67)	2 (33.33), (0.67)	34.09
	8-30 days	63 (21.0)	36 (39.13), (12)	26 (12.88), (8.67)	1 (16.67), (0.34)	57.1
	+30 days	2 (0.67)	1 (1.09), (0.34)	1 (0.49), (0.34)	0	50.0
	Asymptomatic	147 (49.0)	25 (27.17), (8.33)	119 (58.91), (39.67)	3 (50.0), (1)	17.0
Days from the symptoms to sampling time	1-7 days	11 (3.73)	3 (3.26), (1)	7 (3.55), (2.33)	1 (16.67), (0.34)	27.27
	8-30 days	25 (8.47)	12 (13.04), (4)	11 (5.58), (3.67)	2 (33.33), (0.67)	48.0
	31-60 days	28 (9.5)	14 (15.22), (4.67)	14 (7.11), (4.67)	0	50.0
	61-90 days	16 (5.42)	8 (8.7), (2.67)	8 (4.06), (2.67)	0	50.0
	+90 days	68 (23.05)	30 (32.61), (10)	38 (19.29), (12.67)	0	44.12
	Asymptomatic	147 (49.83)	25 (27.17), (8.33)	119 (60.41), (39.67)	3 (50.0), (1)	17.0
<b>Total</b>		<b>300</b>	<b>92</b>	<b>202</b>	<b>6</b>	<b>30.67<sup>b</sup></b>

<sup>a</sup> Percent in the related category

<sup>b</sup> Percent in the total population

<sup>c</sup> Percent in the seropositive population



**Figure 1.** Comparison of the disease symptoms and N antibody status in the total population.

## Discussion

In this cross-sectional screening study, the seroprevalence of SARS-CoV-2 among the staff of three hospitals affiliated to Mashhad University of

Medical Sciences who participated in the care of patients with COVID-19 were examined.

The total seroprevalence of 30.67%, among the personnel with a higher positive percentage among healthcare and nurse assistants was observed. Other

job titles also showed a serum prevalence ranging from 23.53% percent to 29.76% percent. The lowest prevalence was observed among cleaning staff. This is indicative of the fact that the less contact with patients, results in the lower risk of infection. It is important to note that there is a high percentage of positive people among the staff who did not show any symptoms of the disease. In other words, 17.1% of personnel can get an infection without symptoms who may inadvertently spread the virus.

The most prevalent was in the individuals with more than 60 age, due to physiological changes that come with aging and potential underlying health conditions. older ages were also associated with more history of infection.

A prevalence of antibodies similar to our understudy population has been reported in other cities. In a study among the staff of the Masih Daneshvari hospital as one of the main COVID-19 admission centers in Tehran, the prevalence rate was reported to be 27.8% (16) and in the childrens' hospital staff in Tehran, the prevalence was reported to be 29.4 % (17). Odds ratios and 95% confidence intervals were reported in the results. The significant difference indicates a statistically significant association with a p-value less than 0.05. (P-value=0.001).

In other countries, there are reports in the same period, so that in a hospital in Italy 17.11% of the hospital staff were serologically positive (18). In the total staff of a hospital in Spain including covid and non-covid departments, the seroprevalence in the first wave of the pandemic was reported to be 2.8% (19).

In the most comprehensive report published from Iran, the prevalence of antibodies in Mashhad was reported 14.8% and among high-risk people in 18.7 % (20). Our study shows a higher prevalence because the population we studied was in direct contact with patients with Covid-19 and was considered a very high-risk population. Our study has several limitations. First, the population that participated in some study groups was small, and it was also better to consider the sensitivity and specificity of the kits in statistical calculations.

However, the data in this study permit an early assessment of the Seroprevalence of SARS-CoV-2

among ICU Healthcare Workers in Mashhad, Iran. The findings of this review should trigger improved research methods and better reporting of any future studies on seroprevalence. In addition, further efforts should be made to compensate for the above-mentioned limitation in future studies. further studies are required on the Seroprevalence of this virus with larger study populations among the staff of the COVID-19 ICU unit in other cities of Iran. Efforts and initiatives at the national, regional, and global levels should also be made to cut the disease transmission chain.

## Conclusion

This study demonstrated that health care and nurse assistants who spent a lot of time interacting with patients with COVID-19 were at higher risk for infection. Also, among seropositive individuals, 27.17% did not show any history of the disease symptoms.

## Acknowledgments

We would like to thank Mashhad University of Medical Sciences for providing valuable specimens.

## Conflict of Interest

The authors declared that they have no conflict of interest associated with this study.

## Funding/Support

This research was funded by a grant of Research and Technology (National Institute of Genetic Engineering and Biotechnology) and the school of medical sciences of Tarbiat Modares University.

## Ethics

The Ethics Committee of Tarbiat Modares University (IR.MODARES.REC 1399.009) approved the study. Written informed consents were obtained from all participants before sampling.

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