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ORIGINAL RESEARCH

Prevalence of Anti-SARS-CoV-2 Antibodies and Associated Factors Among Health Care Workers in Santiago De Cali, Colombia

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Purpose: This study aims to determine the seroprevalence of coronavirus disease (COVID-19) among health care workers and describe the associated sociodemographic and labor features.

Patients and Methods: An observational study with an analytical component was conducted at a clinic in Cali, Colombia. The sample size was 708 health workers and they were selected by stratified random sampling. A Bayesian analysis was developed to determine the raw and adjusted prevalence. A Poisson regression model was used to estimate the prevalence ratios.

Results: Overall seroprevalence of COVID-19 among healthcare workers was 29%. Miscellaneous services workers, healthcare, and administrative workers, was 38%, 33%, and 32%, respectively. Factors related to seropositivity were having a contact with a COVID-19 patient for >120 minutes and being diagnosed with COVID-19 by laboratory tests.

Conclusion: The present study shows a adjusted seroprevalence of 29% in health workers, indicating a high level of disease transmission and an increased risk of infection in this population group.

Keywords: antibodies, seroprevalence, SARS-CoV-2, health care workers, epidemiology

Introduction

The COVID-19 disease was declared a pandemic due to the rapid spread of the virus in several countries in Asia, Europe, Africa, America, and Oceania.[1] However, Colombia followed strict measures even before registering the first reported case of COVID-19 on March 06, 2020, to prevent the spread of virus and protect the population at high risk from serious illness and death by a joint and articulated effort for developing containment and mitigation strategies.[2]

Owing the timely adaptation of preventive measures, the case fatality rate and other epidemiological parameters of the pandemic can be less severe. Therefore, controlling the seropositivity (presence of antibodies) in a population is expected to limit the extent of infection and the cumulative incidence rate of the viral infections. A study to confirm the hypothesis can be conducted either on the general population or on the people involved in the sectors of public health interest, such as health care workers.[3]

Thus, seroprevalence of COVID-19 in a population is determined by the detection of IgG and IgM anti-SARS-CoV-2 antibodies. The IgM antibodies provide the baseline defense during viral infections, whereas IgG antibodies are important as an indicator of long-term immunity. Therefore, the detecting these antibodies can provide information on the timeline of the infection and the proportion of asymptomatic and symptomatic individuals in different sets of population. Therefore, studying the seroprevalence can help in understanding the immunological status of a specific population group against the COVID-19 infection.[4]

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Seroprevalence may underestimate the true exposure of a population as shown by the Scottish population study where less than one in ten people had antibodies to SARS-CoV-2 after the second wave of the pandemic.[5] In addition, the majority of the word's human population in mid-2021 was susceptible to the virus, strengthening the need to implement immunization with vaccines.[6]

Frontline workers in the health care system, including those working in the health care services, security services, administrative and clerical support, social services, and maintenance, have a higher risk of exposure to SARS-CoV-2. The initial epidemiological studies have confirmed the high incidence rates of COVID-19 among healthcare workers. It has also been reported that among the healthcare workers, exposure to the virus was greater through infected coworkers than through direct contact with the infected patients, and higher occupational transmission was observed among the nursing staff.[7] These findings highlight the need for increased attention to reduce the risk of infections in these workers during and after the pandemic.[8] In northern Italy in Emilia-Romagna. A population very affected by the pandemic since its inception showed that among occupations with the highest risk of exposure to SARS-CoV-2 are health workers with a seroprevalence of 22.9%.[9] Although seroprevalence in this group may not be as high compared to other groups if personal protective equipment is used properly.[10] Likewise, among non-health workers in Italy, the positivity of anti-SARS-CoV-2 serological antibodies was higher for the sector with meat processing and transportation activities.[11]

Till date, only a few studies have evaluated the seroprevalence for COVID-19 in health care workers involved in the primary care of patients with this infection. Therefore, the current study focused on studying the seroprevalance for COVID-19 in health workers who will help control the transmission of the disease, which has been predicted to prevail for a few more years.[12]

Thus, the aim of this study was to determine COVID-19 seroprevalence and describe the sociodemographic and labor features of the health care workers in a highly complex setting of a clinic that was being used as a national reference center for the management of this health condition.

Materials and Methods

Study Design

A cross-sectional observational study with an analytical component was conducted at a clinic in the city of Santiago de Cali, Colombia. This clinic was a highly complex setting for this study as this was the regional reference center for the care of COVID-19 patients, it has five intensive care units, emergency department and hospitalization. The city is located in the southwestern region of Colombia and concentrates an important portion of the health services network, thus providing care to the population of the entire area. The study included the active health care workers who were hired by the clinic during the second semester of the year 2020 and agreed to participate in the study. Informed consents were obtained from each participant. However, subjects who tested positive for the antigen or polymerase chain reaction (PCR) tests for SARS-CoV-2 in the past three months were excluded from the study.

To calculate the sample size, the total study population of the 2000 workers included, an expected seroprevalence value of 50%, a confidence level of 95% and a 5% error were used. The design effect was 1.5 due to stratification and a non-response rate of 30%, resulting in a sample of 708 subjects. Subjects were selected through random and stratified sampling. The groups or categories of workers of the clinical institution were used as a stratum.

Data Collection

The studied variables included test result, age, sex (female, male), socioeconomic stratum (level 1 low to level 6 high), educational level (technical, technological, and professional level), profession, service provided by the subject, additional work in another health entity, response in the questionnaire regarding the COVID-19 symptoms and contact with COVID-19 patients, number of people the worker was exposed to, history of obesity, arterial hypertension, diabetes mellitus, dyslipidemia, metabolic and pulmonary alterations, cancer, use of medications, physical activity, diet, and smoking.

The information was obtained by filling out a survey developed in Google Forms® called "Encuesta para la vigilancia de COVID-19 en trabajadores de la salud" [Survey for the surveillance of COVID-19 in healthcare workers]. It contained

selection questions related to sociodemographic and occupational characteristics, symptoms, and risk factors. The first step was the explaining the content of the informed consent form and it was ensured that the participant was able to define their acceptance to participate in the study. Once the participant filled out the survey, an identification code was assigned that was only known to the participant and the people in charge of information processing to ensure confidentiality. Data consolidation was carried out in a master database containing the variables included in the data collection instrument. Then, the concordance and statistical validation of the database was evaluated that helped in organizing the final information to be processed in the study.

The sample collection for the IgG and IgM antibody tests was performed at the institutional clinical laboratory. The serological test for the detection of antibodies was based on flow cytometry. The samples were collected by trained and certified workers. All internal and external quality protocols were followed to ensure the reliability of the test results.

According to the COVID-19 antibody test results, the following scenarios were considered: IgM-negative IgG-positive, the worker was exposed to COVID-19 but the acute period was over and no further tests were conducted; IgM positive IgG positive, the worker was considered as a subject with intermediate exposure to COVID-19 who was then isolated according to the corresponding epidemiological fence; IgM positive IgG-negative, the worked had an early exposure of COVID-19 and a PCR test was conducted to determine the measures to be taken according to the current guidelines stipulated by the Ministry of Health of the country.

Data Analysis

The information was analyzed by followed a similar methodology used for studying the SARS-CoV-2 seroprevalence during the epidemic in Colombia: Estudio mi país[4] [My country study] using a Bayesian method with the OPENBUGS®, program to adjust the seroprevalence estimate considering the uncertainty of the sensitivity and specificity of the study test. According to the reference study model, prevalence was determined with the following formula:

$$P_{\mathbf{raw}} = P_{\text{adjusted}} * \text{Sensitivity} + \left(1 - P_{\text{adjusted}}\right) * (1 - \text{Specificity})$$

The sociodemographic factors of the study subjects were described for categorical variables using absolute (cases) and relative (proportions) frequencies and for numerical or quantitative variables such as age, it was described with measures of central tendency and dispersion. Likewise, we first estimated the prevalence of positive rapid-antigen tests among workers and then the raw and adjusted prevalence ratios were calculated while considering the main sociodemographic factors and personal history associated with the positive or negative test result. This adjustment allowed for obtaining the adjusted seroprevalence results with the corresponding 95% Bayesian credible interval (95% BCI). Finally, prevalence ratios (PR) were estimated using a Poisson regression model with their respective 95% confidence intervals (95% CI).

The research was conducted in accordance with the international recommendations based on the Declaration of Helsinki.[13] The project was approved by the Technical Scientific Committee of the Clinical Institution and the Ethics and Bioethics Committee of the Department of Health of the Universidad Santiago de Cali (Act N° 20/2021). According to national regulations, Resolution 8430 of 1993, and Resolution 2378 of 2008, this research was considered without any risks to the participants.[14]

Results

Characteristics of Study Population

A total of 708 workers were included in this study. Women were a predominant part of the included subjects (76%; n = 537) with the median age of 34 years (18–75 years). In addition, the highest proportion of workers were 28–37 years of age (women, 43.2% (n = 232); men, 39.2% (n = 67)).

The studied sociodemographic variables showed that 66.9% (n = 474) participants belonged to the socioeconomic stratum 2 and 3. Moreover, 55.1% (n = 390) had a technical or technological level of education, whereas 21.9% (n = 155) subjects were medical professionals. Meanwhile, 12% (n = 88) workers who participated in the study had a contact with a person with COVID-19 infection for >120 minutes.

Of the studied subjects, 14% (n = 99) exhibited at least one COVID-19 symptom, including cough, fever, respiratory distress, fatigue, sore throat, or decreased sense of taste and smell, in the last 14 days. In the clinical risk history, 26.8% (n = 190) workers reported having the history of at least one studied ailments that included obesity, hypertension, diabetes, dyslipidemia, cancer, cardiac alterations, pulmonary or metabolic alterations, and lifestyle alterations. It was also observed that 7% (n = 51) subjects were active smokers, 39% (n = 277) workers performed at least 150 minutes of physical activity per week, and 52% (n = 267) workers consumed at least five portions of fruit and vegetables per day.

Prevalence of IgG and IgM Antibodies

According to the antibody tests results of the workers, it was found that 542 workers were not exposed to the virus, whereas 107 workers had a negative IgM and positive IgG test result, which indicated an exposure to COVID-19 after the acute period (three months). On the other hand, 42 workers exhibited a positive IgM and positive IgG result, indicating an intermediate exposure to the virus and a PCR test was done to corroborate the diagnosis as a Gold Standard test. The remaining 17 participants obtained a positive IgM and negative IgG result, they were considered to have had an early exposure to the virus, and their samples were collected for the PCR test (Table 1).

PCR test was performed on the samples collected from the 59 workers who tested positive for IgM in the antibody test and 14 workers tested positive for COVID-19. (Table 2). While observing the results of the PCR tests, it was observed that the probability of having the COVID-19 disease in case of a positive IgM result in the antibody test was 23.7%, whereas the probability of having the disease if a positive IgM and positive IgG result was obtained in the antibody test was 30.9%. The workers with a positive IgM and negative IgG result had 5.8% probability of being infected.

Of the 708 samples collected for the IgM and IgG antibody test from the participating workers, 166 (23%) samples showed previous exposure to the virus (IgM-negative and IgG-positive, IgM positive and IgG-positive, and IgM positive and IgG negative). Of those exposed to the virus, 79 (47.6%) workers denied having a history of COVID-19 infection. Among these 79 workers, 58 (73.4%) workers had been asymptomatic. In addition, of the 121 workers with a history of COVID-19 infection diagnosed by a health professional, 34 (28%) workers did not have a positive result for the antibodies compatible with previous exposure (Figure 1).

Furthermore, workers were classified into three large groups on the basis of their professional roles in the clinic: administrative workers, health care workers (who are continuously in contact with patients with COVID-19 infection),

Table 1 IgM and IgG Antibody Test Results of the Health Care Workers

Antibody Test Results	Cases	Proportion
Exposed (IgM− IgG+)	107	15.1%
Intermediate Exposure (IgM+ IgG+)	42	5.9%
Early Exposure (IgM+ IgG−)	17	2.4%
Not Exposed (IgM− IgG−)	542	76.6%
Total	708	100%

Table 2 Antibody Test and PCR Test Results of the Health Care Workers

Antibody Test Results	PCR Test		
	Positive	Negative	Total
IgM+ IgG−	1	16	17
IgM+ IgG+	13	29	42
Total	14	45	59

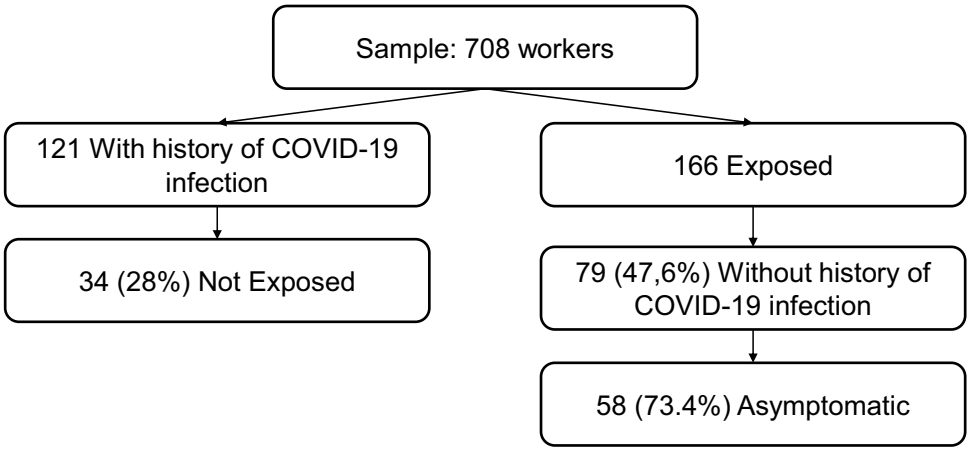

Figure 1 Exposure and antecedent history of infection by COVID-19.

and miscellaneous services workers (workers in the areas of general services, maintenance, electromedicine, pharmaceutical service, sterilization center, and security services). Of the population previously exposed to the virus, 38, 109, and 19 subjects were included in the groups of administrative, health, and various services workers, respectively. With reference to the raw proportion of previous exposure to the virus, the highest proportion of workers exposed to the virus was in the health care workers group (27%; IBC95%: 22–31). This groups was followed by miscellaneous services workers (20%; IBC95%: 12–29) and administrative workers (18%, IBC95%: 13–24) (Table 3).

Subsequently, adjustments were made to the estimate of the proportion of workers with exposure to the virus while considering the uncertainty of the sensitivity and specificity of the antibody test at the two points in time. The first adjustment was made after 7 days of the initial PCR result confirmation for the subjects with positive IgM antibody test. The test had a sensitivity of 91.7% and a specificity of 100%. The second adjustment was made 7 days after the initial confirmation of the PCR results for the subjects with positive IgG antibody result. The test had a sensitivity of 79.2% and a specificity of 100%. Based on these results, the adjusted estimation of workers exposed to COVID-19 at each moment was done by the Bayesian methods, considering the model used by the National Institute of Health in the study, seroprevalence of SARS-CoV-2 during the epidemic in Colombia.[5]

The adjusted estimates for the first instance of being exposed to the COVID-19 virus in all the workers were 29% (IBC95%: 26–32). The estimates for workers included in the miscellaneous services, health care, and administrative services groups were 38% (IBC95%: 33–44), 33% (IBC95%: 30–37), and 32% (IBC95%: 28–37), respectively. The adjusted estimate for the second instance of COVID-19 exposure in the workers was 28% (IBC95%: 25–31). The estimates for workers included in the miscellaneous services, health care, and administrative services groups were 36% (IBC95%: 30–42), 32% (IBC95%: 28–36), and 30% (IBC95%: 26–35), respectively.

Table 3 The Proportion of the Exposed Workers Categorized on the Basis of Roles in the Clinic

Proportion of Health Care Workers			**Raw Ratio**		**Adjusted Proportion S:91.7% E:100%**		**Adjusted Proportion S:79.2% E:100%**	
Workers	**Number Samples**	**Number Exposed**	**Proportion**	**$_{95\%}$BCI**	**Proportion**	**$_{95\%}$BCI**	**Proportion**	**$_{95\%}$BCI**
Administrative	206	38	18%	13–24%	32%	28–37%	30%	26–35%
Health Care	409	109	27%	22–31%	33%	30–37%	32%	28–36%
Miscellaneous Services	93	19	20%	12–29%	38%	33–44%	36%	30–42%
Total	708	166	23%	20–27%	29%	26–32%	28%	25–31%

Abbreviations: S, Sensitivity; E, Specificity; $_{95\%}$BCI, 95% Bayesian Credibility Interval.

Table 4 Test Results for the Workers Based on the Studied Characteristics

Characteristics	Exposed	Not Exposed	Prevalence Ratio ($_{95\%\ CI}$)	*p*-value
Has been diagnosed with COVID-19				
Yes No	87 (52.4%) 79 (47.6%)	34 (6.3%) 508 (93.7%)	8.35 (5.85–11.93)	<0.001
Any symptoms in the last 14 days				
Symptomatic Asymptomatic	27 (16.3%) 139 (83.7%)	72 (13.3%) 470 (86.7%)	1,22 (0.81–1.83)	0.332
Contact for more than 120 minutes with COVID-19 patient				
Yes No	30 (18.3%) 134 (81.7%)	58 (10.8%) 478 (89.2%)	1.69 (1.13–2.53)	0.011
150 minutes of physical activity per week				
Yes No	68 (41%) 98 (59%)	209 (38.8%) 330 (61.2%)	1.06 (0.85–1.30)	0.613
Consumes five serving of fruits and vegetables daily				
Yes No	89 (53.9%) 76 (46.1%)	278 (51.4%) 263 (48.6%)	1.05 (0.89–1.23)	0.565
Has any medical history				
Yes No	46 (27.7%) 120 (72.3%)	144 (26.6%) 398 (73.4%)	1.04 (0.79–1.38)	0.771
Works in a health entity other than the Clinic				
Yes No	8 (4.8%) 158 (95.2%)	30 (5.6%) 509 (94.4%)	0.87 (0.40–1.85)	0.709

Note: Subjects who tested positive for the antigen or polymerase chain reaction (PCR) tests for SARS-CoV-2 in the past three months were excluded from the study.
Abbreviation: $_{95\%\ CI}$, 95% Confidence interval.

Table 4 shows the relationship between the test results and different features reported among the workers, where many PR did not show much statistical significance, although it is reported that the exposed workers were slightly more symptomatic compared to the exposed. However, the factors like having a contact with a confirmed COVID-19 patient for >120 minutes and having been diagnosed with COVID-19 by laboratory tests duly read by a health professional presented a positive association ($p < 0.05$) with being exposed to the virus.

Discussion

Seroprevalence studies are a useful tool for understanding the dynamics and trajectory of a pandemic. Currently, and especially in Latin America, not enough studies have been conducted to assess the seroprevalence for COVID-19 in health care workers who are involved in the primary care of patients with COVID-19 infection.[15] The present study is one of the first reports in Colombia to study the seroprevalence in health care workers with a high burden of patients with SARS-CoV-2 infection.

The present investigation reported an adjusted seroprevalence of 29% in health workers, which varied with the place of work, wherein a higher adjusted seroprevalence of 38% was noticed in health workers who performed various services, followed by workers who only performed health care services (33%) and administrative workers (32%). This observation is comparable to that of the Estudio País [Country Study] where the adjusted seroprevalence in the city of

Cali for health care workers was 35%, whereas the highest seroprevalence was observed in cities such as Guapi (70%) and Villavicencio (55%), highlighting the issue of the occupational medicine in this labor sector in these cities.[4]

Similarly, research conducted in a hospital in Mexico reported that 31% health care workers had anti-SARS-CoV-2 antibodies and only 13.1% reported a history of positive reverse transcription polymerase chain reaction (RT-PCR) test results. In addition, the showed that cohabitation with a person with COVID-19 and testing positive in RT-PCR test were factors associated with seropositivity. Laboratory workers had the lowest seroprevalence (12.0%), while social workers reported the highest prevalence (35.7%).[16] These findings are comparable with our observation regarding the similarity between the seroprevalence and related factors, focusing on the contact with COVID-19 patients and a history of diagnosis of this infection.

Further, a recent study conducted in 18 cities of Iran categorized individuals according to their occupations with a high risk of exposure to SARS-CoV-2 and also included healthcare workers. The study found an average seroprevalence of 20% that varied only slightly on the basis of subjects' occupation. However, the findings described a seroprevalence of 17.1% in the general population that was not categorized as high risk.[17] Another study conducted in Wuhan, China, which was the epicenter of the COVID-19 pandemic, reported a seroprevalence of 1.8% among health care workers. It showed a significantly lower frequency of the cases that can possibly be explained by the exhaustive personal protection measures taken at the time of the investigation. It must be noted that the study was carried out a few months after the beginning of the pandemic, thus achieving a lower total exposure rate.[18]

Moreover, the study conducted by García-Basteiro et al[19] reported the 11.2% seroprevalence of antibodies against SARS-CoV-2 in the healthcare workers of a national reference hospital in the city of Barcelona, Spain. The study included 578 subjects with a high burden of care for people with COVID-19, which is lower than that of the present study.

Contrasting results regarding the seroprevalence of 2.9% for COVID-19 among health care workers and outpatients were obtained in a study conducted in 1282 workers in Minnesota. The low frequency in the study population suggested different patterns of using the personal protective equipments and various governmental regulatory measures during the pandemic.[20] Similar report has been made by a study conducted in Germany wherein a seroprevalence of 1.6% was found among the third-level healthcare workers.[21] The large variation observed in seroprevalence between studies may be due to different factors, including the type of work activities, the different laboratory tests used to detect antibodies, the selection criteria of health workers, and different patterns of use of personal protective equipment.

The results of these studies denoted a high level of heterogeneity in the mode of transmission of SARS-CoV-2 experienced globally. The same has been presented in our study in Colombia, which is one of the most affected Latin American countries by the COVID-19 pandemic, whose Estudio País [Country Study] involving ten major cities reported an estimated seroprevalence of 21%–78%. The Estudio País [Country Study] also showed great variation in seropositivity among different cities that largely driven by the socioeconomic status, which was the strongest independent predictor of seropositivity. Similar results were obtained in our study where 45% of the exposed cases corresponded to the socioeconomic strata 1 and 2.

One of the greatest challenges of this disease is the significant number of asymptomatic subjects.[22] As a consequence, the real number of people with COVID-19 infection is not effectively known.[19] The major concern regarding the asymptomatic population is their ability to spread the disease up to 19 days after infection to healthy individuals.[23] Therefore, many studies have reported the behavior of asymptomatic infections in the development of the pandemic with varying results. Thus, in the Diamond Princess cruise ship in Yokohama, Japan, 17.9% of asymptomatic cases were found.[22] On the contrary, high percentages have been determined in the study by Al-Qahtani et al[24] which was carried out in Bahrain, showing of the proportion of asymptomatic cases of 76.6%. The variation in these results in studies carried out in healthcare workers is also notorious. In a study carried out in the departmental hospital of Villavicencio, Colombia, the serological incidence of asymptomatic patients was found to be 12.4%.[25] Likewise, a study of healthcare workers in a large hospital in Spain described that 40% workers had not been previously informed of the diagnosis of COVID-19. This study revealed that the proportion of asymptomatic patients among the workers exposed to the virus without prior diagnosis was 86%.

In regards to the diagnostic tests for this disease, Xie et al[26] showed that antibody tests for COVID-19 had a significantly higher positive rate than PCR, which is considered the standard diagnostic method for this infection. This was also indicated by our study where only 14 (23.7%) of workers with early and intermediate exposure had a positive test for SARS-CoV-2 PCR, thus indicating that the antibody test has a superior effectiveness when looking for a person with exposure to the virus. Seroprevalence studies are a useful tool for understanding the dynamics and trajectory of a pandemic. Currently, and especially in Latin America, not enough studies have been conducted to assess the seroprevalence for COVID-19 in health care workers who are involved in the primary care of patients with COVID-19 infection.[15] The present study is one of the first reports in Colombia to study the seroprevalence in health care workers with a high burden of patients with SARS-CoV-2 infection.

The present study has several strengths including the number of participants, the high participation rate, and the use of a serological assay with increased levels of sensitivity and specificity. One of the limitations of the study was the lack of neutralizing antibodies obtained from the participants, because antibodies alone do not equate to immunity to infection by the virus causing COVID-19 infection.[27–29] The test used in this study (total IgM and IgG antibodies detection) establishes previous exposure to the virus, but it is not yet known to what extent a positive result in this test correlates with protective immunity against new exposure to the virus.[4] In addition, it is recommended for future studies to include measurement of occupational variables such as the use of personal protection elements.

Conclusion

We found an adjusted seroprevalence of 29% in health workers, which varied with the workplace, where a higher seroprevalence was noted was in health workers who Miscellaneous Services, followed by workers who only Health Care, and finally administrative workers. SARS-CoV-2 seroprevalence in healthcare workers was linked to having contact with a COVID-19 patient for more than 120 minutes and have been previously diagnosed with COVID-19. These findings indicate a high level of disease transmission and an increased risk of infection in this population group, which implies a problem for public health, which must be addressed through local policies.

Abbreviations

DM, Diabetes mellitus; PR, Prevalence ratios; WHO, World Health Organization; COVID-19, Coronavirus disease; SRS-CoV-2, Severe acute respiratory syndrome coronavirus 2; PCR, Polymerase chain reaction; 95% CI, 95% confidence intervals; 95% BI, 95% Bayesian credible interval; RT-PCR, Reverse transcription polymerase chain reaction.

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Disclosure

The authors report no conflicts of interest in this work.

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