SARS-CoV-2 Seroprevalence Among Healthcare Workers by Workplace Exposure Risk in Kashmir, India

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BACKGROUND: SARS-CoV-2 infection (COVID-19) poses a tremendous challenge to healthcare systems across the globe. Serologic testing for SARS-CoV-2 infection in healthcare workers (HCWs) may quantify the rate of clinically significant exposure in an institutional setting and identify those HCWs who are at greatest risk.

METHODS: We conducted a survey and SARS-CoV-2 serologic testing among a convenience sample of HCWs from 79 non-COVID and 3 dedicated COVID hospitals in District Srinagar of Kashmir, India. In addition to testing for the presence of SARS-CoV-2–specific immunoglobulin G (IgG), we collected information on demographics, occupational group, influenza-like illness (ILI) symptoms, nasopharyngeal reverse transcription polymerase chain reaction (RT-PCR) testing status, history of close unprotected contacts, and quarantine/travel history.

RESULTS: Of 7,346 eligible HCWs, 2,915 (39.7%) participated in the study. The overall prevalence of SARS-CoV-2–specific IgG antibodies was 2.5% (95% CI, 2.0%-3.1%), while HCWs who had ever worked at a dedicated COVID-19 hospital had a substantially lower seroprevalence of 0.6% (95% CI, 0.2%-1.9%). Higher seroprevalence rates were observed among HCWs who reported a recent ILI (12.2%), a positive RT-PCR (27.6%), a history of being put under quarantine (4.9%), and a history of close unprotected contact with a person with COVID-19 (4.4%). Healthcare workers who ever worked at a dedicated COVID-19 hospital had a lower multivariate-adjusted risk of seropositivity (odds ratio, 0.21; 95% CI, 0.06-0.66).

CONCLUSIONS: Our investigation suggests that infection-control practices, including a compliance-maximizing buddy system, are valuable and effective in preventing infection within a high-risk clinical setting. Universal masking, mandatory testing of patients, and residential dormitories for HCWs at COVID-19–dedicated hospitals is an effective multifaceted approach to infection control. Moreover, given that many infections among HCWs are community-acquired, it is likely that the vigilant practices in these hospitals will have spillover effects, creating ingrained behaviors that will continue outside the hospital setting. *Journal of Hospital Medicine* 2021;16:XXX-XXX. © 2021 Society of Hospital Medicine

India is emerging as one of the world's largest hotspots for SARS-CoV-2 infection (COVID-19)—second only to the United States—with more than 13,000,000 documented infections since the first case was recorded on January 30, 2020.[1,2] Kashmir, a northern territory of India, reported its first case of COVID-19 on March 18, 2020, from the central District Srinagar; this region has accounted for more cases of COVID-19 than any other district throughout the pandemic.[3] The large majority of healthcare in District Srinagar is provided by three tertiary care institutions, one district hospital, two subdistrict hospitals, and 70 primary healthcare centers. Potential occupational exposures place healthcare workers (HCWs) at higher risk of acquiring SARS-CoV-2 infection, which in turn may serve as an important source of infection for their families and other community members.[4-6] Given the high frequency and geographic variability of asymptomatic infection, growing evidence suggests this hidden reservoir is a source of infection for the general population.[7,8]

Many countries have started testing for antibodies against SARS-CoV-2, both at the population level and in specific groups, such as HCWs. Seroepidemiological studies are crucial to understanding the dynamics of SARS-CoV-2 infection. Many seroepidemiological studies have been conducted among community populations, but there are insufficient data on HCWs. The World Health Organization also encouraged its member states to conduct seroepidemiological studies to attain a better understanding of COVID-19 infection prevalence and distribution.[9-11] Therefore, to quantify the prevalence of SARS-CoV-2 infection among HCWs, we conducted a seroepidemiological study by testing for SARS-CoV-2–specific immunoglobulin (IgG) to gain insight into the extent of infection among specific subgroups of HCWs and to identify risk-factor profiles associated with seropositivity.

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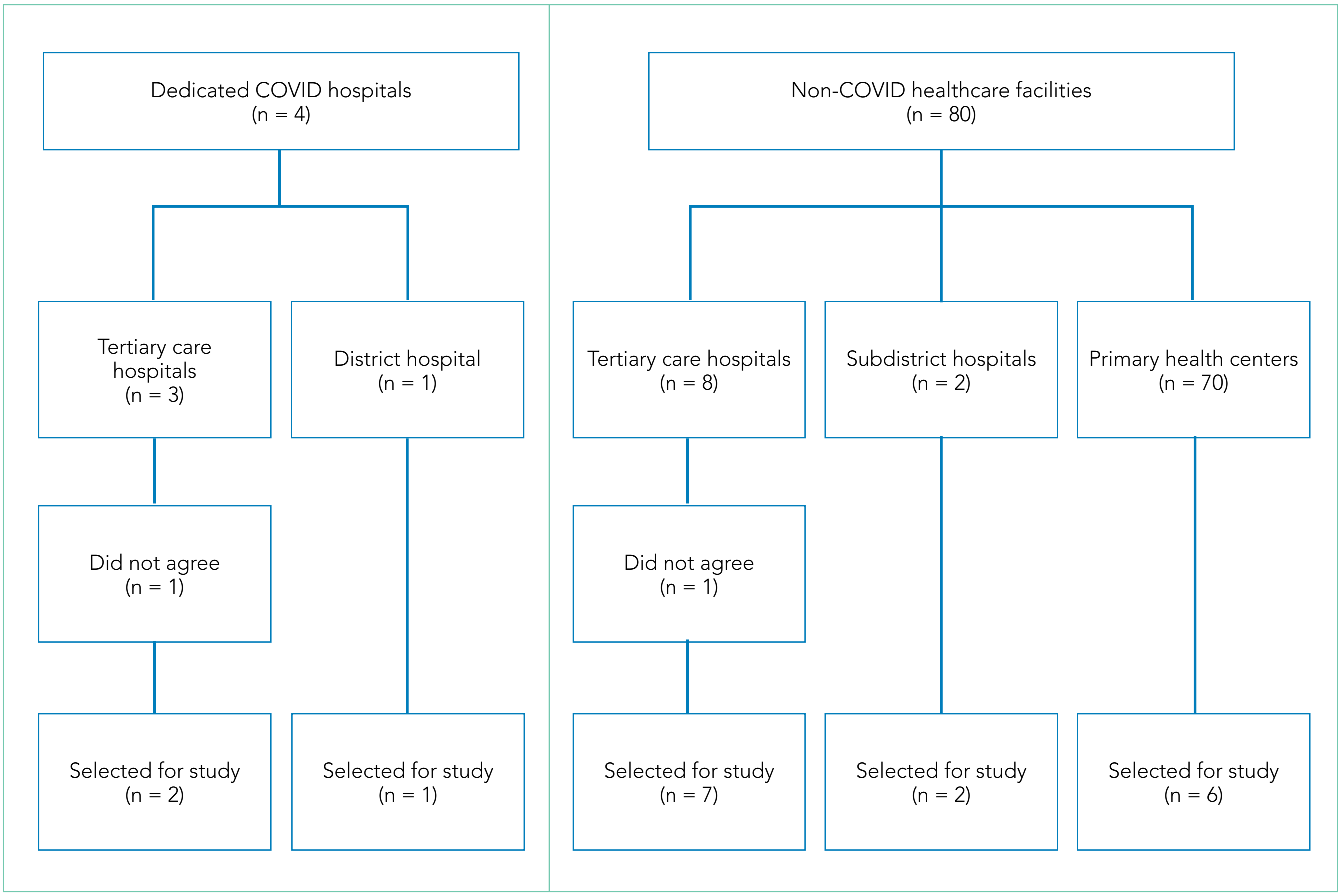

FIG 1. Healthcare Facilities in District Srinagar and the Number of Hospitals and Facilities Selected for the Study

METHODS

Study Design and Settings

We conducted this seroepidemiological study to ascertain the presence of IgG antibodies against SARS-CoV-2 among HCWs in the District Srinagar of Kashmir, India. The 2-week period of data collection began on June 15, 2020. As part of healthcare system pandemic preparedness efforts, India's Ministry of Health provided specific guidelines for health facilities to manage COVID-19. Hospitals were categorized as dedicated COVID and non-COVID hospitals. Dedicated COVID hospitals provided comprehensive care exclusively to patients with COVID-19 and were equipped with fully functional intensive care units, ventilators, and beds with reliable access to oxygen support.[12] In addition, infection prevention and control strategies to limit the transmission of SARS-CoV-2 infection were implemented according to guidelines specified by India's National Center for Disease Control.[13] To strengthen service provision, HCWs from other hospitals, including resident physicians, were relocated to these dedicated COVID hospitals. The additional staff were selected by administrative leadership, without input from HCWs.

Study Population and Data Collection

We approached administrative heads of the hospitals in District Srinagar for permission to conduct our study and to invite their HCWs to participate in the study. As Figure 1 shows, we were denied permission by the administrative heads of two tertiary care hospitals. Finally, with a point person serving as a study liaison at each institution, HCWs from three dedicated COVID and seven non-COVID tertiary care hospitals, two subdistrict hospitals, and six primary healthcare centers across the District Srinagar were invited to participate. The sample primary healthcare centers were each selected randomly, after stratification, from six major regions of the district. All frontline HCWs, including physicians, administrative and laboratory personnel, technicians, field workers involved in surveillance activity, and other supporting staff were eligible for the study.

We collected information on an interview form using Epicollect5, a free data-gathering tool widely used in health research.[14] Physicians specifically trained in the use of Epicollect5 conducted the face-to-face interview on a prespecified day and recorded the collected information through mobile phones. This information included the participants' role in providing care to patients with COVID-19 and risk factors for SARS-CoV-2 infection (eg, history of travel since January 1, 2020, symptoms of an influenza-like illness [ILI] in the 4 weeks prior to the interview, close contact with a COVID-19 case). We defined close contact as an unmasked exposure within 6 feet of an infected individual for at least 15 minutes, irrespective of location (ie, community or the hospital).

Following the interview, trained phlebotomists collected 3 to 5 mL of venous blood under aseptic conditions. We strictly adhered to standard operating procedures during collection, transportation, and testing of blood samples. Following collection, the blood samples remained undisturbed for at least 30 minutes before centrifugation, which was performed at the collection site (or at the central laboratory for sites lacking the capability). The samples were then transported for further processing and testing through a cold chain supply line, using vaccine carriers with conditioned icepacks. All testing procedures were conducted with strict adherence to the manufacturers' guidelines.

Laboratory Procedure

In accordance with the manufacturer's recommendations, we used a chemiluminescent microparticle immunoassay to detect SARS-CoV-2–specific IgG antibodies in serum samples. The assay is an automated two-step immunoassay for the qualitative detection of IgG antibodies against the nucleocapsid of SARS-CoV-2 in human serum and plasma. The sensitivity and specificity of this test are 100% and 99%, respectively. The test result was considered positive for SARS-CoV-2 IgG if the index value was ≥1.4, consistent with guidance provided by the manufacturer.[15]

The IgG values were also entered into Epicollect5. Two trained medical interns independently entered the laboratory results in two separate forms. A third medical intern reviewed these forms for discrepancies, in response to which they referenced the source data for adjudication. The information gathered during the interview and the laboratory results were linked with the help of a unique identification number, which was generated at the time of the interview.

Statistical Analysis

We estimated the proportion (and logit-transformed 95% CI) of HCWs with a positive SARS-CoV-2–specific IgG antibody level, the primary outcome of interest. We compared seroprevalence rates by gender, age group, specific occupational group, and type of health facility (dedicated COVID hospital vs non-COVID hospital). Seroprevalence was also estimated separately for HCWs who reported symptoms in the past 4 weeks, had a history of exposure to a known case of COVID-19, or had undergone testing by reverse transcriptase-polymerase chain reaction (RT-PCR). In the case of zero seroprevalences, Jeffreys 95% CIs were reported. We used a chi-square test to report two-sided *P* values for comparison of seroprevalence between groups. When the expected frequency was <5 in more than 20% of the cells, the exact test was used instead of the chi-square test. We additionally performed multivariable logistic regression analysis to evaluate the independent association between place of work (primary independent variable) and seropositivity (dependent variable). We adjusted for the following observable covariates by including them as categorical variables: age, gender, occupational group, and history of close contact with a patient who was COVID-positive. We performed data analysis using Stata, version 15.1 (StataCorp LP). The Institutional Ethics Committee of Government Medical College, Srinagar, approved the study (Reference No. 1003/ETH/GMC dated 13-05-2020). We obtained written, informed consent from all participants.

RESULTS

Of the 7,346 HCWs we were granted permission to approach, 2,915 (39.7%) agreed to participate in the study. The participation rate was 49% at the dedicated COVID hospitals (57% physicians and 47% nonphysicians) and 39% at the non-COVID hospitals (46% physicians and 36% nonphysicians). We analyzed information gathered from 2,905 HCWs (Epicollect5 interview forms were missing for nine participants, and the laboratory report was missing for one participant).

The mean age of the participants was 38.6 years, and 35.8% of participants identified as female (Table 1). One third (33.7%) of the participants were physicians, nearly half of whom were residents. In our sample, the overall seroprevalence of SARS-CoV-2–specific antibodies was 2.5% (95% CI, 2.0%-3.1%). The distribution of the IgG index value among the study participants is shown in Figure 2.

Of the 2,905 participating HCWs, 123 (4.2%) reported an ILI (ie, fever and cough) in the 4 weeks preceding the interview, and 339 (11.7%) reported close contact with a person with COVID-19 (Table 2). A total of 760 (26.2%) HCWs had undergone RT-PCR testing, 29 (3.8%) of whom had a positive result. Stratifying by workplace, history of nasopharyngeal RT-PCR positivity was reported by 4 of 77 (5.1%) participants from dedicated COVID hospitals compared to (3.7%) participants from the non-COVID hospital (*P* = .528).

As Table 2 also demonstrates, we found a significantly higher seropositivity rate among HCWs who had a history of ILI (*P* < .001), a history of positive RT-PCR (*P* < .001), history of ever being put under quarantine (*P* = .009), and a self-reported history of close contact with a person with COVID-19 (*P* = .014). Healthcare workers who had ever worked at a dedicated COVID hospital had a significantly lower seroprevalence of infection (*P* = .004).

Among HCWs who reported no ILI symptoms in the 4 weeks prior to the interview but who had positive RT-PCR test, 20.8% were seropositive. Of HCWs who reported both ILI and a positive RT-PCR test result, 60.0% were seropositive. Compared to employment at a non-COVID hospital, HCWs working in dedicated COVID hospitals had a reduced multivariate-adjusted risk of seropositivity (odds ratio, 0.21; 95% CI, 0.06-0.66).

DISCUSSION

We aimed to estimate the seroprevalence of SARS-CoV-2 infection in HCWs in different hospital settings in the District Srinagar of Kashmir, India. In general, seroprevalence was low (2.5%), with little difference across gender or occupational group.

Seroprevalence studies of HCWs across divergent workplace environments have revealed estimates ranging from

TABLE 1. **Seroprevalence of SARS-CoV-2–specific IgG Antibodies by Baseline Characteristics of Healthcare Workers**

	No. (%) of participants	Seroprevalence (95% CI), %	*P* value
Overall	2,905	2.5 (2.0-3.1)	
Sex			.347
Male	1,865 (64.2)	2.7 (2.0-3.5)	
Female	1,040 (35.8)	2.1 (1.4-3.2)	
Age, y			.186
<30	705 (24.3)	3.4 (2.3-5.0)	
30-49	1,612 (55.5)	2.2 (1.6-3.1)	
≥50	588 (20.2)	2.0 (1.2-3.6)	
Occupational group			.353
Physician	980 (33.7)	2.8 (1.9-4.0)	
Nurse	321 (11)	2.8 (1.5-5.3)	
Medical technician[a]	397 (13.6)	2.5 (1.4-4.6)	
Pharmacist	109 (3.7)	0	
Field staff[b]	141 (4.9)	0	
Ambulance driver	57 (2)	3.5 (0.9-13.3)	
Hospital sanitation staff	624 (21.5)	2.4 (1.5-4.0)	
Other housekeeping staff	276 (9.5)	3.3 (1.7-6.2)	
Designation of physicians			.223
Administration	61 (2.1)	3.3 (0.8-12.5)	
Faculty[c]	274 (9.4)	1.1 (0.4-3.4)	
Intern	58 (2)	3.4 (0.8-13.1)	
Medical officer- PHC	130 (4.5)	2.3 (0.7-7.0)	
Resident[d]	457 (15.7)	3.7 (2.3-5.9)	
Physician specialty			.252
Critical care	57 (2)	1.8 (0.2-11.9)	
Medical	343 (11.8)	3.5 (2.0-6.1)	
Surgical	327 (11.2)	3.7 (2.1-6.4)	
Nonclinical	138 (4.7)	0.7 (0.1-5.0)	
MBBS	115 (4)	0.9 (0.1-6.0)	

[a] Medical technician includes persons who handle sophisticated equipment and have expertise in working in different areas such as laboratories of biochemistry/pathology/microbiology/blood bank, operation theater, ophthalmology, and radiology.
[b] Field staff includes female multipurpose healthcare workers, community health officers, accredited social health activists, and health visitors.
[c] Faculty physicians participate mainly in teaching, research, administration, as well as in clinical care based on their field of expertise.
[d] Residents are physicians who are receiving postgraduate training in a particular specialty
Abbreviations: IgG, immunoglobulin G; MBBS, Bachelor of Medicine and Bachelor of Surgery.

1% to 10.2%.[16-19] Generally, the seroprevalence rates among HCWs are not significantly different from those of the general population, which reflects how different the dynamics of COVID-19 are compared to other infections in healthcare settings. The low seroprevalence observed in our study coincides with the overall low infection rate in the community population. During the study period, District Srinagar reported a median of 28 new infections daily (interquartile range, 17-46), which is indicative of the early phase of the pandemic in the population at the time of the study.[20]

Among the HCW occupational groups, ambulance drivers and housekeeping staff had the highest seroprevalence rates, followed by nurses and physicians. Possible explanations for higher seropositivity in these groups are improper use or inadequate supply of protective gear and lack of training on the use of personal protective equipment (PPE), resulting in increased exposure risk.[21] Concordance of HCW and community infection rates in specific geographic areas suggests that community exposure may be the dominant source of healthcare exposure and infection. Additionally, careful in-hospital behavior of HCWs in dedicated COVID hospitals may have had a spillover effect on their out-of-hospital behavior, which may partially explain our finding that employment at dedicated COVID hospitals was associated with a markedly lower chance of seropositivity. A study of 6,510 HCWs in Chicago, Illinois, showed high seropositivity rates among support service workers, medical assistants, and nurses, with nurses identified as having a markedly higher adjusted odds of seropositivity relative to administrators. The authors of the study concluded that exposure in the community setting plays a crucial role in transmission among HCWs.[22] Similarly, higher seroprevalence among housekeeping, nonadministrative staff, and other support service staff has been reported elsewhere.[23] Certain underlying factors related to socioeconomic status and lifestyle may also contribute to higher seroprevalence in some occupational groups.[24] Nonadherence to masking, social distancing, and proper hand hygiene outside the hospital setting could result in community-acquired infection.

Interestingly, participants who were working in a dedicated COVID hospital or who had ever worked at one had a seroprevalence of 0.6%, much lower than the 2.8% observed among other participants. This difference remained statistically significant after controlling for age, sex, place of work, and occupational group. As these facilities were dedicated to the management and care of patients with COVID-19, the hospital staff strictly adhered to safety precautions, with particular vigilance during patient contact. These hospitals also strictly adhered to infection prevention and control practices based on the latest guidelines released by India's Ministry of Health and Family Welfare.[13]

A commitment was made to provide adequate PPE to the dedicated COVID hospitals and staff, commensurate with expected infected patient volumes and associated exposure risks. Healthcare workers were specifically trained on proper donning and doffing of PPE, self-health monitoring, and protocols for reporting symptoms and PPE breaches during pa-

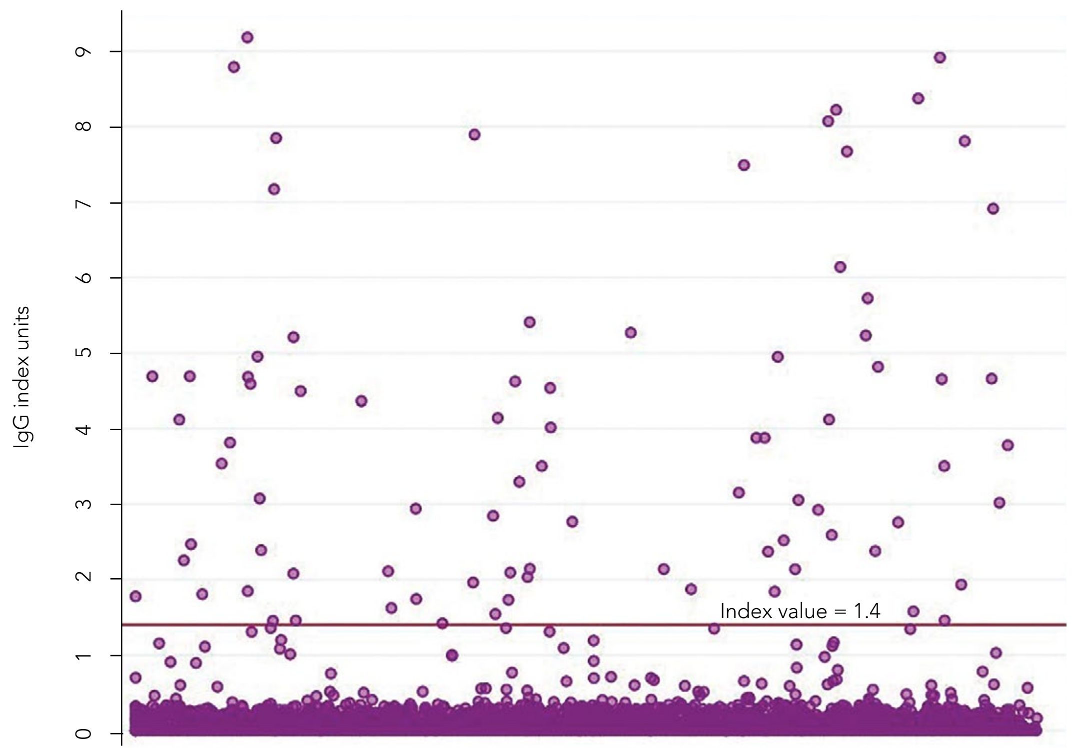

FIG 2. Scatter Diagram Displaying Immunoglobulin G (IgG) Index Value of the Study Participants

tient encounters. Healthcare workers were regularly tested for COVID-19 using nasopharyngeal RT-PCR. Of critical importance, these hospitals implemented a buddy system wherein a team of two or more staff members was responsible for ensuring each other's safety, proper PPE use, conformance to other protective measures, and reporting breaches of PPE compliance.[25] Universal masking was mandatory for all hospital staff and patients at the COVID-focused facilities, with the additional use of N-95 masks, gloves, and face shields during times of patient contact. Administrative measures, including visitor restrictions and environmental sanitation, were rigorously enforced. Also, being a potentially high-risk area for transmission of infection, these facilities implemented staff-rationing to reduce the duration of exposure to the healthcare staff. Third, the HCWs of COVID-dedicated hospitals were provided with separate living accommodations during the period in which they were employed at a dedicated COVID hospital.

In contrast, in non-COVID hospitals, with the exception of HCWs, patients and the hospital visitors were not subject to a masking policy. Moreover, an adequate and timely supply of PPE was not prioritized at the non-COVID facilities due to resource constraints. Further, lack of testing of asymptomatic patients at non-COVID hospitals may have resulted in nosocomial transmission from asymptomatic carriers. Though routine infection prevention and control activities were performed at non-COVID hospitals, we did not assess adherence to infection prevention and control guidelines in the two different categories of hospitals. Our results are also supported by evidence from studies conducted in different hospital settings, the findings of which reiterate the importance of fundamental principles of prevention (eg, proper masking, hand hygiene, and distancing) and are of particular importance in resource-limited settings.[17,26,27] The only published study quantifying seroprevalence among HCWs in India was performed in a single hospital setting with separate COVID and non-COVID units. The authors of that study reported a higher seroprevalence among HCWs in the COVID unit. However, this difference seems to be confounded by other factors as revealed by the multivariable analysis result.[23]

We found a two-fold higher seroprevalence (4.4%) in HCWs who reported close contact with a patient with COVID-19. Respiratory infections pose a greater health risk to HCWs in an occupational setting. Substantial evidence has emerged demonstrating that the respiratory system is the dominant route of SARS-CoV-2 transmission, with proximity and ventilation as key predictive factors.[28] Globally, among thousands of HCWs infected with SARS-CoV-2, one of the leading risk factors identified was close contact with a patient with COVID-19;

TABLE 2. **Seroprevalence of SARS-CoV-2–specific IgG Antibodies by Clinical Characteristics and Specific Risk Factors**

	No. (%) of participants	Seropositivity (95% CI), %	*P* value
Symptoms of an influenza-like illness[a]			<.001
Present	123 (4.2)	12.2 (7.4-19.3)	
Absent	2,782 (95.8)	2 (1.6-2.6)	
RT-PCR status			.390
Ever done	760 (26.2)	2.9 (1.9-4.4)	
Never done	2,145 (73.8)	2.3 (1.8-3.1)	
RT-PCR result (n = 760)			<.001
Positive	29 (3.8)	27.6 (14.0-47.2)	
Negative	731 (96.2)	1.9 (1.1-3.2)	
Ever put under quarantine			.009
Yes	268 (9.2)	4.9 (2.8-8.2)	
No	2,637 (90.8)	2.2 (1.7-2.9)	
Ever worked at a quarantine ED			.667
Yes	60 (2.1)	3.3 (0.8-12.7)	
No	2,845 (97.9)	2.5 (2.0-3.1)	
Ever worked in a dedicated COVID hospital			.004
Yes	480 (16.5)	0.6 (0.2-1.9)	
No	2,425 (83.5)	2.8 (2.3-3.6)	
History of close contact with a COVID-19 case			.014
Yes	339 (11.7)	4.4 (2.7-7.2)	
No	2,566 (88.3)	2.2 (1.7-2.9)	
History of travel after 1/1/2020			.963
Yes	165 (5.7)	2.4 (0.9-6.3)	
No	2,740 (94.3)	2.5 (2.0-3.1)	

[a] A history of fever and cough with or without other symptoms, within 4 weeks preceding the date of interview.
Abbreviations: ED, emergency department; IgG, immunoglobulin G; RT-PCR, reverse transcription polymerase chain reaction.

other identified risk factors were lack of PPE, poor infection prevention and control practices, work overload, and a preexisting health condition.[29]

The seroprevalence estimate among participants who reported an ILI in the 4 weeks preceding the interview was only 12.2%, suggesting an alternative etiology of these symptoms. Among those who reported a previously positive RT-PCR for SARS-CoV-2, only 27.6% showed the presence of SARS-CoV-2–specific IgG antibodies. The inability to mount an antibody-mediated immune response or early conversion to seronegative status during the convalescence phase has been suggested as an explanation for such discordant findings.[30] On the contrary, seropositivity among participants who reported having a negative RT-PCR test was 1.9%. There are few plausible explanations for such observations. First, several studies have reported false-negative result rates from RT-PCR testing ranging from 2% to 29%.[31-33] Second, the sensitivity of the SARS-CoV-2 assay is influenced by the timing of the test after the onset of symptoms or RT-PCR positivity. The sensitivity of the assay we used varies from 53.1% at day 7 to 100% at day 17 postinfection.[34] Variable viral load and differences in duration of viral shedding are other possible reasons for false-negative RT-PCR results.[35,36]

In our study, seroconversion among asymptomatic HCWs who were RT-PCR-positive was 20.8%. Among HCWs who reported an ILI and were RT-PCR-positive, seropositivity was 60%. In one study, 40% of asymptomatic and 13% of symptomatic patients who tested positive for COVID-19 became seronegative after initial seropositivity—that is, 8 weeks after hospital discharge.[37]

Serological testing offers insight into both the exposure history and residual COVID-19 susceptibility of HCWs. However, current immunological knowledge does not allow us to conclude that seropositivity conveys high-level immunity against reinfection. As the epidemic evolves, HCWs will continue to be exposed to COVID-19 in the community and the workplace. Serial cross-sectional serosurveys can help monitor the progression of the pandemic within the healthcare setting and guide hospital authorities in resource allocation.

Strengths and Limitations

We used the Abbott Architect SARS-CoV-2 IgG assay, which has exhibited a high level of consistency and performance characteristics when tested in different patient populations. The participation rate was acceptable compared to similar studies, and we included all the major hospitals in the District Srinagar. The findings from our study can therefore be considered representative of the HCWs in the district.

The study results should be interpreted in the context of the following limitations. First, information on risk factors for seropositivity were based on participant report. Also, we did not collect information on the timing of symptoms or the date on which a participant became RT-PCR-positive. Second, information regarding place of exposure (ie, community or hospital setting) was not recorded, limiting conclusions regarding the effect of workplace exposures. Third, given the voluntary nature of participation in the study, there is a possibility of selection bias that may have limited the generalizability of our findings. For example, some HCWs with a recent exposure to COVID-19 or those who were symptomatic at the time of the study might not have participated based on the absence of an individual benefit from IgG testing in the early phase of infection. Conversely, some HCWs who had symptoms in the distant past might have been more likely to have participated in the study. However, we believe that selection bias does not vitiate the validity of the associations based on the plausible assumption that infection risk should be similar between respondents and nonrespondents due to comparable work environments. Finally, with a cross-sectional study design, we cannot ascertain the reconversion from an initial positive-IgG to negative-IgG status, which warrants a cohort study.

CONCLUSION

We conclude that the seroprevalence of SARS-CoV-2 infection was low among HCWs of District Srinagar at the time of the study. Healthcare workers in a dedicated COVID hospital or HCWs who had ever worked in such a facility had lower seroprevalence, suggesting both adherence to and effectiveness of standard protective measures during contact with patients who had COVID-19. Nonetheless, the careful in-hospital behavior of the HCWs at the COVID hospitals may have had a spillover effect on their out-of-hospital behaviors, which lead to community-acquired infection. On the contrary, lack of testing of asymptomatic patients at non-COVID hospitals may have resulted in nosocomial transmission from asymptomatic carriers. We believe that our findings highlight the value of implementing infection prevention and control measures in the hospital setting. Moreover, training and retraining of sanitation and other housekeeping staff on standard hygienic practices and appropriate use of the protective gear may further help reduce their rates of exposure.

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Data availability statement: Data shall be made available on request through the corresponding author.

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