



Original Research Article

Seroprevalence of COVID-19 infection among healthcare professionals in Central India using SARS-CoV-2 antibody test

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ARTICLE INFO

Article history:

Received 21-09-2020

Accepted 03-10-2020

Available online 11-12-2020

Keywords:

COVID-19

Siemens healthineers

Seroprevalence

ABSTRACT

Introduction: The diagnosis and monitoring of SARS-CoV-2 infection (COVID-19 illness) are based on two different types of tests: (i) RT-PCR (reverse-transcription polymerase chain reaction) test that detects the presence of viral RNA, and (ii) antibody test that detects antibodies to SARS-CoV-2. Studies have demonstrated that antibody testing is useful for the identification of asymptomatic or subclinical infection of SARS-CoV-2 among close contacts with COVID-19 patients, including the HCP.

Objectives: This study presents the first SARS-CoV-2 seroprevalence study among 307 HCP in Central India. This study also evaluates the risk of exposure of the HCP of different roles/departments to COVID-19 infection by the SARS-CoV-2 antibody seroconversion rate.

Materials and Methods: A cross-sectional study was conducted using serum obtained from 307 HCP, who were on duty in the hospitals in Indore City of Central India during the COVID-19 pandemic from March till June 2020. Siemens Healthineers COV2T assay that detects total antibody (including IgM and IgG) against the S1-RBD (receptor binding domain of spike protein subunit 1) antigen was selected to be used in this study due to its robust sensitivity and specificity, compared to IgG or IgM assay alone.

Results: Overall, the prevalence of COVID-19 infection among HCP in Central India hospital is 7.82% (n=24/307) as evaluated using SARS-CoV-2 total antibody test. Of the 307 HCP, Seropositivity rate varies widely by professions/departments ranging from intensivists (66.7%), general surgeons (25%), ophthalmologist (20%), pediatrician (20%), anesthetist (12.5%), radiologist (10%), general physician (9.7%) to gynaecologist (4.9%).

Conclusion: This seroprevalence study, along with other studies, highlights the importance of SARS-CoV-2 antibody in seroprevalence and epidemiology studies which may subsequently guide the policy-making in implementing an effective infection control strategy to curb SARS-CoV-2 transmission in the hospital settings; on top of the use as aid-in-diagnosis, contact-tracing, pre and post vaccination screening and evaluation of convalescent plasma therapy.

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1. Introduction

COVID-19 has infected over 27.2 million people worldwide, and over 4.2 million people in India as of 9th Sep 2020 with 3.27% death rate (WHO). The route of transmission of SARS-CoV-2 (the causative virus for COVID-19 infection) is primarily through respiratory

droplets when a person is in close contact (within 1 meter). The frontline healthcare professionals (HCP) are playing a critical role in the COVID-19 outbreak response caring for the COVID-19 patients and are at high risk. Asymptomatic COVID-19 infection has been described. Various studies have shown that the prevalence of COVID-19 among these healthcare professionals vary from 1.6% in Germany,¹ 6.0% in United States of America,² 6.4% in Belgium³ and 24.4% in UK.⁴ The seroprevalence among HCP in India remains largely unknown.

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The diagnosis and monitoring of SARS-CoV-2 infection (COVID-19 illness) are based on two different types of tests: (i) RT-PCR (reverse-transcription polymerase chain reaction) test that detects the presence of viral RNA, and (ii) antibody test that detects antibodies to SARS-CoV-2. Studies⁵ have demonstrated that antibody testing is useful for the identification of asymptomatic or subclinical infection of SARS-CoV-2 among close contacts with COVID-19 patients, including the HCP.

2. Objectives

This study presents the first SARS-CoV-2 seroprevalence study among 307 HCP in Central India. This study also evaluates the risk of exposure of the HCP of different roles/departments to COVID-19 infection by the SARS-CoV-2 antibody seroconversion rate.

3. Materials and Methods

A cross-sectional study was conducted using serum obtained from 307 HCP, who were on duty in the hospitals in Indore City of Central India during the COVID-19 pandemic from March till June 2020. Participants were largely grouped based on the self-declared symptoms into (i) symptomatic and (ii) asymptomatic groups. Sera were collected by thorough aseptic technique in serum tubes of HCP between 1st July 2020 to 7th July 2020 to be screened for SARS-CoV-2 antibodies. Participants were asked to declare any COVID-19-associated symptoms, diagnosis of previous SARS-CoV-2 infection by RT-PCR test and their profession/departments. Siemens Healthineers COV2T assay that detects total antibody (including IgM and IgG) against the S1-RBD (receptor binding domain of spike protein subunit 1) antigen was selected to be used in this study due to its robust sensitivity and specificity, compared to IgG or IgM assay alone.⁶ Participants were categorized as seropositive if SARS-CoV-2 antibodies were detected at threshold of ≥ 1.0 index value; or seronegative if SARS-CoV-2 antibodies were below the threshold. Previous validation work with this assay demonstrated a 100% sensitivity (14 days post-PCR) and 99.8% specificity. Notably, independent head-to-head evaluation performed by Public Health of England suggested that the Siemens Healthineers COV2T has the best overall performance compared to other comparator manufacturers.⁷ Independent validations of the COV2T by several Indian hospitals also demonstrated 100% positive percent agreement (PPA) and 100% negative percent agreement (NPA) using RT-PCR-confirmed positive samples and negative samples (data not shown; via personal communication).

4. Results

Overall, the prevalence of COVID-19 infection among HCP in Central India hospital is 7.82% (n=24/307) as

evaluated using SARS-CoV-2 total antibody test. Of the 307 HCP, 8.5% (n=26/307) reported symptoms associated with COVID-19 infection (Table 1). Of this symptomatic group, 84.6% (n=22/26) were positive for SARS-CoV-2 total antibody, suggesting a recent or previous COVID-19 infection and seroconversion. Four others (15.4%, n=4/26) symptomatic HCP were seronegative (Table 1 and Figure 1). Of these four, only one HCP who experienced fever was tested for SARS-CoV-2 RNA and was found to be negative. Of the other 3; one had fever, one experienced runny nose and the other experienced body ache. Two hundred and eighty-one (91.5%, n=281/307) of the study HCP were asymptomatic. Of these, 279 (99.3%) were seronegative for SARS-CoV-2 (Table 1). Only two HCP (0.7%; n=2/281) were positive for SARS-CoV-2 total antibody indicating asymptomatic COVID-19 infection (Table 1 and Figure 1).

RT-PCR test result was available on only 21 HCP. Of these, only 5 (23.8%, n=5/21) were positive for SARS-CoV-2 RNA (Table 2). All these 5 HCP were also positive for SARS-CoV-2 antibody. All these 5 HCP were also seropositive for SARS-CoV-2. Fifteen other HCP (71.4%, n=15/21) who were negative for SARS-CoV-2 RNA were also negative for SARS-CoV-2 antibody tests. Only one HCP who had a negative SARS-CoV-2 RNA was seropositive for SARS-CoV-2. The 307 study HCP were from 26 distinct specialties/departments (Figure 2). Seropositivity rate varies widely by professions/departments ranging from intensivists (66.7%), general surgeons (25%), ophthalmologist (20%), pediatrician (20%), anesthetist (12.5%), radiologist (10%), general physician (9.7%) to gynaecologist (4.9%). Among the study HCP, general physician represented the largest individual group (33.6%, n=103/307). In terms of risk of exposure, these 307 HCP were generally grouped into (i) general physicians, and (ii) other healthcare professionals (Table 3). The seroconversion rate was higher among the general physician (9.7%, n=10/103) than the other healthcare professionals (6.9%, n=14/204).

The relative antibody level in human sera is indicated by the arbitrary units represented in numerical index value (0.05-10.0). Siemens Healthineers COV2T assay has an assay cut-off threshold of index value 1.0, in which index value ≥ 1.0 indicates reactive (presence of SARS-CoV-2 antibodies) and < 1.0 indicates non-reactive. Symptomatic group who seroconverted had very high level of SARS-CoV-2 antibody with median and mean index values of 10.0 and 8.39, respectively (Figure 3). The asymptomatic group had median and mean index value of 7.26.

5. Discussion

This study is, to our best knowledge, the first study of seroprevalence among the healthcare professionals in Indore City of Central India who were on duty in the hospitals

Table 1: Demographic of 307 healthcare professionals participated in the study

Demographic	Symptomatic		Asymptomatic		Overall	
		%		%		%
Male	16	5.2%	191	62.2%	207	67.4%
Female	10	3.3%	90	29.3%	100	32.6%
	26	8.5%	281	91.5%	307	
Age Median	42		43		43	
Profession						
General physician	11	10.7%	92	89.3%	103	33.6%
Other healthcare professionals	15	7.4%	189	92.6%	204	66.4%
SARS-CoV-2 total antibody (COV2T)						
Reactive	22	84.6%	2	0.7%	24	7.8%
Nonreactive	4	15.4%	279	99.3%	283	92.2%

Table 2: SARS-CoV-2 RNA and antibody results

	RT-PCR		COV2T		
	+	-	+	-	
Symptomatic	+	-	+	-	5
	-	-	+	-	1
	-	-	-	-	1
	Not tested	-	+	-	16
	Not tested	-	-	-	3
Asymptomatic	-	-	-	-	14
	Not tested	-	+	-	2
	Not tested	-	-	-	265

Table 3: Seroconversion between general physician and other healthcare professionals

SARS-CoV-2 Total Antibody (CoV2T)				
Profession	Reactive	%	Nonreactive	%
General physician	10	9.7%	93	90.3%
Other healthcare professionals	14	6.9%	190	93.1%

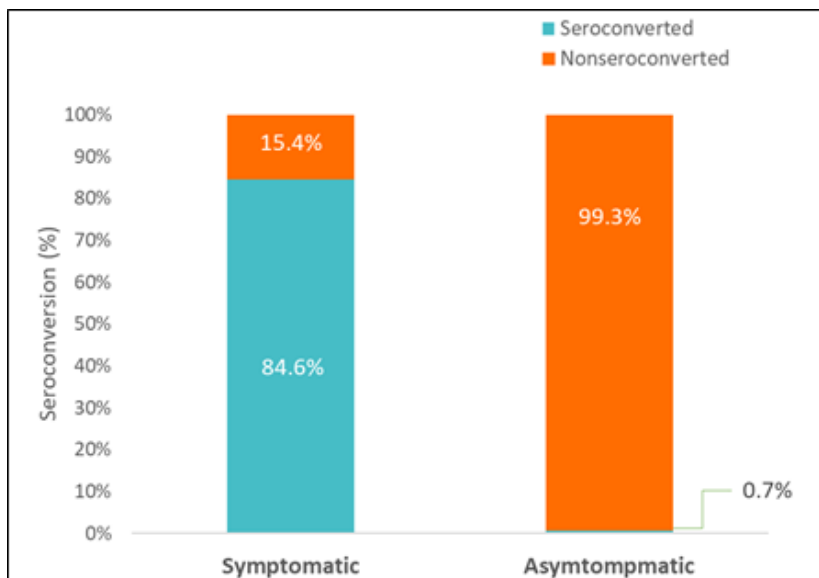


Fig. 1: Seroconversion rates of healthcare professionals, with self-declared COVID-19 symptoms

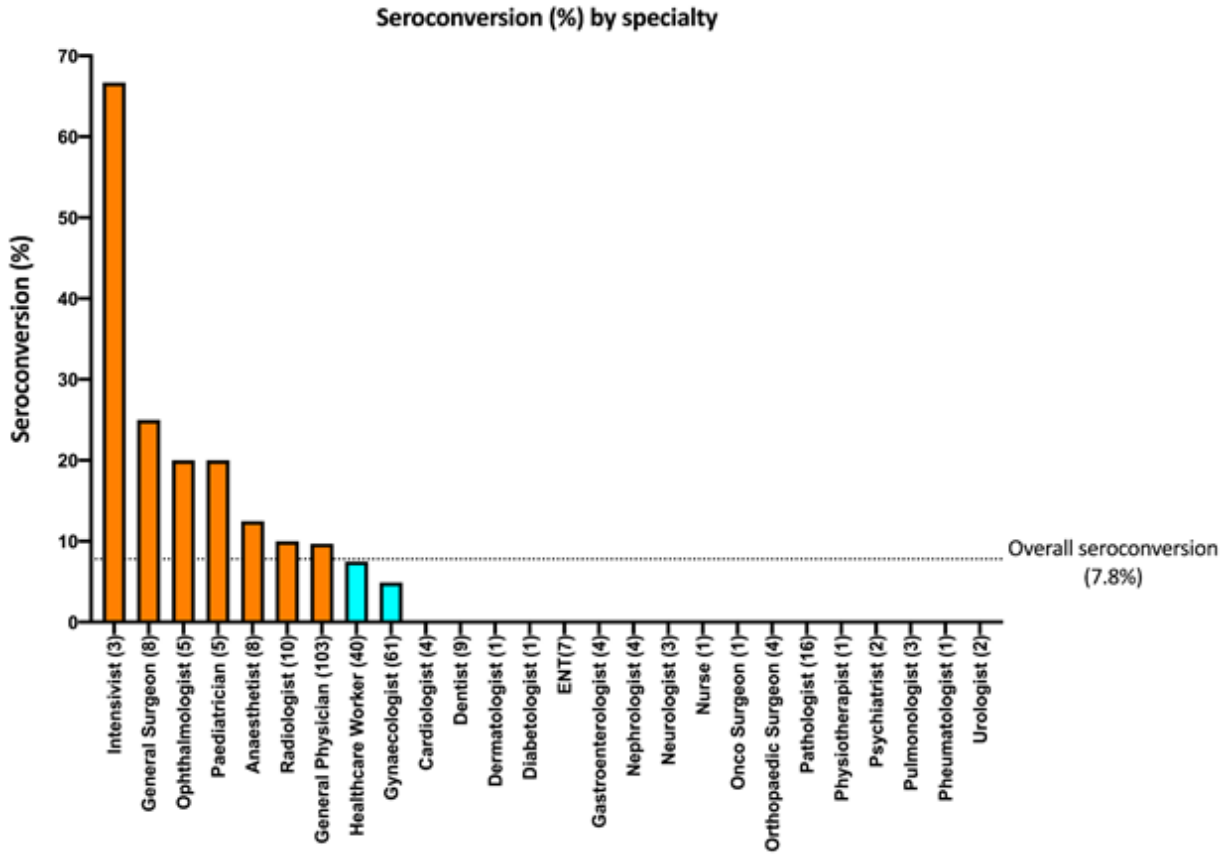


Fig. 2: Seroconversion rate by healthcare professional specialty. The overall seroconversion among the healthcare professionals participated in this study is at 7.8%

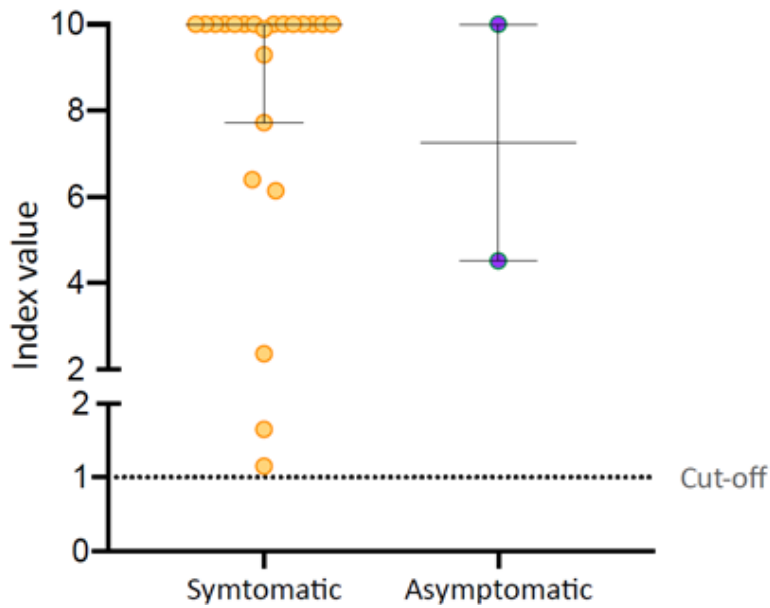


Fig. 3: Distribution of index value (numerical result) obtained for antibody test. Assay thresholds (cut-off at 1.0) is shown as dashed line.

caring for the patients during the COVID-19 pandemic. Study has shown that people infected with COVID-19 develop antibodies that is detectable generally after 2-3 weeks after symptom onset,⁵ though the antibody level may be lowered or delayed in people with milder symptoms or immune-compromised. In this cohort of 307 HCP, 24 (7.8%) developed detectable IgM and/or IgG antibodies against SARS-CoV-2. In comparison to the estimated 0.3% COVID-19 prevalence (4,204,613 cases recorded on WHO as of 7th Sept 2020 at 4.24pm CEST) in the 1.353 billion Indian population, this study implies that HCP is indeed a high-risk population. The study finding – 91.7% (n=22/24) reported symptoms consistent with COVID-19 and 8.3% (n=2/24) did not experience any symptoms – confirms the fact that COVID-19 infection can be asymptomatic. This suggests that some of the COVID-19-infected HCP may be undetected and unrecognized; and may subsequently lead to unintentional SARS-CoV-2 transmission to their hospital colleagues and patients. This study also identified an important factor that certain department/profession within the hospital is at higher-risk and potentially associated with the SARS-CoV-2 infection among the HCP. General physicians represented the highest individual seropositive group (9.7%; n=10/103) (compared to the average of 7.8% seropositivity across the study group) indicates a higher risk of exposure of general physician to COVID-19 infection. This is likely due to the nature of the job of the general physician coming into a closer proximity and/or prolonged period of interaction with (in-house or walk-in) unsuspected COVID-19-infected patients in the hospital. This underlines the importance of continued vigilance and the need for frequent testing of the HCP to protect both the HCP and patients.

In this study, all the five HCP who had a previous RT-PCR positive were also seropositive for SARS-CoV-2. Consistently, all these 5 HCP had a reportable index values of ≥ 10.0 (the highest limit measuring range) and reported COVID-19-associated symptoms. All these supports the previous findings⁵ that symptomatic COVID-19 patients may mount a higher antibody level. This group also represents a 100% PPA (positive percentage agreement) of SAR-CoV-2 antibody and RT-PCR tests. Contrary, the 15 HCP who had previous negative RT-PCR result were seronegative. Notably, this study also identified one HCP who had a previous negative RT-PCR but seropositive for SARS-CoV-2. This individual is a 36 years-old general physician who reported symptoms including fever, cough and body ache. Considering the high-risk of exposure to COVID-19, COVID-19-associated symptoms and the high antibody level (index value >10.0) displayed by this subject, this is likely a true COVID-19 case missed by RT-PCR. This highlights the importance of SARS-CoV-2 antibody test as an aid-of diagnosis for identifying individual who had a recent or previous COVID-19 infection. Although

RT-PCR test is the first test developed to diagnose SARS-CoV-2 infection, some of these RT-PCR tests in the market have been plagued with false negative rate of up to 48%.⁸ This high false-negative rate is largely attributed to the preanalytical errors such as sample collection and handling, and the tedious RT-PCR procedure. More importantly, study has demonstrated that combining both the RT-PCR and antibody test improves the sensitivity in detecting COVID-19 patients.⁶

Studies have also described patients with undetectable antibodies after 2-3 weeks of symptom onset,⁵ one possibility is that the antiviral treatment received by the patients affect the immune response development. Another reason could be attributed to the T-cell response, in which the mild SARS-CoV-2 infection is possibly cleared by the T-cells⁹ before the antibody is elicited. There are debates that people who have recovered from a COVID-19 infection may experience a secondary infection. However, a study¹⁰ by South Korean CDC showed that those recovered COVID-19 patients may be tested positive again weeks later; but these re-positive individuals are not infectious. This is evident by the fact that (i) the close contacts of this group did not contract the virus from these re-positive group, and (ii) scientists failed to culture the virus in the secretions of these re-positive patients.

It is believed that SARS-CoV-2 antibody may confer immunity against secondary infection. Although the extent of immunity and longevity of the antibodies are currently unclear, understanding the individual's serological status against SARS-CoV-2 may shed some lights to guide the policy makers, particularly once the vaccine becomes available. These individual serological profiles will enable the policy maker to make an informed decision on identifying the most susceptible group to be prioritized for the vaccination program. A recent longitudinal study of the Iceland population revealed that SARS-CoV-2 antibodies may rapidly rise and fall in the early stage but stabilized over time, for at least 4 months.¹¹ These stabilized detectable antibodies enable a reliable seroprevalence of the population; and further signify the potential immunity and vaccination strategy against COVID-19.

6. Conclusion

All in all, this seroprevalence study, along with other studies, highlights the importance of SARS-CoV-2 antibody in seroprevalence and epidemiology studies which may subsequently guide the policy-making in implementing an effective infection control strategy to curb SARS-CoV-2 transmission in the hospital settings; on top of the use as aid-in-diagnosis, contact-tracing, pre and post vaccination screening and evaluation of convalescent plasma therapy.

7. Source of Funding

None.

8. Conflict of Interest

The author(s) declare(s) that there is no conflict of interest.

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Cite this article: Hawalдар R, Sodani S, Sodani V, Sodani RK. Seroprevalence of COVID-19 infection among healthcare professionals in Central India using SARS-CoV-2 antibody test. *J Community Health Manag* 2020;7(4):146-151.