Research article

SARS-CoV-2 sero-surveillance among healthcare workers at a tertiary care reference centre in Central India: A cross-sectional study

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Abstract:

Introduction: Health care workers (HCW), as the primary caregivers in the management of COVID-19 cases, are at a higher risk of acquiring infection. As such, they are associated with challenges to themselves including adverse health outcomes and emotional burdens. Additional challenges include compromised continuity of patient care, potential spread to patients and household contacts and increased mortality . Assessment of seroprevalence of SARS-CoV-2 IgG antibodies among HCWs can provide important data on pathogen exposure, infectivity and vaccine efficacy. This study aims to estimate the seroprevalence among different cadres of HCW and explore associations with demography, category of exposure to COVID-19 and vaccination status.

Methods: This cross-sectional study was conducted over a five-month period from January to May 2021 during the second wave of the COVID-19 pandemic. HCWs from various professional categories were recruited and tested for SARS-CoV-2 IgG antibodies. Data capturing demographic details, comorbidities, job role, work environment, history of exposure to COVID-19 patients, prior COVID-19 diagnosis, and vaccination status were collected and analysed.

Results: Out of 461 HCWs, anti-SARS-CoV-2 IgG antibodies were detected in 260 (56.4%; 95%CI: 51.8%-60.9%) individuals. Factors associated with significant higher seropositivity included age <35 years ($p = 0.038$), professional category ($p = 0.0001$), vaccinated status ($p < 0.0001$), previous RTPCR positive for COVID-19 ($p = 0.017$), posting in COVID unit ($p=0.014$), and close contact with COVID -19 cases ($p=0.015$). Upon logistic regression analysis, vaccination was the sole significant factor (OR: 5.52; 95% CI: 2.98 – 10.23; $p < 0.0001$) associated with greater antibody positivity.

Conclusion: We report higher seroprevalence in HCWs immediately following the rollout of vaccination in India. Role of antigenaemia in individuals with low seroprevalence in faculties and resident doctors is a matter of further research.

Keywords: *Sero epidemiologic studies, SARS-CoV-2, Health personnel, Vaccination, COVID-19*

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Introduction

Over the last three years, the COVID-19 pandemic—attributable to the novel coronavirus SARS-CoV-2—has led to substantial worldwide morbidity and mortality. Health care workers (HCW) being the frontline workforce have borne a major brunt of the virus. Due to occupational exposure to suspected and confirmed COVID-19 cases and infectious material, HCWs are at a higher risk of acquiring the disease than the general population.[1] On the contrary, there are some reports that HCWs risk a similar or lower rate of infection than the community owing to the preventive strategies practised.[2,3] A number of occupational factors such as the role of the HCW, work settings and availability of personal protective equipment (PPE) are proposed as impacting the exposure risk to HCWs.[2,4–8]

While detection of the viral RNA in throat and nasal swabs of infected individuals by PCR has served as the gold standard for diagnosis of active infection, antibody testing has been widely used to assess exposure to the virus. Following symptom onset, IgG antibodies directed against SARS-CoV-2 proteins generally peak within 3 to 4 weeks, with a sustained humoral response persisting in most individuals for at least three months.[9] Demonstration of these antibodies is a marker of vaccination and infection with the virus. Seroprevalence studies offer valuable insights into the proportion of individuals with prior or recent infections. While they are informative at the community level, they are equally important for high-risk groups such as healthcare workers. Numerous seroprevalence studies have been conducted on HCWs across the globe but differ in the platforms used and performance characteristics of the assays, rendering head to head comparisons challenging.

Our institute is a tertiary health care centre having approximately 2500 HCWs belonging to different cadres. This study aims to estimate the seroprevalence of antibodies against SARS-CoV-2 and characterise the antibody profile in HCWs at our institute, one of the primary reference centres in Chhattisgarh for the diagnosis and treatment of COVID-19 disease. The seroprevalence rate found in this study is compared with that of other centres across the country.

Methods

Study design, population and setting. This is a cross sectional study conducted during a 5 month period from January to May 2021 at the All India Institute of Medical Science (AIIMS), Raipur during the second wave of COVID-19. A total of 493 HCWs belonging to various categories including faculty members, resident doctors, nursing staff, laboratory workers, housekeeping staff, canteen staff, security guards and administrative staff were recruited to the study. Those unwilling to give consent or presenting with a history of a COVID compatible illness within the last 14 days were excluded from the study. A detailed case record form including information on demographic data, comorbidities, professional category, nature of work (whether directly involved in providing health care to COVID-19 patients or not or working in the environment where COVID-19 patients are admitted), history of contact with COVID-19 patients, previous diagnosis of COVID-19 and vaccination status was filled. Three ml of venous blood was withdrawn for detection of SARS-CoV-2 IgG antibodies. Serum samples were aliquoted and stored at -80 ºC until analysis.

Laboratory procedures. SARS-CoV-2 IgG antibodies were detected using the ADVIA Centaur® SARS-CoV-2 IgG (COV2G) assay, an in-vitro diagnostic test designed for both qualitative and semi-quantitative analysis on the ADVIA Centaur® XP and XPT systems. This fully automated, two-step sandwich immunoassay employs indirect chemiluminescent technology on the CLIA platform (Siemens Pvt. Ltd). The amount of IgG antibodies in the sample is directly proportional to the relative light units (RLUs) measured by the system. Results are reported as Index Values and categorised as Reactive or Nonreactive, with values below 1.0 considered Nonreactive and those above 1.0

considered Reactive. The procedure was done on a single serum sample of the participants according to manufacturer's instructions.

Statistical analysis. Descriptive statistics including frequency, mean and SD were calculated for the demographic data. Categorical variables were expressed as percentages or proportions, while continuous variables were summarised using means with corresponding 95% confidence intervals. Associations between variables were assessed using the Chi-square test or Fisher's exact test for categorical variables, and the Student's t-test for continuous quantitative variables. Odds ratios were calculated for risk factors, and variables with a p-value less than 0.05 were included in a binary logistic regression model. A p-value of ≤0.05 was considered statistically significant for all analyses. All statistical analyses were performed using Epi info version 7.2.5.0.

Results

A total of 493 HCWs were enrolled in the study and 461 samples included for testing and analysis. Samples from 32 HCWs were haemolysed and could not be tested for SARS-CoV-2 IgG antibody.

The mean age of participants was 30.6 years (SD: 7.1) and male to female ratio was 1.3:1. Nursing officers represented 30.8% of the participants, followed by laboratory workers (14.1%) and residents (13.0%). At the time of recruitment, 114 healthcare workers (HCWs) had received one dose of the vaccine, while 37 had completed both doses. The remaining participants were unvaccinated. Anti-SARS-CoV-2 IgG antibodies were detected in 260 (56.4%; 95%CI: 51.8%-60.9%) individuals with higher seropositivity in males (59.62%) and in HCWs less than 35 years. Seropositivity was highest among administrative staff (24/33, 72.73. The difference among the professional groups was found to be statistically significant (p value = 0.0001) (Table 1).

All vaccinated individuals had received COVISHIELD^{TM} vaccine (ChAdOx1-S [recombinant]). Of the 461 participants, 241 (52.3%) were posted in a COVID-19 unit, amongst whom 158 (65.6%) were working in the COVID-19 ward and the remaining 41 (17.1%) in the COVID-19 ICU. Of those posted in COVID-19 units, 115 (47.7%) reported close contact with COVID-19 patients . Of the 134 participants with a previous diagnosis of COVID-19, 88 (65.67%; OR: 1.66; 95% CI: 1.09; 2.53; p=0.017) were found to be seropositive which is significantly higher than those who did not have a history of a previously diagnosed COVID-19 infection (168/314, 53.50%). Seroprevalence in HCWs posted in a COVID-19 area (169/277, 61.01%) was significantly higher than those posted in non-COVID-19 areas (91/184, 49.46%). However, there was no significant association between seropositivity and different places of posting in the COVID units : ICU, ward, OPD or laboratory (p value=0.512). Contact with COVID-19 confirmed or suspected cases was significantly associated with higher seroprevalence (p value=0.015) (Table 2).

Among the vaccinated individuals, 83.48% (OR: 5.60; 95% CI: 3.28;9.57; p <0.0001) were seropositive for SARS-CoV-2 IgG antibodies, which was significantly higher than non-vaccinated individuals (164/346, 47.55%). Even a single dose of the vaccine was found to be associated with a significant increase in seroprevalence (76.92%, p value < 0.0001) in comparison to those who were not vaccinated at all (Table 3).

Table 1: Demographic details and occupational roles of HCWs at AIIMS, Raipur

Factors		Antibody Positive		Antibody Negative		Total	OR	(95%CI)	P value
		n	%	n	%	n			
Sex	**Female**	105	51.47	99	48.53	**204**	1		0.057
	Male	155	60.31	102	39.69	**257**	1.43	(0.99;2.07)	
Age groups	**< 35 years**	210	58.99	146	41.01	**356**	1.58	(1.02;2.45)	**0.038**
	> 35 years	50	47.62	55	52.38	**105**	1		
Professional category	**Administrative staff**	24	72.73	9	27.27	**33**	1		**0.0001**
	Hospital attendants	15	44.12	19	55.88	**34**	0.29	(0.10;0.82)	
	Faculty	15	37.50	25	62.50	**40**	0.22	(0.08;0.61)	
	Canteen staff	14	29.79	33	70.21	**47**	0.16	(0.06;0.43)	
	Resident doctors	34	56.67	26	43.33	**60**	0.49	(0.19;1.23)	
	Nursing Officers	91	64.08	51	35.92	**142**	0.66	(0.28;1.55)	
	Laboratory workers	44	67.69	21	32.31	**65**	0.78	(0.31;1.98)	
	Security	16	64.00	9	36.00	**25**	0.66	(0.21;2.04)	
	Others	7	46.67	8	53.33	**15**	0.32	(0.09;1.17)	

Table 2: Vaccination status and COVID-19 unit deployment of HCWs

Factors		Antibody Positive		Antibody Negative		Total	OR	(95%CI)	P value
		n	%	n	%	n			
Vaccination status	**Vaccinated**	96	83.48	19	16.52	**115**	5.60	(3.28;9.57)	**<0.0001**
	Non vaccinated	164	47.40	182	52.60	**346**	1		
Previously diagnosed as COVID positive by RTPCR	**Yes**	88	65.67	46	34.33	**134**	1.66	(1.09;2.53)	**0.017**
	No	168	53.50	146	46.50	**314**	1		
Posting in COVID unit	**Yes**	169	61.01	108	38.99	**277**	1.59	(1.09;2.33)	**0.014**
	No	91	49.46	93	50.54	**184**	1		
Place of posting in COVID 19 unit	**ICU**	26	53.06	23	46.94	**49**	1		0.512
	Laboratory	25	60.98	16	39.02	**41**	1.38	(0.59;3.20)	
	OPD	8	53.33	7	46.67	**15**	1.01	(0.31;3.22)	
	WARD	110	63.95	62	36.05	**172**	1.56	(0.82;2.98)	
	TOTAL	**169**	**61.01**	**108**	**38.99**	**277**			
Close contact with COVID-19 confirmed or suspected case	**Yes**	97	59.88	65	40.12	**162**	1.52	(1.00;2.30)	**0.015**
	No	104	49.52	106	50.48	**210**	1		
	Not known	59	66.29	30	33.71	**89**			

Table 3: Association of the vaccination status with seroprevalence of anti-SARS-CoV-2 IgG in HCWs

No of doses of vaccines	Antibody positive		Antibody negative		Total
	n	%	n	%	n
One dose	60	76.92	18	23.08	**78**
Two doses	36	97.30	1	2.70	**37**
Unvaccinated	165	47.55	182	52.45	**347**

Seroprevalence increased from January to May among all participants (Figure 1).

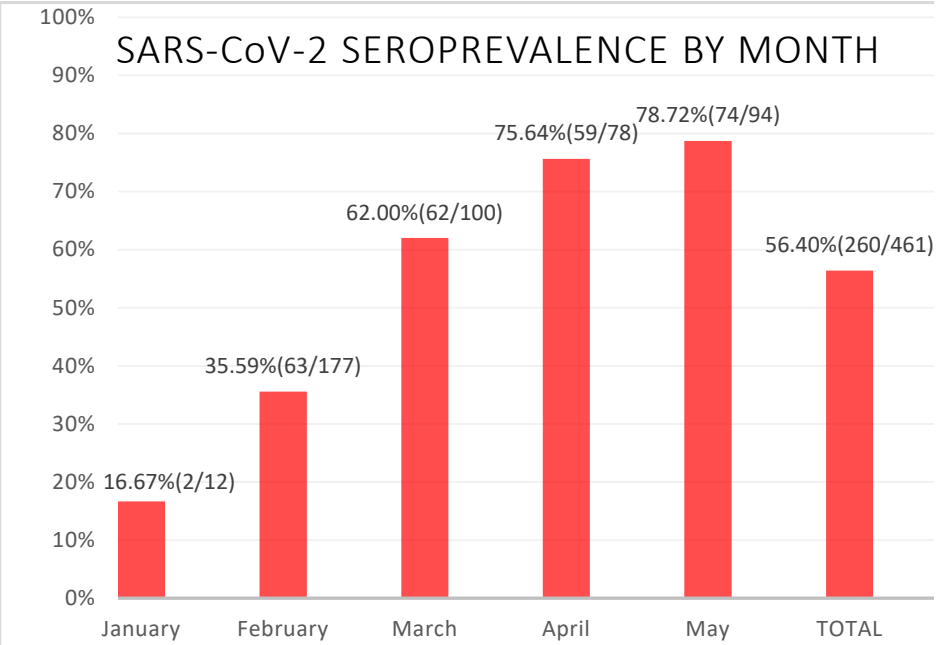

Figure 1: Month wise variation in SARS-CoV-2 antibody positivity in HCWs over the study period (January to May 2021)

Figure 2 depicts the seroprevalence rates amongst HCWs obtained in studies done across the country.[10]

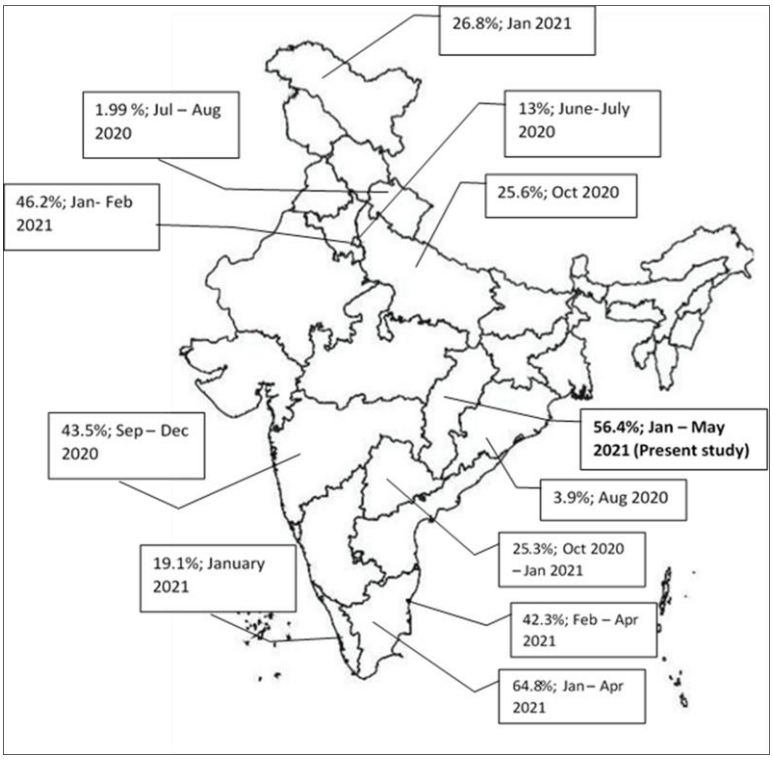

Figure 1: SARS-CoV-2 seroprevalence rates amongst HCWs obtained in studies done across India, along with the time periods

Upon logistic regression analysis of factors of significance in the univariate analysis, vaccination emerged to be sole significant factor (OR: 5.52; 95% CI: 2.98 – 10.23; $p < 0.0001$) associated with a greater antibody positivity.

Table 4 enlists other studies done in India which have analysed association of various demographical and clinical characteristics with SARS CoV-2 seroprevalence.

Table 4:Comparison of various studies across India to determine SARS-CoV-2 seroprevalence

Study	Study Time period	Age	Sex	Profession	Previous diagnosis of COVID-19	Posting in COVID-19 units	Contact with COVID cases	Symptoms in past	Vaccination
Haq et al[11]	January 2021	NS	NS	NS	S	NA	NA	A	NA
Murhekar et al[12]	Dec 2020-Jan 2021	NS	NS	NS	S	NA	S	S	NA
Murhekar et al[13]	June – July 2021	NS	NS	NA	S	NA	NA	S	S
Kataria et al [14]	Jan – Feb 2021	NA	NS	S	S	NA	NA	NA	NA
Jessy et al [15]	January 2021	NS	S	S	S	S	NA	S	NA
Elangovan et al[16]	January – April 2021	NS	NS	S	S	NA	NA	NA	S
Basheer et al[17]	February – April 2021	S	NS	NS	NS	NS	NS	NA	S
Dudeja et al[18]	December 2020 – June 2021	S	NS	S	NA	S	NA	S	S
Present study	**January – May 2021**	**S**	**NS**	**S**	**S**	**S**	**S**	**S**	**S**
NS – Not significant; S – Significant; NA – Not analysed									

Discussion

HCWs are frontline personnel involved in diagnosis and management of suspected or confirmed COVID-19 patients, exposing them to a higher risk of acquiring the infection as compared to the general population. This study aimed at determining SARS-CoV-2 seroprevalence among HCWs at AIIMS, Raipur. In this study, 56.4% of HCWs were positive for SARS-CoV-2 IgG antibodies which is greater than many studies done previously in India and across the globe.[19–22] However, many of these studies were carried out before the introduction of COVID-19 vaccines in India, while the present study coincided with the launch of the COVISHIELD™ vaccine (ChAdOx1-S [recombinant]) in January 2021[23] as well as during start of the second wave of COVID pandemic in March – April 2021 and peak in May 2021.[24]

According to the World Health Organisation (WHO), India reported an average of 390,000 new cases during the first week of May 2021 with the peak of 414,188 cases reported on May 7th, 2021. In Chhattisgarh, there were 12,962 active COVID cases as of 1st January 2021 which decreased in February but again crossed more than 100,000 active cases till the end of April 2021.[25] During the same period, vaccination coverage also increased from 50,000 beneficiaries in February 2021 to more than 6.5 lakhs till the end of April 2021.[26,27] The third serosurvey in India was conducted between December 2020 and January 2021 in which among 7385 HCWs, the seroprevalence of anti-S1-RBD

IgG antibodies was 25.6% [12] while in the fourth survey done in June – July 2021, the seroprevalence rose to 85.2%.[13] This increase in seroprevalence over months has been also observed in this study. The increase in seroprevalence over a period of time could be due to natural infection and COVID vaccination.

In the present study, seroprevalence did not differ by sex groups but differed significantly by age groups. Other studies have found similar seropositivity across age and sex groups.[12,22] Interestingly, highest seropositivity in the current study was seen in administrative staff (72.73%) followed by laboratory workers (67.69%), nursing officers (64.08%), security guards (64.00%) and resident doctors (56.67%). Only 35.7 of faculty staff including clinical consultants tested positive for COVID-19 antibodies. This finding is similar to another study done by Gupta *et. al* (2021)[28] in which administrative staff had the highest seropositivity while nurses and physicians had low seroprevalence.

Another observation of our study was that vaccination coverage was highest for administrative staff (48.48%) and lowest for faculty staff (17.50%) and residents (28.33%) (Data not shown). Low vaccination rates and probably better infection control practices could probably be the reasons for a lower seroprevalence in faculty staff and residents. An alternative hypothesis suggests that continuous exposure to SARS-CoV-2 may lead to a sustained and elevated presence of viral components—or the virus itself—in the bloodstream, potentially saturating available antibodies and hindering their detection until antigenaemia or viraemia declines below a detectable threshold.[29] Belogiannis *et al* (2021)[29] in their study found that prolonged SARS-CoV-2 antigenemia/viraemia could mask humoral responses and be a confounding factor in immunodiagnostic assays. Thus, role of antigenaemia in non-responders is a matter of further investigation and large-scale research.

Among the various factors affecting seroprevalence, vaccination status was the most significant factor ($p < 0.0001$) as compared to previously diagnosed COVID positive ($p=0.017$), posting in COVID unit ($p =0.014$) and close contact with COVID cases ($p =0.015$). An observational multi-centre study among HCWs in India reported a seropositivity of 98.1% among COVISHIELD™ recipients.[30] In another study in UK, authors estimated 6% of participants to be non- responders.[31] In our study, only one (1/36, 2.8%) individual was seronegative even after receiving two doses of Covishield vaccine. This sero-negativity among fully vaccinated individuals may be due to lower antibody response or a decline in antibodies due to some specific host factor. The reason could not be ascertained due to the cross sectional nature of the study. The seroprevalence in previously COVID-19 positive HCWs was found to be 65.67%, similar to the findings of Verma *et al* (2022).[22] The role of HCWs in patient care activities is an important risk factor of acquiring SARS-COV-2 infection. HCWs in ICUs have a higher risk of exposure to COVID-19 patients, possibly due to more aerosol generating procedures (AGPs) being performed in these high-dependency units. In a study by Wiggen *et al*(2022)[32], 30% of participants working in ICUs reported a direct COVID-19 exposure within the past two weeks as compared to 6% of HCWs in ambulatory clinical settings. In contrast to this, our study did not find any significant association between different locations in the hospital setting and seropositivity. This is probably due to meticulous training and strict implementation of infection control practices including hand hygiene and appropriate use and constant availability of PPE at our institute. It was the protocol of the institute that all healthcare workers were posted in COVID areas on rotation basis and they had to undergo mandatory infection control practices training regarding hand hygiene, donning and doffing of PPE, and disinfection of patient care items and work surfaces. Infection control nurses were posted in all COVID areas to oversee compliance of HCWs to infection control practices.

The limitation of this study is the cross sectional nature of the study with lack of follow up testing to check for seroconversion which might have been missed due to single testing, which could have been

either done early (window period) or delayed (waning antibody response). Another lacunae of the study is that the duration between vaccination and testing for antibodies were not analysed due to lack of information of vaccination dates.

Conclusion

This study found that vaccination, along with younger age-group (<35 years) played a significant role in seroconversion as compared to other factors like in-hospital location, environment or contact with COVID-19 patients. Significantly lower seroprevalence among HCWs with constant virus exposure highlights the need for future research.

Declaration

Conflict of interest: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.
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Ethics Statement: The study was approved by Institute ethical committee (letter no. 1425/1EC-AIIMSRPR/2021 dated 18.01.2021), AIIMS, Raipur. Informed written consent was obtained from the participating health care workers.
Author contributions:

Kumar Vikram:	Writing - original draft, Data curation, Formal analysis;
Anudita Bhargava:	Conceptualization, Funding acquisition, Writing - review & editing;
Pragya Agarwala:	Conceptualization, Writing - review & editing, Data curation;
Eli Mohapatra:	Conceptualization ,Resources, Writing - review & editing;
Padma Das:	Conceptualization, Writing - review & editing ;
Ujjwala Gaikwad:	Conceptualization ,Writing - review & editing

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