

Immunoglobulin-G Antibodies against Severe Acute Respiratory Syndrome – Coronavirus-2 among Health-Care Workers: A Serosurveillance Study from India

Abstract

Background: Seropositivity among health-care workers (HCWs) may help in better understanding of the immune response after COVID-19 infection. **Objectives:** To estimate seropositivity among HCWs and to compare available variables with seropositivity to understand the factors affecting seropositivity. **Materials and Methods:** A serosurveillance among HCWs was carried out using population proportion sampling during the second half of October 2020 in the city of Ahmedabad using the Covid-Kavach (immunoglobulin G [IgG] ELISA Antibody testing kit). Simple proportions and appropriate statistical tests were used as needed. **Results:** As on October 2020, HCWs in Ahmedabad demonstrated a seropositivity of 20.84% (95% confidence interval [CI] 19.00–22.81%). Seropositivity among HCWs was lower than that of the general population (24.20%) which was estimated as part of the same study. Female HCWs had higher seropositivity 22.14% (95% CI 19.74–24.74%) as compared to 18.82% (95% CI 16.06–21.93%) among male HCWs and the difference was statistically not significant ($Z = 1.66, P = 0.097$). Age groups with increasing age show increasing trend in the seropositivity among HCWs. **Conclusion:** As on October 2020, with 20.84% seropositivity among HCWs in Ahmedabad, one in every five HCW already demonstrate IgG antibodies against severe acute respiratory syndrome– coronavirus-2. Further scientific studies on seropositivity and the factors affecting the seropositivity may be carried out to uncover more details of immune reaction after COVID-19 infection.

Keywords: Covid Kavach, COVID-19, health-care workers, immunoglobulin G antibodies, immunity, severe acute respiratory syndrome – coronavirus-2, sero-surveillance

Introduction

Severe acute respiratory syndrome – Coronavirus-2 (SARS-CoV2), the causative agent of COVID-19, spread across the world in pandemic proportion during 2020.^[1] A large percentage of people infected with SARS-CoV-2 present either no symptoms or relatively mild disease.^[2] Since those who exhibit symptoms are more likely to get tested than asymptomatic individuals, confirmed cases are a skewed underestimate of the number of active cases.^[3] In view of the above scientific facts, serological survey indicating cumulative incidence are powerful tool as well as an effective supplementary indicator for monitoring the development and progression of the epidemic.^[4,5]

Health-care workers (HCWs), on account of their occupational exposure, are at

higher risk of getting infected.^[6] HCWs with asymptomatic infection could be a source of infection to other HCWs and patients.^[7] It is therefore important to know the seropositivity among HCWs to get better scientific insight into disease situation. HCWs working at COVID hospitals and COVID health centers are at significantly higher risk as compared to other HCWs and this has been reflected in seroprevalence studies.^[8]

Situated in the western part of India, Ahmedabad city from Gujarat, was one of the earliest cities to witness very high number of COVID-19 cases.^[9] As per the Indian Council of Medical Research (ICMR) directives, a population-based serosurveillance study was carried out during the second half of October 2020. HCWs, cases, and contacts of cases were the additional serosurvey sampling categories apart from the representative

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Submitted: 05-Aug-2021

Revised: 20-Oct-2021

Accepted: 01-Dec-2021

Published: 31-Jan-2022

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Access this article online

Website:
www.ijabmr.org

DOI:
10.4103/ijabmr.ijabmr_516_21

Quick Response Code:



How to cite this article: Prakash O, Solanki B, Sheth J, Acharya H, Acharya S, Vinzuda M, et al. Immunoglobulin-G antibodies against severe acute respiratory syndrome – Coronavirus-2 among health-care workers: A serosurveillance study from India. Int J App Basic Med Res 2022;12:18-23.

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general population. The present study focuses only the HCWs category from the serosurveillance. With the primary objective of assessing the seroprevalence among HCWs, we also tried to correlate seropositivity among HCWs with available demographic and other factors affecting their immunity.

Materials and Methods

During the early 2020, ICMR issued directives to all the state governments for conducting repeated serosurveillance studies to monitor the pandemic, predict its progression and to take appropriate corrective public health measures in a timely manner.^[10] Ahmedabad Municipal Corporation (AMC) had already completed two serosurveillance studies during June 2020 and August 2020 with a number of scientific research papers documenting its findings.^[11-15] To study the changing level of seropositivity, another serosurveillance study in the general population of Ahmedabad was planned during the second half of October 2020. To decide the minimum required sample size, we referred to the seropositivity results of our earlier sero-survey in the general population of Ahmedabad. We considered 99% confidence level and 1% margin of error in a population of 70 lakhs. Population-based stratified sampling was used for the study and the required minimum samples for each of the Urban Primary Health Center (UPHC) was determined based on the population proportion.

Apart from the general population, there were three additional categories which included COVID-19 cases, contacts of cases, and HCWs. The minimum sample size for these additional three sample categories was calculated as at least 10% of the general population sample for each of the UPHC area. For the same purpose, the general population sample size for each of the UPHC was rounded up to the next "0". This also interprets that the sample size for HCWs for each UPHC was also based on population proportion. On written informed consent, HCWs working at UPHCs, working at private dispensaries/clinics/hospitals etc., from the field area of the UPHC were eligible to get enrolled in the study as HCWs. Selective sampling was followed, and HCW enrollment continued till the desired HCWs were enrolled from the UPHC field area.

Institutional Ethics Committee of the AMC MET Medical College, Ahmedabad, approved the study protocol. Informed written consent was obtained from each of the enrolled individual for participation in the study. Confidentiality was ensured at all levels. With the purpose of reducing the sample rejection rate, we used SST-Gel Vacutec for the blood sample collection. Testing of the collected serum samples was carried out by the laboratories with state-of-the-art facilities, desired equipment, and national level accreditation. "Covid-Kavach" (capture ELISA test for anti-SARS-CoV2 immunoglobulin-G [IgG] antibody) kits were being developed and manufactured

by Zydus Diagnostics. The National Institute of Virology, Pune, India had validated these kits and its results were quite reliable with sensitivity of 92.37% and specificity of 97.9%.^[16] ICMR had permitted the use of these kits for the sero-surveillance studies and the same kits were used for the present study. As per the manufacturer report, these kits did not have any cross-reactivity with other viruses in the serum from the real-time reverse-transcription polymerase chain reaction confirmed patients of various other infections. Testing procedures were followed as directed by the manufacturer's instructions for testing.

Microsoft Excel and Epi-Info were the tools used for the purpose of data management and data analysis. A positive Covid-Kavach test result indicates the presence of IgG antibodies against SARS-CoV-2 and the proportion of positive tests give the crude seropositivity among HCWs. We also tried to compare the seropositivity with the limited number of variables (age, sex, and zone) which were collected as part of the study. Simple proportions were calculated from the data, and appropriate statistical tests were applied as needed.

Results

A total of 1738 samples were collected out of which 1 sample was rejected and results were available for 1737 samples from HCWs. Analyzing the results 1346 (77.49%) samples were negative and 29 (1.67%) had indeterminate results. Remaining 362 samples were positive for the IgG antibodies against SARS-CoV2 giving an overall positivity of 20.84% (95% confidence interval [CI] 19.00–22.81%).

Detailed analysis of 1737 HCWs [Table 1] show that there were 1057 female and 680 male HCWs for whom results were available. A total of 234 samples were positive among female HCWs giving a positivity rate of 22.14% (95% CI 19.74–24.74%), whereas 128 samples were positive among male giving a positivity of 18.82% (95% CI 16.06–21.93%). The percentage positivity was higher among female HCWs as compared to the male HCWs [Figure 1], and the difference was statistically not significant ($Z = 1.66, P = 0.097$).

The age distribution of the HCWs typically followed age-heaping bias [only grouped data shown in data Table 1] as the age of the enrolled HCWs was recorded as replied by them and not verified with any official document. The age of the HCWs ranged from 18 to 75 years with a mode of 25, median of 32 and an average of 33.45 ± 10.51 years. Among the sample, the mean age of females was 34.45 ± 9.94 years, whereas the mean age of males is 31.90 ± 11.18 years. Considering the sero-positive HCWs, the mean age for females was 36.18 ± 10.14 years, whereas that of male is 34.68 ± 11.63 years.

The age group wise analysis of seropositivity among HCWs [Figure 2] shows that the lowest seropositivity is

Table 1: Analysis of coronavirus disease-2019 sero-survey positivity in health care workers

	Female			Male			Total			95% CI
	Results	Positive	Percentage positivity	Results	Positive	Percentage positivity	Results	Positive	Percentage positivity	
Total	1057	234	22.14	680	128	18.82	1737	362	20.84	19.00-22.81
Age group										
10-19	14	3	21.43	20	4	20.00	34	7	20.59	08.70-37.90
20-29	360	63	17.50	350	47	13.43	710	110	15.49	13.02-18.34
30-39	344	76	22.09	158	34	21.52	502	110	21.91	18.51-25.74
40-49	250	70	28.00	78	25	32.05	328	95	28.96	24.32-34.09
50-59	85	20	23.53	53	14	26.42	138	34	24.64	17.71-32.69
60-69	2	1	50.00	16	2	12.50	18	3	16.67	03.58-41.42
70-79	2	1	50.00	5	2	40.00	7	3	42.86	09.90-81.59
80-89	1	1	100	0	0	0.00	1	1	100	02.50-100.0
Zone										
CZ	137	31	22.63	54	6	11.11	191	37	19.37	14.02-25.70
EZ	212	50	23.58	112	19	16.96	324	69	21.30	17.19-26.08
NWZ	86	12	13.95	70	11	15.71	156	23	14.74	09.58-21.30
NZ	217	54	24.88	136	39	28.68	353	93	26.35	22.02-31.18
SWZ	78	11	14.10	78	16	20.51	156	27	17.31	11.73-24.17
SZ	177	44	24.86	121	23	19.01	298	67	22.48	17.87-27.65
WZ	150	32	21.33	109	14	12.84	259	46	17.76	13.31-22.97

CI: Confidence interval, CZ: Central zone, WZ: West Zone, NWZ: North WZ, SWZ: South WZ, NZ: North Zone, SZ: South Zone, EZ: East Zone

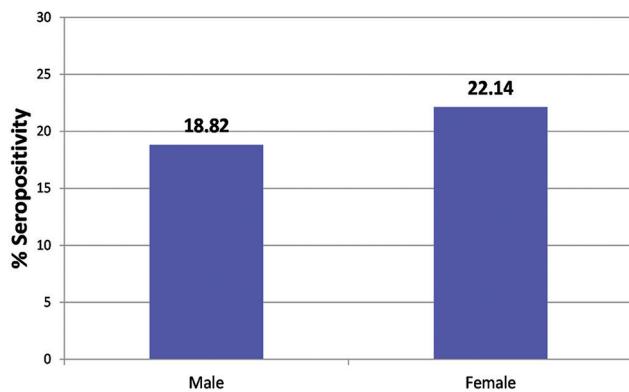


Figure 1: Sex wise seropositivity among health care workers

for the 20–29 years' age group (15.49%) and the highest seropositivity is for 70–79 years age group (42.86%). The linear trend line shows increasing trend from just above 15% to around 30% as the age group increases from 10 – 19 and 70 – 79 years. When the same comparison of age group and sero-positivity is done for both the sex groups [Figure 3], it shows that both the sex categories of HCWs have almost similar levels of seropositivity with slight variation from one age group to another. However, the variation is wider toward the elderly groups, i.e., 60–69 and 70–79 years.

The zone wise analysis of total tests and positive tests when compared to calculate percent positivity shows that the positivity in various zones varies widely. The zone wise positivity ranges from 14.74% to 26.35%. The zone wise positivity shows that the North Zone (NZ–26.35%) had the highest seropositivity followed by South Zone

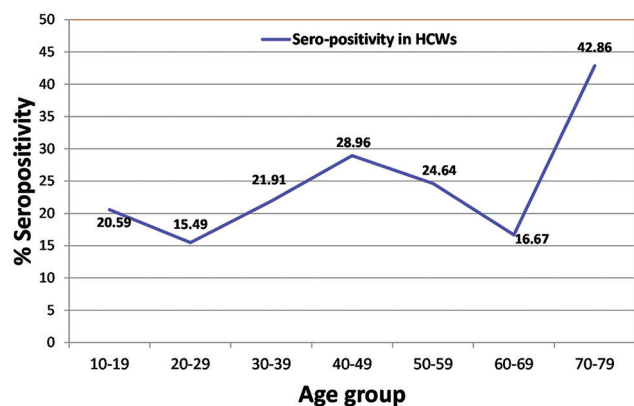


Figure 2: Age group wise seropositivity in health care workers

(SZ–22.48%), whereas North West Zone (NWZ–14.74%) and the South West Zone (SWZ–17.31%) were the zones with lowest seropositivity.

Seropositivity among HCWs for each zone was compared with the reported COVID-19 cases from the respective zone to check for any correlation. The zones with low number of reported cases before the start of the study (as on October 15, 2020), i.e., NWZ and SWZ, also had the lowest seropositivity among HCWs. Other zones with higher number of reported cases have wider variation in the seropositivity among HCWs.

Discussion

Immune response during and after COVID-19 infection is still largely evolving.^[17] So far, serological surveys

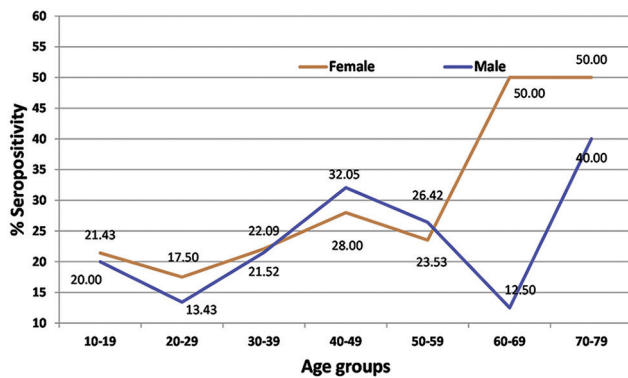


Figure 3: Age group and sex wise seropositivity in health care workers

have been found to be extremely useful in understanding the progress of the pandemic. Scientifically, it was recommended to have repeated serosurveillance studies to estimate and monitor the growing burden of the pandemic.^[18] Since the seropositivity is markedly affected by a variety of factors, understanding the various factors affecting immune response is extremely important while interpreting the results of the serosurveillance.^[19]

The present study discusses the seropositivity among HCWs of Ahmedabad city from Gujarat, India. During the COVID-19 pandemic, HCWs were the most at risk on account of their profession as they were exposed to suspected/confirmed cases while providing the health care services to the affected people. Many HCWs developed symptoms on account of their exposure. However, COVID-19 has reported more of asymptomatic infections.^[2] That is why many HCWs developed immune response in form of IgG antibodies without developing any symptoms after being exposed to subclinical/preclinical cases in their incubation. Seroprevalence among HCWs is an important indicator as it gives an idea of communicability of the infection and transmissibility of the infectious agent along with the level of preventive/protective measures applied by the HCWs.

As of October 2020, the seropositivity for IgG antibodies against SARS-CoV2 among HCWs from Ahmedabad [Table 1] was 20.84% (95% CI 19.00–22.81). The present study documented lower seroprevalence among the HCWs as compared to our earlier study carried out during August 2020, which reported seropositivity of 23.65% among HCWs.^[14] Our present study enrolled HCWs irrespective of their participation in the previous study, and the enrolment in the present study might be affected based on their serosample results of the previous study which might be the reason for the reported seropositivity. Studies among HCWs from hospitals of India reported wide range of seropositivity from 2.5% to 19.1% depending on the transmission dynamics of the pandemic during the study period.^[20-22] However, most studies enrolled HCWs from hospitals, whereas in our study, they are HCWs from the field area.

In general, HCWs are better informed, more aware about the disease transmission dynamics and provided with appropriate personal protective equipment and so we may expect them to have lower infection rate and thus lower seropositivity as compared to the general population. The same is observed in the present study where the seropositivity among HCWs (20.84%) is lower than that of seropositivity among the general population (24.20%) which was estimated as part of the same study and results are shared separately.^[23] At the same time, this estimated seropositivity level among HCW indicates that almost 1 in every 5 HCW have already acquired symptomatic/asymptomatic infection and thus demonstrated IgG antibodies against SARS-CoV2.

Our study included field level HCWs from the UPHC field area. Apart from HCWs from the private sector, our study included Urban Accredited Social Health Activist (ASHA), Aanganwadi workers as well as Multipurpose Health Workers, etc., and covered them as HCWs in the present study. This may be the reason why our study had enrolled more of female HCWs as compared to the male HCWs. Female HCWs had higher positivity of 22.14% (95% CI 19.74–24.74%) as compared to male HCWs who demonstrated IgG Antibody seropositivity of 18.82% (95% CI 16.06–21.93%). This difference in seropositivity according to sex group was statistically not significant ($Z = 1.66, P = 0.097$). Our finding was similar to some of the other research studies where the difference in seropositivity was statistically not significant.^[24]

Analysis of the age of the HCWs shows that the mean age (33.45 years) was higher than median (33 years) which is also higher than the mode (25 years). This indicates skewed distribution.^[25] The interpretation is that there are many young adults enrolled in our study as HCWs as compared to the elderly HCWs. This finding is correct in view of the existing human resources in the public health sector, contractual appointment to large number of HCWs on different posts in urban health setup during the pandemic and deputation/deployment of many medical-paramedical students/staff for health care delivery during the COVID pandemic times.

The age data were grouped according to 10 years age groups. Seropositivity according to age group [Figure 2] shows increasing trend from just above 15% to around 30% as the age group increases from 10 – 19 to 70 – 79 years. Scientifically, it has been recorded that younger people are more likely to have asymptomatic or milder infection.^[26,27] Even the duration of the illness is shorter among the younger individuals.^[28,29] Considering the severity of symptoms, younger people have milder symptoms as compared to the elderly, who are more likely to have severe symptoms for longer duration.^[30-32] All the factors discussed above play a crucial role in resulting in higher seropositivity among elderly as compared to the younger people and this is also applicable for the category

of HCWs. Since we have collected a limited number of data and clinical symptoms as well as their severity etc., it was not possible to check this association. The same comparison for both the sex groups [Figure 3] shows almost similar levels of seropositivity with wide variation toward the higher age groups due to smaller size of the sample in those respective age groups.

Research studies from the field of immunology have documented that antibody is not immediately available and they do take some time to develop after an infection, around 1–3 weeks, with an average of about 2 weeks (14 days).^[33,34] This means that we need to have around 14 day time gap before the antibodies demonstrate their presence in the serum sample after an infection. In other words, our study reflects the seropositivity of around 2 weeks before the study sample collection. Since our study was carried out in the second half of October 2020 and completed by the end of October 2020, we can say that the study reflects the findings as on October 15, 2020.

Ahmedabad city have a population of around 70 lakhs, covered through 75 UPHCs spread across 48 wards and 7 zones. As described in methodology, in our study, HCWs from UPHC and its field area were selected with population proportion. During the pandemic times, HCWs are working in the field area for containment and control of the pandemic. Consequently, these HCWs are more at risk and the risk is higher for the HCWs from those area where the case load is very high. This is the same reason why we compared the estimated seroprevalence among HCWs with the COVID-19 cases reported from the respective zone [Figure 4] which shows wide variation. The first to get affected zones e.g., Central Zone and SZ had higher seropositivity as compared to the zones affected recently, e.g., NWZ and SWZ. These zones show similar trend in reported cases and seropositivity. However, NZ and West Zone have marked variation in seropositivity and reported cases. Differential proportion of asymptomatic cases, testing and reporting of cases, apart from sampling may be responsible for this variation.

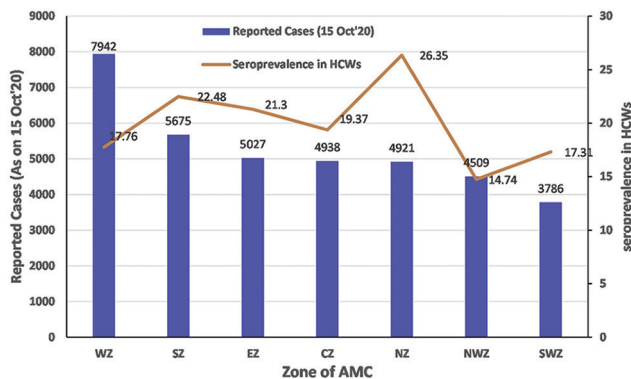


Figure 4: Zone wise comparison of cases and seropositivity in health care workers

Considering some of the limitations of our study, all the limitation of the testing method (Covid Kavach) applies to our study. Moreover, as our study tool collected only a limited number of information, we could compare the seropositivity only with a limited number of variables like age, sex, zone, etc., Looking to the limited amount of inference from our study data analysis, further scientific studies on seropositivity and the factors affecting the seropositivity may be carried out to uncover more details of immune reaction after COVID-19 infection.

Conclusion

As of October 2020, seropositivity among field level HCWs in Ahmedabad is 20.84% and so one in every five HCW already demonstrate IgG antibodies against SARS-CoV2. Female HCWs have higher seropositivity as compared to male HCWs, but the difference was statistically not significant. Seropositivity according to the age group shows increasing trend. Further scientific studies on seropositivity and the factors affecting the seropositivity may be carried out to uncover more details of immune reaction after COVID-19 infection.

Ethical clearance

Protocol was approved by the IEC of the AMC MET Medical College. (DCGI Registration No: ECR/17/inst/Guj/2013/RR-20 with Letter No. “NIL” dated 15/10/2020)

Acknowledgments

We are extremely thankful to respected Dr Rajiv Kumar Gupta, IAS (Additional Chief Secretary, Government of Gujarat) and Mr. Mukesh Kumar, IAS (Municipal Commissioner, Ahmedabad) for their whole hearted support. We acknowledge the full support from all the Deputy Health Officers, Assistant Health Officers and Medical officers of the UPHCs and paramedical workers in conducting the sero-surveillance. Finally, we are indebted to all the participants whose willingness and support has generated the much-desired data for the study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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