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## Original Research Article

# Seroprevalence of SARS-CoV-2 IgG antibodies in health care workers and the associated risk factors during the covid-19 pandemic period at a tertiary care health center in South India

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## ABSTRACT

**Background:** Most of the published studies across the globe so far have demonstrated a highly variable seroprevalence rate of SARS-CoV-2 IgG antibodies in health care workers [HCW's] during the pandemic period. Multiple risk factors were studied that influenced the seropositivity.

**Aim & Objective:** The primary aim of the study was to determine the seroprevalence of SARS-CoV-2 IgG in HCW's in local settings during the pandemic period. The secondary objective was to categorize the HCW's based on the history of symptoms of covid-19 and also to evaluate the relation between the various risk factors and seropositivity amongst the HCW's.

**Materials and Methods:** A cross sectional prospective study was conducted on health care workers at a tertiary care hospital in Telangana state during the pandemic period between March to April 2021. Following enrollment and verbal consent from the participants descriptive data was collected using a validated questionnaire. SARS-CoV-2 IgG antibodies estimation was done using ELFA technology after obtaining IERB clearance.

**Results:** Of the 230 enrolled participants 141 [61.30%] fulfilled the inclusion criteria. The overall SARS-CoV-2 IgG seropositivity in the present study was 48 [34.04%]. Of the 72 [51.06%] symptomatic HCW's, 19 [26.38%] were seropositive and of the 69 [48.93%] asymptomatic, 29 [42.02%] were seropositive. Among the various risk factors studied none were found to be significantly associated with seropositivity.

**Conclusion:** in the present study a greater number of asymptomatic HCW's were found seropositive which could be due to several of the reasons discussed below one being silent transmission of the virus and demands further enquiry into the cause by improved research methodology.

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## 1. Introduction

Most of the published studies have demonstrated a highly variable seroprevalence rate of SARS-CoV-2 IgG antibodies in health care workers [HCW's] across the globe during the pandemic period which clearly indicates a high impact of various socio demographic factors.<sup>1,2</sup> In this context

many authors have investigated multiple risk factors that were supposed to influence the seropositivity in HCW's.<sup>1,2</sup> The overall seroprevalence from various independent, systematic studies and scoping reviews has been shown to be in the range of 0.1- 46% in developing countries especially from south Africa.<sup>1,2</sup> Studies from various geographic regions of India has demonstrated seropositivity in the range of 1-26%.<sup>3,4</sup> Seroprevalence studies aims to determine the proportion of HCW's who had been exposed

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to infection irrespective of the symptoms, the level of exposure and identifying the high-risk locations and the professionals within the health care system. It helps the hospital administration to avoid unnecessary quarantines in times when there is dearth of staff, and also help plan appropriate use of health care resources. Clarity on the immunological response to SARS-CoV-2 is still under study; the exact time of seroconversion, the levels of antibody produced are still not well understood. Moreover, the correlation between seropositivity, antibody levels, protection against reinfection and duration of protective immunity remains a gray zone.<sup>5</sup>

## 2. Aim & Objective

The primary aim of the study was to determine the seroprevalence of SARS-CoV-2 IgG in health care workers in local settings during the pandemic period. The secondary objectives being to determine seroprevalence in two different groups of health care workers as symptomatic and asymptomatic. In addition to determine the relation between the various risk factors and seropositivity amongst these group of HCW's.

## 3. Materials and Methods

### 3.1. Study type

Cross sectional prospective study on health care workers at a tertiary care health center.

### 3.2. Study period and place

One month; from March 2021-April 2021 at a tertiary health care center and teaching hospital of Ayaan institute of medical sciences and research center Kankamamidi village, RR district, Telangana state in south India.

### 3.3. Sample size

Sample size estimated using information on seroprevalence from already published studies ranging between 10% -26% at a CI. of 95% and a precision of 5%.

### 3.4. Sampling technique

Non probability sampling technique using purposive method.

### 3.5. Inclusion criteria

Health care workers above 18 years of age, who are recruited through HR department on permanent basis and are on regular duties during the pandemic period. Those who are not vaccinated against SARS-CoV-2 and didn't have rt RT-PCR confirmed COVID-19 disease in the recent past 14 -21days before the sampling time

as the study aimed on determining seroprevalence of SARS-CoV-2 IgG and not on the incidence of disease or diagnosing acute infection. Participants were grouped into symptomatic and asymptomatic based on the history of presence of symptoms of COVID-19 disease in the past 3-6 months according to WHO clinical grading of the disease as mild, moderate and severe disease and documented in the questionnaire admitted. Results of detection of SARS-CoV-2 RNA by rt RT-PCR 3- 6 months before if available from the symptomatic group were recorded from the documented questionnaire. Risk assessment for work place-based exposure was done using CDC guidelines on healthcare personal risk assessment on exposure to COVID-19 patients and participants were grouped as high risk, intermediate or medium risk and low risk group based on the information documented by them in the questionnaire.<sup>6,7</sup> IERB clearance was obtained prior to the study.

### 3.6. Data collection

Descriptive data was collected from the participants on sociodemographic factors like, age, gender, professional category, risk group, travel history and presence of comorbid conditions, having COVID-19 confirmed disease, and history of vaccination against it using validated questionnaire.

### 3.7. Statistical tools used

Chi-square test and unpaired student t test and Fisher exact test were applicable using R language software.

### 3.8. Test performed

5ml blood samples was collected under aseptic precautions in gel tube from BD India and tested for SARS-CoV-2 antibodies using ELFA technology from Biomerieux India.

### 3.9. Principle of the test

Is a qualitative /semiquantitative sandwich assay wherein anti spike protein antibodies [RBD] to SARS CoV-2 was detected using recombinant spike protein antigen and antihuman IgG conjugated with alkaline phosphate enzyme which hydrolyzes the fluorescent substrate [4 methyl umbelliferon phosphate] to 4 methyl umbelliferon; the fluorescence of which was proportional to the amount of antibody in the test sample. The sensitivity of the assay was 100% and specificity as almost 99.98%.

### 3.10. Interpretation

The sample relative fluorescence is measured as index value and the assay cutoff value of  $\geq 1$  was taken as positive and  $<1.0$  as negative as mentioned by the manufacturer<sup>8</sup>

## 4. Results

Around 141 HCW's were included out of the 230 enrolled. Three participants who were rt RT-PCR positive for SARS-CoV-2 RNA in recent past i.e., 14-21 days from the sampling time and 86 who were vaccinated against COVID-19 were excluded from the disease. Overall seropositivity noted was 48/141 (34.04%). In symptomatic group we had 19/72 (26.38%) seropositive subjects and in asymptomatic we had 29/69 (42.02%).

### 4.1. Gender

With respect to gender the male to female ratio in the study participants was noted as 1.2:1 i.e.; 77/64. The female gender had higher seropositivity in overall and in symptomatic group of subjects but in asymptomatic HCW's males predominated as shown in (Tables 1, 2 and 3).

### 4.2. Age

In the present study the age range of HCW's was between 20-80 years. Maximum no. of participants in descending order of frequency were observed in the age range of 21-30 years, followed by 31-40, 41-50, 61-70, 51-60, and 71-80 years shown in Table 1. The overall mean age of the participants was noted as  $39.01 \pm 13.04$ . The mean age for symptomatic group was greater as  $41.16 \pm 14.27$  compared to asymptomatic group as  $36.68 \pm 11.19$  with a p value of 0.04 and t test value of 2.06. gender wise when checked, the mean age for symptomatic males was greater as  $43.18 \pm 14.03$  compared to asymptomatic males  $39.37 \pm 12.48$  with p value of 0.22 and t value of 1.24. In females the mean age of the symptomatic was greater than asymptomatic group as  $36.65 \pm 13.79$  vs.  $34.58 \pm 9.29$  with p value of 0.48 and t value of 0.72. Similar pattern of age distribution was observed with respect to gender in seropositive and seronegative subjects in symptomatic and asymptomatic participants with symptomatic participants being greater in age than asymptomatic participants. Overall seropositivity was observed to be higher as 15/30 [50%] in the age group 41-50 years. However, the findings differed when the symptomatic and asymptomatic HCW's were compared. Highest seropositivity of 50% was observed in the age group 51-60 years in symptomatic and 100% seropositivity in asymptomatic as 2/2 in the age group 61-70 years as shown in (Tables 1, 2 and 3).

### 4.3. Symptomatic health care workers

Of the 72 [51.06%] symptomatic participants 71 (98.61%) experienced mild influenza like illness with symptoms of upper respiratory tract infection like cough, cold, mild fever, myalgia, loss of taste and loss of smell sensation. Only 1 (1.29%) of the participant had moderate disease with symptoms of pneumonia and required hospitalization. Of

the 72 participants 23 (31.94%) gave history of undergoing SARS-CoV-2 RNA by rt RT-PCR in the past 3-6 months and 3 (13.04%) of them were detected positive. The remaining 49 (68.05%) didn't reveal any information on the diagnostic test they underwent. However, they experienced ILI symptoms. Of the symptomatic participants only 19 (26.38%) were seropositive for IgG antibodies as seen in (Table 3).

### 4.4. Asymptomatic health care workers

Were around 69 [48.93%] and of which 29(42.02%) were seropositive for IgG antibodies. Except for the age group 31-40 and 51-60 years and presence of travel history as risk factors, asymptomatic HCW's were seropositive in greater number than symptomatic health care workers.

### 4.5. Risk category

According to the CDC risk assessment category of HCW's for covid-19 disease we had majority of the HCW's in high-risk group as 62/141 (43.97%) followed by intermediate /medium risk group as 42/141 (29.78%) and low risk group as 37/141 (26.24%). Overall highest seropositivity was noted in the intermediate risk group as 17/42 (40.47%) with similar observation in asymptomatic group of HCW's as 11/20 (55%). However, in symptomatic group of participants maximum seropositivity was noted in high-risk group as 10/36 (27.77%) as shown in (Tables 1, 2 and 3).

### 4.6. Comorbid conditions

The common comorbid conditions observed in HCW's in descending order of frequency are diabetes mellitus [DM], hypertension [HTN], asthma. Very few of them documented presence of neurological disorder and immunosuppression. Some even had a combination of two to three disorders together like DM with HTN or DM with HTN and asthma. Around 22/141 (15.60 %) had comorbid conditions of which 15/72 (20.83%) were in symptomatic and 7/69 (10.14%) in asymptomatic group. Of the 15 symptomatic HCW's with comorbid conditions, 6 members had DM of which 2 were seropositive and of 4 with asthma one was seropositive, of the remaining five, 2 with DM and HTN, another 2 members with DM, HTN and asthma and one with neurological deficit all were seronegative. In asymptomatic subjects of the total 7 subjects with comorbidity, 4 members had DM and hypertension of which one was seropositive and of the 2 hypertensive subjects one was seropositive, one with asthma was seronegative as seen in (Tables 1, 2 and 3).

### 4.7. Travel history

Travel to high prevalence zones of covid -19 confirmed cases at international, national and local level was noted in 19/141 (13.47%) HCW's of which 12/72 [16.66%]

**Table 1:** Overall SARS-CoV-2 IgG antibody sero positivity in HCW’s against the various risk factors studied.

<b>Risk factor studied</b>	<b>Total HCW’s included in the study = 141</b>	<b>Total seropositive for SARS-CoV-2 IgG</b>	<b>Total seronegative for SARS-CoV-2 IgG</b>	<b>P value using chi square test</b>
Male	77	26	51	0.99
Female	64	22	42	
21-30 years	50	22	28	0.29
31-40 years	38	7	31	
41-50 years	30	15	15	
51-60 years	11	3	8	
61-70 years	9	2	7	
71-80 years	3	0	3	
High risk group	62	21	41	0.81
Intermediate risk group	42	17	25	
Low risk group	37	10	27	
Mild disease	140	47	93	0.37
Moderate disease	1	1	0	
Comorbid condition present	22	5	17	0.48
Comorbid condition absent	119	43	76	
Travel history present	19	3	16	0.19
Travel history absent	122	45	77	

**Table 2:** SARS-CoV-2IgG antibody seropositivity in symptomatic HCW’s

<b>Risk factor studied</b>	<b>Total symptomatic HCW’s included in the study</b>	<b>Total symptomatic &amp; seropositive for SARS-CoV-2 IgG</b>	<b>Total symptomatic &amp; seronegative for SARS-CoV-2 IgG</b>	<b>P value using chi square test</b>
Male	43	11	32	0.98
Female	29	8	21	
21-30 years	22	6	16	0.57
31-40 years	21	4	17	
41-50 years	13	6	7	
51-60 years	6	3	3	
61-70 years	7	0	7	
71-80 years	3	0	3	
High risk group	36	10	26	0.99
Intermediate risk group	22	6	16	
Low risk group	14	3	11	
Mild disease	71	18	53	0.7
Moderate disease	1	1	0	
Comorbid condition present	15	3	12	0.7
Comorbid condition absent	57	16	41	
Travel history present	12	2	10	0.82
Travel history absent	60	17	43	

**Table 3:** SARS-CoV-2 IgG antibody seropositivity in asymptomatic HCW's

Risk factor studied	Total asymptomatic HCW's included in the study	Total asymptomatic & seropositive for SARS-CoV-2 IgG	Total asymptomatic & seronegative for SARS-CoV-2 IgG	P value using chi square test
Male	34	15	19	0.94
Female	35	14	21	
21-30 years	28	15	13	0.11
31-40 years	17	3	14	
41-50 years	17	9	8	
51-60 years	5	0	5	
61-70 years	2	2	0	
71-80 years	0	0	0	
High risk group	26	11	15	0.62
Intermediate risk group	20	11	9	
Low risk group	23	7	16	
Comorbid condition present	7	2	5	<b>0.05</b>
Comorbid condition absent	62	27	35	
Travel history present	7	1	6	0.29
Travel history absent	62	28	34	

**Table 4:** Comparison of SARS-CoV-2 IgG seropositivity for the various risk factors studied between symptomatic and asymptomatic health care workers

Risk factor studied	Total No. of participants = 141	Symptomatic Health Care Workers		Asymptomatic Health Care Workers		P value
		Symptomatic group total No. of participants =72	Symptomatic group sero positives for IgG antibodies =19	Asymptomatic group total No. of participants =69	Asymptomatic group sero positives for IgG antibodies =29	
Males	77	43	11	34	15	0.6748 [Chi square test]
Females	64	29	08	35	14	
21-30 years	50	22	06	28	15	0.0896 [Fisher exact test]
31-40 years	38	21	04	17	03	
41-50 years	30	13	06	17	09	
51-60 years	11	06	03	05	0	
61-70 years	09	07	0	02	02	
71-8 years	03	03	0	0	0	
High risk group	62	36	10	26	11	0.5822 [Chi square test]
Intermediate risk group	42	22	06	20	11	
Low risk group	37	14	03	23	07	0.321 [Fisher exact test]
Travel history present	19	12	02	07	01	
Travel history absent	122	60	17	62	28	
Co morbid conditions present	22	15	03	07	02	0.324 [Fisher exact test]
Co morbid conditions absent	119	57	16	62	27	

**Table 5:** Comparison of seroprevalence rates for SARS-CoV-2 IgG antibodies in asymptomatic group of health care workers from previous studies.

S.No.	Author	Month & Year of study	Sample size	Over all sero prevalence	Seroprevalence in asymptomatic HCW's	Significant risk factors	Remarks
1.	Goldblatt et al	06-08/2020	222	10.4	68.9	None	Periodic screening of HCW's and education & training of all
2.	Kassem et al	06/2020	74	12.2	62.5	Age, gender Occupation Contact Comorbid conditions	Do
3.	Mostafa et al	04-05/2020	4040	1.3	68.2	Do	Do
4.	Mostafa et al	05-06/2020	2282	4.0	64.0	Do and pregnancy also	Do
5.	Mukwege et al	07-08/2020	359	41.2	77.7	Contact	Do
6.	Olayanju et al	04/2020	133	45.1	45.1	-	Do
7.	Mukhtar et al	05-06/2020	455	7.9	31.0		Do
8.	Present study	03-04/2021	141	34.04	42.02	Comorbid condition	Do

were in symptomatic group and 7/69 (10.14%) were in asymptomatic group. Of this 3/19 (15.78%) were seropositive and 2/12 (16.66%) in symptomatic group and 1/7 (14.28%) in asymptomatic group as seen in (Tables 1, 2 and 3).

When the two groups of HCW's symptomatic and asymptomatic were compared for the association of risk factor with IgG seropositivity to SARS-CoV-2. Overall, the asymptomatic participants were seropositive in greater number than symptomatic for most of the risk factors studied except for the age group 31-40 years and 51-60 years of age wherein a greater number of symptomatic HCW's were seropositive as 4/21 (19.09%) against 3/17 (17.64%) and as 3/6 (50%) against 0/5. Similarly, when checked for presence of travel history more of the symptomatic HCW's were seropositive than asymptomatic as 2/12 (16.66%) against 1/7 (14.28%).

### 5. Discussion

The overall seroprevalence of SARS-CoV-2 IgG antibodies in the present study is noted as 34.04% which is similar to the reports by other authors as 33%.<sup>9,10</sup> In the present study greater number of asymptomatic HCW's as 42.02% were seropositive than symptomatic ones as 26.38% which has been observed in other studies too<sup>9-18</sup> and summarized in the (Table 5) for comparison purpose.

Presence of greater no. of seropositive for SARS-CoV-2 IgG in asymptomatic group of HCW's can be explained for reasons like:

1. Silent transmission from pre symptomatic and asymptomatic subjects to the susceptible HCW's.<sup>12-16,19</sup>
2. The period of study also matters, as most of the studies conducted so far were during the 1<sup>st</sup> wave of the pandemic were in the clarity on time required for development of demonstrable humoral immune response and its duration was vague. The present study was done during the 2<sup>nd</sup> wave which might have resulted in generation of good humoral immune response following repeated and mild exposures to the virus as reported by other authors too.<sup>14,15</sup>
3. Presence of preexisting's antibodies to circulating HCoV's like HKU-1, OC-43, NL63, 229E etc. during the annual seasonal outbreaks of ILI might have resulted in seropositivity in asymptomatic group due to cross reactive antibodies against spike protein, NTD & RBD and N protein and also for the presence of reactive T cells to SARS-CoV in the pre pandemic samples as demonstrated by one author in his original research study.<sup>20</sup>
4. Effective training and education, implementation and monitoring of infection control practices among the symptomatic and HRG of subjects with resultant lower exposure rates and less seropositivity and suboptimal assurance of same in IRG & LRG category of HCW's as reported by many authors.<sup>1,2,13,14</sup>
5. Exposure to confirmed cases of COVID-19 disease outside the hospital premises could also be a reason for high seropositivity.<sup>9-16</sup>

Greater no. of HCW's in the middle age group were seropositive in symptomatic group when compared to asymptomatic group wherein it was found to be highly variable and in descending order of frequency, maximum participants were observed in the age group 61-70 years, followed by 41-50 years and then in age group of 21-30 years. However, most of studies have related seropositivity with increasing age and more so above 50 years of age<sup>16,17,19</sup> which is observed by us too as overall finding. In symptomatic group greater no. of HCW's in HRG were seropositive while in asymptomatic it is observed in medium or IRG as shown in Tables 1, 2 and 3 and also reported by other authors which is related with the type of occupational exposure and personal observation and adherence to infection prevention and control measures by them.<sup>19</sup> The most common comorbid condition associated with seropositivity in our study are diabetes mellitus, hypertension and asthma. Presence of comorbid conditions in HCW's was significantly associated with higher seropositivity especially in asymptomatic HCW's in our study. This has been well explained by previous authors by demonstration of polyfunctional helper CD4 cells and antibodies and variations in innate immune response in activation of T helper cell response in the sera of HCW's studied.<sup>1,2,9,10,21</sup> Majority (97.92%) of the symptomatic HCW's had mild form of disease while only 1.38% had moderate disease as pneumonia and required hospitalization as seen in (Table 2) and observed by other authors too.<sup>1-3</sup> In Table 4 above we have compared the two groups of HCW's for the risk factor association with seropositivity using statistical test like chi square and fisher exact test. None of the risk factors studied showed any positive association with seropositivity when two groups were compared indicating that no individual group had any specific high or low risk of getting seropositive to SARS-CoV-2 and demands further enquiry into its causal relationship with more improved testing strategy like determination of baseline and follow up titres of IgG antibodies to get clarity on genuine exposure and avoid unnecessary quarantines when there is significant dearth of HCW's.

## 6. Conclusion

The results of present study indicate greater proportion of asymptomatic transmission of the infection in HCW's during the pandemic which possess a substantial risk of infection to other healthy staff, vulnerable patients in the hospital setting and their families<sup>22-24</sup> with its recommendations and limitations mentioned below.

## 7. Recommendations

Results of the present study warrants periodic testing, education and training of all HCW's irrespective of the risk category, presence of symptoms, prioritization for

vaccination and adequate supply & uniform distribution of PPE and education on its use to mitigate source and curb onward transmission of SARS-CoV-2 infection.<sup>1,2,22-24</sup> Further studies determining seroprevalence rates in symptomatic and asymptomatic groups of participants need paired sera testing.

## 8. Limitations

The results of the present study couldn't be generalized for reasons like we failed to perform baseline and follow up sampling of the HCW's for demonstrating true exposure and fourfold rise in IgG titre. The major constraints noted were financial and apprehension of health care workers with resultant seropositivity and even sample size studied is too small for the purpose.

## 9. Conflict of Interest

None

## 10. Source of Funding

None.


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