Seroprevalence of SARS-CoV-2 among the Healthcare Workers of a Tertiary Care Hospital of Northeast India during First Wave of COVID-19 Pandemic: A Hospital-based Cross-sectional Study

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ABSTRACT

Introduction: During Coronavirus Disease-2019 (COVID-19) pandemic, Healthcare Workers (HCWs) are the frontline personals who are engaged in different facilities of the health system. So they always remain at a greater risk of exposure and acquiring the disease. They may also become a potential source of infection to the other patients as well to the community.

Aim: To estimate the seroprevalence of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) specific Immunoglobulin G (IgG) antibodies among asymptomatic, COVID-19 negative HCWs of a tertiary care hospital.

Materials and Methods: This hospital-based cross-sectional study was conducted in the Department of Microbiology in a tertiary care hospital of Northeast India. A total of 215 HCWs were recruited from 15th October to 14th December 2020 after taking written and informed consent. Inclusion criteria were: a) >18 years of age and both genders, b) asymptomatic, negative for COVID-19 either by Rapid Antigen Test (RAT) or Reverse Transcription Polymerase Chain Reaction (RT-PCR), c) working in the hospital

for atleast last four months. Predesigned questionnaire was used for data collection. Serum samples were tested for SARS-CoV-2 IgG antibodies by Enzyme Linked Fluorescence Assay (ELFA) using VIDAS (VITEK ImmunoDiagnostic Assay System) platform. Chi-square test was used (Epi Info version 7 software) for data analysis.

Results: The prevalence of SARS-CoV-2 IgG was 54 (25.12%) out of 215, which was highest in ≤30 years age group, 27 (32.14%) out of 84 (p=0.0261). Significant seropositivity was found among cleaners 22 (61.11%) out of 36 (p<0.01) and participants who reported having COVID-19-related symptoms in the previous months (p<0.013). However gender, daily patient contact, close contact with COVID-19 cases and working in COVID-19 units showed no significance.

Conclusion: The study highlighted a high burden of asymptomatic SARS-CoV-2 infection among HCWs. A proper surveillance system is needed for estimating the burden of COVID-19 among HCWs as well as in the community for better understanding of the dynamics of the infection.

Keywords: Coronavirus disease-2019, Enzyme linked fluorescence assay, Frontline severe acute respiratory syndrome coronavirus-2

INTRODUCTION

The COVID-19 is a novel disease caused by SARS-CoV-2 and the virus was first detected in Wuhan, China in December 2019 [1]. World Health Organisation (WHO) declared it as a pandemic in March 2020 [2]. This newly emerging virus was also declared as public health emergency by WHO [3].

During the pandemic, HCWs are the frontline personals who are engaged in patient care in different facilities of the health system. So they always remain at a greater risk of exposure as well as acquiring the disease. As they have access to the other patients also, they may become a potential source of infection to the other patients as well to the community [4-6]. During the early stages of the SARS epidemic, a high incidence was observed among the HCWs [6]. Serosurvey data can provide relevant information about recent or past infection of a disease as serological tests can detect antibodies for a long period after recovery and these data also tell us the extent of disease transmission. The knowledge of seroprevalence is crucial in the pandemic because it helps to predict the future course of the pandemic [7-9].

Indian Council of Medical Research (ICMR) conducted Nation-wide population-based serial serosurveys in 70 Indian districts. The first and second survey reports indicated a significantly high

10 fold increase in the prevalence of SARS-CoV-2 infection among adults from 0.73% in May-June 2020 to 7.1% in August-September 2020 [10,11]. The report of third serosurvey showed an overall seroprevalence of 24.1% and in HCWs it was 25.7% [12]. The fourth ICMR survey showed state-wise data and the seropositivity in Assam was found to be 50.3% [13].

The data regarding the burden of asymptomatic infection among HCWs are very limited from Northeast part of the country [13]. Therefore, this study was conducted to estimate the seroprevalence of SARS-CoV-2 specific IgG antibodies among asymptomatic, COVID-19 negative HCWs of a tertiary care hospital of Assam to know the burden of the disease and its association with different parameters like demographic, clinical, occupational etc.

MATERIALS AND METHODS

This hospital-based cross-sectional study was carried out in the Department of Microbiology in a tertiary care hospital of Northeast India for a period of two months from 15th October to 14th December 2020. HCWs who deliver care and services to patients, either directly as physicians and nurse or indirectly as assistants, technicians, and other support staff (administrative staff, cleaning, kitchen, laundry, maintenance, etc.,) employed under the institution were part of this study. Ethical approval for the study was obtained from Institutional

Ethics Committee (IEC) (Human) (No.AMC/EC/5928 Dibrugarh dated 10th June, 2021).

Inclusion criteria: The HCWS with >18 years of age and both genders, asymptomatic, negative for COVID-19 either by RAT or RT-PCR, working in the hospital for at least last four months were included in the study.

Exclusion criteria: Previously, COVID-19 positive or IgG positive HCWs were excluded from the study.

Sample size calculation: Convenient sampling method was used and participants were approached telephonically. Participation in the study was voluntary. A total of 435 HCWs were approached and 215 participants were enrolled. Written and informed consent was obtained from the study subjects prior to the enrolment.

Study Procedure

A predesigned proforma was used for collection of following information from each participants: demographics (age, sex, etc.,), professional information (occupation, department etc.,), clinical information about the history of COVID-19 compatible symptoms during the previous months (cough, sore throat, runny nose, fatigue, shortness of breath, fever, headache, vomiting, diarrhoea, loss of smell, chills etc.,), history of COVID-19 test (RT-PCR/RAT), co-morbidities and history of close contact with COVID-19 cases. The symptoms were categorised according to Ministry of Health and Family Welfare, Govt. of India guideline [14].

A 2 mL of venous blood samples was collected from the study subjects in a clot activator vial maintaining standard precautions. Serum was separated by centrifugation and samples were analysed immediately. The SARS-CoV-2 IgG was tested by ELFA with VIDAS SARS-CoV-2 IgG II (VIDAS 9COG) test kit (biomerieux SA, France, lot no- 1008193120, REF- 423834)) using VIDAS platform according to manufacturer's instructions. It is an automated qualitative assay which measures antibodies against the Receptor Binding Domain (RBD) of the spike glycoprotein of SARS-CoV-2.

STATISTICAL ANALYSIS

Data were entered and analysed in Epi Info version 7. Chi-square test was done and p<0.05 was considered to be statistically significant.

RESULTS

The baseline characteristics of the 215 study participants are summarised in [Table/Fig-1]. The mean±SD was 36.33±10.74 years. Of them 120 (55.81%) were males and 95 (44.19%) were females. 39 (18.14%) nurses, 36 (16.75%) cleaners, 45 (20.93%) laboratory technicians, 18 (8.37%) staff and 77 (35.81%) physicians were included in the study. Co-morbidities were reported by 13 (6.05%) participants. Total 30 (13.95%) participants reported having COVID-19-compatible symptoms in the previous months but they all were negative by RT-PCR.

Characteristics		N (%)
Age (years)	≤30	84 (39.07)
	31-40	65 (30.23)
	41-50	39 (18.14)
	>50	27 (12.56)
Sex	Males	120 (55.81)
	Females	95 (44.19)
Professional categories	Nurse	39 (18.14)
	Physician	77 (35.81)
	Lab technician	45 (20.93)
	Staff	18 (8.37)
	Cleaner	36 (16.75)

Daily contact with general patients	Yes	134 (62.33)
	No	81 (37.67)
Working in a COVID-19 unit	Yes	159 (73.95)
	No	56 (26.05)
Close contact with confirmed COVID-19 patients	Yes	138 (64.19)
	No	77 (35.81)
Co-morbidities	Yes	13 (6.05)
	No	202 (93.95)
Reporting COVID-19 compatible symptoms within previous months	Yes	30 (13.95)
	No	185 (86.05)

[Table/Fig-1]: Baseline characteristics of study participants.

The seroprevalence of COVID-19 IgG was 54 (25.12%) out of 215 in the present study. Prevalence was observed to be highest in ≤30 years age group and lowest in >50 years (p=0.026). Although IgG positivity was higher in males i.e., 33 (27.50%) out of 120 compared to female 21 (22.11%) out of 95, no statistical significance was found [Table/Fig-2]. Different occupational categories of HCWs were compared and observed that most affected group was the cleaners, followed by other staff, nurses, laboratory technicians, and doctors (p<0.01) [Table/Fig-2].

Parameters		Positive number of cases (%)	Negative number of cases (%)	p-value
Age (years)	≤30	27 (32.14)	57 (67.86)	0.0261*
	31-40	19 (29.23)	46 (70.77)	
	41-50	6 (15.38)	33 (84.62)	
	>50	2 (7.41)	25 (92.59)	
Sex	Male	33 (27.50)	87 (72.50)	0.365
	Female	21 (22.11)	74 (77.89)	
Symptoms compatible to COVID-19 within previous month	Yes	13 (43.33)	17 (56.67)	0.0131*
	No	41 (22.16)	144 (77.84)	
Occupation	Cleaner	22 (61.11)	14 (38.89)	<0.01*
	Doctor	5 (6.49)	72 (93.51)	
	Lab technician	9 (20.00)	36 (80.00)	
	Nurse	10 (25.64)	29 (74.36)	
	Other staff	8 (44.44)	10 (55.56)	
Working in COVID-19 unit	Yes	37 (23.27)	122 (76.73)	0.2929
	No	17 (30.36)	39 (69.64)	
Contact with confirmed COVID-19 cases	Yes	35 (25.36)	103 (74.64)	0.9113
	No	19 (24.68)	58 (75.32)	
Daily contact with general patients	Yes	29 (21.64)	105 (78.36)	0.1308
	No	25 (30.86)	56 (69.14)	

[Table/Fig-2]: Different parameters and their association with seroprevalence among the study subjects.
*p-value <0.05 is considered to be statistically significant

Out of the 30 participants reporting COVID-19 compatible symptoms in the previous months, 22 (73.33%) reported fever, 13 (43.33%) cough, 10 (33.33%) sore throat, 10 (33.33%) nasal discharge, 6 (20.00%) body ache, 6 (20.00%) headache, 5 (16.67%) fatigue and 4 (13.33%) diarrhoea [Table/Fig-3]. The symptoms were considered as mild. Seropositivity was found to be significantly high in these previously symptomatic participants (p<0.0131). It was observed that having daily contact with general patients, close contact with COVID-19 cases and working in COVID-19 units had no significance in developing SARS-CoV-2 IgG [Table/Fig-2].

Presence of co-morbidities did not show significance regarding antibody development (p=0.0417). All the 13 participants reported to have co-morbidities were seronegative. The co-morbidities reported are shown in [Table/Fig-3].

Characteristics		Frequency (%)
Co-morbidities among the study subjects (n=13)	Asthma	5 (38.46%)
	Diabetes and hypertention	1 (7.69%)
	Hypertension	4 (30.77%)
	Hypothyroidism	2 (15.39%)
	Hypothyroidism and hypertension	1 (7.69%)
COVID compatible symptoms reported by the study subjects in previous months (n=30)	Fever	22 (73.33%)
	Cough	13 (43.33%)
	Sore throat	10 (33.33%)
	Nasal discharge	10 (33.33%)
	Bodyache	6 (20.00%)
	Headache	6 (20.00%)
	Fatigue	5 (16.67%)
	Diarrhoea	4 (13.33%)

[Table/Fig-3]: List of co-morbidities and COVID-19 compatible symptoms in the past reported by the study subjects.

DISCUSSION

This hospital based seroprevalence study of SARS-CoV-2 IgG, estimated 25.12% of positivity among HCWs, who did not have a confirmed laboratory diagnosis of COVID-19. However, studies conducted among HCWs in different countries reported a lower IgG positivity. Studies conducted by Korth J et al., in Germany, Garcia-Basteiro AL et al., in Spain, Sotgiu G et al., in Italy and Stock AD et al., in New York showed lower seroprevalence than the present study [9,15-17]. Similar studies conducted in different states of India also reported lower IgG positivity than present study. Goenka M et al., from West Bengal found 11.94% IgG seroprevalence [18]. Kumar A et al., from Kerala showed no IgG positivity among their study subjects [19]. Dave M et al., from Rajasthan reported that among seropositive cases 8% developed IgM antibody, 8% developed both IgM and IgG, while none had IgG antibody positivity [20]. Positivity of 17.61% and 2.5% was reported by Prakash O et al., from Ahmadabad and Khan MS et al., from Kashmir, respectively [21,22]. Singhal T et al., from Mumbai showed 4.3% prevalence of infection in asymptomatic HCWs but 70% in previously symptomatic untested HCWs [23]. Gupta R et al., reported 13% positivity [24]. However, a study from China showed 38.89% seropositivity among doctors exposed to COVID-19 patients [25] [Table/Fig-4]. The findings of the present study indicate that a substantial proportion of the HCWs have been exposed in our institution and a large percentage of infections remained undetected. As all of these individuals were engaged in patient care, they could have become the source of infection for others. Tian S et al., also observed similar result in their study conducted in Beijing [26]. This signifies that periodic screening programs to be implemented among HCWs and the hospital infection control system to be strengthened to decrease hospital transmission of the disease [27].

The significant higher seropositivity in <30 years age group may be explained by higher enrollment of younger age groups in COVID-19 related duties. It was observed that these seropositive HCWs were without any complications of COVID-19, which could be explained by low viral load, younger age groups, absence of associated co-morbidity and good immune function in them. Among the participants, those reported having mild symptoms compatible with COVID-19 in the previous months (but RT-PCR negative), the seropositivity was found to be higher. The symptoms include fever, cough, sore throat, headache, nasal discharge, body ache, fatigue. A study done by Garcia-Basteiro AL et al., found 80% positivity in HCWs with mild-to-moderate symptoms [15]. As the antibody level is known to decline after mild infection with COVID-19, so even a negative serological test result might not be reliable to exclude previous infection [28]. Cleaner, staff, laboratory technicians and nurses had higher seroprevalence rate than doctors which was

Sl. No.	Study	Year of study	Seroprevalence data of SARS CoV-2 among health care workers (in %)
1	Korth J et al., from Germany [9]	March-April, 2020	1.6% IgG positive
2	Garcia Basteiro AL et al., from Spain [15]	March-April, 2020	6.2% IgM, 7.6% IgG, and 8.1% IgA positive
3	Sotgiu G et al., from Italy [16]	April, 2020	14.4% IgM and 7.4% IgG positive
4	Stock AD et al., from New York [17]	April, 2020	11.2% PCR-negative and IgG positive
5	Goenka M et al., from West Bengal [18]	July-August, 2020	11.94% IgG positive
6	Kumar A et al., from Kerala [19]	July, 2020	No seropositivity
7	Dave M et al., from Rajasthan [20]	April-May, 2020	8% IgM positive, 8% both IgM and IgG positive, none was IgG antibody positive
8	Prakash O et al., from Ahmadabad [21]	June-July, 2020	17.61% IgG positive
9	Khan MS et al., from Kashmir [22]	June, 2020	2.5% IgG positive
10	Singhal T et al., from Mumbai [23]	June, 2020	4.3% asymptomatic HCWs and 70% previously symptomatic untested HCWs seropositive
11	Gupta R et al., from AIIMS, New Delhi [24]	June-July, 2020	13% SARS-CoV-2 total antibody positive
12	Chen Y et al., from China [25]	January-February, 2020	17.1% overall seropositive
13	Present study from Assam	October-December, 2020	25.12% IgG positive

[Table/Fig-4]: Comparison of studies on seroprevalence of SARS CoV-2 among HCWs conducted by different authors [9,15-25].

also observed by Goenka M et al., [18]. This signifies that higher awareness about the disease spread and prevention measures, better adherence to infection control protocols could be responsible for lower infection rate among doctors. However, Garcia-Basteiro AL et al., did not find any relation between professional categories and seropositivity [15]. Although male showed higher percentage of positivity than female in this study, it was not statistically significant. Garcia Basteiro AL et al., also found no significance related to gender (female 76% vs male 24%, p=0.52) [15]. Similarly, Prakash O et al., from Ahmedabad observed that the positivity percentage was higher among women as compared to the men but the difference was statistically insignificant [21]. Sotgiu G et al., showed no significance in IgG positivity but IgM positivity was significantly high in male (male vs female: 10% vs 6.1% for IgG and 24.3% vs 9.1% for IgM) [16]. However, Goenka M et al., and Gupta R et al., reported significantly higher seroprevalence in male. (male vs female 13.76% vs 8.51% and 63% vs 37%, respectively) [18,24].

Working in COVID-19 unit, contact with confirmed COVID-19 positive cases and daily contact with general patients was not associated with seroprevlence, which might be explained by the fact that the higher perception of risk, makes people to strictly follow precautionary measures, so the risk of acquiring the infection become lower. Garcia-Basteiro AL et al., also explained that there was no significant association between the presence of SARS-CoV-2 antibodies with the above mentioned categories of HCWs [15]. Sotgiu G et al., in their study on Italian HCWs also found that the percentage of IgG and IgM positive cases did not differ depending on history of contact with COVID-19 patients in comparison with non contacts (6.8% vs 3.5% for IgG, p-value: 0.86; 15.9% vs 13.9% for IgM, p-value: 0.74) [16].

The study showed that, the burden of asymptomatic COVID-19 was high among HCWs and a prior negative testing does not preclude infection.

Limitation(s)

It was a hospital-based study conducted in a less number of subjects and convenient sampling was done. Only serum IgG was tested not other antibodies like IgM and IgA due to which some of the cases in the early part of their antibody generation may be missed. Some of the exposed cases might also have been missed in this cross-sectional study as antibody level is known to wane over a few months.

CONCLUSION(S)

A high IgG seropositivity among the COVID-19 negative HCWs of our institution in this cross-sectional seroprevalence study conducted during the first wave of COVID-19 pandemic was observed. The findings of the study guided us about the burden of the infection among the HCWs in prevaccination period of this pandemic. There is a need of well managed, organised, systematic and periodic surveillance system for estimating the burden of COVID-19 among HCWs as well as in the community which will help in better understanding of the dynamics of the infection with this novel virus and the future of this ongoing pandemic.

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