DOI: 10.7860/JCDR/2021/50235.15422

Original Article

Pathology Section

COVID-19 Seroprevalence Study in Asymptomatic Healthcare Workers at a Tertiary Healthcare Centre, India

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ABSTRACT

Introduction: The Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) infection has evolved into a pandemic disease. The present knowledge is mainly based on available numerator data of confirmed positive cases only. The asymptomatic and mildly symptomatic cases are not brought into picture for testing at all, which is a major contributor to the pandemicity and hence creating bias in the documentation and understanding of the disease. The magnitude of the exposure of Healthcare Workers (HCW) and their potential for asymptomatic transmission makes it critical to know the incidence of infection in the healthcare population.

Aim: To evaluate the seroprevalence of Immunoglobulin G (IgG) SARS-CoV-2 among the asymptomatic HCW.

Materials and Methods: This was a cross-sectional study conducted between January 2021 to February 2021 in SRM Medical College Hospital and Research Centre a tertiary care hospital in Potheri, Chengalpattu district, Tamil Nadu, India. The HCW were asked to complete the standardised questionnaire including the basic information, symptoms of COVID-19 illness and utility of Personal Protective Equipment (PPE) based on World Health Organization (WHO) risk assessment and management of exposure of HCW in the context of COVID-19. They were divided into two groups, the staff who had direct patient exposure as group 1 with 82 participants and staff without direct patient exposure as group 2 with 46 participants. The serodetection of IgG SARS-CoV-2 antibodies was done using the Chemiluminescence Immunoassay (CLIA). The obtained results were statistically analysed with Statistical Package for the Social Sciences (SPSS) version 20.0. A Chi-square test (χ^2) was performed and a p-value less than 0.05 was considered statistically significant.

Results: A total of 128 HCW were studied. In group 1, there were 64.1% (n=82) of HCWs and in group 2 there were 35.9% (n=46) of HCWs. There were total of 74 (57.8%) males and 54 (42.2%) females. No gender-specific differences were observed. The mean age in group 1 was 28.93 years and group 2 was 32.2 years. The staffs older than 40 years were more commonly affected. Adherence to strict PPE protocol was observed in 92.6% (76/82) in group 1 and 82.6% (38/46) in group 2. The difference between the groups were statistically significant (p=0.025). In this study, though the seroprevalence of COVID-19 infection was 9.8% (n=8) in group 1 and 13% (n=6) in group 2, it was statistically not significant.

Conclusion: SARS-CoV-2 Serology study helps to identify the asymptomatic (unestimated) cases. The results of the seroprevalence suggest that the strict adherence to PPE protocol helps to prevent COVID-19.

Keywords: Coronavirus disease-19, Personal protective equipments, Serology

INTRODUCTION

COVID-19 pandemic has spread and affected more than 220 countries [1]. At the outset of the infection, healthcare system was submerged with the increase in many severe cases of pneumonia [2]. Eventually, as the patients were channeled to the hospital, many of the HCW were at high risk of being struck with the ailment [3]. In the early phase, the nature of the disease was incomprehensible. As a result, the repercussions were on patient care, hopes of the common people and morale of professionals. In the course of COVID-19 infection, immunoglobulin IgG was detected after a median of 14 days {Interquartile Range (IQR) 10-18 days}, from the onset of symptoms [4]. An IgG immune response indicates apparent and inapparent infection as well as potential immunity (still a matter of debate) [5,6].

A proportion of cases of COVID-19 infection can also occur without any symptoms. An unestimated 'dark figure' of the unreported infection was prevalent [7]. Very few studies on COVID-19 seroprevalence among asymptomatic HCW from Southern India were available. Identification of the asymptomatic cases in healthcare professionals plays an important role to break the chain of silent transmission. Therefore, the purpose of the study was to evaluate the seroprevalence of SARS-CoV2 IgG among the asymptomatic HCW of tertiary care hospital.

MATERIALS AND METHODS

A cross sectional, monocentric study was done on seroprevalence of SARS-CoV-2 IgG among the asymptomatic HCW, during the period of January 2021 to February 2021 in a tertiary care, SRM Medical College Hospital and Research Centre, Potheri, Chengalpattu district, Tamil Nadu, India. Institutional Scientific and Ethical Committee approval (IEC no.:2166/IEC/2020) was obtained.

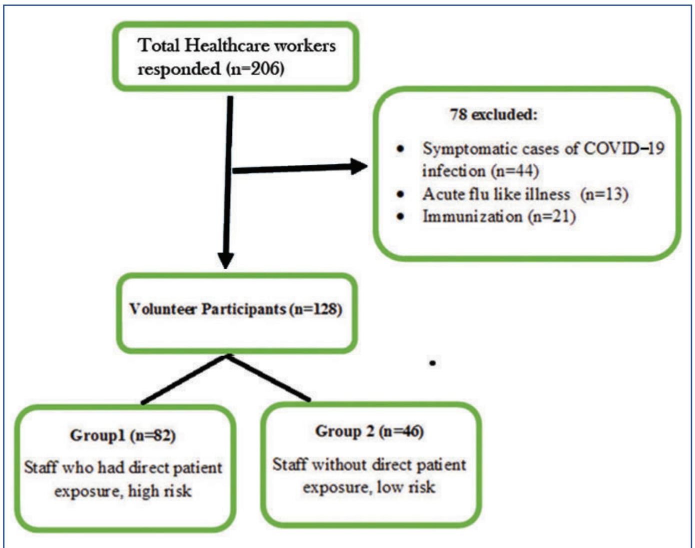
A standardised questionnaire was prepared and the basic information such as age, gender, type of healthcare personnel, designation, type of healthcare facility they were working at, chronic underlying medical condition, travel abroad in recent days, acute flu like symptoms, immunisation, contact with COVID-19 infection in household and neighbourhood and utility of PPE (based on the WHO risk assessment and management of exposure of HCW in context of COVID-19) [8]. It was circulated among the HCWs through their phone number and e-mail address. Utility of PPE was grouped as adhered to PPE (>50%) if the responses given by the participants as "Always (>95%) or Most of time" (50- 95%) and not adhered to PPE (<50%) if responded "Occasionally (20-50%) or Rarely (<20%)" for purpose of statistical analysis.

Inclusion criteria: Asymptomatic HCW between 18 to 60 years of age in SRM Medical College Hospital and Research Centre, a tertiary care hospital in Potheri, Chengalpattu district, Tamil Nadu, India, were included in the study.

Exclusion criteria: Healthcare professionals of more than 60 years of age, those who had history of travel abroad in recent days, typical symptoms of COVID-19, immunised against COVID-19 and not giving consent were excluded from the study.

Sample size calculation: The sample size was calculated using the following formula, $n=4pq/d^2$. The seroprevalence rate (Chen Y et al.,) [9] is p=17.1%,; q=1-p; d- allowable error. So, the total sample size required for this study was 115.

In the present study, 206 responses were received, of which 78 were excluded as they had history of COVID-19 infection (44), immunisation (21), acute flu like symptoms during the study (13) [Table/Fig-1]; none had travelled abroad during recent times of COVID-19 outbreak. Volunteers (128 HCWs) were eager to participate in the study to know their serology status. The eligible participants were categorised into two groups, staff who had direct patient exposure (high risk, group 1) and staff without direct patient exposure (low risk, group 2).



[Table/Fig-1]: Flowchart of participant recruitment.

For the participants, under aseptic precaution, 2 mL of venous blood was collected in plain vacutainer without any anticoagulant. The serum was separated and processed for detection of IgG SARS-CoV-2 antibodies, by Chemiluminescence Immunoassay (CLIA) method. This technology follows a similar concept to Enzyme Linked Immunosorbent Assay (ELISA) by taking advantage of high binding affinity between the viral antigen(s) and host antibodies but uses chemical probes that yield light emission through a chemical reaction to generate a positive signal (>1s/co positive). CLIA has an average time-to-result of 1-2 hours [10].

STATISTICAL ANALYSIS

The results were statistically analysed using the Statistical Package for the Social Science (SPSS) software version 20.0. The frequencies and percentages were representation of categorical variables. Quantitative variables were presented as mean and median. The differences in proportion between groups were analysed by Chi-square test (χ^2) and p-value less than 0.05 was interpreted as statistically significant.

RESULTS

In the present study, a total of 128 HCWs were tested out of 1200 (10.7%) HCWs in the hospital. There were 64.1% (n=82) of HCWs in group 1 with direct COVID-19 patient exposure; the health personnel included physicians, anaesthetists, intensivists, casualty medical officers and nurses and in group 2, there were 35.9% (n=46) of HCWs without direct patient exposure; the healthcare personnel included pathologists, microbiologists, biochemists and laboratory technicians. There were 69% (n=88) participants in the age group of 21-30 years, 25% (n=32) in the age group of 31-40 years, 3% (n=4) in the each age group of 41-50 and 51-60 years, respectively. The mean age in group 1 is 28.93 years and group 2 is 32.2 years. The median age in group 1 is 28 years and group 2 is 30 years. Of the study population, there were 68.3% (n=56) males, 31.7% (n=26) females in group 1 and 39.1% (n=18) males and 60.9% (n=28) females in group 2 [Table/Fig-2]. Participants worked for 6-12 hours shift; average of 5.4 days a week. After approximately a week duty they were advised self-isolation for a period of 14 days and also to take immune boosters, vitamin supplements and traditional medicine "Kabasura kudineer" [11].

Past medical illness was observed in 9.3% (n=12) in entire study population. The chronic medical illnesses among study population reported were hypothyroidism followed by bronchial asthma, and others include migraine and chronic eczema [Table/Fig-2].

Overall, in 10.9% of HCW, IgG SARS-CoV-2 antibodies were detected. The seroprevalence was 13% in the group 2 (6/46) whereas 9.8% in group 1 (8/82), but was statistically not significant [Table/Fig-3].

In this study, there was 4.5% (4/88) seropositive in the age group of 21-30, 18.75% (6/32) between 31-40 years and 50% (4/8) in the age group above 40 years and was statistically not significant. The COVID-19 seropositive males were 10.8% (8/74) and females were 11.1% (6/54) [Table/Fig-4].

Adherence to strict PPE protocol was observed in 92.7% (76/82) in group 1 and 82.6% (38/46) in group 2. Seroprevalence of 7.89% (6/76) in group 1 and 10.52% (4/38) in group 2 among staff who strictly adhered to PPE protocol. It was observed that 7.3% (6/82) in group 1 and 17.4% (8/46) in group 2 were not strictly adherent to

Characteristics	No. of cases (N=128)								Total
	Group 1 (n=82)				Group 2 (n=46)				
	Serology <1 s/co		Serology >1 s/co		Serology <1 s/co		Serology >1 s/co		
Age (years) / Gender	Male	Female	Male	Female	Male	Female	Male	Female	
21-30	38	20	2	2	10	16	0	0	88 (68.8%)
31-40	12	4	4	0	6	4	0	2	32 (25%)
41-50	0	0	0	0	0	2	0	2	4 (3.1%)
51-60	0	0	0	0	0	2	2	0	4 (3.1%)
Type of healthcare personnel	• Physician • Anaesthetists • Emergency medicine • Post graduates • Medical interns • Nurse				• Pathologists • Microbiologists • Biochemists • Laboratory technicians				-
Past medical illness	8				4				12 (9.3%)
Adherence to PPE protocol (>50%)	70		6		34		4		114 (89.1%)
Adherence to PPE protocol (<50%)	4		2		6		2		14 (10.9%)

[Table/Fig-2]: Characteristics of Healthcare workers
PPE: Personal protective equipment; s/co: sample-to cut-off ratio

Category	Ig G Serology (s/co) <1	Ig G Serology (s/co) >1	Seroprevalence	Chi-square	p-value
Group 1 (n=82)	74	8	9.8%	0.33	0.567
Group 2 (n=46)	40	6	13.0%		
Total (n=128)	114	14	10.9%		

[Table/Fig-3]: Seroprevalence among healthcare workers.

A study from Italy had reported high seropositivity among females, whereas the present study did not observe any gender specific differences in serological response and so were the studies conducted in Ahmedabad, Spain and USA [22-25].

The Spain study reported higher infection rate among doctors, nurses, and nurse assistant than technicians [21]. In contrast, the present study noted that slightly high seroprevalence among low risk HCWs Laboratory personnel (group 2) than the high risk HCWs

Parameters	No. of cases (n=128)								p-value*
	Group 1 (n=82)				Group 2 (n=46)				
	Serology <1		Serology >1		Serology <1		Serology >1		
Age (years) / Gender	Male	Female	Male	Female	Male	Female	Male	Female	
21-30	38	20	2	2	10	16	0	0	0.067
31-40	12	4	4	0	6	4	0	2	0.076
41-50	0	0	0	0	0	2	0	2	-
51-60	0	0	0	0	0	2	2	0	0.167
Adherence to PPE protocol (>50%)	70		6		34		4		0.025
Adherence to PPE protocol (<50%)	4		2		6		2		

[Table/Fig-4]: Seroprevalence among subgroups of Healthcare workers.
PPE: Personal protective equipment
*chi-square test

PPE protocol. Seroprevalence of 33.3% (2/6) in group 1 and 25% (2/8) in group 2 among staff who did not strictly adhere to PPE protocol. The difference between the group is statistically significant (p-value=0.025) [Table/Fig-4].

DISCUSSION

In March 2020, COVID-19 infection was declared a pandemic disease, and until then in Tamil Nadu, there were only 20 cases. There was a significant increase in COVID-19 infected cases between the months of August and October 2020 in India [1]. Again in March 2021, there was surge of COVID-19 infection considered to be the second wave. The frontline healthcare professionals were at higher risk of contracting the infection due to their direct contact or indirect contact, with the infected patients. An infected HCW poses a risk to other patients under his or her care as well as to their fellow HCWs and family.

Serosurveillance of HCW is an important indicator of spread of SARS-CoV-2 and also helps in assessing the rate of infections within our HCWs [12]. Early identification of asymptomatic COVID-19 individuals provide opportunity for close follow-up with screening test, to prevent end organ damage [13]. The screening methods for COVID-19 are employed only for symptom based screening by real time Reverse Transcription Polymerase Chain Reaction (RT-PCR), which is used widely to detect the infection [14].

However, several false negative cases have been reported owing to low viral load and inappropriate sample collection. There are recent studies showing that such cases can be screened by serology tests as they produce detectable quantities of immune response [15-17]. The serology testing was done using CLIA which has high sensitivity and high specificity. The results of seroprevalence study of the COVID-19 infection across the globe are varied according to the geographical location and outbreak of the infection. Few countries have recorded as high as 32.6% prevalence rate and others less than 2% [18,19]. In the present study, the seroprevalence was 10.9% in asymptomatic HCWs.

A slight high seroprevalence among people aged more than 40 years was observed. Similar finding was noted by Baveja S et al., where the seroprevalence was high among people aged more than 50 years [20]. This was considered to be either due to good serological response or higher exposure. Galan MI et al., did not report such age specific differences [21].

(group 1). However, it was not significant statistically. Similarly, in a study conducted in Mumbai, there were no differences in seropositivity between staff of COVID-19 and non COVID-19 area of the hospital [20]. The low seroprevalence among COVID-19 Intensive Care Unit (ICU) HCWs in New Jersey Hospital, United states [18] whereas high prevalence among HCWs not treating COVID-19 patients in Essen Hospital, Germany [19]. A study conducted in Belgium by Steensels D et al., showed 6.4% seroprevalence among hospital staff was associated with household contact of COVID-19 patients and not due to contact with COVID-19 patients in hospitals [26].

In the present study, it was noted that the staff those who adhered to PPE protocol were less affected than those who did not and the difference was statistically significant. This observation was supported by the study conducted in China during the second wave that none of the 42600 HCWs caring for COVID-19 patients were infected, suggesting efficient, judicious and strict enforcement of precautionary Infection Prevention Control (IPC) measures. The strict adherence to PPE usage plays a key role for eliminating the COVID-19 infection [27]. Therefore, the risk of COVID-19 infection among HCWs was thought to be higher with community based transmission or by unprotected hospital exposure.

Limitation(s)

The limitation includes small sample size and single centre hospital based study. Many such multicentre seroprevalence studies with larger sample size will help in understanding the epidemiology of the illness.

CONCLUSION(S)

It is concluded that it would be more appropriate to study seroprevalence among healthcare workers at frequent intervals irrespective of exposure and symptoms, which helps not only to detect the asymptomatic cases but also assess the effectiveness and adherence to IPC measures. There should be strict, committed adherence to PPE protocol with utmost concentration. Increasing the awareness programme on PPE utility enhances understanding, carefulness, appropriate usage and disposal of PPE. It also reduces the non compliance of PPE especially among auxillary workers.

REFERENCES

[1] World Health Organization: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports.

[2] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet (London, England). 2020;395(10223):497-506.
[3] Erdem H, Lucey DR. Healthcare worker infections and deaths due to COVID-19: A survey from 37 nations and a call for WHO to post national data on their website. Int J Infect Dis. 2021;102:239-41.
[4] Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. New England Journal of Medicine. 2020;382(18):1708-20.
[5] Duysburgh E, Mortgat L, Barbezange C, Dierick K, Fischer N, Heyndrickx L, et al. Persistence of IgG response to SARS-CoV-2. Lancet Infect Dis. 2021;21(2):163-64.
[6] Okba NMA, Müller MA, Li W, Wang C, GeurtsvanKessel CH, Corman VM, et al. Severe acute respiratory syndrome coronavirus 2-specific antibody responses in coronavirus disease patients. Emerg Infect Dis. 2020;26(7):1478-88.
[7] Rothe C, Schunk M, Sothmann P, Bretzel G, Froeschl G, Wallrauch C, et al. Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany. N Engl J Med. 2020;382(10):970-71.
[8] WHO Considerations for quarantine of individuals in the context of containment for coronavirus disease (COVID-19): Interim guidance 28 February 2020 (https://www.who.int/publications-detail/considerations-for-quarantine-of-individuals-in-the-contextof-containment-for-coronavirus-disease-(covid-19).
[9] Chen Y, Tong X, Wang J, Huang W, Yin S, Huang R, et al. High SARS-CoV-2 antibody prevalence among healthcare workers exposed to COVID-19 patients. J Infect. 2020;81(3):420-26.
[10] Vashist SK. In Vitro Diagnostic Assays for COVID-19: Recent Advances and Emerging Trends. Diagnostics (Basel). 2020;10(4):202.
[11] Ramya JE, Subash Chandran G, Alagesan S, Ravichandran M, Victoria S, Rathi Devi M, et al. A Prospective observational study of the outcome of treatment with Kabasura Kudineer among patients with SARS-nCOV-2 infection. Int J of Nutr Pharmacol Neurol Dis. 2021;11(2):169-73.
[12] Prakash O, Solanki B, Sheth J, Makwana G, Kadam M, Vyas S, et al. SARS-CoV2 IgG antibody: Seroprevalence among health care workers. Clin Epidemiol and Glob Health. 2021;11:100766.
[13] Chang MC, Lee W, Hur J, Park D. Chest computed tomography findings in asymptomatic patients with COVID-19. Respiration. 2020;99(9):748-54.
[14] Rivett L, Sridhar S, Sparkes D, Routledge M, Jones NK, Forrest S, et al. Screening of healthcare workers for SARS-CoV-2 highlights the role of asymptomatic carriage in COVID-19 transmission. Elife. 2020;9:e58728.
[15] Pang J, Wang MX, Ang IYH, Tan SHX, Lewis RF, Chen JI, et al. Potential rapid diagnostics, vaccine and therapeutics for 2019 Novel Coronavirus (2019-nCoV): A systematic review. J Clin Med. 2020;9(3):623.
[16] Shirin T, Bhuiyan TR, Charles RC, Amin S, Bhuiyan I, Kawser Z, et al. Antibody responses after COVID-19 infection in patients who are mildly symptomatic or asymptomatic in Bangladesh. Int J Infect Dis. 2020;101:220-5.
[17] Ko JH, Joo EJ, Park SJ, Baek JY, Kim WD, Jee J, et al. Neutralizing Antibody Production in Asymptomatic and Mild COVID-19 Patients, in Comparison with Pneumonic COVID-19 Patients. J Clin Med. 2020;9(7):2268.
[18] Mughal MS, Kaur IP, Patton CD, Mikhail NH, Vareechon C, Granet KM. The prevalence of severe acute respiratory coronavirus virus 2 (SARS-CoV-2) IgG antibodies in intensive care unit (ICU) healthcare personnel (HCP) and its implications-a single-center, prospective, pilot study. Infect Control Hosp Epidemiol. 2021;42(5):638-39.
[19] Korth J, Wilde B, Dolff S, Anastasiou OE, Krawczyk A, Jahn M, et al. SARS-CoV-2-specific antibody detection in healthcare workers in Germany with direct contact to COVID-19 patients. J Clin Virol. 2020;128:10443.
[20] Baveja S, Karnik N, Natraj G, Natkar M, Bakshi A, Krishnan A. Rapid volunteer-based SARS-Cov-2 antibody screening among health care workers of a hospital in Mumbai, India. Indian J Med Sci. 2020;72(3):148-54.
[21] Galán MI, Velasco M, Casas ML, Goyanes MJ, Rodríguez-Caravaca G, Losa-García JE, et al. Hospital-Wide SARS-CoV-2 seroprevalence in health care workers in a Spanish teaching hospital. Enferm Infecc Microbiol Clin (Engl Ed). 2020;S0213-005X(20)30418-3.
[22] Hanage W, Xueting Q, Lee KS. Snowball sampling study design for serosurveys in the early COVID-19 Pandemic (2020).
[23] Bryant JE, Azman AS, Ferrari MJ, Arnold BF, Boni MF, Boum Y, et al. Serology for SARS-CoV-2: Apprehensions, opportunities, and the path forward. Sci Immunol. 2020;5(47):eabc6347.
[24] Stringhini S, Wisniak A, Piumatti G, Azman AS, Lauer SA, Baysson H, et al. Seroprevalence of anti-SARS-CoV-2 IgG antibodies in Geneva, Switzerland (SEROCoV-POP): A population-based study. Lancet (London, England). 2020;396(10247):313-19.
[25] Prakash O, Solanki B, Sheth JK, Joshi B, Kadam M, Vyas S, et al. Assessing seropositivity for IgG antibodies against SARS-CoV-2 in Ahmedabad city of India: A cross-sectional study. BMJ Open. 2021;11:e044101.
[26] Steensels D, Oris E, Coninx L, Nuyens D, Delforge ML, Vermeersch P, et al. Hospital-wide SARS-CoV-2 antibody screening in 3056 staff in a tertiary center in Belgium. JAMA. 2020;324(2):195-97.
[27] Zhan M, Qin Y, Xue X, Zhu S. Death from Covid-19 of 23 Health Care Workers in China. N Engl J Med. 2020;382(23):2267-68.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: May 08, 2021
- Manual Googling: Jun 16, 2021
- iThenticate Software: Aug 11, 2021 (15%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. No

Date of Submission: **May 07, 2021**
Date of Peer Review: **Jun 17, 2021**
Date of Acceptance: **Jul 14, 2021**
Date of Publishing: **Sep 01, 2021**