VOLUME - 9, ISSUE - 12, DECEMBER - 2020 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Microbiology

SEROPREVALENCE OF SARS COV-2 AMONG HEALTHCARE WORKERS IN A MUMBAI TERTIARY CARE HOSPITAL

Dr. Nishat Khan*	Assistant Professor, Department Of Microbiology, TNMC & BYL Nair Ch Hospital, Mumbai. *Corresponding Author
Dr. Sachee Agrawal	Associate Professor, Department Of Microbiology, TNMC & BYL Nair Ch Hospital, Mumbai.
Dr. Jayanthi S. Shastri	Professor And Head, Department Of Microbiology, TNMC & BYL Nair Ch Hospital, Mumbai.

ABSTRACT

INTRODUCTION: Since its emergence in 2019, COVID has rapidly spread to countries other than China through international travel. Infection is spread through droplets and direct or indirect contact with infected patients. WHO declared this as pandemic on 11th March 2020. The first positive case was detected on 11th March 2020 in Mumbai. This tertiary care MCGM hospital was declared a COVID hospital on 20th April 2020.HCW in this hospital have been constantly involved in screening and managing infected and quarantined COVID 19 patients regularly. Hence were exposed to COVID positive patients frequently. Serologic assays for SARS-CoV-2, can play an important role in understanding the virus's epidemiology in the general population and identifying groups at higher risk for infection. Serologic tests detect waning or past SARS-CoV-2 virus infection indirectly, by measuring the host humoral immune response to the virus. These tests can help determine the proportion of a population previously infected with SARS-CoV-2 and provide information about populations that may be immune and potentially protected. This study was designed to screen the healthcare workers working in ICU settings, screening OPDs isolation wards and administration work for the seroprevalence of IgM/IgG antibodies against SARS-CoV-2 by rapid tests and Chemiluminescence assay for IgG antibodies. **OBJECTIVES:** To study the seroprevalence of IgM/IgG antibodies in doctors against SARS-CoV-2 in a tertiary care hospital in Mumbai using rapid kits and detecting IgG antibodies by Chemiluminescence assay. **MATERIAL AND METHODS:** 132 HCWs were screened for the presence of IgM/IgG antibodies against SARS CoV-2 using two different Rapid tests (Rapid test 1 and Rapid test 2) and IgG antibodies by Chemiluminescence (CLIA) assay. **RESULTS:** In this serosurvey 84 were frontline workers and 48 were backline workers. Two HCWs were IgG antibody positive for SARS CoV-2 by both the rapid kits. IgM was not detected in any HCW. CLIA was positive in 6 HCWs for IgG antibody against SARS CoV-2. **CONCLUSION:** The high specificity of the rapid assays will definitely contribute to rapidly confirm the presence of past infections of COVID-19 in the populations but a negative test will be unreliable due to its sensitivity. Therefore, these rapid assays should be used in correlation with other testing modalities.

KEYWORDS : SARS CoV-2, Antibody, Rapid, CLIA, HCW

INTRODUCTION

Coronaviruses (CoVs) are a group of enveloped viruses with non-segmented positive sense RNA belonging to the family Coronaviridae and the order Nidovirales. The World Health Organization (WHO) reported cases of pneumonia of unknown aetiology in Wuhan city, Hubei province of People's Republic of China, on December 31, 2019[1]. On January 7, 2020, Chinese authorities officially announced that the illness was caused by a novel CoV [2]. The WHO has named the disease as COVID-19, and based on its similarity to SARS-CoV (2002-2003), the CoV Study Group of the International Committee on Taxonomy of Viruses (ICTV) has named the virus as SARS-CoV-2 [3,4,5].

Since its emergence, the disease has rapidly spread to other countries through international travel. Infection is spread through droplets and direct or indirect contact with infected patients. WHO declared this as pandemic on 11th March 2020.

The first positive case was detected on 11th March 2020 in Mumbai. Subsequently screening OPDs, Isolation wards and Quarantine facilities were started in Municipal Corporation of Greater Mumbai (MCGM) hospitals. This tertiary care MCGM hospital was declared a COVID hospital on 20th April 2020.

Healthcare workers from the hospital were involved in screening and managing infected and quarantined COVID 19 patients in the isolation wards, ICU and quarantine facilities. Interns from this tertiary care hospital were posted at airports to screen the incoming travellers. Hence were exposed to COVID positive patients frequently.

Therefore, there was an urgent need to understand the level of exposure among healthcare workers involved in screening and managing COVID 19 positive patients. IgG antibodies against SARS-CoV-2 generally start appearing after two weeks of onset of infection, and last for several months. Detection of IgG antibodies for SARS-CoV-2 are useful in Serosurveys to understand the proportion of individual HCWs exposed to infection with SARS-CoV-2 including asymptomatic individuals. Depending upon the level of seroprevalence of infection, appropriate public health interventions can be planned and implemented for prevention and control of the disease. Periodic serosurveys are useful to guide the policy makers. Survey among high risk or vulnerable populations (health care workers, frontline workers, immunocompromised individuals, individuals in containment zones etc) is required to know the extent of infected and recovered population.

This study was designed to screen the healthcare workers for the seroprevalence of IgM/IgG antibodies against SARS CoV-2 using rapid tests and Chemiluminescence assay for IgG antibodies. The test was done in healthcare workers (HCWs) working in ICU settings, screening OPDs isolation wards and administration work. Estimates of seroprevalence will enable us to understand the impact of this disease in one of the most vulnerable groups -- doctors, nurses and frontline workers working in a COVID hospital.

OBJECTIVES

To estimate the seroprevalence of SARS Cov-2 antibodies in HCWs using Rapid IgM/IgG kits and to assess the performance of these rapid kits as compared to Chemiluminescence assay (CLIA) in a tertiary care hospital in Mumbai.

Inclusion Criteria: Healthcare workers involved in screening and managing of infected and quarantined patients in the isolation wards, ICU and quarantine facilities.

MATERIALS AND METHOD

132 HCWs were screened for the presence of IgM/IgG antibodies against SARS CoV-2 using two different Rapid tests (Rapid test 1 and Rapid test 2) and IgG antibodies by Chemiluminescence (CLIA) assay. 3 ml blood was collected in EDTA bulb and transported to the Microbiology laboratory of the tertiary care hospital. Rapid tests for antibody was performed by Rapid Test 1 and Rapid Test 2 as per kit insert. Plasma was also processed for CLIA using SARS-CoV-2 IgG Architect system for Nucleocapsid antigen as per kit insert.

RESULTS

In the distribution of the healthcare workers enrolled in the study as per designation and nature of work is as shown in Table 1, majority of the HCW were residents (n=50), followed by Professor, Associate professor and Assistant Professor. Others included Infection control nurses, blood bank officers and medical officers. 84 of these were frontline workers involved in patient care and 48 were backline workers involved in administrative work or not directly in contact with patients. The healthcare workers were mainly involved in the Special screening OPD (SSO), wards and ICU (Fig 1). The frontline workers were generally had 6-hour duty every alternate week for the entire week with one-week quarantine. 5 healthcare workers had developed COVID 19 disease and 9 had been quarantined due to high risk close contact.

Table 1: Distribution of HCW as per designation and Nature of work

Designation	Number	Frontline	Backline
Junior residents	31	30	1
Senior residents	19	16	3
Assistant professor	20	15	5
Associate professor	24	10	14
Professor	31	10	21
Medical officers	3	1	2
Blood bank officers	2	0	2
Infection Control Nurse (ICN)	2	2	0

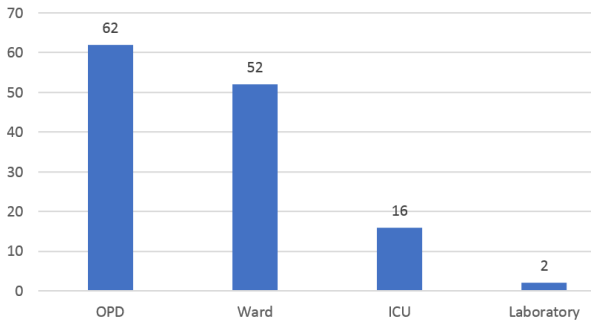

Fig 1 : Area of work (n=132)

Rapid tests for antibody detection was performed by two different rapid tests (n=132) for IgM and IgG antibodies. Two HCWs were positive for IgG by both the rapid tests but none of the samples were positive for IgM antibodies. Plasma was processed for CLIA using SARS-CoV-2 IgG Architect system against Nucleocapsid antigen. CLIA was positive in 6 HCWs. The results of the rapid tests were correlated with the CLIA results. (Table: 2) Kappa agreement was done. When both the decisions were compared it was shown that overall agreement was 96.9% with simple kappa value 0.48 (Moderate agreement) which was statistically significant (P <0.001). The results of the Rapid tests along with the CLIA indices is shown in Table :3.

Table 2: Comparison of Rapid IgM/ IgG antibody with CLIA

		CLIA (n=132)		Total
		Positive	Negative	
Rapid Kit (n=132)	Positive	2	0	2
		33.3%	0%	1.5%
	Negative	4	126	130
		66.7%	100.0%	98.5%
Total		6	126	132

Kappa = 0.488 (Moderate agreement)
P < 0.001 (Significant)

Table No :3 Results of Rapid kit and CLIA result

Serial Number	Rapid Kit 1	Rapid Kit 2	CLIA
Concordant Rapid kit and CLIA Results			
1	IgG	IgG	Positive 5.36
2	IgG	IgG	Positive 8.07
Discordant Rapid kit and CLIA Results			
3	Neg	Neg	Positive 1.74
4	Neg	Neg	Positive 2.76
5	Neg	Neg	Positive 3.75
6	Neg	Neg	Positive 6.48

The sensitivity, specificity, PPV and NPV of the rapid results on comparison with CLIA were calculated. (Table: 4).

Table 4: Sensitivity, Specificity, PPV and NPV of the rapid results on comparison with CLIA

Name of Test	Sensitivity	Specificity	PPV	NPV
Rapid Test 1	33%	100%	100%	96.9%
Rapid Test 2	33%	100%	100%	96.9%

Total 6 HCWs were positive for IgG SARS CoV-2 antibodies by CLIA. 3 out of 6 of HCWs had recovered from symptomatic COVID disease whereas 3 HCWs were asymptomatic. 2 HCWs who had tested positive for COVID previously by RT PCR were CLIA negative. (Table: 5)

Table 5: CLIA results in HCW

Symptomatic/ Asymptomatic	CLIA Positive	CLIA Negative
Symptomatic (COVID Positive)	3(2.27%)	2(1.51%)
Asymptomatic (COVID Negative)	3(2.27%)	124(93.93%)

DISCUSSIONS

Understanding seroprevalence, the proportion of people infected/ exposed with SARS-CoV-2, is essential to know the true spread of Covid-19 in the community and then plan strategies to prevent further spread and more importantly, to plan policies for relaxing lockdown and related restrictions in a planned and phased manner.

The Indian Council of Medical Research (ICMR) recommended the use of serological tests to evaluate the burden of the COVID infection in certain populations like frontline workers, nurses, doctors and other high-risk groups. Hence this study was conducted in the HCWs of this tertiary care hospital.

In this serosurvey 132 HCWs were included, 84 were frontline workers and 48 were backline workers. Two HCWs were IgG antibody positive for SARS CoV-2 by both the rapid kits. IgM was not detected in any HCW. CLIA was positive in 6 HCWs for IgG antibody against SARS CoV-2. 5 out these 6 of these HCWs were frontline workers. The overall low seroprevalence in our study could be due the presence of backline healthcare workers in the study population.

In this study 3 HCW were known symptomatic or COVID positive and 3 HCW were asymptomatic and had never been PCR positive were positive by CLIA. CLIA positivity in asymptomatic HCWs could be due to the fact that they may have had mild or moderate symptoms and had not realized it.

CLIA was negative in 2 previously COVID positive HCW. A negative antibody response in a previously COVID positive patient could mean the patient's immune system is not able to mount a measurable antibody response or a false positive PCR test in individuals who have not had the SARS-CoV-2 infection at all. In others, it is possible Nucleocapsid antibody levels must have waned over time to undetectable levels as half-life of these antibodies is only 70 days .[6]

The HCWs with positive rapid tests had a high CLIA index of above 5. In 4 HCW rapid and CLIA results were discordant, 3 had indices above 2.5. Rapid negative results could be due to prozone phenomenon. An evident prozone effect was detected, in a study done by Jääskeläinen et al where an initially negative rapid test became positive at serum dilution 1:4 up until dilution of 1:16. This maybe an important cause of false negative test results in rapid tests.[7]

The sensitivity, specificity, PPV and NPV of the rapid kits in our study was found to be 33%, 100%, 100% and 96.9% respectively. When the decisions of rapid test and CLIA were compared it was shown that overall agreement was 96.9% with simple kappa value 0.48 (Moderate agreement) which was statistically significant (P <0.001). Despite the differences in sensitivity, all rapid assays had sufficient positive predictive value (PPV) in this COVID-19 hospital.

In a pilot study done by Ong et al, sensitivity characteristics of rapid tests were very heterogeneous, ranging from 10% to 55% in hospitalised patients [8]. In a study done by Traugott et al comparing sensitivities and specificities of 4 commercial ELISA and 2 rapid tests in patients with symptomatic SARS-CoV-2 infection in different groups of patients. They found that the test sensitivities were low (<40%) within the first 5 days of infection but increased to >80% between days 6 and 10 after start of symptoms for immunoglobulin (Ig) M, IgA and total antibody ELISAs. The evaluated tests which included IgG ELISAs and rapid tests were positive in all patients at or after Day 11 of symptoms. The specificities of the evaluated ELISAs were 83% (IgA), 98% (IgG) and 97% IgM and total antibody [9]. But both these studies were done in symptomatic patients and did not include the kits which were used in our study.

As per EUA Authorised Serology performance published on 8/7/2020 the Sensitivity, Specificity, PPV and NPV at prevalence of 5% is 100%, 99.6%, 92.9% and 100% respectively of Abbott Architect SARS CoV-2 IgG [10]. Sensitivity and Specificity is 92.7% and 99.9% respectively in an evaluation study published by Public Health England [11]. Since this is an emerging infection there is no gold standard against which these antibody test can be evaluated.

CONCLUSION

Antibody assays can help determine the proportion of a population previously infected with SARS-CoV-2 and provide information about populations that may be immune and potentially protected. But the medical community needs to determine whether positive serologic tests are indicative of protective immunity against SARS-CoV-2. WHO also states that there is currently no evidence that people who have recovered from COVID-19 and have antibodies, will be protected from re-infection. Presence of antibodies will not serve as an "immunity passport" or "risk-free certificate" that would enable individuals to travel or to return to work assuming that they are protected against re-infection.[12]

Fully automated CLIA and ELISA assays allow the quantitative determination of antibodies against SARS-CoV-2 by clinical laboratories with increased screening capacity. Rapid serological tests can be performed in the laboratory or used as point-of-care tests (POCT). The latter will provide accurate results within 10−15 min with equivalent sensitivity and specificity as the quantitative automated immunoassays, particularly two weeks after onset of symptoms.

Drawbacks of the tests such as cross reactivity with other coronaviruses leading to a false positive result should also be kept in mind.

The high specificity of the rapid assays will definitely contribute to rapidly confirm the presence of past infections of COVID-19 in the populations but a negative test will be unreliable due to its sensitivity. Therefore, these rapid assays should be used in correlation with other testing modalities.

REFERENCES

1. World Health Organization (WHO). WHO Statement Regarding Cluster of Pneumonia Cases in Wuhan, China. Beijing: WHO; 9 Jan 2020. [Accessed 26 Jan 2020]. https://www.who.int/china/news/detail/09-01-2020-who-statement-regarding-cluster-ofpneumonia-cases-in-wuhan-china
2. Weiss SR, Leibowitz JL. Coronavirus pathogenesis. Adv Virus Res 2011;81:85-164. PMID:22094080 DOI:10.1016/B978-0-12-385885-6.00009-2
3. Su S, Wong G, Shi W, et al. Epidemiology, genetic recombination, and pathogenesis of coronaviruses. Trends Microbiol 2016;24:490-502. PMID:27012512 DOI:10.1016/j.tim.2016.03.003
4. Cui J, Li F, Shi ZL. Origin and evolution of pathogenic coronaviruses. Nat Rev Microbiol 2019;17:181-192.PMID:30531947 DOI:10.1038/s41579-018-0118-9
5. World Health Organization (WHO). Coronovirus. https://www.who.int/health-topics/coronavirus Index
6. Cheryl Yi-Pin Lee , Raymond T. P. Lin, Laurent Renia and Lisa F. P. Ng; Serological Approaches for COVID-19: Epidemiologic Perspective on Surveillance and Control; Front. Immunol., 24 April 2020 | https://doi.org/10.3389/fimmu.2020.00879
7. AJ Jääskeläinen, S Kuivanen, E Kekäläinena , MJ Ahava , R Loginov , H Kallio-Kokko , O Vapalahtia , H Jarvaa , S Kurkela , M Lappalainen; Performance of six SARS-CoV-2 immunoassays in comparison with microneutralization; Journal of Clinical VirologyVolume 129, August 2020, 104512.
8. D.S.Y. Ong , S.J. de Man , F.A. Lindeboom , J.G.M. Koeleman , Comparison of diagnostic accuracies of rapid serological tests and ELISA to molecular diagnostics in patients with suspected coronavirus disease 2019 presenting to the hospital, Clinical Microbiology and Infection 26 (2020) 1094.e7e1094.e10.
9. Traugott M, Aberle SW, Aberle JH, et al. Performance of SARS-CoV-2 antibody assays in different stages of the infection: comparison of commercial ELISA and rapid tests [published online May 30, 2020]. J Infect Dis. doi:10.1093/infdis/jiaa305/5849070
10. Coronavirus Disease 2019 (COVID-19) Emergency Use Authorizations for Medical Devices, EUA Authorized Serology Test Performance published on 8/7/2020.
11. Evaluation of sensitivity and specificity of four commercially available SARS-CoV-2 antibody immunoassays Public Health England, Porton Down; Nuffield Department of Medicine, University of Oxford, Oxford University Hospitals NHS Foundation Trust; July 2020
12. World Health Organization (WHO). WHO Statement "Immunity passports" in the context of COVID-19: Scientific Brief 24 April 2020 https://www.who.int/news-room/commentaries/detail/immunity-passports-in-the-context-of-covid-19