

## Original Article

## Non-COVID Health Care Workers with Positive Antibody Responses: Are We Heading Towards Herd Immunity?

Sudhir Bhandari<sup>1</sup>, Nitya Vyas<sup>2</sup>, Shivankan Kakkar<sup>3</sup>, Bhoopendra Patel<sup>4\*</sup>, Amitabh Dube<sup>5</sup>, Jitendra Gupta<sup>6</sup>, Natwar K. Swarnkar<sup>7</sup>, Sunil Kumar<sup>7</sup>, Nisha Patidar<sup>8</sup>

<sup>1</sup>Senior Professor, Department of Medicine, S. M. S. Medical College and Attached Hospitals, Jaipur, Rajasthan, India

<sup>2</sup>Senior Professor and Head, Department of Microbiology, S. M. S. Medical College and Attached Hospitals, Jaipur, Rajasthan, India

<sup>3</sup>Assistant Professor, Department of Pharmacology, S. M. S. Medical College and Attached Hospitals, Jaipur, Rajasthan, India

<sup>4</sup>Assistant Professor, Department of Physiology, All India Institute of Medical Sciences (AIIMS), Bilaspur, Himachal Pradesh, India

<sup>5</sup>Senior Professor, Department of Physiology, S. M. S. Medical College and Attached Hospitals, Jaipur, Rajasthan, India

<sup>6</sup>Professor, Department of Physiology, S. M. S. Medical College and Attached Hospitals, Jaipur, Rajasthan, India

<sup>7</sup>Third Year Resident, Department of Physiology, S. M. S. Medical College and Attached Hospitals, Jaipur, India

<sup>8</sup>Senior Resident, Department of Physiology, S. M. S. Medical College and Attached Hospitals, Jaipur, India

**Corresponding Author:** Dr. Bhoopendra Patel, E-mail: bhupendra.kool9999@gmail.com

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## ABSTRACT

**Background:** Antibody testing against SARS-CoV-2 complimentary to RT-PCR could be an effective method for its detection. Development of immunity against COVID-19 in context of reinfection and herd immunity still remains debatable and needs further elucidation. The present study was conducted to investigate the immunity status against SARS-CoV-2 in terms of IgG antibody positivity in health care workers at a tertiary care center. **Methodology:** This single center study was conducted at a tertiary care center, that involved 1039 healthcare workers and other staff members. The testing of all subjects was performed using ELIFAST (SARS-CoV-2 IgG ELISA) kits. The sample population was then segregated into RT-PCR positive and negative/status unknown groups. Groups were further segregated on the basis of IgG positivity status and the sensitivity and specificity was also calculated. **Results:** Among the 1039 enrolled subjects, 179 (17.23%) were RT-PCR positive for SARS-CoV-2 positive and remaining were either RT-PCR negative or status unknown cases. Among 179 COVID-19 recovered subjects, 19 (10.61%) were negative for IgG, whereas 160 (89.39%) came out IgG positive. Out of 860 (82.77%) RT-PCR Negative/Status unknown, 248 (28.84%) came out IgG positive and the remaining 612 (71.16%) were negative for IgG. The overall sensitivity and specificity were 89.39 and 71.16, respectively. **Conclusion:** A combined approach of testing for COVID-19 using RT-PCR and rapid antibody assays could be more beneficial. Serological studies project a higher antibody response in population that compel us to think about plausibility of herd immunity. However, variability in serological response could be affected by several factors and the underlying complex immune process of COVID-19 is yet to be fully understood.

## INTRODUCTION

The sphinx of the journey of COVID-19 has been very confounding that has left the medical fraternity bewildered and baffled. There are still many questions that remain answered relating to origin of the virus and its probable definitive management [1]. The infection of COVID-19 since its emergence in December 2019 spread like a wildfire across geographical borders in 223 countries worldwide, such that, as of 11<sup>th</sup> February 2021, the confirmed cases have crossed the 100 million mark causing 2, 347, 015 confirmed deaths [2]. After an uncertainty and misery of almost one year there has been a hope against COVID-19 with the advent of vaccines. A systematic vaccination program has been already launched

in several countries. Yet, there are several questions regarding the elimination of COVID-19, herd immunity and long-term complications that need further elucidation [3, 4].

It remains the endeavor of our scientific community at large, to learn and apply knowledge to limit or eradicate COVID-19. Laboratory testing is a significant component of the COVID-19 response. Diagnostics are essential not only for identifying the infection but also for controlling and eventually eradicating the disease [[5]. The backbone of COVID-19 diagnosis in the state of Rajasthan has been the World Health Organization (WHO) and Indian Council of Medical Research (ICMR) recommended molecular testing using reverse transcriptase-polymerase chain reaction

(RT-PCR). With the rapid increase in the cases worldwide, India scaled up testing for COVID-19 [6].

Beside RT-PCR technique, antibody testing for IgM and IgG against SARS-Cov-2 has also been used. Long et al. [7] observed a seroconversion of IgM or IgG antibodies in COVID-19 patients within 20 days after symptom onset. The median duration for both antibodies was 13 days post symptom onset. Since the COVID-19 outbreak, most studies have focused on etiopathogenesis and management strategies. Acquired immunity is still a predicament. The underlying complex immune response needs unraveling. In this context, the present study was undertaken to investigate the antibody responses among health workers at Sawai Man Singh Medical College and Attached Hospitals, Jaipur, who were non-COVID at the end of nine months into this pandemic.

## METHODOLOGY

A single center, investigator initiated, pilot study was conducted by Department of Microbiology and Medicine, S. M. S. Medical College and Attached Hospitals, Jaipur (Rajasthan). RT-PCR test were performed on people as well as health care staff working across all departments and hospitals with symptoms suggestive of suffering from the COVID-19. The RT-PCR testing has an established role in diagnostics [8]. Since the pandemic happened, staff comprising of medical, nursing and paramedical personnel has been working tirelessly serving the public and patients with COVID-19. All the COVID-19 protocols with regard to protection of staff were followed. It has been a good strategic control, but a need was felt to find the antibody status among those non-COVID health care staff that was continuously being exposed during the past nine months in the pandemic. These staff either did not have any symptoms suggestive of COVID-19 or had tested PCR negative following symptoms during their working tenure at our setting.

An initiative was undertaken at this institute and all staff was informed that non-COVID-19 members will be tested for their antibody status. Although, if COVID-19 recovered members approached for being tested, they were not refused testing. Three working days were kept exclusively for testing all such members. The participation for COVID-19 antibody testing was kept voluntary and first come, first serve basis only. Prior consent for procedure was undertaken. The inventiveness received an overwhelming response. The testing of all samples

was done using ELIFAST (SARS-CoV-2 IgG ELISA) kits for SARS-CoV-2 IgG antibody with chemiluminescent assay.

## OBSERVATION AND RESULTS

A total of 1039 samples were tested, wherein 860 samples had RT-PCR status negative/unknown/non-COVID and remaining were previously diagnosed RT-PCR positive/known/COVID recovered cases. IgG antibody status among RT PCR unknown and known cases are depicted in Figure 1, 2 and Table 1.

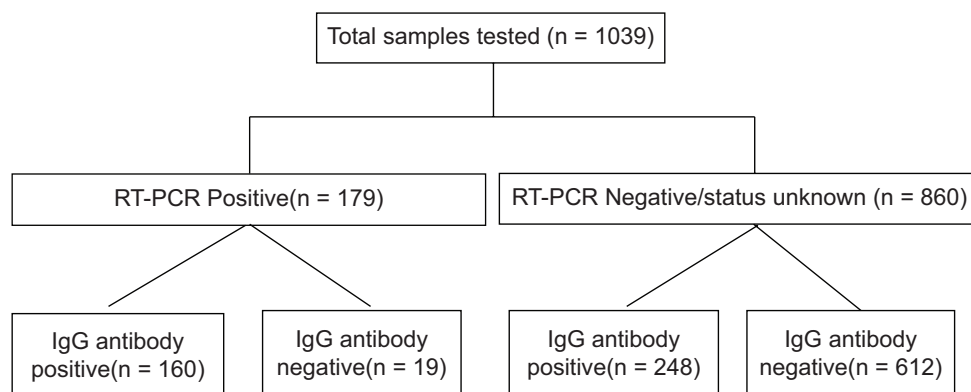
## DISCUSSION

As is the practice of any disease process with protean manifestations afflicting humans across the globe, COVID-19 pandemic has witnessed a deluge of conflicting information. It has challenged the frontiers of medical science, tested its limits through extremes and taken humankind for a ride. The development of definitive management protocols along with vaccines is vital to do away with the specter of the present pandemic. Although, certain people are more likely to suffer worse or die from COVID-19 based on age, underlying health conditions, deprivation and ethnicity, there are no guarantees, and there have been young people in intensive care and 90-year-olds who have recovered.

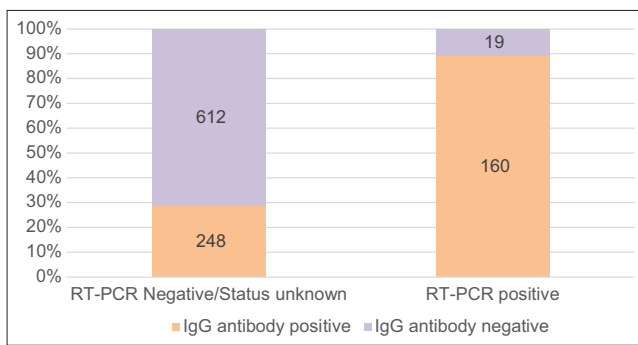
As for the resource's constraint, we reprogrammed our gene expert machines (being used for TB testing) to support

**Table 1.** Number and percent distribution of healthcare workers on the basis of RT-PCR

Particular	Number (n)	Percent (%)
Total sample tested	1039	100
RT-PCR Negative/Status unknown	860	82.77
IgG antibody positive	248	28.84
IgG antibody negative	612	71.16
RT-PCR Positive	179	17.23
IgG antibody positive	160	89.39
IgG antibody negative	19	10.61
Sensitivity		89.39
Specificity		71.16



**Figure 1.** Schematic representation of the results of the present study



**Figure 2.** Comparison of IgG positivity status among RT-PCR negative/unknown and known cases

molecular testing. It became an effective strategy in reducing the costs and waiting time. Whilst the endeavor remained to continue doing the gold standard RT PCR testing, something had to be done about its limitation of giving false results. Hence the present study focused on using rapid antibody (serological) tests that detect human antibodies generated in response to infection. It is pertinent to mention that an antibody test which is usually a blood test doesn't inform you whether an individual has virus infection or not [9].

In the present study, a positive IgG antibody response was observed in COVID-19 negative and status unknown group. A negative RT PCR test may not necessarily guarantee a negative IgG response especially among the healthcare workers continuously involved in treatment of COVID-19 patients. The antibody tests may gain particular relevance among health workers continuously involved in COVID care with unknown infection status and achieve diagnosis in those with persistently negative RT PCR.

RT-PCR technique has been the mainstay for detection of SARS-CoV-2. However, it has several limitations, that may be longer turnaround times and false negative results in up to 30% of cases [9-12]. The available literature suggested the suitability of various immune assays for detection of IgG antibodies against in COVID-19 patients [13-15].

Several studies have tested the accuracy of the available antibody testing methods against SARS-CoV-2 [10, 16-19]. The sensitivity and specificity in one such study was reported to be 88.66% and 90.63% [10], respectively, whereas another one reported 71.1% and 96.2% [16], respectively. On 11<sup>th</sup> September 2020, WHO gave Interim guidance about Antigen-detection in the diagnosis of SARS-CoV-2 infection using rapid immunoassays [20]. Following this the ICMR, New Delhi also approved rapid antigen based diagnostic tests. This was in response to the rapidly growing COVID-19 cases and shortages of laboratory-based PCR molecular testing capacity. Diagnostic test manufacturers across the world started developing rapid diagnostic tests (RDTs). The available rapid tests are either antigen (detecting proteins of the SARS-CoV-2 virus) or antibody (serological) tests that detect human antibodies generated in response to COVID-19. Rajasthan state Government did not allow antigen based RDTs (except under exceptional circumstances) since they can never be preferred over the gold standard RT PCR [21]. Indian Council of Medical Research issued advisory for using rapid antibody-bases blood test in areas

reporting clusters (containment zone) and in large migration gatherings/evacuee centers [22].

Wang [23] suggested that combination of RT-PCR and antibody assay could be a more accurate diagnostic method for SARS-CoV-2 detection, providing a higher sensitivity and specificity. Moreover, this method could prove more beneficial for timely management of suspected patients, epidemiological investigation, and monitoring of the ongoing pandemic. A comparative study of various commercially available antibody testing methods suggested a variable sensitivity [24]. These contradictory results were attributed to time point in course of the COVID-19, when the test was performed. This variability in developing detectable immune response against COVID-19 in some patients was also evident by findings of Wang et al. [25]. In this study some COVID-19 infected pneumonia patients exhibited delayed development of IGM or IgG antibodies against. Moreover, two RT-PCR confirmed cases of COVID-19 failed to show IgM or IgG reactivity.

Cancellata de Abreu et al. reported positive IgG/IgM antibody response in one fifth of the RT-PCR negative patients [26]. Thus, RT-PCR testing alone could not be sufficient for identifying COVID-19 infected patients. Cassaniti et al. reported 8.3 % cases of COVID-19 in emergency department being positive for IgM or IgG antibodies, even after being RT-PCR negative [17]. Döhla et al. also observed a similar trend in RT-PCR negative COVID-19 patients [18]. Variability in SARS-CoV-2 IgG responses has also been observed to depend upon the severity of COVID-19. Severe illness was associated with higher titers of IgG as compared to the milder illness. Moreover, severely ill patients seroconverted earlier as compared to the patients with milder diseases [27-29].

Cervia et al. suggested a protective role of SARS-CoV-2-S-protein-specific IgA present in nasal and tear fluid in asymptomatic health care workers [29]. This could also be contributing to the variable antibody reactions as has been observed by various researcher. This response might also be influenced by the duration and the viral load of SARS-CoV-2 [30, 31]. The IgM-IgG combined assay has better utility and sensitivity compared with a single IgM or IgG test. It can be used for the rapid screening of SARS-CoV-2 carriers, symptomatic or asymptomatic, in hospitals, clinics, and test laboratories [10].

Recently ICMR, New Delhi recently shared the finding of the third pan-India serological survey for COVID-19, that revealed a seroprevalence of 25.3% in children aged 10-17 years and 25.3%, and people above the age of 60 showed a prevalence of 23.4%. The healthcare workers, especially doctors and nurses exhibited a seroprevalence of 26.6%. These findings support results of the present study on healthcare workers [32]. The projected positive antibody response from such studies even in asymptomatic and RT-PCR negative cases compel us to think about the plausibility of herd immunity against COVID-19 in near future. The term herd immunity [33] has been in use since 1923 that indicates a level of sufficient immunity in a community, against a particular infectious disease that could be indirectly beneficial to those who are not immune to the disease. It is estimated that for achieving such a level of herd immunity and exploiting its benefits 75-90% population needs to develop immunity

against SARS-CoV-2 assuming 80% vaccine efficacy and basic reproductive rate (R0) value between 2.5 to 3.5 [34].

However, it has been argued that immunity against COVID-19 may not last long, hence the possibility of protection against reinfection and achieving herd immunity through natural infection still remain a topic of debate [35]. Although, with the advent and availability of COVID-19 vaccines, the gap between the existing immunity level of country and the level required to achieve herd immunity seems plausible. India and other countries have already begun its vaccination drive against COVID-19, that gives hope to the mankind.

In conclusion the RT-PCR alone could not identify every SARS-CoV-2 infected individual. Rapid antibody assays may fill this gap and hence a combined approach could be beneficial. Also, the serological surveys project a higher proportion of population being exposed to COVID-19. These findings compel us to think about the plausibility of herd immunity in near future. Moreover, with the availability of vaccines give hope against COVID-19. Although, variability in serological response is governed by several factors and the underlying complex immune process is yet to be fully understood.

#### Abbreviation

SARS-CoV-2: Severe Acute Respiratory Syndrome – Corona Virus – 2, RT-PCR: Reverse Transcriptase – Polymerase Chain Reaction, COVID-19: Corona Virus Disease- 2019, ELISA: Enzyme-Linked Immunosorbent Assay, IgG/IgM: Immunoglobulin – G/M, WHO: World Health Organization, ICMR: Indian Council of Medical Research, RDT: Rapid Diagnostic Test, R0: Basic Reproductive Rate.

#### DECLARATION

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None.

##### Authors' Contributions

SB designed the study and coordinated all aspects of the research, including all steps of the manuscript preparation. SB and BP are responsible for the study concept, design, writing, reviewing, editing, and approving the manuscript in its final form. NV, SK, AD, and JG contributed to the study design, analysis, interpretation of data, writing the manuscript and reviewed and approved the final manuscript. All authors read and approved the final manuscript.

##### Ethics Approval and Consent to Participate

We conducted the research following the Declaration of Helsinki. The ethical protocol was approved by Institutional Ethics Committee of S. M.S. Medical College and Attached Hospitals, Jaipur (India).

##### Consent for Publication

Not applicable.

#### Competing Interest

The authors declare that they have no competing interests.

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