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Antibody Response in COVID-19 among Healthcare Workers

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Abstract

Objectives: To determine association between Polymerase Chain Reaction (PCR) and antibody positivity by assessing the antibody response in PCR positive Versus PCR negative COVID-19 exposed symptomatic/ asymptomatic healthcare workers.

Methods: A Total of 102 healthcare workers (HCW) were included in this cross-sectional study after written informed consent including doctors, nurses, laboratory and janitorial staff who were working in isolation ward admitted with symptomatic COVID-19 patients and their samples. Specimen swabs from posterior oropharyngeal wall and nasopharynx were taken and kept in viral transport medium to perform Polymerase Chain Reaction (PCR) testing of SARS-CoV-2 either at onset of symptoms or at 6 weeks (42 days) after first day of duty with COVID-19 patient and blood samples were drawn to measure the serum antibody response after recovery or at completion of 6 weeks (42 days) of their first duty in COVID-19 wards. Serum C- reactive protein (CRP) in mg/L was measured by immuno-turbidimetry in both groups at the time of PCR.

Results: Mean age of our study participants was 31 ± 8.9 years. Of 102 HCW, 60(58.8%) were males and 42(41.2%) were males; 42 (36.23%) were PCR positive and 60(63.76%) were PCR negative, 57(50.72%) had reactive antibodies and 45(49.28%) had non-reactive antibodies. Of 35 PCR positive subjects, 11 remained asymptomatic. There were 76% subjects who had positive PCR & reactive antibodies, 63.6% subjects with negative PCR and Non-reactive antibodies. Interestingly, (22)36.4% subjects had negative PCR but reactive antibodies. Likewise, 16.7% subjects had positive PCR but non-reactive antibodies. However, statistically moderate significant association (x2(1) =10.02; P=0.00) was found between PCR positivity and antibody positivity. Serum CRP in PCR positive and negative HCWs was 1.5 mg/L and 1 mg/L correspondingly.

Conclusion: Antibody response may be used as a screening tool for COVID-19 infection particularly in asymptomatic exposed subjects.

Keywords: Antibody; COVID 19; Health care workers; PCR

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Introduction

COVID-19 has been declared a Pandemic by World Health Organization (WHO) in March 2020 due to the rapid spread of disease outside china affecting a growing number of countries; about 218 countries have been affected worldwide including Pakistan [1]. With the start of infection in December last year in Wuhan city of China the source of infection was identified as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) [2].

Pakistan is dealing with huge burden of disease, with the first case reported in Pakistan on 26 February 2020. By 28 November 2020, 392356 confirmed cases have been reported in Pakistan with 7942 deaths [3]. HCWs are involved in management of the cases of this infectious disease. With increased working hours and working in a potentially infectious environment is fatiguing both mentally and physically. On 25 February 2020, China reported 3387 infected HCWs in Hubei alone, at least 18 of whom died, causing growing concern among HCWs [4].

For diagnosis of infection, two methodologies are used, reverse transcription Polymerase Chain Reaction (RT-PCR) which is considered gold standard. The diagnosis of COVID-19 is based on PCR testing of severe acute respiratory distress syndrome corona virus-2 (SARS-CoV-2) in nasopharyngeal/ oropharyngeal swab specimen of symptomatic patients [5]. This PCR testing takes longer time and may underrate the disease burden; it is expensive and requires trained staff. While second technique is antibody testing [6], which are formed in the body in response to virus and are required to encounter the infectious agent; antibody testing is easy to perform, fast and less expensive. Antibodies developed against SARS-CoV-2 may be used as a screening tool to assess the prevalence of COVID-19 infection; which can be overlooked by inadequate/ unreachable PCR testing particularly among asymptomatic patients. But sensitivity of antibody tests is too low in the first week since onset of symptoms to be considered for the diagnosis, but they complement other testing in individuals presenting later, when RT-PCR tests are negative, or are not done at all. Similarly Antibody testing can have a useful role for detecting previous SARS-CoV-2 infection if performed after more than 15 days after onset of symptoms. However, the duration of antibody rises is currently not clear, and we found very little data beyond 35 days post-symptom onset [7]. Antibody tests have been developed to detect IgG only, both IgG and IgM, or total antibodies. In a review of 54 available studies, mostly from China, the accuracy of pooled results for combination IgG/IgM tests was 91% at 15 to 21 days after onset of symptoms [8].

As Fast and accurate laboratory diagnosis of active COVID-19 infection is one of the cornerstones of pandemic control. With the numerous tests available in the market, the use of correct specimen type and laboratory testing technique in exact clinical situation remains a challenge [9]. The assessment of the clinical utility of these tests in different scenarios in COVID-19 is helpful in management of COVID-19 cases and early prediction of complications [10]. Further studies in this field are required to validate assays for precise diagnosis and newer biomarkers for monitoring treatment and progression of disease. In view of above present study was carried out to determine association between PCR and antibody positivity by assessing the antibody response in PCR positive vs PCR negative COVID-19 exposed symptomatic/ asymptomatic HCWs.

Materials and Methods

A total of 102 HCW were included in this cross-sectional study after written informed consent including doctors, nurses, laboratory and janitorial staff who were working in different wards with symptomatic COVID-19 patients and their samples. We performed antibody testing to see the development of antibodies in PCR positive HCWs and also in PCR negative HCW who were exposed to SARS COV-2 while working in closed contact with the COVID 19 positive. Specimen swabs from posterior oropharyngeal wall/ nasopharynx were taken and kept in viral transport medium to perform PCR testing of SARS-CoV-2 either at onset of symptoms or at 6 weeks (42 days) after first day of duty with COVID-19 patient and blood samples were drawn to measure the corresponding serum antibody response after recovery or at completion of 6 weeks (42 days) of their first duty in COVID-19 wards. Serum COVID-19 total antibody test was performed on fully automated chemiluminescence based immunoassay analyser Roche-COBAS 6000 with FDA approved kits.8 Pharyngeal swab RT- PCR was done on CFX-96 Biorad fully automated amplifier after RNA extraction on fully automated extractor- super extract Systaaq diagnostic products.5 Serum CRP (mg/L) was measured by immunoturbidimetry in both groups at the time of PCR test [11]. Chi-square was applied between string data for PCR and antibodies. P value of <0.05 was taken as significant.

Results

Total 102 health care workers were included in this cross-sectional study with mean age of 30.6 ± 8 comprising of 60(58.8%) females and 42(41.2%) males. 35(83.6%) COVID 19 PCR positive patients had developed reactive antibodies for COVID-19 while no antibodies were detected in 7(16.7%) with PCR positive COVID-19 subjects. In PCR negative group of HCW 22(36.3%) developed antibodies with no signs/ symptoms of COVID-19 while 38(63.7%) subjects had negative COVID-19 PCR and antibodies in their serum. Mean serum CRP in PCR positive HCWs was 1.5 mg/L and PCR negative HCWS was 1 mg/L **(Figure 1).**

Chi-square was applied between string data for PCR result and antibodies. The result was significant with P-value of 0.000. SPPS version 20.00 was used to analyse the results and chi-square test was applied to see the degree of association between PCR positivity and antibody response. A P-value <0.05 was taken as significant **(Table 1).**

Discussion

HCWs involved in management of COVID-19 positive individuals are most susceptible to get infected [12]. Our result suggests that there is a high possibility of patients to develop antibodies for COVID-19 if they acquire the infection. Development of antibodies due to COVID-19 and its use for diagnosis has also been evaluated in by Woo PC et al. suggesting that the development of antibodies can be used as a alternate marker for diagnosis of infection which was observed in this study also [13].

Similarly Chughtai OR et al. (n=154) studies young male policemen

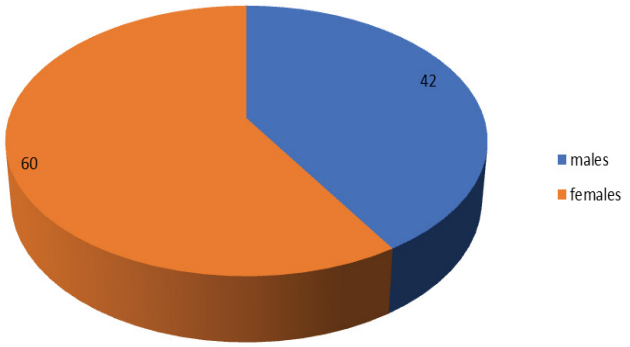

Figure 1 Gender distribution among participants (n=102).

Table 1 Antibody response in PCR positive & negative HCW (n=102).

Variables	Antibodies reactive	Antibodies non-reactive
PCR positive	35 (83.3%)	7 (16.7%)
PCR negative	22 (36.3%)	38 (63.7%)

(mean age 27 ± 3.8 years) to find out the prevalence of COVID-19 IgG antibodies among policemen doing duties at high risk areas of Lahore, Pakistan. Out of 154 subjects, 24 were reactive for COVID-19 IgG antibodies. These COVID-19 IgG reactive cases were asymptomatic. It was concluded that COVID-19 IgG antibody reactive cases may be asymptomatic which supports present study [14].

Similarly Meng QB et al. (n=652) studied suspected COVID-19 patients, out of them 237 (36%) had positive PCR, 311 (48%) were reactive for IgM and 592 (91%) had developed IgG. Using the RT-PCR results as a gold standard sensitivity, specificity & accuracy of IgM/ IgG combined tests for SARS-CoV-2 infection were 96%, 98% & 97% respectively [15]. Another Cohort Study done on detection of antibodies to COVID-19 suggested that antibodies response is different in different individuals, patients recovered from COVID-19 showed difference in the level of counterbalancing antibodies to SAR-COV-2 and it depends on many factors like age, CRP level and lymphocytes in blood which supports present study [16]. While majority of asymptomatic subjects and PCR negative also had no antibodies, but a small subset of HCW developed antibodies suggesting that it is possible to get an asymptomatic infection and there is a need to study the basis of such a response. Similarly a study conducted on patients coming for hemodialysis showed that about 40% of cases were positive for COVID-19 infection but were either asymptomatic and had Negative PCR results [17].

Bao et al. have concluded that COVID-19 IgG antibodies measurement in the population can gauge the number of individuals who have developed an immune response and represent subclinical mode of infection or past exposure to the virus and may also advocate recovery. Some of the recent studies have shown that these antibodies remain positive for at least 4 weeks [18]. Studies have shown that seroconversion is usually achieved after a median of 10 days for IgM and 14 days for IgG after start of symptoms. The maximum level of seroconversion can be seen at 2 weeks for IgM & at 3 to 6 weeks for IgG and by 7 weeks IgG shows maximum positivity; whereas, IgM starts to vanish [19].

In present study we found that 83% PCR positive HCWs were found to be reactive for anti SARS COV-2 antibodies and 36% PCR negative HCWs had developed antibodies which are supported by other researchers. Recently, an epidemiological study was carried out in Spain by Polan M et al. to find out frequency of people anti SARS COV-2 antibodies among general population and to estimate the spread of Pandemic across the country. More than 35,000 household individuals were selected through two-stage random sampling. 5.0% individuals were found to be reactive for anti SARS COV-2 antibodies; and 33% of them were asymptomatic [20]. Young et al. used serological testing in Singapore to trace PCR negative COVID-19 cases and was useful to limit the spread of infection by providing an estimate in the community [21].

Zhao J et al. have revealed that SARS CoV-2 IgG antibodies were positive in >90% of COVID-19 patients 2 weeks after the onset of symptoms which also supports present study [22].

A recent study conducted in the city of Wuhan, China estimated IgG and IgM levels in >17,000 persons and found a seropositivity of 3.8% in different cohorts. It was found that patients regularly visiting the hospitals and HCW had higher seroprevalence as compared to the general population which is in accordance with present study [23]. Similarly Sood et al. found a seroprevalence of 4.6% in a serological survey in California [24] and Bendavid et al. found seroprevalence of COVID-19 IgG upto 2.8% in Santa Clara County and stated that infection may be more widespread than indicated by the number of PCR confirmed cases only which is also in accordance with present study [25].

Conclusion

Antibody response may be used as a screening tool for COVID-19 infection particularly in asymptomatic exposed subjects.

Recommendation

There is a need to study the basis of antibody response with reference to immune response and genetic factors involved in it.

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Conflict of Interest

All authors declare no conflict of interest regarding the publication of this paper.

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