European Journal of Molecular & Clinical Medicine

ISSN 2515-8260 Volume 09, Issue 02, 2022

Antibody response in healthcare workers to COVISHIELD vaccination in a tertiary care hospital

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Abstract

Background: SARS CoV-2 infection has become a major public health concern. India started Covid-19 vaccination from January 16, 2021, after the approval of two candidate vaccines namely COVISHIELD ™ and COVAXIN ™. The present study was conducted to see the neutralizing antibody response to trimeric S protein of SARS CoV-2 in health care workers (HCWs) with 2 doses of COVISHIELD vaccination in a tertiary care hospital.
Methodology: A prospective cohort study was conducted among 156 healthy adult health care workers in a tertiary care centre, vaccinated during January-March 2021. They were divided into two groups, the first group comprised of individuals who were previously RT-PCR positive (n=36) for SARS CoV-2, and second group comprised of those who were RT-PCR negative (n=120). Blood samples were collected from all participants, the first sample on the day of vaccination, second sample after 4 weeks of vaccination, and third after 8 weeks of vaccination to measure the IgG antibodies against the SARS CoV-2 'S' protein using a chemiluminescent quantitative immunoassay.
Results: The spike protein-specific IgG antibody titre was demonstrated reactive cut-off in 98.3% of the participants after 2 doses of vaccine. The median antibody titre declined from 710.5 (IQR, 338.5-1577.5) to 266 (IQR, 116-557.75) in RT-PCR positive HCWs after 8 weeks of vaccination whereas it increased from 45.1 (IQR, 31.475-76.575) to 83.4 (IQR, 52.075-104) in RT-PCR negative HCWs.
Conclusion: We could demonstrate the development of an adequate spike protein-specific IgG titre against SARS CoV-2 following vaccination with 2 doses of COVISHIELD in HCWs.

Keywords: SARS CoV-2, Spike protein, IgG Antibodies, COVISHIELD, Vaccination, RT-PCR, Immunoassay

Introduction

SARS CoV-2 is the causative organism of COVID 19 pandemic, and this has recently created a worldwide crisis. The pandemic started in January 2019, has spread to almost all countries and we are still not seeing the end of it. SARS CoV-2 is a novel virus of *Betacorona* virus genus, this has a spike protein on its surface that bind to the human angiotensin converting enzyme 2 (ACE2) protein receptors. This binding helps the virus in its entry into the host cell.

ISSN 2515-8260 Volume 09, Issue 02, 2022

The effects of the disease are due to the replication of virus and the response of the host's immune system to the virus. The coronavirus neutralizing IgM and IgG antibodies are produced after 1-2 weeks of natural infection. They primarily target the trimeric spike (S) glycoproteins on the viral surface [1]. These neutralising antibodies against spike protein are also produced after vaccination.

Many pharmaceutical companies of the world are making enormous efforts to develop safe and effective vaccines against COVID-19. To assess the safety and efficacy of newer vaccine candidates, rapid clinical trials are being undertaken [2]. More than 200 vaccines are under development with COVID-19, and a few have finished phase-3 trials and approved for emergency use. The vaccines developed by Pfizer, Moderna, Johnson & Johnson, AstraZeneca are approved for emergency use [3]. In India, three vaccines have been approved on date for emergency use-COVISHIELD, COVAXIN and Sputnik V [4, 5]. All these vaccines have reported 70-95% of efficacy.

A suitable measure of vaccine-induced immunity is the estimation of protective antibody titres after vaccination. The protective antibodies are ideally assessed by plaque neutralisation assays. However, once the specific types of neutralising antibodies are identified, they can be quantified by ELISA or CLIA. The neutralizing antibodies, especially the ones produced against the spike protein of SARS CoV-2, have shown correlation with protection against COVID-19 disease [7]. These antibody responses to the vaccine are easily quantified by assays in lab [6]. We wanted to see the neutralizing antibody response to trimeric S protein of SARS CoV-2 in health care workers (HCWs) to 2 doses of COVISHIELD vaccination in a tertiary care Hospital.

Materials and Methods

After obtaining Institutional Ethical Committee approval, this prospective cohort study was carried out in a tertiary care hospital in Lucknow from January to March 2021. A total of 156 healthy, adult HCWs were enrolled and were divided into two groups, the first group comprised of individuals who were previously RT-PCR positive (n=36) for SARS CoV-2, and the second group comprised of those who were RT-PCR negative (N=120).

Informed consent was taken from all participants, and they were administered two doses of COVISHIELD {ChAdOx1 nCoV-19 Corona Virus Vaccine (Recombinant) intramuscularly. The time interval between the two doses was 4 weeks as advised by ICMR initially. All those participants who were previously RT-PCR positive were vaccinated after 1 month of being symptom-free. Sequential blood samples were collected from all participants, the first sample on the day of vaccination, the second sample after 4 weeks of vaccination, and the third after 8 weeks of vaccination.

Serum was extracted from all samples and processed immediately after collection. The IgG antibodies against SARS CoV-2 'S' protein were determined using chemiluminescent quantitative immunoassay with LIAISON® SARS-CoV-2 Trimeric S IgG assay (DIASORIN). The clinical sensitivity and specificity of the assay were 98.7% and 99.5%, respectively. The kit had a correlation with microneutralization test showing PPA of 100% and NPA of 96.9%. Antibody titre of 14 AU/mL was considered as a reactive cut-off.

The IgG titres of the two groups were determined and statistical analyses were performed using SPSS Version 25 (IBM). Continuous variables were expressed as median (IQR) and were compared with Mann-Whitney *U*-test. Categorical variables were expressed as numbers (%) and were compared by Fisher's exact test. A p value <0.05 was considered statistically significant.

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Results

The median age of these participants was 41 years (IQR, 32-46 years). All RT-PCR positive HCWs cohorts had an antibody titres reactive cut-off at the time of first dose of vaccination. Median antibody titre in RT-PCR positive HCWs at the time of vaccination with the first dose was 44.5 (IQR, 31-114). Median antibody titre in RT-PCR positive HCWs after 4 weeks of vaccination was 710.5 (IQR, 338.5-1577.5). The median antibody titre declined from 710.5 (IQR, 338.5-1577.5) to 266 (IQR, 116-557.75) in RT-PCR positive HCWs after 8 weeks of vaccination (Figure 1). All RT-PCR positive HCWs maintained an antibody titres reactive cut-off of 14 AU/mL for 8 weeks after vaccination.

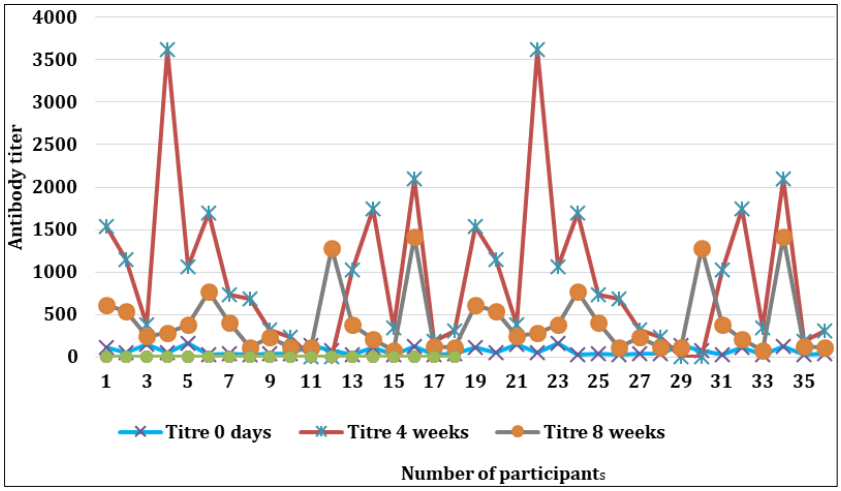

Fig 1: Antibody titer in RT-PCR positive HCWs

In all RT-PCR Negative HCWs, the antibody titre was below the reactive cut-off at the time of vaccination. The median antibody titre in RT-PCR negative HCWs at the time of vaccination was 0.088 (IQR, 0.083-0.165). After 4 weeks of vaccination, 91.6% of RT-PCR negative HCWs developed an antibody titres reactive cut-off respectively. Median antibody titre in RT-PCR negative HCWs after 4 weeks of vaccination was 45.1 (IQR, 31.475-76.575). After 8 weeks of vaccination, median antibody titre in RT-PCR negative HCWs increased from 45.1 (IQR, 31.475-76.575) to 83.4 (IQR, 52.075-104). After 8 weeks of vaccination, 98.3% of HCWs generated an antibody titres reactive cut-off (Figure 2). All participants except one RT-PCR negative health care worker maintained an antibody titres reactive cut-off for 8 weeks after vaccination.

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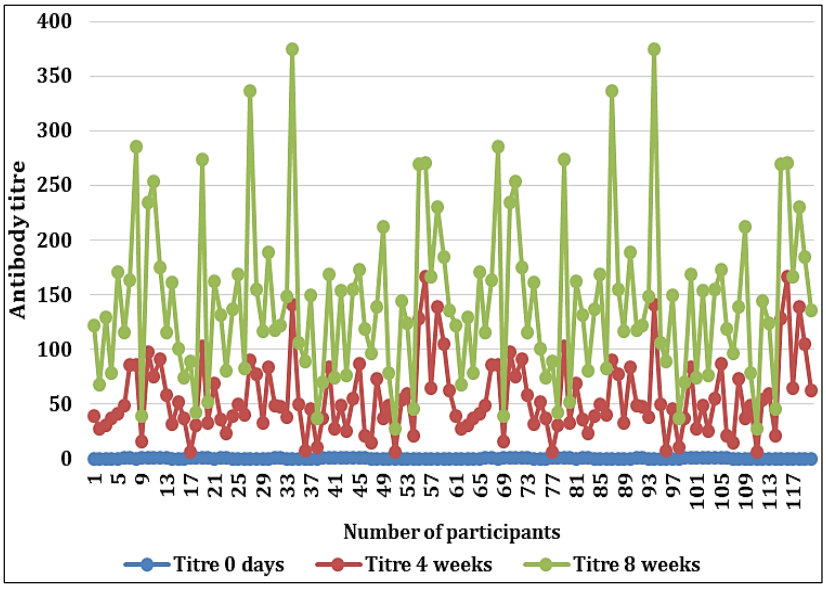

Fig 2: Antibody titer in RT-PCR Negative HCWs

Using Fisher's exact test, there is no statistically significant association between the two groups in the generation of antibody titres cut off values following 2 doses of vaccination. The *p* values after 4 weeks and 8 weeks of vaccination are 0.568 and 0.999, respectively (Table 1).

Table 1: Association between two groups in the generation of antibody titres cut off values following 2 doses of vaccination

Cohort	Median antibody titre (IQR)		
	At the time of Vaccination	After 4 Weeks of Vaccination	After 8 weeks of Vaccination
RT-PCR Positive	44.5 (IQR, 31-114)	710.5 (IQR, 338.5-1577.5)	266 (IQR, 116-557.75)
RT-PCR Negative	0.088 (IQR, 0.083-0.165)	45.1 (IQR, 31.475-76.575)	83.4 (IQR, 52.075-104)

Discussion

The COVID-19 pandemic presents an unprecedented health care challenge globally. It is still uncertain how individuals are developing enduring immunity following natural infection and vaccination against SARS CoV-2. People who have survived after the SARS CoV-2 infection when checked for immunity, about 90% had virus-neutralising antibodies [8, 9]. To combat SARS CoV-2, development of neutralising antibodies preferably through vaccination is required. Antibody kinetic profiles varies widely with patients, some display inclining neutralizing antibody levels while others develop constant or fluctuating levels [10, 11].

In present study, only 23% of HCWs (N=18) were infected (RT-PCR positive) with SARS CoV-2 during the first wave (June to Dec 2020) of COVID-19 in India. These RT-PCR positive cohorts had a spike protein specific IgG titre above the reactive cut-off before the first dose of vaccination and it remained above the reactive cut-off after the first and second dose. After 4 weeks of the first dose of vaccination, the increases in antibody titres were notably higher in the RT-PCR positive cohort of HCWs compared to RT-PCR Negative cohort. After the second dose of vaccine, the median antibody titre (AU/mL) of RT-PCR positive HCWs declined from 710.5 to 266. This finding is in concordance with the study conducted by Ujjainia *et al*. in New Delhi for monitoring COVISHIELD vaccination program of seropositive HCWs. They reported an increase in median antibody levels after the first dose and it remained relatively at the same levels after the second dose of vaccine [12].

In the RT-PCR Negative cohort, after the first and second doses, spike protein-specific IgG

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antibodies were detected above the reactive cut-off of 14 AU/mL in 91.6% (n=110) and 98.3% (n=118) of HCWs respectively. After the second dose of vaccine, the median antibody titre (AU/mL) increased from 45.1 to 83.4. Multicentric study conducted by Ewer *et al*. in U.K among ChAdOx1 n-Cov-19 vaccine trial participants reported a rose of anti-spike IgG response by day 28 and it boosted following a second dose of vaccine [13, 14]. Another study conducted in New Delhi reported seroconversion in 98% of seronegative HCWs with the first dose of COVISHIELD vaccine [12]. Cross sectional study conducted among SARS-CoV-2 naïve HCWs in West Bengal for antibody response after first dose of COVISHIELD vaccine reported seroconversion in 77.2% of participants and history of SARS-CoV-2 infection elicited a significantly greater median antibody titre compared to SARS-CoV-2 naïve (400.0 vs. 48.0 AU/ml) [15].

In current study, infection-induced immunity got boosted up after vaccination, suggesting that infection-induced and vaccination induced immune response are complimentary. Jabal *et al*. also made similar observations in their study [16].

The severity and complications of COVID-19 in vaccinated individuals are likely to be reduced due to the complementary nature of the vaccine and infection-induced immune responses. The spike protein-specific IgG antibody titres never fell below the reactive cut-off in 98.7% of the participants during our study frame, suggesting that it will be maintained above the reactive cut-off for at least 8 weeks. It has been observed that after natural infection and vaccination, waning of antibodies occurs after 3-6 months [10]. Few studies suggested better induction of immune response by AstraZeneca/Oxford vaccine with longer interval between vaccine doses. It is also recommended 8-12 weeks interval between 2 doses of COVISHIELD for better generation of immune response [12, 17, 18, 19].

Conclusion

In present study, we could demonstrate the development of an adequate spike protein-specific IgG titre against SARS CoV-2 following vaccination with 2 doses of COVISHIELD in HCWs. Seropositive individuals had developed a robust immune response after the first dose of vaccination, these individuals might require only a single dose. This still needs further evaluation with a larger sample size. It is also a need to be studied that whether antibody titres achieved after COVISHIELD offer protection against COVID-19 disease caused by mutants/variants of SARS CoV-2.

Acknowledgments

We thank all lab staff and administrative authorities of our hospital for making this study possible.

Competing interests

The authors declare that there are no competing interests.

Data availability

Data available on request from the authors.

Author’s contributions

All authors contributed equally to all aspects of the study.

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