

Antibody Response to SARS-COV-2 Vaccination in Healthcare Workers of Uttarakhand: A Prospective Follow-up Study

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Abstract

Background: Countries around the world are now racing to vaccinate people against SARS-CoV-2, the virus that causes COVID-19. The Government of India also rolled out its vaccination drive from 16th January '2021.

Aims: To estimate the antibody response of the COVID-19 vaccine in the form of SARS-COV-2 IgG antibodies in vaccinated healthcare workers.

Methods: Prospective follow-up was study conducted on healthcare workers (HCWs) of a Medical college in Dehradun, Uttarakhand. Healthcare workers who have been vaccinated for COVID-19 were tested for SARS-CoV-2-IgG antibodies at regular intervals i.e at 4 weeks after the 1st dose and then again at 4 weeks after the 2nd dose. The third sample was taken 6 months after the 2nd dose.

Results: A total of 302 HCWs were enrolled in the study who gave their samples for IgG antibody estimation after the covishield vaccine. After 4 weeks of completion of both doses, 96% HCWs formed SARS-COV-2 IgG antibodies, whereas 4% didn't. Then after 6 months of follow-up, 14% HCWs have become negative for antibodies and better immunity is seen in people who also got infected with COVID-19 during this time.

Conclusion: This study concludes that the immunity gained after vaccination is waning off in around 6 months and there is a need for a booster dose, especially for people at high risk. The infection control practices still play a crucial role in the prevention of this deadly disease.

Keywords: Humans, COVID-19 Vaccines, Immunoglobulin G, SARS-CoV-2, ChAdOx1 nCoV-19, Follow-Up Studies, COVID-19, Prospective Studies, Antibodies, Viral vaccination, Vaccines, Government.

INTRODUCTION

World is facing an ongoing pandemic caused by a novel virus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which was first identified in December 2019 in Wuhan, China.^[1] After its escalating spread globally, even in India, the total number of cases is 1 crore as reported on 5th February '2020 and active cases reported are 1.4% of the total and deaths also 1.43% of total cases till date as per MOHFW. According to WHO, the virus spreads mainly through the air when people are near each other.^[2]

To respond quickly and effectively to the COVID-19 pandemic, a broad range of vaccines have come into the global

market. These include viral-vectored, protein subunit, nucleic acid (DNA, RNA), live attenuated and inactivated vaccines. The Government of India also rolled out its vaccination drive from 16th January '2021 by giving regulatory licenses to two vaccines i.e. Covishield, ChAdOx1 nCoV-19 Coronavirus recombinant vaccine developed by Serum Institute of India and Covaxin, an inactivated vaccine developed by Bharat

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Table 1: Level of SARS-COV 2 IgG Antibody titre in relation to Gender

Gender	No. of subjects N (%)	level of AB titre High N (%)	level of AB titre Low N (%)	level of AB titre Negative N (%)	p-value
Male	232(76.8)	80(34.5)	133(57.3)	19(8.2)	0.713
Female	70(23.2)	21(30)	44(62.9)	5(7.1)	
Total	302	101(33.4)	177(58.6)	24(8)	

Biotech. A study done by A Widge showed that the mRNA-1273 vaccine has the potential to provide durable humoral immunity.^[3] Some workers have demonstrated induction of SARS-CoV-2 antibodies after vaccination after the second dose.^[4]

The COVID-19 pandemic places healthcare workers (HCWs) at high risk of catching COVID-19 infection. So, Government has planned to vaccinate this workforce on a priority basis. Currently, there are no defined threshold values of antibody levels for protection against COVID-19 infection, and hence the parameters required for vaccine efficacy remain undefined.^[4] Hence this study is planned to estimate the antibody response of the COVID-19 vaccine in the form of “SARS-COV-2 IgG antibodies in vaccinated healthcare workers”.

METHODOLOGY

It was a prospective follow-up study conducted from January 2021 to October 2021 on healthcare workers of the Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Dehradun, Uttarakhand. 302 HCWs who have been vaccinated for COVID-19 were tested for “SARS-CoV-2-IgG antibodies” at regular intervals i.e at 4 weeks after the 1st dose and then again at 4 weeks after the 2nd dose. The third sample was taken 6 months after the 2nd dose. Out of 302, only 155 gave their second antibody estimation sample, and 102 gave the third sample 50 controls were taken in the study, including healthcare workers, who were neither infected with COVID-19 nor vaccinated in the same study duration. A case reporting form was used to collect demographic and clinical data. Anti-SARS-CoV-2-IgG antibodies present in the sample bind with SARS-CoV-2 spike protein coated on wells. This antigen-antibody complex is detected in sera using a semi-quantitative chemiluminescence immunoassay (CLIA) by VITROS, ortho clinical diagnostics, Raritan, NJ, USA. The assay is done by the automated system and is approved by ICMR and US-FDA. As per the kit instructions, a value more than 1 is considered positive, i.e., SARS-COV-2 antibodies are formed. Less than 1 value is negative, i.e., antibodies not formed. Values between 1–12 are considered as low titer, whereas values more than 12 are considered as high titer as mentioned in kit literature.

Data Collection

Convenient sampling method was used for data collection. A case reporting form was used to collect demographic and

clinical data of health care workers. Total 5 mL of blood sample was collected in the plain vial after centrifugation, serum was separated and sample was processed in the serology section.

Sample Size

Samples 302 were taken. Healthcare workers who were willing to participate and gave written informed consent for the study were included.

Inclusion criteria: Healthcare workers who gave consent to participate in the study and could undertake follow-up sampling.

Exclusion criteria: Healthcare workers who are not undergoing vaccination and not willing to participate.

Consent and Ethics Approval

Informed written consent was obtained from all participants in this study and approval from the Institutional ethics committee was obtained. (Ref.: HIMS/RC/2021/87 Dated: 27/04/20221)

Statistical Analysis

All data were tabulated and analyzed in an excel sheet. Analysis of responses is presented in the form of frequency and percentages. The chi-square test is used to assess the association between categorical variables. For comparison of means between 2 groups, an independent T-test is used. The ANOVA test is used to compare means in more than 2 groups. Descriptive statistics is performed using SPSS version 20.

RESULTS

A total of 302 health care workers were enrolled in the study who gave their samples for IgG antibody estimation after 4 to 5 weeks of the first dose of the covishield vaccine. Of these 302 HCWs, 92% (278) had produced antibodies after vaccination, whereas 8% did not form antibodies after 4 weeks of the first vaccination dose. Out of these 278, 33.4% formed antibodies in significant titres whereas 58.6% formed in low titres. Table 1 shows the level of SARS-COV 2 IgG antibody titre in relation to gender, it was not found to be statistically significant (p -value =0.713).

Table 2 shows level of SARS-COV 2 IgG antibody titre in relation to age group (p -value =0.034). It was found to be statistically significant.

Table 3 shows the level of SARS-COV 2 IgG antibody titre in relation to profession, here also no statistical significance was seen (p -value =0.690).

The level of SARS-COV 2 IgG antibody titre in relation to the blood group, no significance was seen (p -value =0.115).

Out of 302 HCWs who gave their samples after the first dose of vaccine, 155 further followed up in the study and gave their samples 4 to 5 weeks after the second dose of vaccine. When a comparison was done in these 155 subjects, 95 (61.3%) showed an increase in antibody level after the second dose, 42 (27.1%) had the almost same level of antibodies and 18 (11.6%)

Table 2: Level of SARS-COV 2 IgG Antibody titre in relation to age group

Age group	No. of subjects N (%)	level of AB titre High N (%)	level of AB titre Low N (%)	level of AB titre Negative N (%)	<i>p-value</i>
20–30	49 (16.2)	22 (44.9)	23 (46.9)	4 (8.1)	
31–40	131 (43.4)	47 (35.9)	79 (60.3)	5 (3.8)	
41–50	86 (28.5)	22 (25.6)	55 (64)	9 (10.4)	0.034
51–60	28 (9.3)	10 (35.7)	14 (50)	4 (14.3)	
> 60	8 (2.6)	0 (0)	6 (75)	2 (25)	
TOTAL	302	101 (33.4)	177 (58.6)	24 (8)	

Table 3: Level of SARS-COV 2 IgG Antibody titre in relation to the profession

Profession	No. of subjects N (%)	level of AB titre High N (%)	level of AB titre Low N (%)	level of AB titre Negative N (%)	<i>p-value</i>
Doctors	91(30.2)	24(26.4)	58(63.7)	9(9.9)	
Nurses	76(25.2)	26(34.2)	45(59.2)	5(6.6)	
Technicians	57(18.8)	20(35.1)	34(59.6)	3(5.3)	0.690
Housekeepers, security staff, Ward attendants etc	30(9.9)	10(33.3)	17(56.6)	3(10)	
Others (office staff, clerks etc)	48(15.9)	21(43.7)	23(47.9)	4(8.3)	
Total	302	101	177	24	

Table 4: Level of SARS-COV 2 IgG Antibody titre at different intervals of study

	<i>Antibody titre More than 1 (protective titre)</i>	<i>Antibody titre less than 1 (non- protective titre)</i>	<i>Mean Antibody levels</i>	<i>Total</i>
1 st sample	278 (92%)	24 (8%)	9.4	302
2 nd sample	149 (96 %)	6 (4%)	10.9	155
3 rd sample	88 (86%)	14 (14%)	8.8	102

Table 5: Comparison of levels of SARS-COV 2 IgG antibody titre in COVID-positive versus COVID-negative study subjects

	<i>Ab titre (high)</i>	<i>Ab titre (low)</i>	<i>p-value</i>
COVID + ve	18	7	25
COVID - ve	20	57	77
Total	38	64	102

showed a decrease in antibody level. Gender, age groups and profession did not show any statistical significance in these 155 subjects.

After 6 months of completion of vaccine doses, blood samples were collected again and SARS-COV-2 IgG antibodies were estimated. Table 4 shows the trend of antibody titres at different study intervals. In between the estimation of the 2nd and 3rd sample, many of our study subjects got infected with COVID-19 infection during the 2nd wave of corona crises; hence the antibody levels were compared between HCWs who were infected with those who were non-infected. Table 5 shows this comparison and the level of antibodies were found to be statistically higher in COVID infected group when compared to the non-COVID group.

Our control group of 50 HCWs who were neither vaccinated nor got COVID infection was also tested for SARS-COV-2 IgG antibodies. Only 1 out of 50 showed positive antibody test results indicating the low incidence of asymptomatic infection and antibody formation.

We would also like to state our study subjects didn't suffer any severe adverse effects from the two doses of the COVID vaccine. Only mild side effects like low-grade fever and pain at the injection site were noted and that too for 2 to 3 days.

DISCUSSION

Countries around the world are now racing to vaccinate their citizens against SARS-CoV-2, the virus that causes COVID-19. It is one of the most ambitious vaccination programs ever. All the healthcare workers in this study received the covishield vaccine.

A pan-India study was conducted on 515 vaccinated healthcare workers 425 received covishield and 90 received Covaxin. Data from 13 states and 22 cities showed that the vaccines could generate an immune response in 95% of recipients 21–36 days after the second dose. Seropositivity was observed in 98% of those immunized with covishield as opposed to 80% of covaxin recipients. This study was published in Times of India, Bombay edition on 7th June'2021.^[5] Our study also showed seropositivity of 96% after 4 weeks of two doses of the COVID vaccine. It also pointed out that factors such as gender, BMI and other co-morbidities didn't seem to play much of a role as also seen in our study. Another similar study conducted by healthcare workers in Turkey showed that 99.6% of the volunteers developed seropositivity 4 weeks after the second dose of the vaccine.^[6]

A study from China that followed their healthcare workers for antibody response to COVID vaccine concluded that antibody response for the CoronaVac vaccine was intense and comprehensive with a 95.08% neutralizing seropositivity rate, while decay was also obvious after 160 days.^[7] Another study from Pakistan also showed similar decline in antibody levels. High antibody titer levels were observed in 84% (21/25) at 61 to 90 days of vaccination, which declined to 80% (20/25) after 91 to 120 days and to 57.1% (32/56) after >120 days of vaccination.^[8]

Our study also focuses on the issue that antibody levels after 6 months of complete vaccination (2 doses of vaccine) have dropped. 86% HCWs who received vaccine still have protective antibody titres and 14% have non-protective titres after 180 days of full vaccination. Therefore, booster doses should be considered in the vaccine strategies.

Our study also did a comparison between the levels of SARS-COV 2 IgG antibody titres in COVID-positive versus COVID-negative study subjects. It showed statistical significance in the levels of antibodies (0.0001) seen in HCWs who got a natural infection with SARS-COV-2. A study by Ahmet Soysal *et al.* also showed significantly higher levels of antibody titers in HCWs with a previous natural infection (median 1220 AU/mL, range: 202–10328 AU/mL) than in uninfected HCWs (median: 913 AU/mL, range: 2.8–15547 AU/mL, $p = .032$).^[9]

No major side effects were reported after vaccination in our study as also reported by study conducted in Israel by N E Raz *et al.*^[10]

This study has certain limitations like it includes short follow-up, small sample size and lack of cellular immunity testing. Larger samples from diverse populations are needed to account for individual variations in immune responses to infection and vaccination.

CONCLUSION

This study emphasizes on the waning immunity provided by the vaccine. Many subjects have nil antibodies after around 6–9 months of complete vaccination i.e, after 2 doses of vaccine. A gap of 3 months or 84 days between 2 doses is better than a gap of just 28 days. The immunity will last longer in people with more gaps between 2 doses. We would like to recommend from our study that a booster dose or precautionary dose is a must for high-risk groups like all frontline workers, aged people and persons with co-morbidities. The overall impact of this study is that the immunity provided by the COVID vaccine seems to be protective for the specified time period and emphasis should also be given to the preventive measures and infection control practices.

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CONFLICTS OF INTEREST

There are no conflicts of interest.

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