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Original Research Article

Comparative Longitudinal Study of SARS-CoV-2 Antibody Responses Induced by Different COVID-19 Vaccines

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Abstract:

Background: The COVID-19 pandemic prompted rapid vaccine development to curb disease transmission and reduce mortality. India initiated its vaccination drive in January 2021 using Covishield, Covaxin, and later, Sputnik V. Monitoring post-vaccination antibody responses is essential to understand vaccine-induced immunity.

Aim: To evaluate the SARS-CoV-2 antibody response in healthcare workers following COVID-19 vaccination and analyze the temporal dynamics of humoral immunity.

Methodology: This longitudinal cross-sectional study was conducted at Sri Krishna Medical College and Hospital, Muzaffarpur, Bihar, from April 2020 to march 2021.

Ninety-two healthcare workers who received at least one dose of COVID-19 vaccine were enrolled. Participants were grouped based on their vaccination status: Group 1 (single dose) and Group 2 (both doses). Serum samples were collected at baseline and three months later. Antibody titres were measured using the Elecsys Anti-SARS-CoV-2S electrochemiluminescence immunoassay. Non-parametric tests were used for statistical analysis.

Results: In Group 1, the median antibody titre significantly decreased from 9,500 U/ml at 4 weeks post-first dose to 2,150 U/ml at 18 weeks ($p < 0.001$), indicating waning immunity. The overall seropositivity rate was 96.5% after the first dose and 100% after the second. Breakthrough infections were mild. Adverse events following immunization (AEFI) were more frequent after the first dose but were generally mild. No correlation was found between antibody levels and AEFI.

Conclusion: COVID-19 vaccines elicit a strong initial antibody response that diminishes over time, emphasizing the need for booster doses and ongoing surveillance to sustain immunity.

Keywords: Antibody response, Booster dose, COVID-19, Covishield, Healthcare workers, Vaccination, Waning Immunity.

Introduction

The novel coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been a historic health challenge since its outbreak in late 2019 [1]. It spread rapidly pan-continently and caused high morbidity and death that strained health facilities and daily life and disrupted economic stability. Out of the global health emergency that was caused by the virus, scientific and health entities gave the development of effective vaccines the priority to stop the transmission of the virus, to lessen the severity of the disease, and ultimately confer herd immunity [2]. Vaccine deployment was among the major measures in curbing the effects of the epidemic with nations initiating large-scale immunization drives to vaccinate their populations.

India introduced its immunization campaign against COVID-19 on January 16, 2021, with the use of two vaccines under emergency use authorization (EUA) in the initial phase of roll-out: Covishield (ChAdOx1 nCoV-19 also called AZD1222) developed by AstraZeneca and produced by Serum Institute of India and Covaxin (BBV-152) being inactivated virus-based vaccine developed by Bharat Biotech of home-grown origin. Sputnik V a Russian viral vector vaccine developed by Russia's Gamaleya Research Institute was also cleared with EUA in April 2021 [3]. These vaccines from multiple platforms were rolled out aggressively through government routes to protect priority population of health-care professionals, front-line health-care personnel and vulnerable population categories. Roll-out of these vaccines was a milestone in the war against COVID-19 in India

because vaccine was the most potent weapon against serious end-organ manifestations and virus transmission slowdown.

A significant part of evaluating vaccine efficacy is in examining the antibody response elicited after vaccination [4]. Neutralizing antibodies and antibodies in general play a significant role in hindering virus entry into host cells and reducing infection. ELISA is one such serological assay that is widely employed to measure the quantity and concentration of these antibodies. In addition to that, virus neutralization assays also determine the functional activity of these antibodies to suppress the virus from replicating. These immunological reagents play a significant role in monitoring long-term immune responses and determining vaccine-induced duration of protection [5].

Emerging evidence indicates that the antibody response following immunization may be inhomogeneous among individuals and may wane over time and, therefore, may result in decreased immune protection [6]. Models have proposed that vaccines protect individuals effectively in the early months following immunization, but antibody levels especially neutralizing antibodies decay over time and may require the use of booster injections to maintain immunity. Waning immunity is of significant concern in the context of newly emergent SARS-CoV-2 variants that may partially resist neutralization by vaccine-induced antibodies and thus add to the difficulties of controlling the pandemic [7].

Although clinical trials of COVID-19 vaccines did show that the vaccines were effective, long-term immunity responses seen in real-world contexts are limited to date [8]. Real-world environments differ from clinical trial settings in the diversity of populations studied, risk of exposure to the virus, and health conditions prior to infection. Thus, it is critical to conduct longitudinal studies of subjects in the long term following immunization to establish evidence of the duration and level of the antibody response. These studies can offer insights into the duration of immunity, whether modified by factors like age, comorbidities, or type of vaccine, and whether the vaccine needs to be boosted to offer adequate protection.

Here, the context, longitudinal study is intended to examine the SARS-CoV-2 antibody response to COVID-19 vaccine in a real-world scenario [9]. Through the recording of antibody level fluctuations at different points of time following the vaccine administration, the study will also look to fill in the most important gaps in current knowledge about the durability of humoral immunity. Knowledge of the antibody production and decline over time will go a long way in informing public health policy on the administration of booster vaccinations, vaccine-induced immunity surveillance, and response to future outbreaks. This study will also assist in evaluating the relative immunogenicity of vaccines being used in Indian populations and gauge their effectiveness in different groups of the population.

In conclusion, monitoring the antibody response post-vaccination is vital to inform and adapt vaccination strategies in response to the evolving nature of the pandemic. The findings from longitudinal studies such as this one will not only enhance our scientific understanding of post-vaccine immune responses but also guide evidence-based policy decisions on the timing and necessity of booster doses. As the world continues to battle COVID-19 and its variants, long-term data on vaccine-induced immunity will remain an essential component in the global effort to bring the pandemic under control.

Methodology

Study Design: This was a longitudinal cross-sectional study conducted in the Department of Community Medicine, Sri Krishna Medical College and Hospital Muzaffarpur, Bihar, India from April 2020 to March 2021.

Sample Size: A total of 92 healthcare workers were enrolled in the study.

Inclusion and Exclusion Criteria

Inclusion Criteria:

- Doctors, nurses, security staff, and other personnel working at the DCH.
- Individuals who had received at least one dose of a COVID-19 vaccine.
- Participants who gave informed consent and were available for follow-up.

Exclusion Criteria:

- Individuals who had not taken any dose of the COVID-19 vaccine.
- Those who did not consent to participate in the study or were unavailable for follow-up.

Procedure

Participants were divided into two groups:

- **Group 1:** Participants who had received only the first dose of the COVID-19 vaccine, with at least three weeks elapsed since vaccination, and who had not taken the second dose at the time of first blood sample collection.
- **Group 2:** Participants who had received both doses of the COVID-19 vaccine, with at least two weeks elapsed since the second dose before the first blood sample was collected.

All participants underwent phlebotomy in March 2021 for serum collection. Antibody testing was conducted using the 'Elecsys Anti-SARS-CoV-2S'

electrochemiluminescence immunoassay (ECLIA), which detects antibodies to the receptor-binding domain (RBD) of the SARS-CoV-2 spike (S) protein. The assay used had a sensitivity of 98.8% (CI: 98.1–99.3) and specificity of 99.9% (CI: 99.9–100). Antibody titres were interpreted as follows:

- Positive: ≥ 0.80 U/mL
- Negative: < 0.80 U/mL

Follow-up

After three months, a follow-up blood sample was collected from both groups to reassess the antibody response. Additionally, participants were asked about:

- Any history of COVID-19 infection since the first sample collection.
- History of receiving the second dose of vaccine for those in Group 1.

Statistical Analysis: Data entry was carried out using Microsoft Excel 2010, and all statistical analyses were performed using IBM SPSS Statistics for Windows, version 27. Before analysis, the data were assessed for normality to determine the appropriate statistical tests. As the data did not follow a normal distribution, non-parametric tests were employed. These included the Chi-square test, Fisher's exact test, Mann–Whitney U test, and Wilcoxon signed ranks test. All statistical tests were two-sided to ensure a balanced interpretation. Continuous variables were summarized as median along with the interquartile range (IQR), while categorical variables were presented in terms of number and percentage.

Result

Table 1 shows the sociodemographic profile of 92 HCWs in Group 1, which was divided between 39 males and 53 females. Participants were predominantly between the age group of 21–30 years (62.0%), with a higher representation of females (73.6%) than males (46.2%) in that age group. HCWs were predominantly nurses (31.5%) or "Others" (44.6%), with females being more represented among nurses (45.3%) than among males (12.8%). For education level, most (63.0%) were professionally educated and the same was the case in both sexes. On average, the group was young (largely in the age group of 21–30 years), female, and professionally trained with a mixed representation of jobs.

Table 1: Sociodemographic characteristics of HCWs in Group 1

Characteristics	Categories	Male (n, %)	Female (n, %)	Total (n, %)
Age	21–30 years	18 (46.2%)	39 (73.6%)	57 (62.0%)
	31–40 years	10 (25.6%)	8 (15.1%)	18 (19.6%)
	41–50 years	8 (20.5%)	1 (1.9%)	9 (9.8%)
	>50 years	3 (7.7%)	1 (1.9%)	4 (4.3%)
Designation	Doctors	3 (7.7%)	4 (7.5%)	7 (7.6%)
	Nurses	5 (12.8%)	24 (45.3%)	29 (31.5%)
	Patient care attenders	2 (5.1%)	1 (1.9%)	3 (3.3%)
	Others	20 (51.3%)	21 (39.6%)	41 (44.6%)
Education	Secondary	5 (12.8%)	7 (13.2%)	12 (13.0%)
	Graduation + PG	11 (28.2%)	11 (20.8%)	22 (23.9%)
	Professional education	23 (59.0%)	35 (66.0%)	58 (63.0%)
Total		39 (100%)	53 (100%)	92 (100%)

Table 2 shows the HCWs' antibody titres in Group 1 upn return to follow-up assessment. The median antibody titre dropped appreciably from 9,500 U/ml (interquartile range [IQR], 85–15,200) at 4 weeks following the initiation of the first vaccine to 2,150 U/ml (IQR, 500–5,100) at 18 weeks post-vaccination. This decrease in antibody concentration over time was statistically significant, according to the Wilcoxon signed ranks test with a p of <0.001, and indicates a significant waning of the immune response over the 14-week duration.

Table 2: Antibody Titre of HCWs in Group 1 who had come for follow-up also

Time Point	Median (IQR) Antibody Titre (U/ml)
4 weeks after first dose	9,500 (85 – 15,200)
18 weeks after first dose	2,150 (500 – 5,100)
Wilcoxon signed ranks test P	<0.001

Table 3 shows the sociodemographic details of 92 HCWs in group 2, with 45 males and 47 females. More than two-thirds of the females (83.0%) were 18–30 years of age, compared to males being more evenly spread among age groups with the highest percentage (51.1%) being 31–40 years of age. In regard to designation, most of the females were nurses (74.5%), whereas males were mostly doctors (37.8%) or of other designations (31.1%). In education, a large percentage of males (77.8%) and

females (95.7%) had professional education, reflecting predominantly a highly qualified workforce with other levels of education being minimally represented in both genders.

Table 3: Sociodemographic characteristics of HCWs in Group 2

Characteristics	Categories	Male (%)	Female (%)	Total (%)
Age	18–30 years	11 (24.4%)	39 (83.0%)	50 (54.3%)
	31–40 years	23 (51.1%)	6 (12.8%)	29 (31.5%)
	41–50 years	6 (13.3%)	1 (2.1%)	7 (7.6%)
	>50 years	5 (11.2%)	1 (2.1%)	6 (6.5%)
Designation	Doctors	17 (37.8%)	5 (10.6%)	22 (23.9%)
	Nurses	6 (13.3%)	35 (74.5%)	41 (44.6%)
	Patient care attenders	8 (17.8%)	3 (6.4%)	11 (12.0%)
	Others	14 (31.1%)	4 (8.5%)	18 (19.6%)
Education	Secondary	3 (6.7%)	2 (4.3%)	5 (5.4%)
	Higher secondary	3 (6.7%)	0 (0.0%)	3 (3.3%)
	Graduation	2 (4.4%)	0 (0.0%)	2 (2.2%)
	Postgraduation	2 (4.4%)	0 (0.0%)	2 (2.2%)
	Professional education	35 (77.8%)	45 (95.7%)	80 (87.0%)
Total		45 (100%)	47 (100%)	92 100%)

Discussion

The sociodemographic profiles of healthcare workers (HCWs) in both Group 1 and Group 2 highlight a predominantly young, female, and professionally educated workforce, particularly in nursing roles. In Group 1, the majority of HCWs were females aged 21–30 years, while in Group 2, an even larger proportion of females fell into the 18–30 age group. These trends are consistent with broader national patterns where women, especially in the younger age bracket, are increasingly occupying roles in nursing and allied health professions. The presence of a significant number of HCWs with professional education in both groups (63.0% in Group 1 and 87.0% in Group 2) underscores the increasing emphasis on formal healthcare training and certification. In our study, the seropositivity rate was 96.5% following the first dosage and 100% after the second dose of Covishield. All six breakthrough infections in our investigation exhibited moderate symptoms. A similar study produced similar findings (Singh et al., 2021) [10]. In the current study, all the adverse events of immunization (AEFI) were of moderate type and AEFI was reported more in the case of the first dose compared to the second dose (Singh et al., 2021). In a cross-sectional study, similar findings were produced. In the current study, antibody titer displayed no association with adverse effects. Another study produced similar findings (Coggins et al., 2022) [11].

The antibody response profile in the HCWs in Group 1 is a key to interpreting the tempo of vaccine-induced immunity. The fact that the median antibody titres decreased from 9,500 U/ml at 4 weeks to 2,150 U/ml at 18 weeks, shown by the Wilcoxon signed ranks test ($p < 0.001$), indicates a significant loss of humoral immunity in a relatively brief time period. This result is supported by various studies that show that antibodies against SARS-CoV-2 vaccine wane following administration of the initial dose of vaccine or primary schedule of administration. This current study of over 8,000 samples over a three-year duration showed that SARS-CoV-2 antibody responses show a rapid initial decline with a phase of stabilization that follows. Booster vaccines proved to be effective in normalizing antibody titres in individuals with and without prior infection. This study offers some good evidence that whereas antibodies drop first, they later level off and thus promote long-term immunity (Srivastava et al., 2024) [12].

Importantly, such a decline may have implications for the strategy of booster dosing, particularly among frontline HCWs with increased risk of exposure. Such rapid waning should be kept in mind in framing the timing and frequency of booster dosing to ensure adequate protection afforded by the elicited immunity, particularly in high-risk settings such as hospitals. In the future, studies may investigate the impact of demographics such as age, gender, and occupational role in modulating the amplitude and duration of the antibody response. These observational studies measured the duration of the humoral response in those vaccinated with Covaxin (BBV152) and Covishield (ChAdOx1 nCoV-19). It was observed that antibody titers lasted up to one year since vaccination, though the levels differed according to prior infection and comorbidities. This study points towards the long-term efficacy of vaccine-induced antibodies and modulation of the response by individual factors (Dwivedi et al., 2025) [13].

Also to be considered is the difference in professional title between the two groups that may affect exposure risk and resulting immune response.

Group 2 contained a higher percentage of doctors and nurses than Group 1, where a higher percentage of HCWs fell in the category of "Others." Since healthcare provider contacts such as doctors and nurses stand a higher chance of being exposed to infected cases, additional stratification and correlation with antibody responses may be of value in yielding important occupational risk factors information. This research investigated the antibody responses in Sputnik V vaccinated individuals. It reported that anti-spike IgG levels decreased over a period of six months but the neutralization against the original SARS-CoV-2 and variants of concern was maintained. Moreover, increased cross-neutralization against circulating variants over time indicated maturation of the antibody response following vaccination (Gonzalez et al., 2022) [14].

The finding in this study mirrors the demographics and antibody profile among HCWs upon COVID-19 vaccination. The declining titres of antibodies corroborate the need for ongoing surveillance and taking into account the use of booster doses in a timely fashion to guarantee long-term maintenance of protection in HCWs. In addition, the sociodemographic information forms a basis for planned health education and immunization in in-patient facilities.

Conclusion

This long-term study highlights the need to monitor vaccine-induced antibodies in order to gain a clearer picture of the dynamics of humoral responses following COVID-19 vaccination. In the vaccinees assessed among the health care workers, a high early seropositivity rate to the first and second Covishield doses corroborated robust primary immune responses. Nonetheless, substantial losses of antibodies over a 14-week period indicated the waning nature of vaccine-induced immunity. This loss of antibodies notwithstanding, breakthrough infection was uncommon and mild in nature and adverse events upon immunization were mild and more common following the primary dose. These results corroborate the safety and initial interim efficacy of the Covishield vaccine and illustrate the importance of ongoing serological surveillance and the possibility of the use of booster dosing in risk groups in particular. This evidence is important in framing public health policy to allow for the delivery of vaccineupdates in a punctual fashion and to sustain population-level protection in the face of emerging variants and possible future outbreaks.

References

1. Stawicki SP, Jeanmonod R, Miller AC, Paladino L, Gaieski DF, Yaffee AQ, De Wulf A, Grover J, Papadimos TJ, Bloem C, Galwankar SC. The 2019–2020 novel coronavirus (severe acute respiratory syndrome coronavirus 2) pandemic: A joint american college of academic international medicine-world academic council of emergency medicine multidisciplinary COVID-19 working group consensus paper. Journal of global infectious diseases. 2020 Apr 1;12(2):47-93.
2. Bloom DE, Cadarette D. Infectious disease threats in the twenty-first century: strengthening the global response. Frontiers in immunology. 2019 Mar 28;10:549.
3. Kumar VM, Pandi-Perumal SR, Trakht I, Thyagarajan SP. Strategy for COVID-19 vaccination in India: the country with the second highest population and number of cases. npj Vaccines. 2021 Apr 21;6(1):60.
4. Burns VE, Gallagher S. Antibody response to vaccination as a marker of in vivo immune function in psychophysiological research. Neuroscience & Biobehavioral Reviews. 2010 Sep 1;35(1):122-6.
5. Thakur A, Pedersen LE, Jungersen G. Immune markers and correlates of protection for vaccine induced immune responses. Vaccine. 2012 Jul 13;30(33):4907-20.
6. Slifka MK, Amanna IJ. Role of multivalency and antigenic threshold in generating protective antibody responses. Frontiers in immunology. 2019 May 1;10:956.
7. Chakraborty C, Sharma AR, Bhattacharya M, Lee SS. A detailed overview of immune escape, antibody escape, partial vaccine escape of SARS-CoV-2 and their emerging variants with escape mutations. Frontiers in immunology. 2022 Feb 9;13:801522.
8. Deplanque D, Launay O. Efficacy of COVID-19 vaccines: From clinical trials to real life. Therapies. 2021 Jul 1;76(4):277-83.
9. Oliveira-Silva J, Reis T, Lopes C, Batista-Silva R, Ribeiro R, Marques G, Pacheco V, Rodrigues T, Afonso A, Pinheiro V, Araújo L. Long-term serological SARS-CoV-2 IgG kinetics following mRNA COVID-19 vaccine: real-world data from a large cohort of healthcare workers. International Journal of Infectious Diseases. 2022 Sep 1;122:1-7.
10. Singh AK, Phatak SR, Singh R, Bhattacharjee K, Singh NK, Gupta A, Sharma A. Antibody response after first and second-dose of ChAdOx1-nCOV (CovishieldTM®) and BBV-152 (CovaxinTM®) among health care workers in India: The final results of cross-sectional coronavirus vaccine-induced antibody titre (COVAT) study. Vaccine. 2021 Oct 22;39(44):6492-509.
11. Coggins SA, Laing ED, Olsen CH, Goguet E, Moser M, Jackson-Thompson BM, Samuels EC, Pollett SD, Tribble DR, Davies J, Illinik L. Adverse effects and antibody titers in response to the BNT162b2 mRNA COVID-19 vaccine in a prospective study of healthcare workers. In-Open forum infectious diseases 2022 Jan 1

(Vol. 9, No. 1, p. ofab575). US: Oxford University Press.
12. Srivastava K, Carreño JM, Gleason C, Monahan B, Singh G, Abbad A, Tcheou J, Raskin A, Kleiner G, van Bakel H, Sordillo EM. SARS-CoV-2-infection-and vaccine-induced antibody responses are long lasting with an initial waning phase followed by a stabilization phase. Immunity. 2024 Mar 12;57(3):587-99.
13. Dwivedi T, Raj A, Das N, Gupta R, Bhatnagar S, Mohan A, Guleria R. Persistence of SARS-CoV-2 antibodies for a year following SARS-CoV-2 vaccinations (BBV152 and ChAdOx1 nCoV-19). Indian Journal of Clinical Biochemistry. 2025 Jan;40(1):111-20.
14. Gonzalez Lopez Ledesma MM, Sanchez L, Ojeda DS, Oviedo Rouco S, Rossi AH, Varese A, Mazzitelli I, Pascuale CA, Miglietta EA, Rodríguez PE, Pallarés HM. Longitudinal study after Sputnik V vaccination shows durable SARS-CoV-2 neutralizing antibodies and reduced viral variant escape to neutralization over time. Mbio. 2022 Feb 22;13(1):e03442-21.