Persistence of antibodies against Spike glycoprotein of SARS-CoV-2 in health care workers post double dose of BBV-152 and AZD1222 vaccines

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Short Report

Abstract

Rationale: Vaccine rollout in India was initiated in mid-January, 2021 and is supposed to be the only antidote against SARS-CoV-2 as of now.

Objectives: To study the dynamicity of vaccine-induced IgG antibody against SARS-CoV-2.

Methodology: The present cross-sectional cohort study was undertaken to determine IgG antibody among health care workers with completed dose of either Covaxin or Covishield and were followed for 24 weeks after first dose of either vaccine to record the periodic changes in titre, concentration, clinical growth and persistence of vaccine-induced SARS-CoV-2 antibodies.

Results: Serum samples were collected from 614 participants during each follow-up and tested them in two CLIA-based platforms for testing SARS-CoV-2 antibodies both qualitatively and quantitatively. Among these participants, 308 (50.2%) were Covishield recipient and rest 306 (49.8%) took Covaxin. A total of 81 breakthrough cases was recorded among the cohort participants for whom infection post vaccination acted as booster. The rest 533 heath care workers without any history of post-vaccination infection showed significant antibody waning either from T3 (Covaxin recipient) or T4 (Covishield recipient).

Conclusion: The clinical implications of waning antibody levels post vaccination are not well understood, and it remains crucial to establish S-antibody thresholds associated with protection against clinical outcomes.

Introduction

The COVID-19 pandemic, caused by SARS-CoV-2 virus, continues to unfold in various waves, that has impacted health, by challenging the mortality rate for individuals with pre-existing health conditions as well as adults in the senior age group (1). Amidst this ongoing pandemic while the nation's community of scientists were trying to curb the impact of the first wave of COVID-19, the entire world got hit by another wave (2). As of 31st July, 2021 195 million people and more had been infected with SARS-CoV-2 and about 4.18 million covid deaths had been reported (3). India, Brazil and USA accounted for majority of the cases worldwide wherein, India reported around 31.48 million cases with 4.22 million deaths (4).

Spike glycoprotein based vaccines against SARS-CoV-2 has being rolled out worldwide to gain control of COVID-19 and reduce the mortality and morbidity due to the virus (5). The Government of India ran a vaccination drive which was the world's larges drive. It was done post approval on the basis of emergency. Throughout the nation the drive was conducted in a phased manner from 16th January 2021. Out of the two vaccines(named BBV-152 (COVAXIN®) and AZD1222), one each was given was given to healthcare workers (HCW).

India, in total has been able to administer vaccines to 351.6 million people out of which 97.9 million of them have been completely vaccinated with either BBV-152 or AZD1222 vaccine. It was seen that in a

similar way, Odisha has successfully given vaccines to about 12 million people out of which about 3.8 million people have been completely vaccinated with either BBV-152 or AZD1222 vaccine, as of mid-june (6).

In view of the increased global incidence of the virus and further emergence and spread of variants of SARS-CoV-2, there is a need for long term studies in order to discover and clarify the dynamics of antibodies and the efficiency level of vaccines. Hence, in this present study, we have analysed the persistence of Antibody among the BBV-152 and AZD1222 recipients in Odisha.

Study settings

This longitudinal cohort study was conducted during 16th January to 31st July 2021 with participants from six different institute from 3 districts of Odisha. Serum samples from 614 vaccinated individuals (Adults – aged 18 years & above) were collected from various private and government healthcare facilities of Odisha and being sent for testing at Cobas Laboratry of ICMR – Regional Medical Research Centre, Bhubaneswar. Demographic characteristics, symptoms present, medical history and vaccination details of each participant were collected using a questionnaire. A written infromed consent was obtained from each participant at the time of participantion in the study. Institutional Human Ethics Committee of ICMR – Regional Medical Research Centre, Bhubaneswar approved the study.

Study design

All the individuals were tested on day 0 (before the 1st dose of vaccine; T0) for IgG against the nucleocapsid (N) protein and Spike RBD IgG against SARS-CoV-2. Antibody against N protein was taken as proxy for previous SARS-CoV-2 infection. Subsequently the samples were collected after 4th (before the 2nd dose of vaccine), 8th, 12th, 16th, 20th and 24th weeks of the first dose of vaccine (noted as T1, T2, T3, T4, T5 and T6 respectively).

Test Method

Serum sample from each participant was used to evaluate the IgG antibody against neucleocapsid (N) and Spike (S) protein antigen using chemiluminescent microparticle immunoassay (CLIA). Total antibody (including IgG) against the Neucleocapsid protein was estimated in Roche Cobas e411 (Roche Diagnostics Int. Ltd.) using a *in vitro* qualitative kit Elecsys® Anti-SARS-CoV-2 and Spike RBD IgG antibodies against SARS-CoV-2 using ARCHITECT i1000SR (Abbott Diagnostics, Chicago, USA) using a commercial quantitative kit ARCH SARS-CoV-2 IgG II Quant as per the manufacturer's instructions. A cut-off index (COI) of ≥1.0 was interpreted as reactive and <1.0 as non-reactive for Elecsys® Anti-SARS-CoV-2. The cut-off value for quantitative kit ARCH SARS-CoV-2 IgG II Quant was 50 AU/mL.

Statistical analysis

Descriptive statistical analyses were performed using GraphPad Prism 9.00 for Windows (GraphPad Software, La Jolla, California, USA) and SPSS software (IBM SPSS Statistics for Windows, version 24.0,

Armonk, NY). The statistical significance threshold was set at 5%.

Study Approval

The study was ethically approved by the Institutional Human Ethical Committee of ICMR – Regional Medical Research Centre, Bhubaneswar vide no ICMR-RMRCB/IHEC-2020/036 dated 07/11/2020.

Results And Discussion

Among 614 participants enrolled in the study, 308 (50.2%) were covishield vaccine recipient and rest 306 (49.8%) had taken covaxin. The participants included 396 (64.5%) male and 218 (35.5%) female. The median age of all the participants was calculated as 37 years (interquartile; IQ: 28–47 years). A total of 257 participants had previous history of SARS-CoV-2 infection before receipt of either vaccine and the median value of antibody titre against N-protein was 19.70 COI (IQ: 6.74–76.2). Among these 614 participants, 81 were breakthrough cases and the Ab production and persistence among them were separately analysed. Among the 257 participants with previous history of COVID-19 infection, 33 were reinfected with SARS-CoV-2 virus after complete dose of either vaccine.

The results of 533 individuals without any history of infection post vaccination indicated a significant drop in Spike RBD IgG concentration for both the vaccines. There was no significant difference in post vaccination antibody production and its persistence throughout gender, age, co-morbidities and blood groups (Table 1). The production of vaccine induced IgG antibodies are significantly higher ($p < 0.001$) in covishield compared to covaxin. Covishield recipients produced a median of 1223.2 AU/mL (IQ: 482.2–5476.0) of anti-S IgG which is higher than covaxin induced antibody concentration of 342.7 AU/mL (IQ: 76.1-892.8) [Figure 1]. In seronegative individuals, the rate of seroconversion after 28 days after the first dose was 81.9% for Covishield and 16.1% for Covaxin (Fig. 1).

Table 1
Demographic date of included participants without breakthrough infection.

		N (%)	T2 (IQR)	*p*-value	T6 (IQR)	p-value
Gender	Male	341 (64.0)	640.30 (1808.93)	0.172	217.20 (962.79)	0.076
	Female	192 (36.0)	959.20 (1779.32)		284.70 (702.36)	
Age Groups	18−44 Years	356 (66.8)	662.55 (1676.23)	0.217	227.45 (744.39)	0.119
	45−59 Years	152 (28.5)	829.60 (2300.79)		288.50 (1230.40)	
	Above 60 Years	25 (4.7)	978.30 (7045.05)		326.60 (2466.60)	
Blood Groups	A + ve	103 (19.3)	557.80 (1371.0)	0.092	179.40 (606.11)	0.157
	B + ve	198 (37.1)	706.05 (2299.67)		290.65 (875.88)	
	AB + ve	42 (7.9)	739.05 (1276.80)		243.35 (1128.93)	
	O + ve	180 (33.8)	2217.46 (1717.28)		244.55 (992.85)	
	A -ve	3 (0.6)	141.60 (0.0)		34.70 (0.0)	
	B -ve	4 (0.8)	994.30 (1384.68)		419.80 (747.12)	
	O -ve	3 (0.6)	2004.31 (0.0)		840.60 (0.0)	
Comorbidities	Present	77 (14.4)	938.20 (2451.05)	0.579	400.70 (1526.40)	0.151
	Absent	456 (85.6)	664.45 (1747.43)		231.00 (773.68)	
Vaccine	Covaxin	255 (47.8)	342.70 (816.69)	< 0.001	95.12 (240.68)	< 0.001
	Covishield	278 (52.2)	1223.25 (4993.83)		637.20 (2868.80)	

Antibody level for Covaxin receipients which was recoreded hightest at T2 with a median value of 342.7 AU/mL (IQ: 76.11−892.8) started to decrease significantly (p = 0.001) from T3 (median = 305.18 AU/mL; IQ: 78.2-771.2) onwards and was recorded as 95.1 AU/mL (IQ; 36.5-277.2) at T6. The maximum median (1299.5 AU/mL; IQ:517.9-5019.07) of anti-S IgG for covishield recipient was recorded at T3, and started

weaning significantly (p = 0.001) from T4 (median = 305.18 AU/mL; IQ: 78.2-771.2) onwards which waned to 637.2 AU/mL (IQ; 186.5-3055.3) after 6 months from the first vaccine shot (p < 0.001).

Among the 224 seropositive cases with no reinfection, median at T0 for Covaxin was 102.7AU/mL (IQ; 75.2-154.4) and for Covishield was 125.3 AU/mL (IQ: 80.5-339.5) which recorded a peak at T2 with median Ab of 884.7 AU/mL (IQ; 579.4-1795.5) and 6286 AU/mL (IQ; 2307.1-12126.5) respectively. The antibody titre started declining and recorded as 276.8 AU/mL (IQ; 179.6-471.9) and 2813.6 AU/mL (IQ; 1417.9-5112.5) for Covaxin and Covishield recipients respectively at T6. The median Ab titre for reinfection cases on T0 was 75.4 AU/mL (IQ; 66.8–99.9) for Covaxin and 78.8 AU/mL (IQ; 62.7-125.9) for Covishield.

The Spike RBD IgG titre of 81 breakthrough cases was recorded as 345.6 AU/mL (IQ: 62.9-879.2) at T2 which further increased to 10550.4 AU/mL (IQ: 3635-21803.9) at T6 (Fig. 2a). Among those, 75 (92.3%) had mild symptoms and 9 (11.1%) participants were hospitalized. Fever was the primary symptom in 85.2% of individuals followed by loss of taste/smell (58.0%), cough (50.6%), sore throat (45.7%) and shortness of breath (32.1%) among the other significant symptoms (Fig. 2b).

In this present study, we report a significant decline of antibody post 2 months and 4 months among Covaxin and Covishield recipients after two doses of the BBV-152 and AZD1222 vaccines. The highest median antibody titre was observed at 4 weeks of double dose for seropositive participants. No significant difference was observed in post vaccination antibody production and its persistence throughout gender, age, co-morbidities and blood groups. Whether previous SARS-CoV-2 infection protects individuals from reinfection and persistence of protection is yet to be understood completely (7). Reinfection cases detected in our study may imply that immunity against SARS-CoV-2 might be weak or decayed relatively quickly or reinfection with variant strains, with implications on how long the vaccines might protect people and what is the antibody threshold required for giving protective immunity (8).

Limited data exists on long-term antibody kinetics among the BBV-152 and AZD1222 vaccine recipients, and to the best of our knowledge the present study first time reports the persistence of spike RBD antibody post vaccination. Various studies carried out with BNT162b2 (Pfizer–BioNTech) and ChAdOx1 nCoV-19 (Oxford–AstraZeneca) detected significant decline of five-fold for ChAdOx1, and by about two-fold for BNT162b2, between 21–41 days and 70 days (5, 9). Although the study has certain limitations like it is cross-sectional with only HCWs, which limits generalization and neutralizing activities of these antibodies are not estimated, however to the best of our knowledge, this is the first ever study undertaken to understand the long-term antibody persistence among the recipients of these two vaccines being administered in India.

The clinical implications of waning antibody levels post vaccination are not well understood, and it remains crucial to establish S-antibody thresholds associated with protection against clinical outcomes. Emerging evidence suggests that antibodies are particularly important for blocking infection and preventing onward transmission of the virus whereas T cells may be particularly relevant for preventing severe disease and death. Findings from this study suggests for a larger cohort study which would help

to define correlates of protection to determine whether there is a need to produce modified vaccines, or booster doses. The study has a follow-up plan for two years which will further help in understanding the kinetics model and also to provide a better estimate of the antibody response in both seropositive and seronegative individuals over a significant period.

Declarations

Funding

So separate funding was obtained for the study.

Ethics approval

The study was ethically approved by the Institutional Human Ethical Committee of ICMR – Regional Medical Research Centre, Bhubaneswar vide no ICMR-RMRCB/IHEC-2020/036 dated 07/11/2020.

Declaration of Competing Interest

The authors have declared that no conflict of interest exists.

Author contributions

DB, S Pati and JSK conceptualised the study. HRC, PKC, KP, NRS, S Podder, AM, SK Pradhan, MP, RRN collected blood samples, information from participants and written informed consents. D Parai, SKS, and UKR performed the laboratory tests. HRC, D Parai, GCD and DB have done the data analysis. HRC, DP and DB drafted the original manuscript. Manuscript review and editing was done by N Mishra, D Pattnaik, SB, SKR, SKM and S Pati. N Mondal, SK, SK Palo, DB and S Pati supervised the study. All the authors have read the manuscript and gave final approval.

Acknowledgement

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Figures
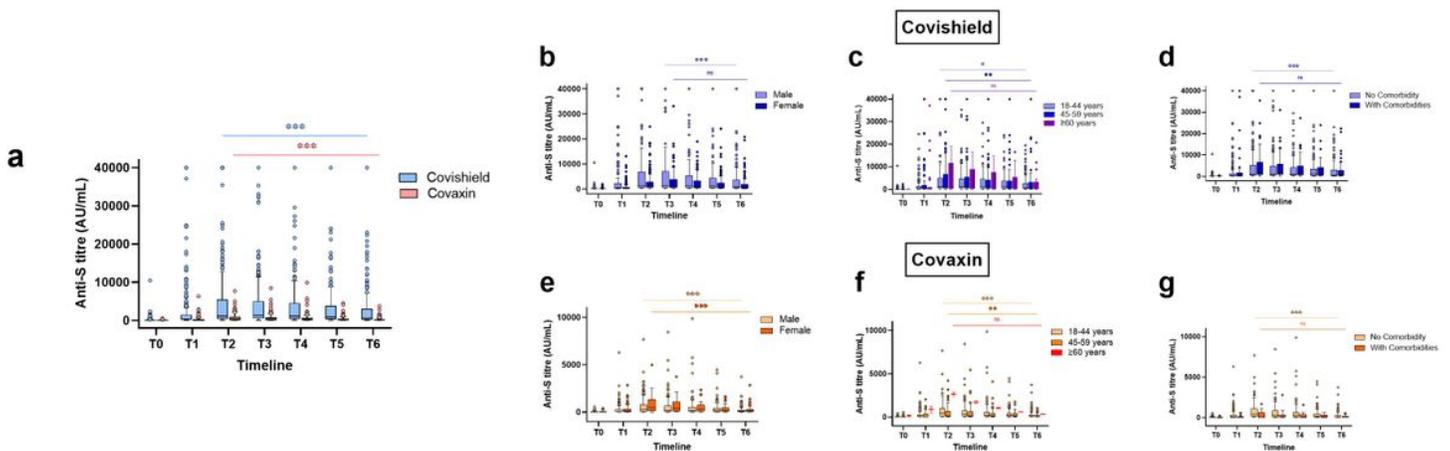
Figure 1

Anti-S IgG antibody levels at various timepoint for covishield and covaxin recipient without any breakthrough infection. The data was further stratified within vaccine type by gender (b, e), age (c, f), and comorbidities (d, g).
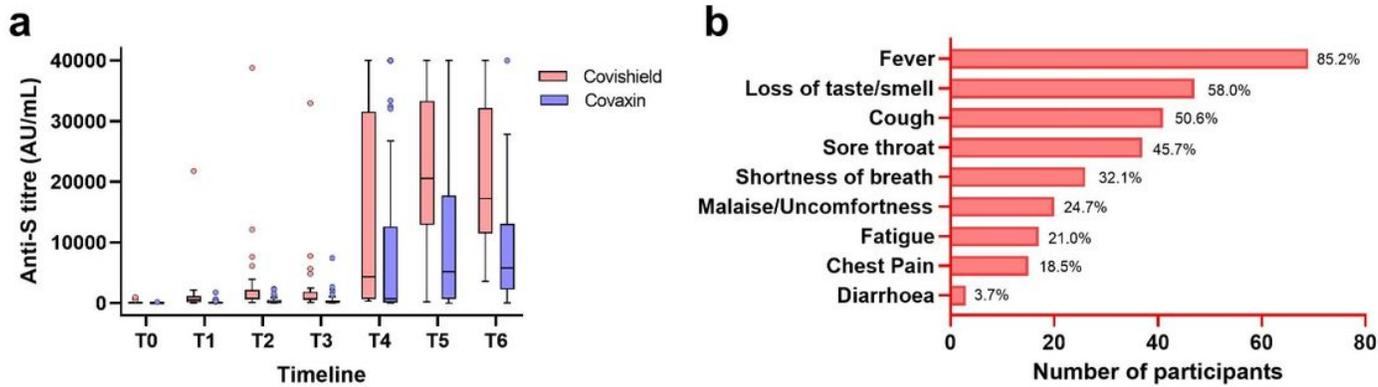
Figure 2

Anti-S IgG antibody concentration for the vaccine recipient having breakthrough infection (a). The symptomatic status of the breakthrough cases (b).