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Single-dose of BBV-152 and AZD1222 increases antibodies against spike glycoprotein among healthcare workers recovered from SARS-CoV-2 infection

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Dear Editor,

The world is currently facing either the second or third wave which is more intense, overwhelming and devastating compared to the first wave of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. As of May 17, 2021, India reported 24.96 million confirmed COVID-19 cases with an average weekly spike of 319,497 cases, and a total of 274,390 deaths to date [2]. Two vaccines named BBV-152 (COVAXIN®) and AZD1222 (COVISHIELD™) were initially available in the Indian market after the government approval for emergency use in the country and became part of India's largest vaccination drive started from January 16, 2021. Later, the Gam-COVID-Vac (Sputnik V) got approval and was subsequently launched on May 14, 2021 [3]. India has administered 0.184 billion citizens with at least a single dose of either BBV-152 or AZD1222 vaccine and among them, only 0.042 billion people got both the dosages (complete vaccination) as of mid-May [3]. Since India is the second most populated country in the world with a population of 1.39 billion, the complete vaccination status is comparatively low (3.0%) and the shortage of adequate shots has already started all over the country [1]. The dissemination of vaccines for the entire population of India is the one of the current ongoing challenges and the situation can be bloomed as well in other LMIC members in near future.

In this study, we assessed the spike (S) and nucleocapsid (N) protein IgG titre during baseline (before vaccination) and subsequently after each dose of vaccines in HCWs to understand the antibody response in both previously infected and non-infected participants. A total of 134 HCWs were included in this study from January 2021 to April 2021. All of them were fully vaccinated either with BBV-152 or AZD1222 as a part of the first vaccination drive to healthcare and frontline workers, both were approved for emergency use in Odisha, India. Demographic details such as age, gender and history of COVID-19 infection were recorded from time to time. Written informed consent was obtained from each participant. No new or reinfection was reported by the cohort participants during the study period. IgG antibody against SARS-CoV-2 was measured by two automated chemiluminescence electro assay (CLIA) based platforms, ARCHITECT i1000SR (Abbott Diagnostics, Chicago, USA) for N- protein and Cobas e411 (Roche Diagnostics GmbH, Mannheim, Germany) for S- protein receptor-binding domain (RBD) which is the primary target of neutralizing antibodies in SARS-CoV-2. The cut-off value for the first platform was 1.4 index. Values $\geq$ 0.80 U/mL were considered as positive and <0.80 U/mL as negative in Cobas e411. The higher detection limit was 2500 U/mL for 10-fold diluted samples.

Among the 134 HCWs, 59 had a previous history of COVID-19 infection confirmed by RT-PCR test and the other 75 HCWs were without any prior infection. At baseline in January 2021, total 21 (35.6%) recovered participants remained IgG positive against N- protein although 55 (93.2%) were seropositive against S- protein (Table S1). We measured the IgG humoral response after 28 days of the first vaccination of all the HCWs and found a significant rise in the antibody concentration for those having earlier COVID-19 infection history irrespective of the given vaccine. For those, the overall median concentration of S-protein IgG was increased significantly ($p < 0.001$) to 588.0 U/mL (IQR, 250.0–2500.0 AU/mL) from 231.4 U/mL (IQR, 81.9–359.1 AU/mL) observed during baseline (Fig. 1). We also found that a time gap of 180 days from recovery significant amount of humoral response against SARS-CoV-2 persists among the recovered individual (Fig. S1). In case of 75 HCWs with no prior infection history, 46 (61.3%) were found to be seropositive after the first dose and the median concentration was low in comparison with recovered individuals and recorded at 7.27 U/mL (IQR, 0.4–116.5 AU/mL). The mean titre of N- protein IgG increased to 1.8 index (IQR, 0.66–2.74 index) from 0.98 index (IQR, 0.54–2.0 index) after the first dose of vaccine in HCWs having previous COVID-19 history although the change was statistically non-significant ($p = 0.06$). The antibody magnitude was further changed after the second dose of the vaccine in both the HCWs categories of prior COVID-19 infection and non-exposed. Median S- protein IgG was measured as 1674.0 U/mL (IQR, 610.3–2500.0 AU/mL) and 46.5 U/mL (IQR, 5.84–839.9 AU/mL) for antibody response in both previous infected and non-infected individuals, respectively (Fig. 1).

In this study, we aimed to investigate the humoral responses against two currently available vaccines BBV-152 and AZD1222 in India. Being the second-largest demography in the world, it is nevertheless challenging to vaccinate a sizeable population to acquire herd immunity.

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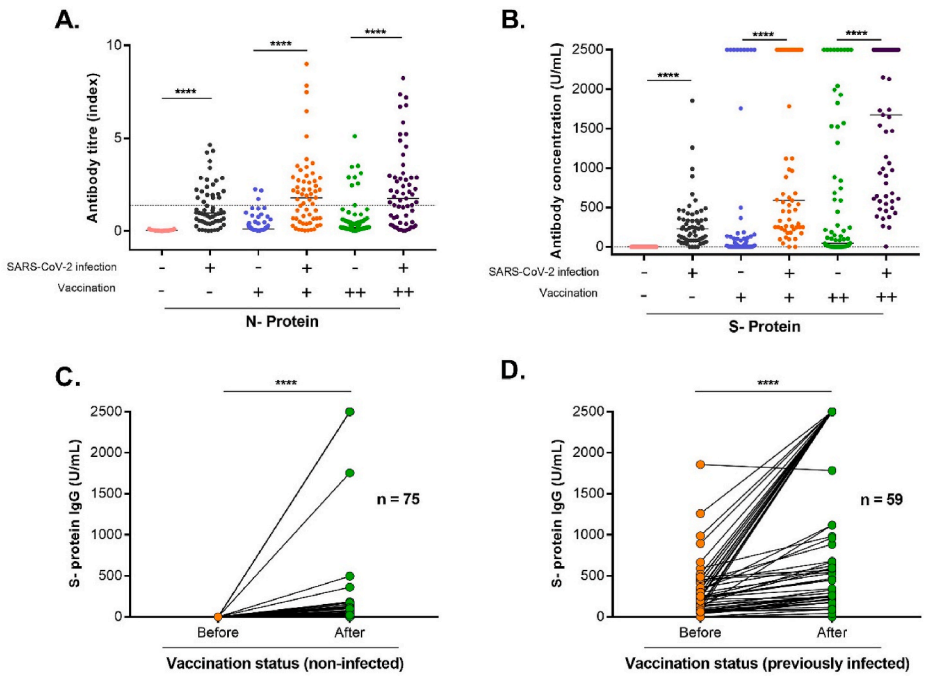

Fig. 1. Antibody responses against SARS-CoV-2 N- protein and S- protein at baseline and after vaccination in previously COVID-19 infected and non-infected HCWs (A & B). Pair-wise comparison of S- protein IgG response after a single dose of vaccine in prior COVID-19 infected and non-infected HCWs (C & D). $p < 0.05$ was considered as significant.

The second wave of the COVID-19 with high morbidity reemphasized the need for vaccination to curtail the mortality and severity of the disease [4]. The study findings even limited in a small cohort suggest a single dose of either of the vaccine can develop a higher level of neutralizing immune response in HCWs with prior COVID-19 infection history compare to non-infected participants. We did not find any significant difference in antibody development across gender ($p = 0.350$) and age groups ($p = 0.556$). Although a handful of works have been published with other vaccines in other countries, the data presented here is the first such report with BBV-152 and AZD1222 in this region [5]. It may be noted that our study was confined to HCWs and may not be extrapolated to the general population.

Our study findings generated preliminary evidence to consider previous infection status before second dose of vaccination for optimization of vaccine policy in view of the current situation in India and a possible future scenario in any country categorised as LMIC. Delay in administration of the second dose among individuals with previous infection history might be an effective strategy as they showed high titre of Spike RBD IgG antibodies against SARS-CoV-2 virus. However, follow-up with a larger cohort at periodic intervals can help us in understanding the protective immunity after first dose of vaccine in Covid-19 recovered individuals.

Ethics approval

The study was ethically approved by the institutional human ethical committee of ICMR – Regional Medical Research Centre, Bhubaneswar.

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Authors contribution statement

DB and SP conceptualised the study. DP, HRC, GCD, SKS, MP, UKR and RRN were involved in testing of the samples. DP, HRC, GCD, JSK and SK were involved in data analysis and valuable inputs. DP and GCD did the statistical analysis. DP, DB and SP wrote the manuscript. All authors have read and approved the final manuscript.

Declaration of competing interest

The authors have no competing interests in any form.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tmaid.2021.102170.

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