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Research Letter

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Antibody responses to Sputnik Vaccination in naïve and COVID 19-recovered vaccine recipients, India

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SARS CoV-2 pandemic challenged the world with emerging multiple variants having high transmissibility and increased infectivity. The limited therapeutic options have boostered the implementation of quick mass vaccination. In India, a total of eight COVID-19 vaccines (Covaxin, Covishield, Spikevax, ZyCoV-D, Corbevax, Covovax and Janssen COVID-19 Vaccine) have been approved including Sputnik V for emergency use,[1] whereas Covaxin, Covishield and Sputnik V are currently used for vaccination. More recently, we have reported the robust antibody response among Covaxin and Covishield vaccine recipients in India.[2–4] However, almost no data are available regarding the humoral immune responses against the Sputnik V vaccine in Indian population. SARS-CoV-2 B.1.617 lineage developing into B.1.617.1 (Kappa), B.1.617.2 (Delta) and Delta sub-lineages, and current omicron variants are being detected globally. The second wave of pandemic (recorded between February and July of 2021) was due to the high transmissibility of Delta variant, which caused serious public health emergency in India.[5]

The rollout of rapid vaccination programs globally has helped in providing protection against the severe course of COVID-19. As a result, COVID-19 disease incidence and related mortality trends are decreasing which further substantiates good efficacy of currently available vaccines against SARS CoV-2 strains.[6]

Sputnik V (Gam-COVID-Vac) is a recombinant human adenovirus based two-vector (rAd type 26 and rAd5.1) viral vaccine.[7] The Ad26-based vaccine is used for the first dose and the Ad5 based vaccine is administered on the 21 day to boost immune response.

Rossi *et al.* demonstrated significant immune responses following the first dose and increase of antibody titres and neutralizing capacity post second dose of Sputnik V.[8] The emerging SARS-CoV-2 variants have multiple mutations in the SARS CoV-2 spike region, which could lead to immune evasion in vaccinated individuals. In our earlier studies with Covaxin and Covishield immunized sera, reduction in the neutralizing antibody (NAb) was observed against Kappa,[9] Delta and Beta variants.[4] In the current study, we assessed the NAb responses of SARS-CoV-2 naïve and recovered individuals immunized with Sputnik V vaccine.

Sera of Sputnik V vaccinated/immunized individuals ($n = 86$) were categorized in four different groups and a comparative assessment of neutralizing antibody responses against Delta, Ay.1 and Beta in comparison with prototype strain B.1 was performed. Sera were classified into four groups: (i) COVID-19 infection naïve individuals who received one dose of vaccine ($n = 29$), (ii) COVID-19 infection naïve individuals who received two doses of vaccine ($n = 27$), (iii) COVID-19-recovered (follow-up samples of COVID-19 qRT-PCR positive patients) patients administered one dose of vaccine ($n = 18$), (iv) COVID-19-recovered subjects administered two doses ($n = 12$). All the sera were collected 4 weeks post-vaccination. Binding antibodies were also tested against S1-RBD in all four groups ($n = 335$) and N protein by

Table 1. The summary of the geometric mean of NAb titres obtained for different strains of SARS-CoV-2 with their 95% confidence interval

	COVID-19 naïve		COVID-19 infected	
	One dose (95%CI)	Two doses (95%CI)	One dose (95%CI)	Two doses (95%CI)
B.1	307.3 (123.7–763.4)	365.6 (195.3–684.2)	4680 (3662–5981)	3542 (1962–6395)
AY.1	87.12 (21.98–345.3)	202.7 (98.05–419)	4025 (3089–5245)	3986 (1946–8165)
Beta	8.273 (1.276–53.63)	70.17 (27.07–181.9)	2023 (1299–3150)	1804 (694.1–4690)
Delta	15.31 (2.313–101.4)	180.2 (84.43–384.6)	4266 (3597–5060)	4601(2429–8717)

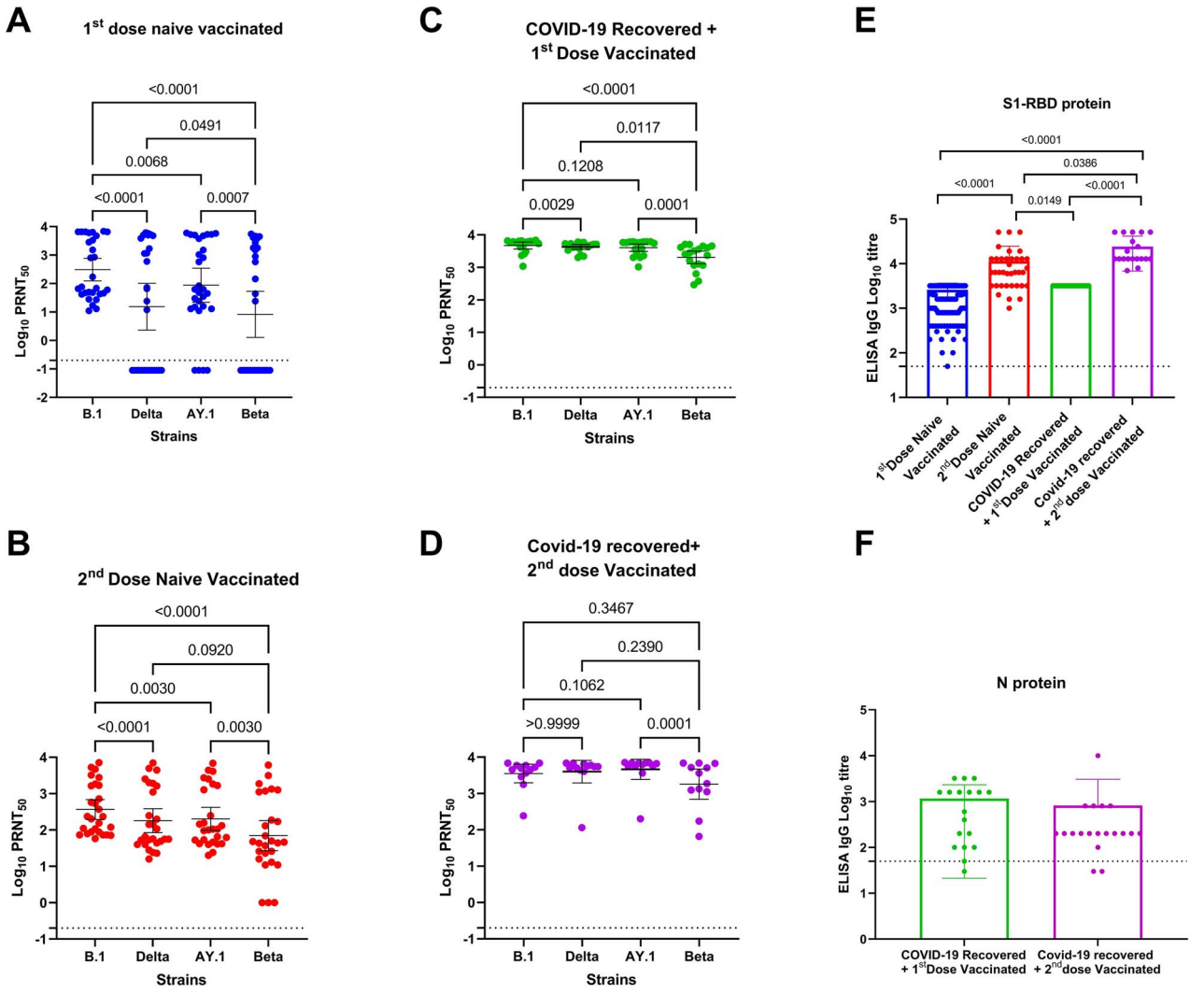

Figure 1. Neutralization of individual sera from COVID 19 naïve and COVID 19 recovered receiving different Sputnik doses with against B.1, Delta, AY.1 and Beta strains along with their ELISA titres: NAb titre of COVID 19 naïve individuals with one dose (A), COVID 19 naïve individuals with two doses (B), COVID-19 recovered plus one dose (C), IV. COVID-19 recovered plus two doses (D) against the B.1, AY.1, Delta and Beta strains. A matched pair two-tailed pair-wise comparison was performed using the Friedman's test to analyse the statistical significance. Anti-SARS-CoV-2 IgG titres of vaccinated individual's sera for S1-RBD protein (E) and N protein (F). The statistical significance was assessed using two-tailed Kruskal–Wallis test with Dunn's test of multiple comparisons. A *P*-value <0.05 were considered to be statistically significant for all the comparison. The dotted line on the figures indicates the limit of detection of the assay. Data are presented as mean values ± standard deviation (SD).

ELISA in Group iii and iv ($n = 37$). (Methods in supplementary material).

The NAb titres against Delta, AY.1 and Beta variants were compared with B.1 for sera of each group. The geometric mean titre (GMT) along with the 95% confidence interval (CI) for COVID-19 naïve receiving one and two doses were 307.3 (95% CI: 123.7–763.4) and 365.6 (95% CI: 195.3–684.2) for B.1 strain; 87.12 (95% CI: 21.98–345.3) and 202.7 (95% CI: 98.05–419) for AY.1 strain; 15.31 (95% CI: 2.313–101.4) and 180.2 (95% CI: 84.43–384.6) for Delta strain and 8.273 (95%

CI:1.276–53.63) and 70.17 (95% CI: 27.07–181.9) for Beta strain, respectively.

The geometric mean titre along with the 95% confidence interval for COVID-19 recovered plus one dose and two doses 4680 (95% CI: 3662–5981) and 3542 (95% CI: 1962–6395) for B.1 strain; 4025 (95% CI: 3089–5245) and 3986 (95% CI: 1946–8165) for AY.1 strain; 4266 (95% CI: 3597–5060) and 4601(95% CI: 2429–8717) for Delta strain, 2023 (95% CI: 1299–3150) and 1804 (95% CI: 694.1–4690) for Beta strain, respectively (Table 1).

The geometric mean NAb titres of the COVID-19 naïve individuals with single dose of Sputnik V were reduced 3.5-, 37.1- and 20- fold for AY.1, Beta and Delta variants, respectively of the SARS-CoV-2 when compared to B.1 strain. Similarly, post two doses of immunization, COVID-19 naïve individuals were observed to have reduced 1.8-, 5.21- and 2.02- fold for AY.1, Beta and Delta variants, respectively as compared to B.1 strain.

When the geometric mean NAb titres of the COVID-19 recovered individuals were assessed, relatively lesser fold differences were observed between the responses to different strains. Post first dose of immunization, the individuals were observed to have geometric mean NAb titres reduced by 1.16-, 2.31 and 1.09- fold for AY.1, Beta and Delta variants respectively when compared to B.1 strain. The COVID-19 recovered individuals administered with both of the doses of the vaccine showed that the geometric mean NAb titre of Beta strain reduced 1.9- fold compared to B.1 whereas the GMT of AY.1 and Delta increased by 1.12- and 1.29-fold as compared to B.1 strain.

A matched pair two-tailed pair-wise comparison was performed using the Friedman's test to analyse the statistical significance.

Anti-SARS-CoV-2 IgG specific to S1-RBD protein showed higher antibody response in all groups (Figure 1E) and N protein-based ELISA indicated a similar pattern of IgG titre in participants of Group III–IV (Figure 1F).

The results indicated that sera of COVID-19 positive recovered subjects who received one and two doses of Sputnik V vaccine had very high antibody response compared to the COVID-19 naïve vaccines with a significant difference in NAb titre against B.1, Delta, AY.1 and Beta variants. In addition, NAb titre to Beta strain (among all four groups) was lowest when compared to other variants tested in this study. Though differences recorded in fold reduction of neutralization capability of Sputnik V vaccine sera were reported earlier by Gushchin *et al.*[10] to Delta and Beta, the pattern of low NAb response to variants in comparison with wild type or prototype strain is in accordance with earlier studies. Further studies regarding the breakthrough cases, immune responses to the vaccines post 4 weeks and cell-mediated immune responses are ongoing. These studies will enlighten the trends of immune response to the Sputnik V vaccine.

Although, we observed a reduction in the neutralizing titre against each variant compared to the B.1 strain, Sputnik V vaccine-induced robust neutralizing antibody response among all groups which may help in limiting the severity of disease and mortality in the vaccinated individuals. Also, COVID-19 recovered individuals who took the vaccine have higher antibody titres, which may ensure long term protection from reinfections.

Supplementary data

Supplementary data are available at JTM online.

Ethical approval

The study was approved by the Institutional Human Ethics Committee of ICMR-NIV, Pune, India.

Authors' contributions

GNS and GND contributed to study design, data analysis, interpretation and writing and critical review. AJ, AV & As contributed in collection of sample, clinical history and demographic details. BNT, AS, RP, CP and NP contributed to data collection and KD contributed in data analysis interpretation and writing. PA, PY contributed to the critical review and finalization of the paper.

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Conflict of Interest

The authors have no conflicts of interest to declare.

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