

**Neutralization of B.1.1.28 P2 variant with sera of natural SARS-CoV-2 infection and recipients of inactivated COVID-19 vaccine Covaxin**

**Authors:** <sup>1</sup>Gajanan Sapkal, Ph.D, \*<sup>1</sup>Pragya D. Yadav, Ph.D, <sup>2</sup>Raches Ella, M.S., <sup>1</sup>Priya Abraham, Ph.D, <sup>1</sup>Deepak Y. Patil, Ph.D, <sup>3</sup>Nivedita Gupta, M.D., <sup>3</sup>Samiran Panda, M.D., <sup>2</sup>V. Krishna Mohan, Ph.D, <sup>3</sup>Balram Bhargava, D.M.

**Affiliations:**

<sup>1</sup>Indian Council of Medical Research-National Institute of Virology, Pune, Maharashtra, India, Pin-411021

<sup>2</sup>Bharat Biotech International Limited, Genome Valley, Hyderabad, Telangana, India Pin-500 078

<sup>3</sup>Indian Council of Medical Research, V. Ramalingaswami Bhawan, P.O. Box No. 4911, Ansari Nagar, New Delhi, India Pin-110029

**\*Corresponding author**

Dr. Pragya D. Yadav,

Scientist 'E' and Group Leader,

Maximum Containment Facility,

Indian Council of Medical Research-National Institute of Virology,  
Sus Road, Pashan, Pune, Maharashtra, India Pin-411021.

Phone: +9120-26006111, Fax No. 91-20-26122669

Email: hellopragya22@gmail.com

### **Teaser**

Our study has shown 1.09 and 1.92 fold reductions in the neutralizing titer with sera of individuals with natural infection and Covaxin vaccine recipients against B.1.1.28.2 variant.

### **Text**

The emergence of SARS-CoV-2 variants with mutations in the spike protein region lead to growing concerns about the efficacy of the currently available COVID-19 vaccines or neutralizing capability of the sera of individuals infected naturally with the earlier circulating strains. Although some of the vaccines seem to be effective against the UK variant.<sup>1,2,3</sup> the efficacy of them against the South African variant has been demonstrated to be less efficacious.<sup>2,4</sup> Earlier we have reported COVID-19 cases infected with the SARS-CoV-2 UK variant (B.1.1.7) and its effectiveness in BBV152 recipient's vaccines.<sup>5, 6</sup> A SARS-CoV-2 vaccine that used an inactivation platform has been reported to be 50.7% efficacious from Brazil, where the B.1.1.28.2 variant is more prevalent (NCT0445659).<sup>7</sup> Similarly, Brazil variant P2 lineage (B.1.1.28.2) virus isolated from international travelers travelled to India from abroad was used to determine the neutralization activity with sera of vaccine recipients and recovered COVID-19 cases.

In this study, we determined the IgG immune response and neutralizing activity of the 19 convalescent sera specimens obtained from the recovered cases of COVID-19 and confirmed for B.1.1.7 (UK) (n=2), B.1.351 (South Africa) (n=2), B.1.1.28.2 (n=2), B1 lineage (n=13) (15-113

days post positive test). The data were compared with 42 participants immunized with an inactivated Covid-19 vaccine, Covaxin (BBV152) as part of phase II clinical trial (two months post the second dose).<sup>8</sup> Neutralizing antibody (NAb) titers of all the serum specimens were evaluated against B.1.1.28.2 variant using plaque reduction neutralization test (PRNT50).<sup>5</sup> Neutralization activity of B.1.1.28.2 was compared to prototype D614G variant as Covaxin vaccine has been developed using D614G variant.

The geometric mean titer (GMT) of an IgG titer for S1-RBD and N protein ELISA (In house assays developed with prototype Wuhan-Hu-1 strain) was observed to be 794.8 and 4627 respectively for the SARS-CoV-2 recovered individuals. Covaxin recipients showed a GMT IgG titer of 2250 with S1-RBD and 3099 with the N protein compared; the former being significantly high compared to natural infection (Figure 1A). The geometric mean titer (GMT) of the neutralizing antibodies (NAb) of the sera with natural infection and Covaxin recipients for the prototype D614G strain was 120.1 and 337.5. In the B.1.1.28.2 variant, the GMT for individuals with natural infection was observed to be 109.2, while that of vaccine recipient was found to be 175.7.

This study shows that the two-dose Covaxin regimen significantly boosted the IgG titer and neutralizing efficacy against both the variants compared to that seen with natural infection. A two-tailed Wilcoxon paired signed-ranks test demonstrated a significant difference between prototype D614G strain and B.1.1.28.2 variant (Figure 1B). Results confirm 1.92 and 1.09 fold reductions in the neutralizing titer against B.1.1.28.2 variant in comparison with prototype D614G variant with sera of vaccine recipients and natural infection respectively.

The robust neutralizing capability of vaccine's sera was reported earlier for B.1.1.7 (UK), reported in earlier studies and again supported by VUI B.1.1.28.2 as well.<sup>5</sup> Findings from

another inactivated vaccine recently reported no neutralization to the P1 (B.1.1.28), albeit sera samples assessed were five months post the second dose.<sup>7</sup> This study further corroborates recent findings indicating high levels of cross-reactivity in sera collected from variant infected individuals.

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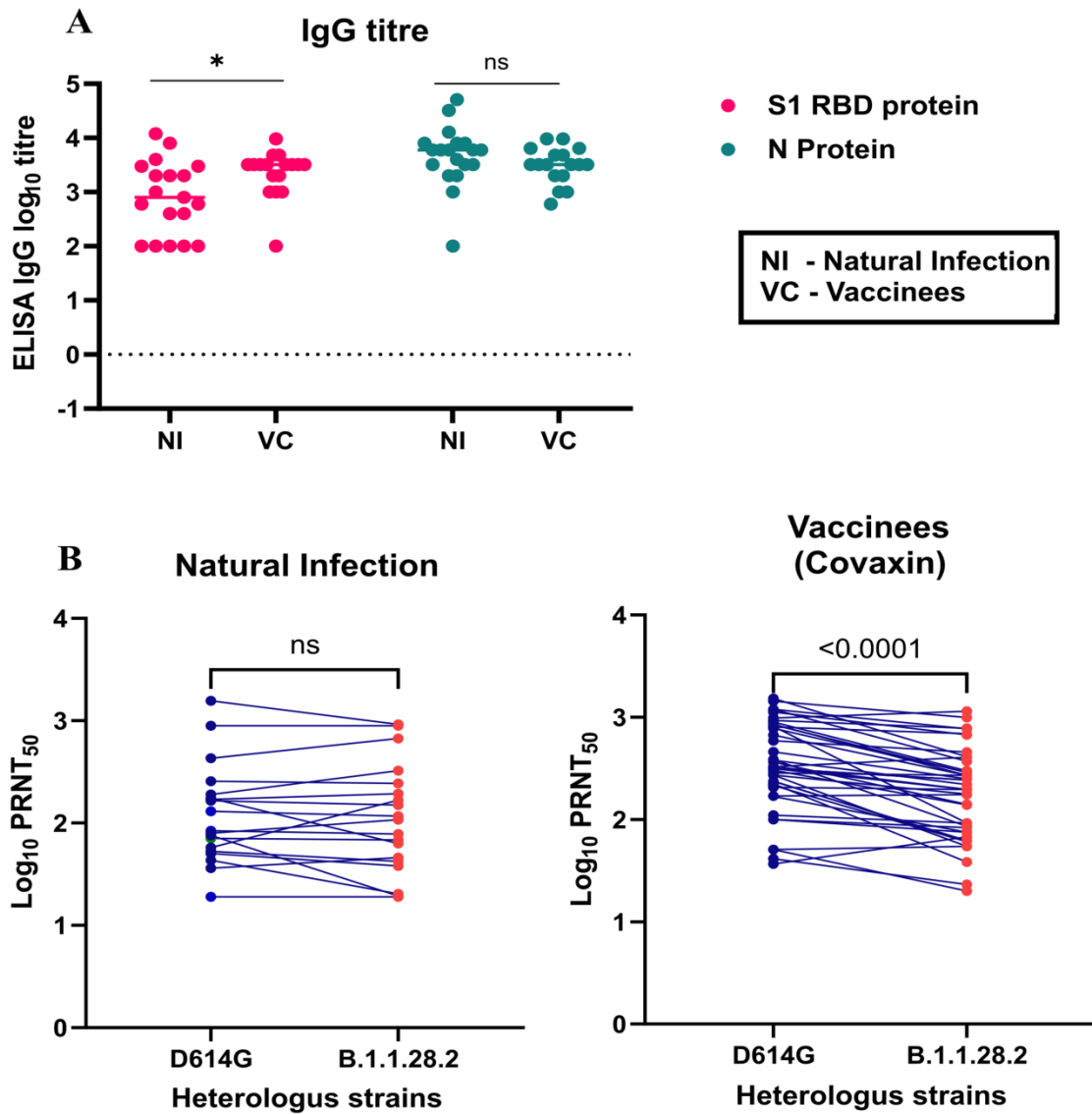
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Figure legend



**Figure 1. IgG response and neutralizing activity post-natural SARS-CoV-2 infection and Covaxin recipients:** **Panel A** depicts the results of S1-RBD protein (Pink circles) and N protein (Blue circles) based SARS-CoV-2 IgG ELISA to determine the IgG titer in sera of naturally infected individuals (n=19) and Covaxin recipients (n=42). Mann-Whitney test was used for the comparison. **Panel B** shows the results of the plaque reduction neutralization test to assess



neutralization activity of the prototype virus D614G (Blue circles) with B.1.1.28 P2 variant (Red circles) with sera of naturally infected individuals (n=19) and Covaxin recipients (n=42). The natural Infection had two samples each from Brazil, South Africa and the UK and thirteen of B1 lineage. Wilcoxon matched-pairs signed-rank test was used to compare the significance. A significant reduction was observed in the samples of the vaccines, whereas a non-significant change was observed in the cases with natural Infection.

### **Ethical approval**

The study is approved by the Institutional Biosafety Committee and Institutional Human Ethics Committee of ICMR-NIV, Pune, India

### **Author Contributions**

PDY, RE and PA contributed to study design, data collection, data analysis, interpretation and writing and critical review. GS and DYP contributed to data collection, interpretation, writing and critical review. NG, SP, VKM and BB contributed to critical review and finalization of the paper.

### **Conflicts of Interest**

Authors do not have conflict of interest.

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