Rapid Communication

Neutralization of Beta and Delta variant with sera of COVID-19 recovered cases and vaccinees of inactivated COVID-19 vaccine BBV152/Covaxin

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In the last several months, several SARS-CoV-2 variants have emerged from various countries worldwide. Among them, variant of concern (VOC) i.e. Alpha (B.1.1.7), Beta (B.1.351), Gamma (B.1.1.28.1) and Delta (B.1.617.2) are serious public health threats because of their association with the higher transmissibility and the potential immune escape. Various reports have been published on the neutralization efficacies with the sera of the currently available COVID-19 vaccines against these variants. However, the immune escape of Beta variant has been serious concern for the COVID-19 vaccination programme. It has shown reduced neutralization to several approved vaccines such as mRNA-1273, BNT162b2, ChAdOx1 nCoV-19, NVX-CoV2373. Another reason of global concern is the recent emergence and detection of highly transmissible Delta variant from India and various other countries. An inactivated SARS-CoV-2 vaccine, BBV152/Covaxin was rolled out under the national COVID-19 vaccination programme in India. The neutralization potential of the BBV152 has been already studied with the B.1, Alpha, Zeta and Kappa found to be effective against these variants.

Here, we assessed the neutralization of sera from COVID-19 recovered cases (n = 20) post 5–20 weeks of infection and vaccinees 28 days after two doses of BBV152 (n = 17) against Beta, Delta variants and compared with prototype B.1 (D614G).

The recovered cases were infected with B.1 (n = 17) and B.1.617.1 lineage (n = 3). SARS-CoV-2 isolates were propagated at Indian Council of Medical Research-National Institute of Virology (ICMR-NIV), Pune from the clinical samples using Vero CCL-81 cells and were used for a 50% plaque reduction neutralization test (PRNT50).

Geometric mean titre (GMT) for vaccinees sera against B.1, Beta and Delta variants were found to be 187.5 [95% confidence interval (CI): 129.3–271.9], 61.57 (95%CI: 36.34–104.3) and 68.97 (95%CI: 24.72–192.4), respectively. The GMT ratio of B.1 to Beta and Delta variants was 3.0 (95%CI: 2.6–3.6) and 2.7 (95% CI: 1.4–5.2).

Similarly, GMT titers in sera of recovered cases against B.1, Beta and Delta variants were 97.8 (95%CI: 61.2–156.2), 29.6 (95%CI: 13.4–65.0) and 21.2 (95% CI: 6.4–70.1), respectively. The GMT ratio of B.1 to Beta and Delta variants was 3.3 (95%CI: 2.6–3.6) and 2.7 (95% CI: 1.4–5.2).

Several studies have reported the reduction in the neutralization efficacy with the sera of naturally infected cases and individuals vaccinated with BBIBP-CorV (1.6×), BNT162b2 (6.5×), mRNA-1273 (8.6×), ChAdOx1 nCoV-19 (86×) against
Beta variant.\(^1,^6\) Reduced neutralization with the vaccinees sera of BNT162b2 mRNA (\(7 \times\)) and one dose of ChAdOx1 nCoV-19 was observed against Delta.\(^2\)

Our study demonstrated that despite a reduction in neutralization titers with BBV152 vaccinees sera against Beta and Delta variants, its neutralization potential is well established. Lastly, the broad epitope coverage in an inactivated vaccine induces immune response against whole virion, which decreases the magnitude of reduced neutralization against emerging variants. Further mutation of Delta variant known as ‘Delta AY.1 and Delta AY.2’ has been identified from India and other countries, which has been a threat to existing vaccine and drugs. We still do not know how reduced neutralization activity results into reduced vaccine effectiveness; hence, vaccine effectiveness studies are absolutely required to fully appreciate the effectiveness of BBV152 against these two variants.\(^7\)

**Ethical Approval**

The study was approved by the Institutional Biosafety Committee and Institutional Human Ethics Committee of ICMR-NIV, Pune, India under the project ‘Comparative assessment of BBV152 vaccine (COVAXINT\(^\text{TM}\)) antibody and antigen-specific responses in immunized population without past COVID-19 infection, individuals vaccinated after recovery from COVID-19 and non-vaccinated individuals with past COVID-19 infection’ (21-2-6N).

**Conflicts of Interest:** R.E. and V.K.M are employees of Bharat Biotech International limited, Hyderabad, with no stock options or incentives. P.D.Y., G.N.S., R.R.S., D.A.N., D.Y.P., G.D., A.M.S., P.A., N.G., S.P. and B.B. are the employees of the Indian Council of Medical Research, New Delhi and they do not have any a financial or non-financial
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**Author Contributions**

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**References**