Clinical Infectious Diseases

CORRESPONDENCE

Neutralization of Variant Under Investigation B.1.617.1 With Sera of BBV152 Vaccinees

To the Editor—The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants in places where the virus is uncontained poses a global threat from the perspective of public health and vaccine efficacy. Peng et al [1] recently reported on the increased transmissibility with the newly emerged Variant of Concern (VOC) (20C/S:452R and 20C/S:452R) with the L452R mutation in San Francisco. We report the immunological characteristics of a Variant under Investigation (VUI) B.1.617.1, playing a critical role in the current surge of coronavirus disease 2019 (COVID-19) in the western state of Maharashtra, India.

Several SARS-CoV-2 variants—B.1.1.7, B.1.351, and B.1.1.28.1—have been reported in India during 2021 [2, 3]. We had sequenced 146 nasopharyngeal/oropharyngeal swabs of COVID-19 cases [4]. Among these, 15 sequences had a combination of L452R and E484Q mutations, which raised concern as both are found in the receptor-binding domain (RBD) of the spike protein. However, the combined effect of these mutations is still unknown.

A total of 23 nonsynonymous changes were observed in the sequences, out of which 7 conserved nonsynonymous changes were found at the spike protein (G142D, E154K, L452R, E484Q, D614G, P681R, Q1071H) along with other conserved mutations (Figure 1A). These sequences were classified as VUI B.1.617.1, a sub-lineage of B.1.617. Phylogenetic analysis of B.1.617.1 sub-lineage sequences led to distinct clusters. The amino acid mutation analysis of the spike protein sequences retrieved from the study revealed them to have independent common mutations: first, T95I; second, H1101D; and third, V382L and V1175Y (Figure 1B). So far, 21 countries have reported the presence of B.1.617 variants [5]. Virus isolation was attempted from 15 specimens using Vero-CCL-81 cells [6]. Twelve specimens displayed cytopathic effects on the fourth post-infection day, which were further passaged and titered for performing a plaque reduction neutralization test (PRNT) [7]. These isolates were obtained from clinical specimens of asymptomatic individuals (age range: 14–55 years) and cases with a low-grade fever, cough, and sore throat (age range: 26–77 years).

The neutralization efficacy of the VUI B.1.617.1 variant was compared with B1 (D614G) and B.1.1.7 variants using sera of 28 BBV152 vaccinated individuals, collected during the phase II clinical trial [8]. The D614G versus B.1.617 Geometric mean titer (GMT) ratio was 1.95 (95% confidence interval [CI]: 1.60–2.38; $P < .0001$). Similarly, the GMT ratio comparison of B.1.1.7 was significantly higher than the GMT for B.1.617.1 (GMT ratio: 1.84; 95% CI: 1.50–2.27; $P < .0001$) (Figure 1C and 1D). The comparison of D614G and B.1.1.7 showed equivalent responses, with a GMT ratio of 1.06 and a 95% CI of 1.02–1.10.

Sera samples collected from individuals recovered from COVID-19 (n = 16) infected with lineage B.1.1.7, B.1.351, B.1.1.28.2, and B1 were used to perform PRNT50 against B.1.617.1 variant, and the results were compared with the vaccine recipients' sera samples. The GMT value for vaccine recipients was 88.48 (95% CI: 62.02–126.2) and for recovered cases was 86.85 (95% CI: 52.04–144.9). The sera of BNT162b2 vaccinees, which effectively neutralized B.1.1.7 and P.1 variants, was reduced with the B.1.351 variant [9]. The B.1.617.1 variant performance with vaccine sera was better than that of recovered cases. The results of B.1.1.7 variant neutralization with BBV152 vaccine sera and findings of B.1.617.1 emphasize that this vaccine is robust against emerging mutation and maintains the efficacy of the vaccine (Figure 1E) [10]. Assessment of the clinical efficacy of BBV152 against such variants is underway.

Notes

Author contributions. P. D. Y., G. N. S., and P. A. contributed to the study design, data collection, data analysis, interpretation, and writing and critical review. R. E., R. R. S., A. M. S., D. Y. P., D. A. N., and G. D. contributed to data collection, interpretation, writing and critical review. N. G., S. P., V. K. M., and B. B. contributed to the critical review and finalization of the paper.

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A

Reference Position	CDS/Gene	Reference	Allele	Amino acid change
241	5' UTR: 5' UTR	C	T	
3037	CDS: ORF1ab, former nsp1	C	T	
3457		C	T	
4965		C	T	Thr1567Ile
11201		A	G	Thr3646Ala
14408	CDS: ORF1ab, nsp12	C	T	Pro4715Leu
17523	CDS: ORF1ab, nsp13	G	T	Met5753Ile
20396	CDS: ORF1ab,nsp15-A1 and nsp15B	A	G	Lys6711Arg
21895	CDS:Spike	T	C	
21987		G	A	Gly142Asp
22022		G	A	Glu154Lys
22917		T	G	Leu452Arg
23012		G	C	Glu484Gln
23403		A	G	Asp614Gly
23604		C	G	Pro681Arg
24775		A	T	Gln1071His
25469	CDS: ORF3a	C	T	Ser26Leu
27638	CDS: ORF7a	T	C	Val82Ala
28881	CDS: N	G	T	Arg203Met
29402		G	T	Asp377Tyr
29742	Stem loop: basepair exception	G	T	

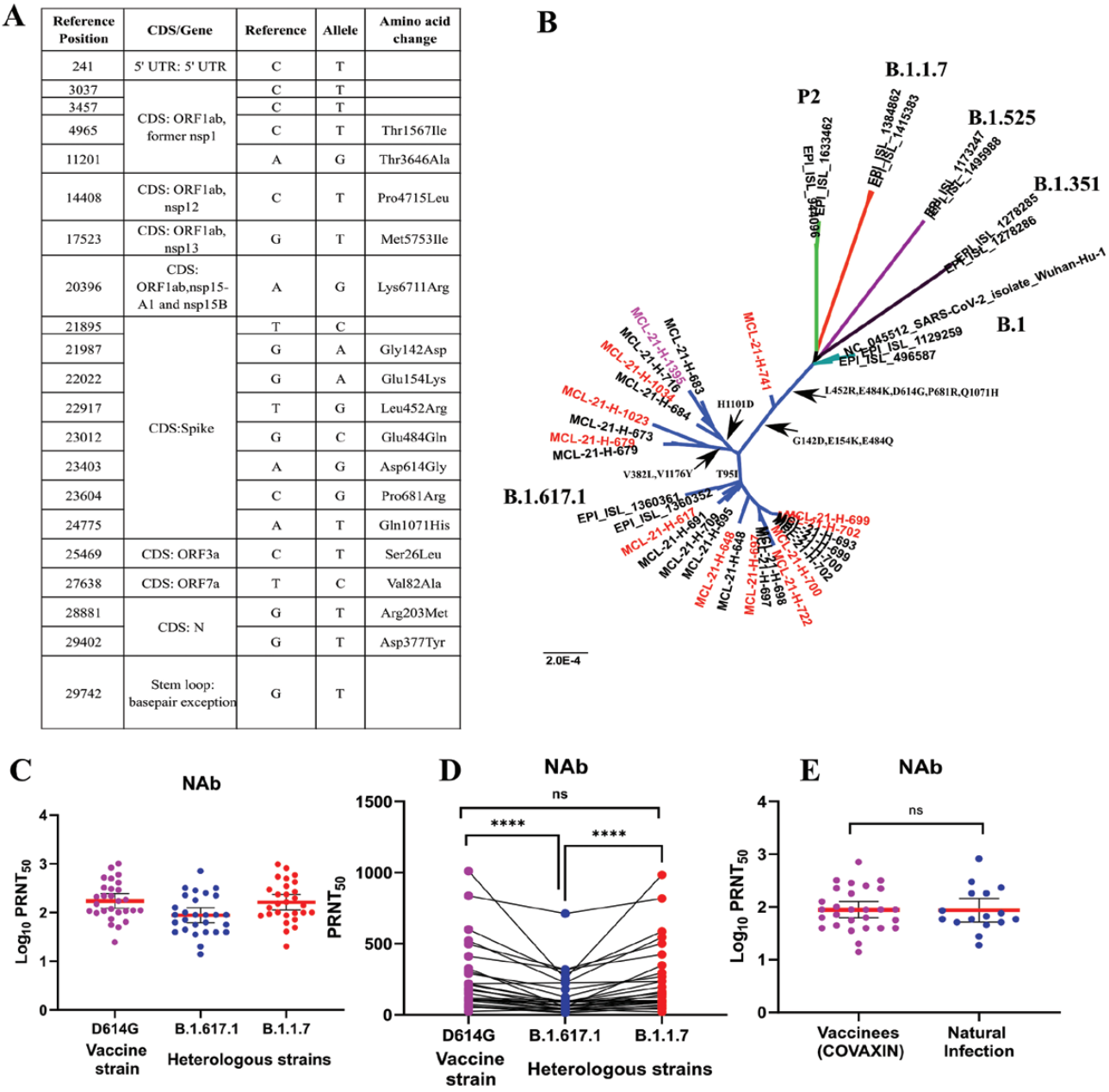

Figure 1. Characteristics and neutralization of the VUI B.1.617.1 variant. *A*, The common nucleotide changes observed in the majority of the isolates and clinical sequences from B.1.617.1 sub-lineage. *B*, A neighbor-joining tree was generated using a Tamura 3-parameter model with gamma distribution and a bootstrap replication of 1000 cycles. Isolates are marked in red and sequences from foreign travelers marked in pink. The representative sequences from other clades are represented as B.1.1.7 (red), B.1.617.1 (blue), B.1.351 (black), B.1.525 (purple) Brazil P2 (light green), and B1 (light blue). Individual spike mutations specific to the clusters are marked using the arrows. One of the sequences (MCL-21-H-741) had an E484K mutation, which led to its distinct clustering, in B.1.617.1 lineage (blue) that belonged to a traveler who had returned from United Arab Emirates to India. *C*, Scatterplot depicting the neutralizing response of the individual sera (n = 28) vaccinated with BBV152 (Covaxin, Bharat Biotech International Ltd., India) collected during a phase II clinical trial for the prototype B1 (D614G) (pink), B.1.1.7 (red), and B.1.617.1 (blue). The red solid line indicates the geometric mean titer and the error bar depicts the 95% confidence interval. *D*, Neutralization of the matched-pair samples compared with prototype D614G (pink), B.1.1.7 (red), and B.1.617.1 (blue). Neutralization reduction by a factor of 1.95 and 1.8 was observed against the B.1.617.1 variant for B1 (D614G) and B.1.1.7 variants, respectively. A reduction factor of 1.06 was observed between the B1 (D614G) and B.1.1.7 variant. A two-tailed pairwise comparison was performed using the Wilcoxon matched-pairs signed-rank test with a *P* value of .05. ****$P < .001$, ns = nonsignificant P value. *E*, Neutralization of the COVID-19 -recovered cases' sera (n = 16) of B.1.1.7 (n = 2), B.1.351 (n = 1), B.1.1.28.2 (n = 2)–infected individuals PRNT50 values against B.1.617.1 variant was compared with vaccine recipient serum samples. A two-tailed pairwise comparison was performed using the Mann-Whitney test with a *P* value of .05. Abbreviations: COVID-19, coronavirus disease 2019; PRNT, plaque reduction neutralization test; UTR, untranslated region CDS: Coding sequence; NAb: Neutralizing antibody.

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