Genetic emergence of B.1.617 in COVID-19

Laxmi Kirola

Submitted to: JMIR Public Health and Surveillance
on: May 17, 2021

Table of Contents

Genetic emergence of B.1.617 in COVID-19

Laxmi Kirola[1] PhD

[1]Banaras Hindu University Banaras IN

Corresponding Author:
Laxmi Kirola PhD
Banaras Hindu University
BHU 221005
Banaras
IN

Abstract

NONE

(JMIR Preprints 17/05/2021:30478)
DOI: https://doi.org/10.2196/preprints.30478

Preprint Settings

1) Would you like to publish your submitted manuscript as preprint?

✓ **Please make my preprint PDF available to anyone at any time (recommended).**
Please make my preprint PDF available only to logged-in users; I understand that my title and abstract will remain visible to all users.
Only make the preprint title and abstract visible.
No, I do not wish to publish my submitted manuscript as a preprint.

2) If accepted for publication in a JMIR journal, would you like the PDF to be visible to the public?

✓ **Yes, please make my accepted manuscript PDF available to anyone at any time (Recommended).**
Yes, but please make my accepted manuscript PDF available only to logged-in users; I understand that the title and abstract will remain v
Yes, but only make the title and abstract visible (see Important note, above). I understand that if I later pay to participate in <a href="http

Original Manuscript

Genetic emergence of B.1.617 in COVID-19

Laxmi Kirola*
*Department of Molecular and Human Genetics
Banaras Hindu University, Varanasi 221005, India

*All correspondence to be addressed to Laxmi Kirola
Department of Molecular and Human Genetics, Banaras Hindu University, Varanasi 221005, India

Email: laxmikirola@gmail.com Phone: +91-8448071292

The Indian SARS-CoV-2 Consortium on Genomics (INSACOG) includes 10 different national laboratories within the country and this group is continuing the sequencing process to map the complete genetic code of COVID-19 virus. COVID-19, a corona virus disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), first reported on December 2019 in

Wuhan China[1]. The first predominating variant D614G was reported later that spread to other countries and across the world during the first wave of COVID-19.

Subsequently, many other variants of SARS-CoV-2 have been identified worldwide and a few of them were classified as variants of concern (VOC), variants of interest (VOI), and variants of high consequence by the Centers for Disease Control and Prevention. As of May 8, 2021, ~158 million cases of COVID-19 have been reported, with ~32.9 lacs total deaths and an increasing number of recovering cases of 94 million; perhaps, these could be underestimated substantial numbers in an expert's opinion.

Three different VOCs namely B.1.1.7, B.1.351, and B.1.1.28 (P.1) started to prevalent within their respective countries later globally. In addition, VOIs such as B.1.617 and B.1.618 have emerged in India and recently B.1.617.2, a sub lineage of B.1.617 is continuously transmitting at higher peak within the country and across the world. Therefore, this is considered now a VOC (https://outbreak.info/latest) and this could possibly link with the second wave of COVID-19. Intriguingly, lineages B.1.617 and B.1.618 have been broadcasted in national and international media as a "double" or "triple" variant.

Like the mutation E484Q is similar to E484K which was seen first time in the B.1.351 and P.1, later this had emerged independently several times in other populations. This simple process discloses the virus mutates within its own family or creating new lineages, to function inversely and later this acts as a VOC. The B.1.427/B.1.429 lineages have such VOC called L452R mutation first identified in the USA and this has been shown to be almost >20% higher transmissibility in comparison to preexisting reported variants[2]. Also, B.1.617.2 is transmitting much rapidly in Indian population and recently this variant has been seen in many other countries. A recent study showed variant B.1.1.7 is 43 to 90% more transmissible in comparison to preexisting lineages in European population including a similar trend seen in other countries[3]. The initial GISAID data explains B.1.617+ variant has reasonably higher transmissibility rate (Figure 1).

Previously, many studies showed an amino acid change inside 438-506 position could considerably associated with increase in virus transmission, infection, or evade immunity, and both E484Q and L452R amino acid substitutions are present in the receptor-binding domain (RBD) of the spike protein like most other VOCs. For example: L452R mutation could involve enhanced interaction with human angiotensin-converting enzyme 2 (ACE2) receptor of the spike protein of COVID-19 that could lead to increased infectivity[4]. Moreover, other mutations such as E484K/E484Q increases the binding affinity via altering electrostatic interactions while analogously creating newer hydrogen bondings and the N501Y increases stronger hydrophobic interactions of RBD–ACE2 and creating more hydrogen-bonding networks. The K417N implicates increasing RBD binding to ACE2 alone or with N501Y and E484K together improved overall binding affinity of this complex and decreases antibody responses and last but not least, the D614G that stabilizes the spike protein for efficient entry within the host cell.

The first time an analysis of the samples collected from India's western Maharashtra state that showed an increase of ~60% samples with E484Q and L452R mutations. Recently, these two mutations along with third mutation P618R have been seen other parts of India (first seen in West Bengal) and this is now called as B.1.618 lineage. Moreover, when the National Centre for Disease Control was looking for samples for hitherto unknown variants such as high transmissibility, fast infectivity etc.; this double mutant strain or lineage B.1.617 came into picture. The B lineage along with other sub lineages are shown in Table 1. Until writing of this report, >60% of the cases in Maharashtra (>770 cases within total cases sequenced), an estimated over 50% higher transmissible and 60% more lethal, most probably ~1.6 deaths for everyone death in comparison to previous version of the virus. Instead, the B.1.1.7 had already dominated in Britain and >114 countries including India; nevertheless, the preliminary data on GISAID from India showed B.1.617 is spreading faster than B.1.1.7. The B.1.617 must be having a selective advantage over others for such a short period of increased transmissibility, infectivity or possibly escape from natural immunity. As

there were many lineages circulating at this time in India, the rapid expansion of B.1.1617.2 over other preceding lineages could be a genetic displacement of COVID-19.

Increased transmission of the virus at this stage is incredible, given the fact what we have understood about the other spike mutations B.1.1.7, B.1.351, B.1.1.28 etc. and what we are still trying to learn about newer emerging variants in other locations. We have very limited SARS-CoV-2 epidemiological, clinical and seroprevalence data from India yet to help us to understand the true extent of the epidemic. The Indian scientists are currently investigating the frequency of transmission, infection and reinfection in the second wave, as well as the clinical presentations of individuals with this variant to better understand the clinical and epidemiological effects of any immune escape, if any. Other groups based out in Hyderabad and Pune are also conducting neutralization assays on plasma from recipients of vaccines and await results of vaccine efficacy trials conducted/continuing in India during the second surge of COVID-19 pandemic.

However, the rate of current hospitalization of diagnosed COVID-19 cases and their clinical profiling are not fully accessible. Moreover, the current preliminary data generated in the country by INSACOG indicated that the B.1.1.7 and B.1.617 (sub lineage B.1.617.2) variants are linked with second wave in the country and in-hospital mortality, higher transmissibility that accounts for about >60% of the total cases. Interestingly a latest study investigated variant B.1.617 with mutations (L452R, E484Q and P681R) in different other combinations, and showed this barely affecting the efficiency of cellular entry and to elude immunity when elicited with neutralizing antibodies and BNT162b2 mRNA vaccine. They also described mutation P681R contributes to increased pathogenesis through syncytium formation as observed in hamsters also in human samples for higher rate of transmission in India[5]. Conversely, a recent study from India showed a likely equal neutralizing capacity for B.1.617 among the vaccinated individuals versus the recovered COVID-19 patients[6].

This cause and effect could be due to mainly greater number of gatherings happened in the country,

inappropriate COVID-19 behaviors among people etc. This also causes congested health facilities, leading to lower numbers of available hospitals beds, harsh shortage of oxygen supply and continued increase in COVID-19 cases that decisively compromised proper patient care. While there is not any valid evidence shown on other antiviral agents and anti-inflammatory usages that are under current treatment for COVID-19 in India and worldwide; nonetheless, these are parallelly important and effective for these variants in emergency practices. The emergence of subsequent novel VOI(s) or VOC(s) one after others highlight the prominence and attentiveness for early identification, detection and extensive genomic surveillance globally. Furthermore, the dynamic virulency of SARS-CoV-2 challenges to develop next-generation vaccines which can help us to stimulate mainly neutralizing activity and longevity against future corona virus.

References

1. Wu F, Zhao S, Yu B, et al. A new coronavirus associated with human respiratory disease in China. *Nature*. 2020;579(7798):265-269. doi:10.1038/s41586-020-2008-3
2. Deng X, Garcia-Knight MA, Khalid MM, et al. Transmission, infectivity, and antibody neutralization of an emerging SARS-CoV-1 2 variant in California carrying a L452R spike protein mutation 2. *medRxiv*. 2021:2021.03.07.21252647. https://doi.org/10.1101/2021.03.07.21252647.
3. Davies NG, Davies NG, Abbott S, et al. Estimated transmissibility and impact of SARS-CoV-2 lineage B.1.1.7 in England. *Science (80-)*. 2021;3055(March):1-16.
4. Circulating SARS-CoV-2 variants escape neutralization by vaccine-induced humoral immunity.
5. SARS-CoV-2 B.1.617 emergence and sensitivity to vaccine-elicited antibodies.
6. Neutralization of variant under investigation B.1.617 with sera of BBV152 vaccinees.

Table 1. Summary details on SARS-CoV-2 lineages including preexisting variants of concerns and recently identified variant B.1.617 from India.

*Shows functionally important mutations probably involved in pathogenesis

Origin	First reported	Lineage/sub-lineage/Designation		Total mutation	Total Amino acid change	Main mutations with amino acid changes in Spike	Countries found	References
United Kingdom (Kent)	December, 2020	B.1.1.7 (VOC-20DEC-01)		23	17	Δ69/70, Δ144, E484K, S494P N501Y, A570D, D614G P681H, T716I, S982A D1118H, K1191N	~114	Rambaut et al., 2020 Davies et al.,2021
South Africa (Eastern Cape)	October, 2020	B.1.351 (VOC-20DEC-02)		23	17	D80A, D215G, Δ241/242/243 K417N, E484K N501Y, D614G A701V	45	Tegally et al., 2020
Japan/Brazil (Rio de Janeiro)	January, 2021	B.1.1.28 (VOC-21JAN-02)		35	17	L18F, T20N P26S, D138Y R190S, K417T E484K, N501Y D614G, H655Y T1027I, K417N	21	Voloch et al., 2020
United States (California)	May, 2021	B.1.427/ B.1.429 (CAL.20C)		11	5	L452R, S13I, W152C	30	Zhang et al., 2021
India (Maharashtra)	February 2021	**B.1.617**	B.1.617.1 *VUI-21APR-01*	>15	6	D614G, L452R* E484Q*, P618R*, Q1071H, E154K del681	~34 Until May 8	Ferreira1 et. Al., 2021 (outbreak.info, cdc.gov)
			B.1.617.2 VOC-21APR-02	>15	6	D614G, L452R*, T478K*, P681R* D950N, T19R del157/158	~31 Until May 8	Ferreira1 et. Al., 2021 (outbreak.info, cdc.gov)
			B.1.617.3 *VUI-21APR-03*	>15	5	D614G, L452R* E484Q*, P618R* T19R	~4 Until May 8	Ferreira1 et. Al., 2021 (outbreak.info, cdc.gov)

Supplementary Files