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Short Communication

Community transmission of SARS-CoV-2 with B.1.1.7 lineage in Mumbai, India

Jayanthi Shastri [a,*,1], Pragya D. Yadav [b,1], Sachee Agrawal [a], Anita M. Shete [b], Dimpal A. Nyayanit [b], Swapneil Parikh [a], Mangala Gomare [c], Rima R. Sahay [b], Deepak Y. Patil [b], Manisha Dudhmal [b], Neelam Kadam [c]

[a] *Molecular Diagnostic Reference Laboratory, Kasturba Hospital for Infectious Diseases, Mumbai, Maharashtra, 400034, India*
[b] *Indian Council of Medical Research-National Institute of Virology, Pune, Maharashtra, 411021, India*
[c] *Public Health Department, Municipal Corporation of Greater Mumbai, Mumbai, Maharashtra, 400 001, India*

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Abstract The B.1.1.7 (Alpha) variant has been detected in Mumbai, India during February 2021. Subsequently, we retrieved 43 sequences from specimens of 51 COVID-19 cases from Mumbai. The sequence analysis revealed that the cases were mainly affected with Alpha variant which suggests its role in community transmission of SARS-CoV-2 in Mumbai, India.

Over the course of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic, multiple variants have emerged across the globe. During late December 2020, a new variant of concern (VOC) B.1.1.7 (Alpha) was identified in the United Kingdom which has spread to more than 135 countries in the world including Europe, Asia, USA.[1] This variant has about 17 mutations, including N501Y, P681H, HV 69—70 deletion in the spike protein and various other mutations. It has been designated as variant of concern due to its high transmissibility, with estimates ranging from 40 to 80% higher transmissibility.[2,3] During the first wave of pandemic in India, SARS-CoV-2 cases showed downward trend since September 2020; however it again started rising in March 2021 with the number of cases being double of last year. Government of India started the genomic surveillance of newly emerging SARS-CoV-2

* Corresponding author. Department of Microbiology T.N. Medical College & B. y. L. Nair Hospital i/c Molecular Diagnostic reference Laboratory Kasturba hospital for infectious diseases Mumbai, 400011, India. Fax: +91 22 23072663.
E-mail address: jsshastri@gmail.com (J. Shastri).
[1] Equal first author.

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variants under 'The Indian SARS-CoV-2 Consortium on Genomics (INSACOG)'. The clinical specimens of all the United Kingdom (UK) travelers were screened using next-generation sequencing (NGS) since January 2021. Genomic surveillance has detected VOC Alpha, Beta (B.1.351), Gamma (B.1.1.28.1) variants. The Alpha was found to be the second most common variant in India among the detected variants till March 2021.[4]

During the first week of January 2021, the new SARS-CoV-2 variant, Alpha was first detected among the UK travelers arriving in Mumbai, Maharashtra, India. Despite the strict mitigation policies, two distinct areas in Mumbai had a spurt in SARS-CoV-2 cases mainly due to dense population, informal settlements and overcrowding. With the ongoing screening of SARS-CoV-2 in government and private laboratories in Mumbai, two private laboratories in Mumbai using TaqPath kits for Real time RT-PCR detected Spike gene target failure (SGTF) among clinical specimens collected from the community during January–February 2021. SGTF has been already identified and assumed to be a surrogate marker for the detection of alpha variant.[3] SGTF clinical samples of SARS-CoV-2 cases from 2 private laboratories received at Reference molecular laboratory at Kasturba Hospital for Infectious Diseases, Mumbai were sent to ICMR-National Institute of Virology (ICMR-NIV), Pune for whole genome sequencing.

Genomic characterization of the referred clinical specimens was carried out with the quantified RNA using next-generation sequencing (NGS). Briefly, the ribosomal RNA depletion was performed using NebnextrRNA depletion kit (Human/mouse/rat) followed by cDNA synthesis using the first strand and second synthesis kit. The RNA libraries were prepared using TruSeq Stranded Total RNA library preparation kit. The amplified RNA libraries were quantified and loaded on the Nexseq Illumina sequencing platform after normalization.[5]

Reference-based mapping was performed to retrieve the genomic sequence of the SARS-CoV-2 from clinical samples using the CLC genome workbench v20.0.4 and submitted to the public repository i.e., GISAID. A phylogenetic tree was generated using the MEGA software version.[7]

Out of 51 SARS-CoV-2 cases, the clinical details of 37 cases (18 male, 19 female) were available. The cases were distributed amongst all the age groups including $<$14 years (n = 3); 15–45 years (n = 14), 46–60 years (n = 8), and $>$60 years (n = 17). Out of 37 cases, 70% were asymptomatic while 27.03% had cough, 21.62% had fever, 18.92% had mild breathlessness and 13.51% had runny nose. The cases were followed till 14 days to check for the development of any kind of symptoms. The cases didn't develop disease severity and recovered completely. The COVID-19 vaccination drive has started in India from 16 January 2021. However, only health care and frontline workers were vaccinated during the initial phase of vaccination. All the study participants were not vaccinated against SARS-CoV-2 during the study period.

SARS-CoV-2 sequences (n = 43) were retrieved with more than 98% genome length from the clinical specimens of the COVID-19 cases. The details of the total read mapped, percent relevant reads and genome length is given in Table 1. The lineage of the retrieved sequences was identified using the pangolin (https://pangolin.cog-uk.io/). Majority of the sequences belong to B.1.1.7 lineage (n = 23) followed by B.1.1.306 lineage (n = 11). Sequences for variant of interest (VUI): Eta [B.1.525] (n = 1), B.1.617.3 (n = 1) and Kappa [B.1.617.1] (n = 2) and other common circulating variants (n = 5) were also retrieved. Fig. 1 depicts the neighbor-joining tree for the retrieved and the reference SARS-CoV-2 sequences. The other sequences retrieved were B.1.1 (n = 2), B.1.36.22 (n = 1), B.1.1.36.29 (n = 1) and B.1.409 (n = 1)common circulating lineages. The percent nucleotide similarity (PNS) of the retrieved SARS-CoV-2 sequences in comparison to Wuhan Hu-1 isolate is given in supplementary table 1.

Mumbai is the India's most populous city and parts of Mumbai have impoverished tenements and large slum areas which are amongst the most densely packed human habitats in the world.[6] Additionally overcrowding in public transport modes like local trains, buses are common in Mumbai. The combination of intense contact between commuters and close inhabitation favors SARS-CoV-2 transmission. This has contributed to rapid community transmission of SARS-CoV-2 among the population in Mumbai City.

The use of SGTF as surrogate marker will not be advisable as many of the SARS-CoV-2 testing laboratories do not use S-gene target for SARS-CoV-2 PCR testing. This could lead to many missed Alpha variant cases, and therefore genome sequencing is warranted.

This genome sequencing study led to identification of a mix of different variants including VOC Alpha variant and few cases of Kappa and B.1.617.3 variants in the local population of Mumbai, Maharashtra. The higher numbers of Alpha variant indicates a local transmission of the virus within the area during the month of February 2021. This could have contributed to rise in cases in this city. Further it is observed that the N501Y mutation present on the spike gene is also not present in the most of the sequences that fall in Alpha lineage. The N501Y mutation influences the binding affinity of the virus to the human ACE2 receptors7, indicating a reduced ACE2 affinity of the Alpha variant in current samples. The SARS-CoV-2 sequences retrieved from the B.1.1.306 lineage have L18F, A27S, E484K, D641G, Q675H mutations in the spike protein. E484K mutation is reported to be an escape mutation, and the presence of this mutation is a cause of concern. The presence of B.1.617.3 and Kappa variant in the samples collected during the February, 2021 indicates early circulation of these variant in Mumbai. During the second wave 2, 89, 11,744 cases and 3, 63,079 deaths have been recorded in India with a crude case fatality rate of 1.24%. As on 11th June 2021, Maharashtra reported cumulative 56, 08,753 cases during the second wave.

Extensive mitigation policies like effective contact tracing of the local and international travelers, strict isolation and quarantine protocols, imposing a ban on

Table 1 Details of the clinical samples of the Community transmission of SARS-CoV-2 cases from Mumbai.

Sr. No	MCL No	Age	Sex	Symptomatic /asymptomatic	Address	Date of onset /testing	SARS-CoV-2 result with CT Value for E gene and ORF1	Percentage genome retrieved	Circulating clade	Updated Pangolin Lineage	GISAID number
1	MCL-21-H-1007	63	M	COUGH, BREATHLESSNESS, FEVER	Sion	16.01.2021	Positive	100	GR	B.1.1.306	EPI_ISL_2483050
2	MCL-21-H-970	65	M	Asymptomatic	Dahisar	28.01.2021	Positive	100	GR	B.1.1.306	EPI_ISL_2483043
3	MCL-21-H-802	82	M	Asymptomatic	Boriwali	Feb-21	22.06	97.85	GR	B.1.1.7	EPI_ISL_3665916
4	MCL-21-H-808	Not provided	F	Not provided	Not provided	Feb-21	Not provided	97.85	_	—	—
5	MCL-21-H-810	Not provided	M	Not provided	Not provided	Feb-21	Not provided	99.22	GR	B.1.1.7	EPI_ISL_3471364
6	MCL-21-H-812	Not provided	F	Not provided	Not provided	Feb-21	18	99.68	GR	B.1.1.7	EPI_ISL_3471365
7	MCL-21-H-813	Not provided	M	Not provided	Not provided	Feb-21	21	99.15	GR	B.1.1.7	EPI_ISL_3665917
8	MCL-21-H-814	Not provided	M	Not provided	Not provided	Feb-21	15	98.5	GR	B.1.1.7	EPI_ISL_3503132
9	MCL-21-H-815	Not provided	M	Not provided	Not provided	Feb-21	15	98.44	GR	B.1.1.7	EPI_ISL_3503133
10	MCL-21-H-816	Not provided	F	Not provided	Not provided	Feb-21	19	99.48	GR	B.1.1.7	EPI_ISL_3471366
11	MCL-21-H-817	Not provided	F	Not provided	Not provided	Feb-21	18	96.87	_	—	—
12	MCL-21-H-819	Not provided	M	Not provided	Not provided	Feb-21	18	93.92	_	—	—
13	MCL-21-H-820	Not provided	M	Not provided	Not provided	Feb-21	26	98.15	GR	B.1.1.7	EPI_ISL_4109501
14	MCL-21-H-821	Not provided	M	Not provided	Not provided	Feb-21	21	99.41	GR	B.1.1.7	EPI_ISL_3471367
15	MCL-21-H-822	Not provided	F	Not provided	Not provided	Feb-21	15	99.25	GR	B.1.1.7	EPI_ISL_3471368
16	MCL-21-H-823	Not provided	M	Not provided	Not provided	Feb-21	28	99.3	GR	B.1.1.7	EPI_ISL_3543285
17	MCL-21-H-824	Not provided	M	Not provided	Not provided	Feb-21	19	99.2	GR	B.1.1.7	EPI_ISL_3543286
18	MCL-21-H-1024	38	M	Asymptomatic	Boriwali	03.02.2021	Positive	99.82	GR	B.1.1	EPI_ISL_2521748
19	MCL-21-H-1025	37	F	Asymptomatic	Borilwali	03.02.2021	Positive	100.02	GR	B.1.1	EPI_ISL_2521749
20	MCL-21-H-1029	31	F	Asymptomatic	Boriwali	03.02.2021	Positive	100.02	GR	B.1.1.306	EPI_ISL_2483053
21	MCL-21-H-1030	56	M	COUGH FEVER	Boriwali	03.02.2021	Positive	100	GR	B.1.1.306	EPI_ISL_2483054
22	MCL-21-H-1031	32	M	Asymptomatic	Boriwali	03.02.2021	Positive	100.02	GR	B.1.1.306	EPI_ISL_2483055
23	MCL-21-H-1033	24	F	cold, cough, fever	Dahisar	03.02.2021	Positive	100.01	GR	B.1.1.306	EPI_ISL_2483056
24	MCL-21-H-1034	77	M	fever, bodyache, cough,	Dahisar	03.02.2021	Positive	100	G	B.1.617.1	EPI_ISL_2483057
25	MCL-21-H-972	71	M	cough breathlessness	Not provided	06.02.2021	Positive	100	GH	B.1.36.22	EPI_ISL_2483044
26	MCL-21-H-615	41	F	Asymptomatic	Dombivali	11.02.2021	26.28	73.1	_	—	—
27	MCL-21-H-616	8	F	Asymptomatic	Mankhurd	11.02.2021	25.05	41.9	_	—	—
28	MCL-21-H-976	68	M	Breathlessness	Sion	16.02.2021	Positive	100	GR	B.1.1.306	EPI_ISL_2483045
29	MCL-21-H-608	57	M	Asymptomatic	Bandra	17.02.2021	16	99.68	GR	B.1.1.7	EPI_ISL_2497900
30	MCL-21-H-609	53	M	Asymptomatic	Mulund	17.02.2021	14	99.73	G	B.1.525	EPI_ISL_2399419
31	MCL-21-H-613	50	M	Asymptomatic	Powai	17.02.2021	19	98.91	G	B.1.1.7	EPI_ISL_3471363
32	MCL-21-H-977	65	M	Breathlessness	Badlapur	17.02.2021	Positive	100	GR	B.1.1.306	EPI_ISL_2483046
33	MCL-21-H-602	48	F	Asymptomatic	Kalbadevi	18.02.2021	32	50.05	_	—	—
34	MCL-21-H-603	25	F	Asymptomatic	Mulund	18.02.2021	21	98.22	GR	B.1.1.7	EPI_ISL_3503131
35	MCL-21-H-604	37	M	Asymptomatic	Mulund	18.02.2021	17	99.68	GR	B.1.1.7	EPI_ISL_2497899
36	MCL-21-H-605	64	F	Asymptomatic	Mulund	18.02.2021	22	98.17	GR	B.1.1.7	EPI_ISL_3471361

(*continued on next page*)

Table 1 (*continued*)

Sr. No	MCL No	Age	Sex	Symptomatic /asymptomatic	Address	Date of onset /testing	SARS-CoV-2 result with CT Value for E gene and ORF1	Percentage genome retrieved	Circulating clade	Updated Pangolin Lineage	GISAID number
37	MCL-21-H-606	54	F	Asymptomatic	Mulund	18.02.2021	25	97.58	GR	B.1.1.7	EPI_ISL_3665914
38	MCL-21-H-607	71	F	Asymptomatic	Mulund	18.02.2021	22	99.41	GR	B.1.1.7	EPI_ISL_3471362
39	MCL-21-H-610	66	F	Asymptomatic	Mulund	18.02.2021	15	99.58	GR	B.1.1.7	EPI_ISL_2497901
40	MCL-21-H-611	12	F	Asymptomatic	Thane	18.02.2021	15	99.78	GR	B.1.1.7	EPI_ISL_2497902
41	MCL-21-H-612	44	M	Asymptomatic	Mulund	18.02.2021	20	99.67	GR	B.1.1.7	EPI_ISL_2497903
42	MCL-21-H-614	30	F	Asymptomatic	Mulund	18.02.2021	18	99.78	GR	B.1.1.7	EPI_ISL_2497904
43	MCL-21-H-978	45	M	Asymptomatic	Digha Navi Mumbai	18.02.2021	Positive	100	GH	B.1.36.29	EPI_ISL_2483047
44	MCL-21-H-801	2	F	Asymptomatic	Dharavi	23.02.2021	Positive	97.39	GR	B.1.409	EPI_ISL_3665915
45	MCL-21-H-1020	21	M	COUGH, BREATHLESSNESS, FEVER	Sion	27.02.2021	Positive	99.88	G	B.1.617.3	EPI_ISL_2497905
46	MCL-21-H-988	53	F	COUGH, FEVER	Kandivali	28.02.2021	Positive	100.01	GR	B.1.1.306	EPI_ISL_2483048
47	MCL-21-H-996	66	F	Asymptomatic	Kandivali	28.02.2021	Positive	100	GR	B.1.1.306	EPI_ISL_2483049
48	MCL-21-H-1022	68	F	COUGH, BREATHLESSNESS, FEVER	Dharavi	28.02.2021	Positive	100	GR	B.1.1.306	EPI_ISL_2483051
49	MCL-21-H-1023	60	M	COUGH, BREATHLESSNESS, FEVER	Goavndi	01.03.2021	Positive	99.99	G	B.1.617.1	EPI_ISL_2483052
50	MCL-21-H-1316	40	M	Asymptomatic	Not provided	08.03.2021	Positive	77.6	_	—	—
51	MCL-21-H-799	26	M	Asymptomatic	Santacruz	18.03.2021	Positive	97.3	_	—	—

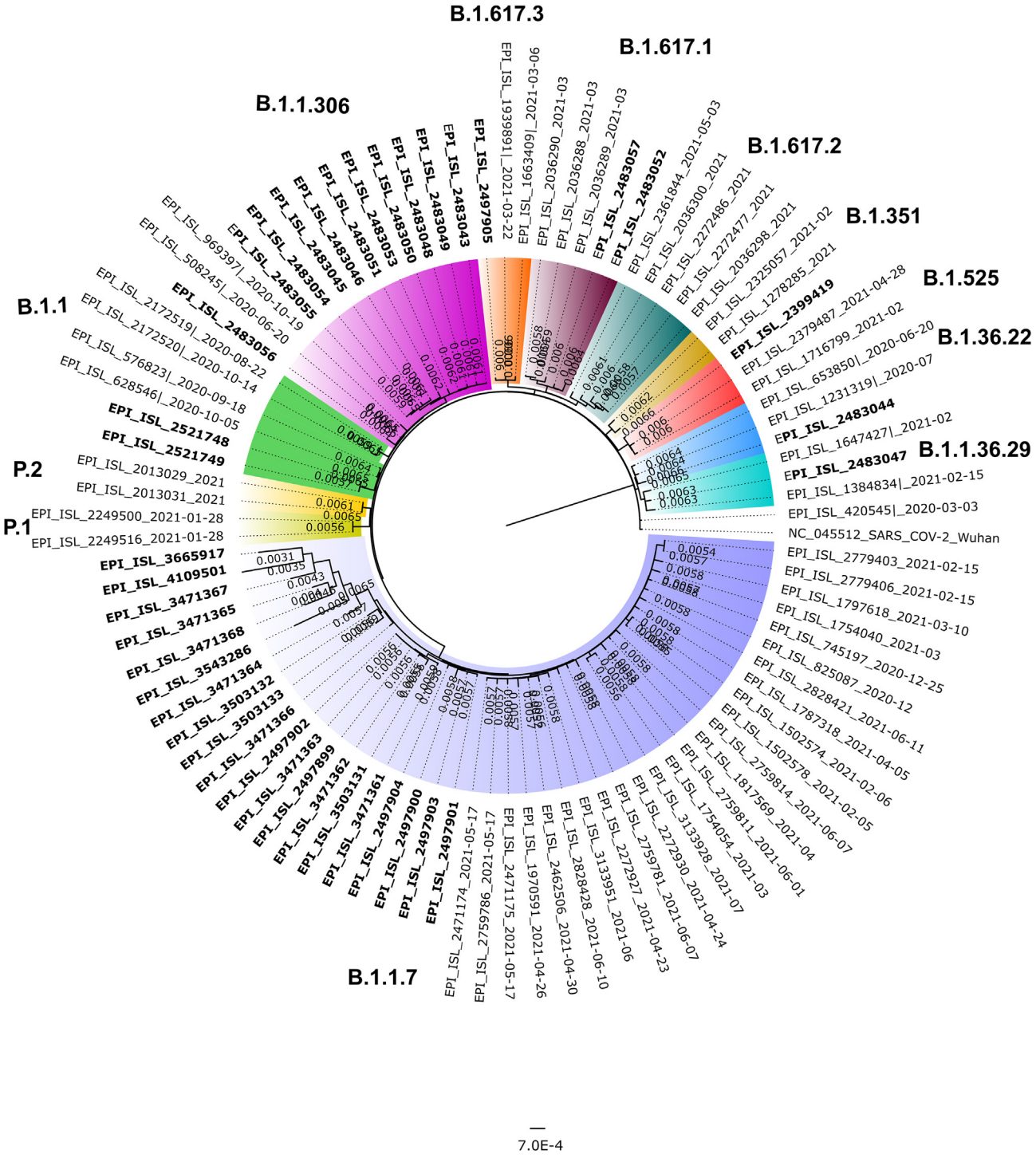

Figure 1. Phylogenetic tree of the SARS-CoV-2 sequences retrieved from Mumbai, Maharashtra: A neighbor joining tree was generated using a Tamura 3-paramter model with gamma distribution and a bootstrap replication of 1000 cycles. The sequences retrieved in this study are marked in boldfaced. The variants of concern, and the variants of interest are marked in different colors on branches; B.1.1.7 (light blue), B.1.525 (Crimson red), B.1.617.3 (orange), B.1.617.1 (brown), B.1.1.306 (pink color).

blic gatherings, community awareness and engagement, stringent lockdown proved to be appropriate strategies to break the chain of virus transmission. Besides this, robust and proactive genomic surveillance of emerging SARS-CoV-2 variants is imperative for the timely identification and control of their transmission in the community. Rapidly increasing vaccine coverage in India would be the most effective way to inhibit further deadly waves of COVID-19.

Ethical approval

The study was approved by the Institutional Biosafety Committee and Institutional Human Ethics Committee of ICMR-NIV, Pune, India under project 'Molecular epidemiological analysis of SARS-COV-2 circulating in different regions of India' (20-3-18N).

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Author contributions

JS, PDY contributed to study design, data collection, data analysis, interpretation and writing and critical review. SA, AS, SP, DAN, MG, RRS, DYP, MD, NK contributed to data collection, data analysis data interpretation, writing and critical review.

Data availability statement

Data set of this study is available within article and any other information will be available from the corresponding author upon reasonable request.

Declaration of competing interest

No conflict of interest exists among authors.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jmii.2021.10.004.