RESEARCH

Commentary

Plausible reasons for purifying selection of SARS-CoV-2 Omicron BF.7 in India

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ABSTRACT

SARS-CoV-2 infection has been playing havoc with emerging variants of concern (VoC.), including the latest Omicron BF.7. Here, we highlight and discuss the role of purifying selection of these unique and common mutations to other populations.

KEYWORDS: Variants of concern, Omicron, SARS-CoV-2, Genomics, Purifying selection.

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The SARS-CoV-2 infections have caused a great economic burden across the world even as numerous variants of concerns (VOC), most importantly, Alpha, Beta, Gamma, and Delta have been on rise (Carabelli et al. 2023; Chopra et al. 2021). While the Omicron variant is the most important currently circulating VOC, it is unclear how malevolent the Omicron variant is. Given that the data on infection and outcome from other countries including China are scanty, there is a need to check Omicron sub-variants such as BF.7 which might likely be more virulent in causing pathogenesis (Focosi et al. 2022).

Based on the available data, the SARS-CoV-2 Omicron BF.7 lineage seems to be hardly ever pathogenic in India (Mohapatra et al. 2022). This, we argue, could be attributed to effective vaccination programmes in India, diet patterns, and perhaps epigenetic spectrum associated. While the Omicron subvariant XBB's immune evading mutations, including R346T, isn't showing pathogenesis, this implies that these could be promiscuously purifying variants that may be drawn attention to. It is important to mention that the mutations in BF.7 in combination with R346T, K444T, F486S, and D1199N could add a high degree of immune escape mechanism rather than just R346T (Chakraborty et al. 2023; Arora et al. 2022). There was a sudden increase in covid cases in China and its neighboring countries such as Japan, Taiwan, Hong Kong, and South Korea; and BF.7 could have had these mutations in combination with either all or maybe any three with R346T as the common among all recombination events (Table 1). We argue that this one of the most important factors could be the epigenetics and diet patterns which are very similar within these countries as compared to others. Until and unless a large data set of BF.7 variants from these above-mentioned countries are known, the epigenetics and diet patterns and meta data pertaining to the immunization programme could delve into greater understanding of these variants. Furthermore, booster vaccines have shown to be variant-resilient and have passive immunotherapy against the new Omicron BQ.1.1, XBB.1, and BF.7 variants (Sullivan et al. 2022). In this pilot study, we sought to ask whether mutational biases influence the purified selection wherein mutations have been adapted and yet don't turn out to be pathogenic (Cano et al. 2022). We found that R346T tends to be purifying (Figure 1). While the previous BA.4/5 sub variants account for an approximate 77% of Omicron lineages, the latter variants have more likely increased immune evasion wherein BF.7 acquiring R346T and BQ.1 acquiring the K444T and N460K mutations in Spike, and probably have a role in enhancing neutralization resistance of these variants (Qu et al. 2022).

Table 1. List of mutations across SARS-CoV-2 variants and lineages

Sl. No.	Variant Name	Lineage	Mutations	Accession
1	Alpha (20I)	B.1.1.7	D614G, N501Y, A570D, P681H, T716I, S982A, D118H	EPI_ISL_2557023 EPI_ISL_2557028

				EPI_ISL_2557030 EPI_ISL_2557017
2	Delta (21A)	B.1.617.2	D614G, T19R, G142D, R158G, L452R, T478K, P681R, D950N	EPI_ISL_11582084 EPI_ISL_11582083
3	Omicron (21K)	BA.1	D614G, T19I, V213G, S371F, T736A, D405N, R408S	EPI_ISL_10630426 EPI_ISL_10630403
4	Omicron (21L)	BA.2	S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R	EPI_ISL_15757269 EPI_ISL_15757263 EPI_ISL_15757264 EPI_ISL_16170539
5	Omicron (22A)	BA.4	L452R, F486V, G142D, V213G, G339D, S371F, S373P, S375F	EPI_ISL_16922457 EPI_ISL_16922442 EPI_ISL_16922437 EPI_ISL_16922435 EPI_ISL_16922434
6	Omicron (22B)	BA.5	E484A, F486V, Q498R, N501Y, Y505H, L452R, D614G	EPI_ISL_16970185 EPI_ISL_17417686 EPI_ISL_14819001 EPI_ISL_13409413
7	Omicron (22C)	BA.2.12.1	L452Q, S704L, D405N, N440K, S477N, Q493R, Q498R, N501Y	EPI_ISL_16701383 EPI_ISL_16701381 EPI_ISL_16701380 EPI_ISL_16701378
8	Omicron (22D)	BA.2.75	K147E, W152R, F157L, I210V, G257S, G339H, N460K, D405N, R408S, K417N, H655Y, P681H	EPI_ISL_15757271 EPI_ISL_15757270 EPI_ISL_15757267 EPI_ISL_15757266
9	Omicron (22E)	BQ.1.1	K444T, N460K, D405N, R408S, K417N, L452R, Q493R, Q498R, Y505H, R346T	EPI_ISL_16701376 EPI_ISL_16633493
10	Omicron (22F)	XBB and XBB.1	H146Q, V213E, R346T, S371F, S373P, S375F, N440K, F490S, Q498R	EPI_ISL_16701382 EPI_ISL_16170535
11	Omicron (23A)	XBB.1.5	D405N, R408S, N460K, T478K, N764K, D796Y, Y505H, H655Y, E484A	EPI_ISL_16701379 EPI_ISL_16701375 EPI_ISL_16613719

12	Omicron	BF.7	G142D, V213G, G339D, R346T, S371F, S373P, S375F, K417N, L452R, S477N, T478K, N501Y, D614G	EPI_ISL_16395183 EPI_ISL_17280446 EPI_ISL_17254860 EPI_ISL_17253547 EPI_ISL_17243396

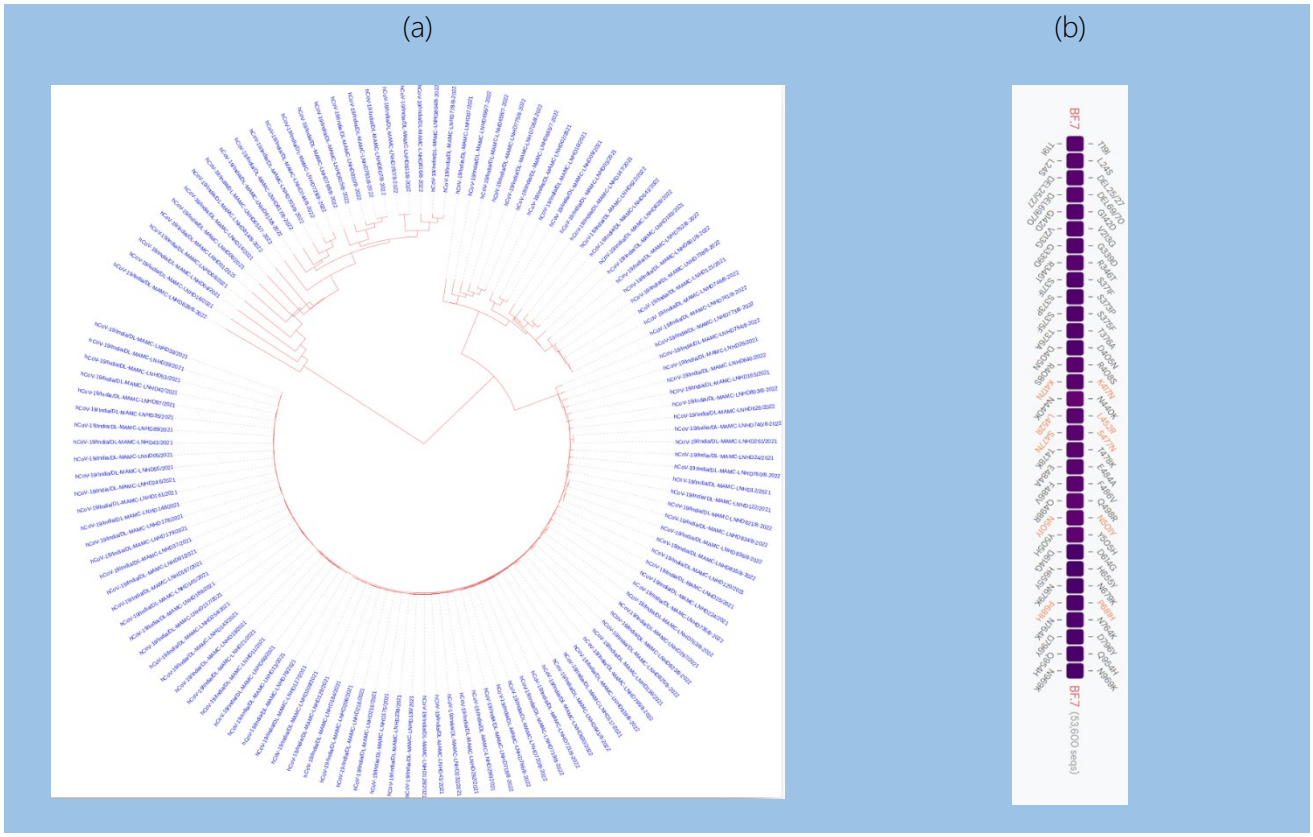

Figure 1: (a) An iTOL image of BF.7 and all other Omicron variants from MAMC/India. A distinct clade is seen to have diverged from this. (b) BF.7 gene lineages.

Conclusions and the way forward

The outbreak of COVID-19 caused by SARS-CoV-2 has swiftly spread worldwide with the probable origin of BF.7 is still unclear. Interestingly, all the emerging case reports are either asymptomatic or oligosymptomatic transmission (Kupferschmidt and Vogel 2021). Given the urgent need for rapid identification and traceability of Omicron variants, an indefatigable checking the antibody titer against deleterious mutations and subsequent single cell genomic assay would have been a better proposition (Kannan et al. 2022). Furthermore, the

difference in viral loads among samples will possibly affect the stability of average depth and genome-wide coverage with increase in whole-genome mapping. We firmly hope that prompt diagnosis and rapid whole-genome analysis would allow a decisive response to the SARS-CoV-2 outbreak that will bring disease under control. In addition, there is an urgent need for developing an inventory of antibodies, affimers, nanomers, and recombinant proteins to support SARS-CoV-2 research with spike and nucleocapsid recombinant proteins as targets.

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Conflicts of interest

The authors declare no conflict of interest.

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Authors' contributions

SKP, SK, AP, AS contributed equally. All other authors chipped in with lateral suggestions.

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