

## Emergence of omicron variant's sublineages BA.4 and BA.5: risks assessment and possible countermeasures

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Dear Editor,

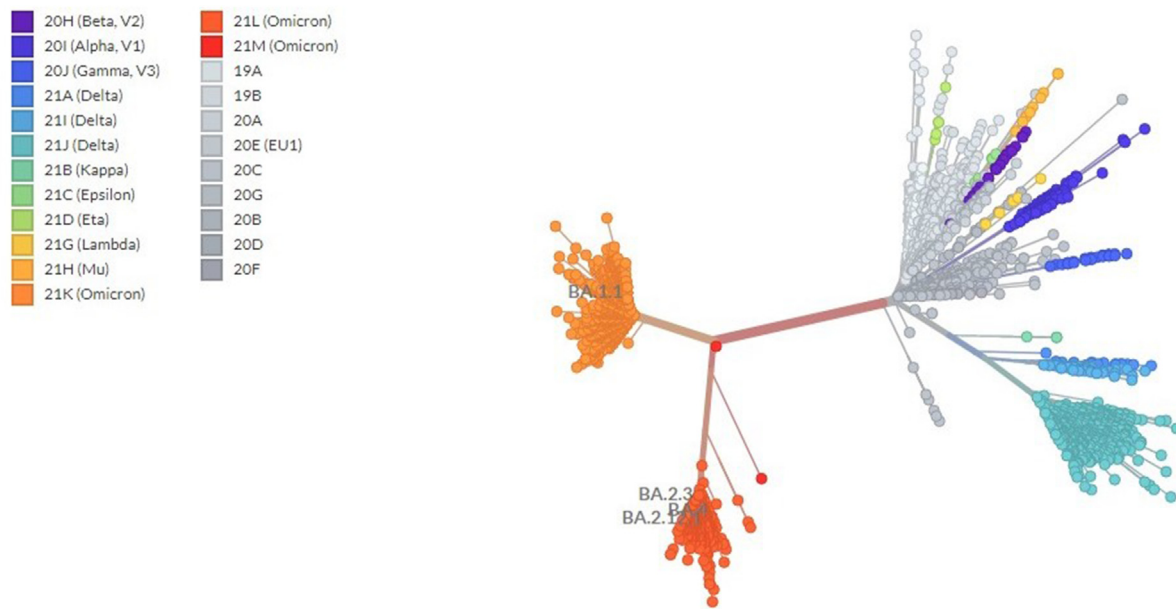
While the globe is still recovering from the COVID-19 pandemic and coping with the widespread negative social, psychological, and economic consequences of this devastating pandemic. The dissemination of the Omicron variant and its subvariants/sublineages possess a severe threat to the public health worldwide amid the serious containment measures such as vaccination. Emerging sublineages/subvariants of the Omicron variant have caused the scientific community to raise a number of concerns associated with them such as their increased transmissibility, increased resistance to the available vaccines and increased probability of reinfection [1]. In the past, computational and sequencing investigations have partitioned the Omicron variant into three sublineages, the most notable of which are the BA.1.1 (B.1.1.529.1), BA.2 (B.1.1.529.2), and

BA.3 (B.1.1.529.3) lineages. Phylogenetic analysis has shown the distinct evolution of the BA.1.1 (B.1.1.529.1) from other sublineages and VOCs such as Alpha and Delta variants (Fig. 1). This suggests that the Omicron variant might have originated from the non-human host. Recent research in South Africa has uncovered traces of two more sublineages, designated BA.4 and BA.5 which have been associated with the increased risk of reinfection in the vaccinated people. The sublineages BA.1, BA.2, BA.4, and BA.5 have been designated as variants of concern (VOCs), whereas BA.3 has been labelled as a VOI (variant of interest) [Table 1]. The appearance of these sublineages in South Africa may be linked to the region's much lower immunization rate in comparison to those of other nations [1,2].

According to early investigations, BA.4 and BA.5 have significantly different pathogenic characteristics than BA.1 and BA.2, particularly when contrasted to BA.1. Furthermore, the dominance of the BA.5 sublineage has been increasing in Portugal during the early May, 2022, supported by a rise in COVID-19 cases. As of May 8, 2022, the Portuguese National Institute of Health assessed that BA.5 was responsible for one-third of the COVID-19 cases. The anticipated daily growth advantage for BA.5 over BA.2 is significantly higher. If the current growth rate continues, BA.5 will possibly become the dominant strain in Portugal by the end of May 2022 [2].

The increased growth of BA.4 and BA.5 and their dominance has been associated with their capabilities to elude immune protection established by past infection and/or vaccination, specifically if the antibody-mediated immune response has weakened over time. In vitro studies examining sera from unvaccinated persons who have previously been infected with BA.1 reveal that both BA.4 and BA.5 are capable of escaping the immunological protection conferred by exposure with BA.1. It is essential to consider that unvaccinated people are far more likely to be infected with BA.4 or BA.5 sublineage [2]. Worryingly, there is a lack of data on the severity of infection caused by sublineage BA.4 or BA.5 [2,3].

On the other hand, South African scientists, believed that the BA.4 and BA.5 might cause a new wave of infection due to their capacity to circumvent antibodies resulting from vaccination and previous infection [4]. The European Centre for Disease Prevention and Control (ECDC) advises governments of various countries to remain aware of BA.4 and BA.5 outbreaks [2]. Comprehensive and accurate testing, as well as genomic surveillance and timely sequence reporting are crucial for early variant discovery [4,5]. Genomic surveillance along with community surveillance have been considered as crucial tools to concisely evaluate the involvement of Omicron's sub-variants in ongoing viral circulation, as well as to accurately determine the extent to



**FIG. 1.** The distinct evolution of the Omicron variant and its sublineages from other VOCs like Alpha and Delta variants suggesting the Omicron variant may have evolved in non-human host. Interestingly, the distinct evolution of other sublineages from BA.1.1 also suggest the distinct characteristics of BA.4 and BA.5 sublineages which may pose severe threat in the future and should be monitored continuously. (Source ([https://nextstrain.org/ncov/gisaid/global?branchLabel=emerging\\_lineage&l=unrooted&m=div](https://nextstrain.org/ncov/gisaid/global?branchLabel=emerging_lineage&l=unrooted&m=div))).

which these sub-variants may contribute to any observed increases in severe outcomes in the population, including a sharp rise in hospital or ICU admission rates. It is important to consider that representative testing policies are necessary worldwide to monitor the outbreaks of these sub-variants [4].

Additionally, the mass vaccination has played a significantly important role in the containment of negative repercussions associated with the advent of the Omicron variant and its subvariants. After receiving the COVID-19 vaccines, booster doses of the vaccine have been provided to reduce the hospitalisations among the vulnerable and immunocompromised population. It has been established that booster doses are effective in increasing the levels of SARS-CoV-2-specific

neutralizing antibodies (nAbs) that are cross-reactive to current VOCs (Variants of Concern) and VOIs (Variants of Interest) [6]. It is interesting to note that a booster dose can dramatically improve levels of nAbs (neutralizing antibodies). The optimal concentration of antibodies (Abs) at the time of infection can give considerable level protection against the infection caused by BA.4 and BA.5 subvariants.

In conclusion, it can be stated that the genomic surveillance, community surveillance, mass vaccination along with providing booster doses of vaccines can substantially reduce any plausible negative effects associated with the emergence of BA.4 and BA.5 sublineages and any other future VOCs, VOIs or their subvariants/sublineages.

**TABLE I.** The differential features of sublineages of the Omicron variant [Source, <https://www.ecdc.europa.eu/en>]

Omicron's sublineage	WHO label VoC/VoI	Place of origin	Impact on transmissibility	Impact on severity	Impact on immune response	Chances of reinfection
BA.1	VoC*	South Africa	Increased	Decreased	Significantly increased	Increased
BA.2	VoC*	South Africa	Significantly increased	Decreased	Increased	Increased
BA.3	VoI**	South Africa	N.A.	N.A.	N.A.	N.A.
BA.4	VoC*	South Africa	N.A.	N.A.	Increased	N.A.
BA.5	VoC*	South Africa	N.A.	N.A.	Increased	N.A.

\* Variant of concern.  
 \*\* Variant of interest.  
 N.A. (Data not available).

## Ethical approval

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This article does not require any human/animal subjects to acquire such approval.

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## Author contribution

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## Declaration of competing interest

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We declare no competing interests.

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