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Could the new BA.2.75 sub-variant lead to another COVID-19 wave in the world? - Correspondence

Dear Editor

Mutations in the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are an ongoing process leading to the emerging new variant Omicron. In February 2022, the World Health Organization (WHO) reported the declaration on the BA.2 variations [1]. A total of 1, 339,120 new cases of the BA.2 variation were documented in European countries in June 2022, Fig. 1, as reported by the European Centre for Disease Prevention and Control (ECDC) [2].

1. The omicron sub-variants

The prevalent omicron sub-variant in the United States is the BA.2.12.1, whereas the prominent in South Africa are the BA.4 and BA.5 sub-variants [3]. Recently, many BA.2 variations showed a transition to become sub-variants generally called BA.2.75, BA.2.74 and BA.2.76. The first sample of the BA.2.75 sub-variant was discovered in India [4], and researchers are now following its likely alterations [4]. According to the WHO, around eight countries have recorded 60 confirmed cases of this new sub-variant. India is the most commonly affected country (n = 23). The mutations in genome sequences of BA.2.75 are high and experts have emphasized that countries should raise concerns on this sub-variant because it has a lot of spike mutations, manifests rapid growth, and has an extensive geographical distribution [5].

As a result of insufficient data being reported on the new BA.2.75 Omicron sub-variant, the evidence of its infectivity, immunity evasion, and severity is still unclear. However, investigations are ongoing by scientific experts to find out details regarding the BA.2.75 sub-variant to suggest best effective methods to restrict its upcoming surge. In India, new cases have increased since the discovery of the BA.2.75 subvariant. The most recent findings on spread and transmissibility support the hypothesis of a greater spread power [6]. For many months, there were fewer than 3000 cases per day in India; however, they gradually rose and reached 18,000 cases per day, which is still under 1/100K of the population [7].

At the same time, mutations that define a lineage (Fig. 2) are the spike K147E, W152R, G446S, and R493Q, and G446S and R493Q, the last two being alarming. The G446S mutation may have an impact on ACE2 binding and immune resistance. It is very conceivable that this mutation might also result in significant immunological escape, although it could lessen the sub-ability variants to attach. All these imply that breakthrough infections and reinfections can fuel the spread of BA.2.75. It might explain why the number of new cases in India is growing [6,7].

2. BA.2.75 sub-variant and vaccines

Accordingly, the Omicron BA.2.75 subvariant may have a larger spread than other sub-variants, indicating a stronger resilience to preventive measures such as vaccinations and treatments. A total of nine alterations, including G446S and R493Q mutations, are found in the surface proteins, mainly the S1 spike proteins which permit cell entrance to generate multiple variations of Omicron, helping it to resist the immune system that has been acquired either naturally or via vaccination [8-10]. BA.2.75's capacity to spread to places where BA.2 infections have already been identified can also be explained by BA.2.75 having the ability to escape the immunity against the BA.2.75 variant [11,12]. Other than BA.2 sub-variants, a high growth rate of 16% each day has been identified in the majority of reported cases in India, competing with other BA.2 sub-variants, notably BA.5, which is now spreading worldwide [13,14]. As a result, adding heterogeneous boosting protection against BA.2.75 to vaccinations is critical in avoiding a surge in BA.2.75 and further dissemination.

The pathogenicity of the **BA.2.75 sub-variant** is attributed to the presence of two distinct mutations in BA.2.75. The first is G446S, a location that contributes significantly to this variant's resistance to antibodies generated by existing vaccinations [11]. The second mutation is R493Q, which permits the virus to connect to ACE2 receptors, allowing it to adhere to cells more easily [12]. Each of these causes is believed to contribute to the recent spike in this variant's dissemination that has been seen over the last two weeks, which has already been recorded in eleven remote Indian states and seven other nations [13]. There is a danger to those immunized, whether through vaccination or by developing natural immunity. However, it is too early to determine whether this lineage will spread rapidly or become the dominant one in the next weeks.

The evidence of the novel BA.2.75 Omicron sub-contagiousness, variant's immunity evasion, and severity are yet unknown because of the dearth of data that has been documented.

Research is being done to discover every aspect of the BA.2.75 subvariant to provide the most effective ways to counter the growing threat [1,2]. The increasing prevalence of the BA.2.75 Omicron sub-variant in India and other countries like the UK, Canada, the U.S., Australia, and Japan might be behind the current COVID-19 surge. Due to its rapid development, wide geographic distribution, and many spike mutations, the World Health Organization (WHO) and specialists have recommended that regions to raise concerns on this new sub-variant [14–16]. In these periods of ambiguity around a new variety, wearing masks, ventilating crowded spaces, and getting vaccinated are still the

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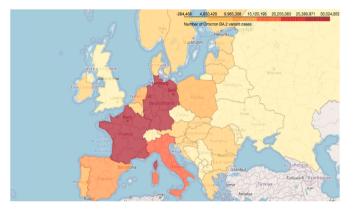


Fig. 1. A map displaying the total number of new BA.2 cases reported each week in various European countries from January 2020 to June 2022.

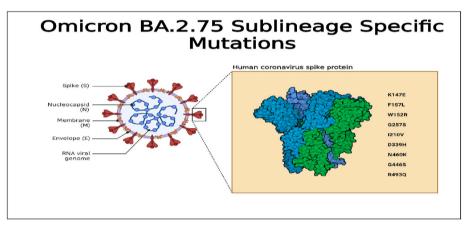


Fig. 2. Sub-lineage mutation of the new omicron BA.2.75.

best ways to stay safe. Combining the COVID shield vaccine with the Covaxin vaccine has been shown to provide better protection than immunization with COVID shield alone. Nevertheless, due to the scarcity of evidence on BA.2.75, there is still debate on the efficacy of such a strategy [17–19]. To further understand the sub-variation's transmissibility, severity, risk of reinfection, and how it differs from other variants of the Omicron virus, studies are required to evaluate the epidemiology of this novel sub-variant.

Previous recommendations to tackle the COVID-19 pandemic ought to be sustained worldwide together with the recently improvised instructions, such as ongoing vaccination for all individuals, preserving social distance, mask-wearing and careful handwashing, and applying quarantine of the BA.2.75 sub-variant positive patients in an alternative area. It is critical to highlight that genome sequencing of all samples could potentially impact disease control and evaluate the threat of new waves in the world ([1,3,4]). Finally, additional control is necessary to prevent the spread of the BA.2.75 sub-variant.

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Nour Shaheen, Abdelrahman Mohamed Alexandria University, Alexandria Faculty of Medicine, Alexandria, Egypt E-mail addresses: nourshaheen40@gmail.com (N. Shaheen), abdelrahman-elgharib@hotmail.com (A. Mohamed).

> Youssef Soliman Assiut University, Faculty of Medicine, Assiut, Egypt E-mail address: youssefrefaat138@gmail.com.

Omar Ahmed Abdelwahab, Rehab Adel Diab Al-Azhar University, Faculty of Medicine, Cairo, Egypt Medical Research Group of Egypt, Cairo, Egypt E-mail addresses: omar3240109@gmail.com (O.A. Abdelwahab), rehab_diab97research@outlook.com (R.A. Diab).

Mariam Tarek Desouki

Alexandria University, Alexandria Faculty of Medicine, Alexandria, Egypt E-mail address: mariamdesouki362@gmail.com.

> Ala' Abdala Rababah King Hussein Medical Center, Internal Medicine, Amman, Jordan E-mail address: aarababah@hotmail.com.

Abdulrhman Khaity Elrazi University, Faculty of Medicine, Khartoum, Sudan E-mail address: abdulrhman.marwan.khaity@gmail.com.

> Mahmoud Tarek Hefnawy Zagazig University, Faculty of Medicine, Egypt Medical Research Group of Egypt, Cairo, Egypt E-mail address: Mahmoudhefnawy77@gmail.com.

Sarya Swed^{*} Faculty of Medicine, Aleppo University, Aleppo, Syria

Ahmed Shaheen

Alexandria University, Alexandria Faculty of Medicine, Alexandria, Egypt E-mail address: ahmeds1999haheen@gmail.com.

Bahaa Elfakharany Pharos University, Faculty of Allied Medical Sciences, Alexandria, Egypt E-mail address: bahaaelfkharany@gmail.com.

Sheikh Shoib Department of Psychiatry, Jawahar Lal Nehru Memorial Hospital, Srinagar, Jammu & Kashmir, India

> * Corresponding author. *E-mail address:* saryaswed1@gmail.com (S. Swed).