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## Correspondence

**The Omicron subvariant BA.2: Birth of a new challenge during the COVID-19 pandemic**

Dear Editor,

In November 2021, many patients presented with the atypical pneumonia due to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in South Africa [1]. Subsequently, the WHO Technical Advisory Group called Omicron the variant B.1.1.529 which caused the rise in the COVID-19 cases in South Africa; WHO classified Omicron as a variant of concern (VOC) [2]. Omicron, which is the fifth SARS-CoV-2 VOC, was detected among individuals who were partially immunized either by natural infection or vaccination. Omicron shares many mutations with the Delta and Alpha VOCs [3]. According to the WHO classification, Omicron has three subvariants, BA.1, BA.2, and BA.3 [4]. All the three subvariants were detected in South Africa, indicating fast evolutionary divergence of the subvariants. The Omicron subvariants share 39 mutations (mostly in the Spike protein); however, BA.1, BA.2, and BA.3 carry 20, 27, and 13 additional mutations, respectively. BA.1, BA.2, and BA.3 contain 13, 10, and 1 unique mutations, respectively. BA.1 has caused a considerable rise in the number of COVID-19 patients so far; however, BA.2 seems to surpass BA.1 and become the dominant Omicron subvariant in many European countries. Scientists have been puzzled by the rapid spread of the new subvariant BA.2. BA.2 has been skyrocketing in more than 57 countries, indicating that it is more highly contagious than its precursor (See <https://outbreak.info/situation-reports?pango=BA.2&selected=ZAF>).

BA.2 has informally been called the “stealth” variant because its PCR identification has been difficult. To differentiate between Delta and Omicron variants, a specific PCR was used to target a region known as “S gene target failure” (SGTF). Unfortunately, BA.2 lacks this signature deletion at 69–70, making its rapid identification difficult in clinical samples. Furthermore, the subvariants contain a combination of mutations. Thus, only sequencing technology can confirm BA.2.

To date, BA.2 is known to have a substantial growth rate, indicating a massive threat for individuals with naïve immune systems. The Omicron variants have three unusual biologic properties compared with previously emerged SARS-CoV-2 variants. First, the high transmissibility has enabled the subvariants to infect many individuals efficiently. Second, weaker virulence has mostly caused less severe disease. Third, the subvariants can subvert the neutralizing antibodies in immune individuals. In January 2022, the Omicron BA.2 increased the case numbers in the United States, Denmark, and France [5,6]. A similar rate of new cases of BA.2 was documented in the United Kingdom [4]. Because not all of the suspected samples could be sequenced, the true numbers and the real prevalence of the circulating subvariant remain unknown.

**Birth of new challenge?**

The high transmissibility of BA.2 causes another major public-health problem, threatening unvaccinated individuals. This high

transmissibility rate explains the high number of positive cases in Europe and other continents. Initial assessments by Denmark’s Statens Serum Institut (SSI) suggest that BA.2 is 1.5-fold more contagious than BA.1. In Denmark, the number of positive cases doubled over a week, signifying the high transmissibility of BA.2 [5]. So far, the risk of high hospitalization rates remains the same.

Evidence shows that both vaccinated and unvaccinated individuals can be infected with the highly transmissible subvariant. Some hypothesize that Omicron is the preferred variant to catch, and the pandemic will be ending soon. However, the best SARS-CoV-2 (sub) variant will be the one that is inactive.

In conclusion, emergence of new SARS-CoV-2 (sub)variants should be monitored by gene sequencing in those countries where an active surveillance program does not exist. The recommended countermeasures including vaccination, physical distancing, correctly donning the recommended types of facemasks, and avoidance of mass-gathering events must continue. Considering nation-wide lockdowns to fight the subvariants could still be pertinent.

**Provenance and peer review**

Not commissioned, internally peer-reviewed.

**Ethical approval**

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

**Sources of funding**

This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

**Author contribution**

**Amin Talebi Bezmin Abadi:** Conceptualization, Data Curation, Writing – Original Draft, Writing – review & editing. **Farid Rahimi:** Writing – Review & editing. All authors critically reviewed and approved the final version of the manuscript before submitting.

**Conflicts of interest**

None.

**Research registration Unique Identifying number (UIN)**

1. Name of the registry: Not applicable.

<https://doi.org/10.1016/j.ijso.2022.106261>

Received 2 February 2022; Received in revised form 4 February 2022; Accepted 7 February 2022

Available online 12 February 2022

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2. Unique Identifying number or registration ID: Not applicable.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): Not applicable.

#### Guarantor

Both authors.

#### Data statement

Data not available/not applicable.

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