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Letter to Editor

Risk of Outbreak Omicron Virus by Increasing the Number of Mutations in the Receptor Binding Domain (RBD)

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HIGHLIGHTS

- Rapid spread of Omicron variant is a serious challenge.
- More than 50 mutations have occurred in Omicron variant.
- The mutations have caused the RBD structure to undergo significant changes.

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Introduction

Omicron (B.1.1.529) is a new variant of the coronavirus that has shown more genetic changes than the Wuhan variant, also more than the Alpha, Beta, Gamma, and Delta variants. The first report was submitted on November 24, 2021, from South Africa and Botswana, and then on November 26, Omicron was approved and an initial warning was issued by WHO. Omicron has been known as the SARS-CoV-2 Variant of Interest (VOI), and in less than a week numerous reports from Australia and the US were recorded and then it was observed in some parts of Europe. These rapid and numerous reports indicate an increase in the prevalence of the disease and the risk in this variant (Karim and Karim, 2021; Sharma, 2021). In this letter, structural changes in the Spike protein regarding to an increase of the risk of Omicron rapid spread have been briefly discussed.

The most important biological feature of Omicron is the high number of mutations compared to the previous Beta variant. There have been more than 50 mutations in the Omicron, of which at least 30 or 32 are in the Spike protein responsible for binding to the angiotensin-converting enzyme 2 (ACE2) receptor (Fig. 1). Spike protein consists of two subunits, S1 and S2, where S1 contains the Receptor Binding Domain (RBD) to ACE2 of the host cell membrane and S2 is involved in the fusion. RBD is the most important component of Spike protein which undergoes the most genetic and structural changes.

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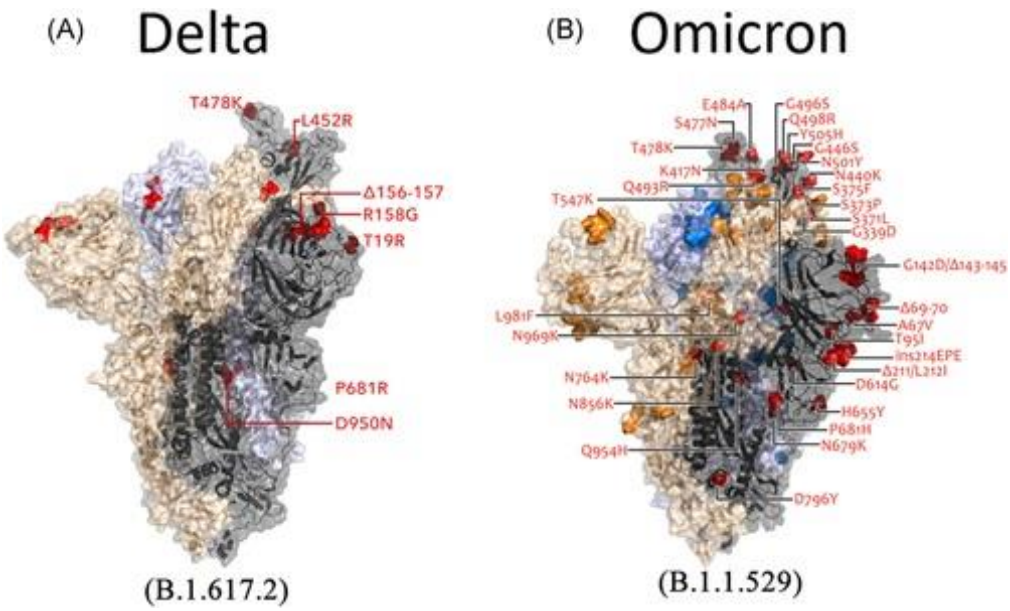

Figure 1: More than 30 mutations have occurred in RBD. Comparison of S protein mutation in Delta and Omicron highlighted on protein structure (reprinted with permission from Kumar, et al., 2021).

This is the reason for the increased biophysical bonding and virus infection of this variant. These changes in the virus appear to be evolutionary and they have emerged in virus to escape the protection created in human body through the natural immunity or after vaccination. The origin of these widespread evolutionary changes is not yet known, but some factors including non-compliance with pandemic protocols, social distancing, low vaccination rates, and the impact of immunosuppressive diseases play a role (Kim et al., 2021; Pooladi et al., 2021; Rath et al., 2020).

Jacob Glanville from the US Therapeutics Company's Research Center believes that there have been 15 mutations in RBD that have altered and strengthened the function in the variant. This domain acts as a hook (grappling hook) for viruses to enter human cells, and there is a strong possibility that mutations in this domain could cause malfunction or challenges in the vaccine-based immunity. It is possible that over time, the immune system created by natural infection or incomplete vaccination will be ineffective against the main virus (Hastie et al., 2021; Meo et al.; 2021).

Diagnosis

Another concern is the diagnosis of COVID-19, for which RT-PCR technique is still the primary diagnostic technique, but one of the three target genes, S gene (S gene dropout), evaluated by RT-PCR is no longer detectable in Omicron (Li et al., 2021).

Vaccine

Spike protein has been an important target for the development of vaccines. This protein stimulates the immune system to make antibodies (Pooladi et al., 2020). The Delta variant has two mutations and the Beta variant has three mutations in this region, while the omicron has at least 15 mutations in RBD. Scientists have been studying a list of mutations in Omicron, but yet have not been completed. These genetic changes, followed by post-translational changes in the proteins of this variant, affect the characteristics of the coronavirus, including connectivity, disease severity, ability to evade the immune system, failure to detect and neutralize therapies offered, and more and the result is its rapid spread in different countries. Cambridge University microbiologist Sharon Peacock uses the term "evolutionary gym" to describe the extent of evolutionary mutations in Omicron (Cohen, 2021; Cross, 2021; Graham, 2021). According to WHO reports, there are three questions that need to be investigated:

- How has the increase in connectivity in Omicron affected the epidemiology of COVID-19?
- What changes have resulted in an increase in severity and symptoms of primary and secondary manifestations in patients with Omicron, compared to previous strains?
- The most important question is whether the available vaccines can provide the necessary immunity against Omicron?

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SARS-CoV-2 VOC is a type of SARS-CoV-2 that challenges the reduction of the effectiveness of health measures. It will create general and social problems, as well as impair diagnosis, reduce the effectiveness of vaccines made, and provide available treatments.

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