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REVIEW

SARS-CoV-2 in relation to global vaccination and booster doses: what is the future of vaccination in the battle against COVID-19?

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ABSTRACT
Many of the deletions and large mutations found in the Omicron version of COVID-19 are identical to those seen in the α, π, β, and δ based VOCs. Such deletions and alterations have long been known to increase the viral risk of transmission and binding ability. Additionally, these changes are anticipated to increase the chances of immunological evasion and antibody secretion. T478K, G339D, Y505H, S373P, S371L, S375F, N440K, K417N, S477N, G446S, Q493R, E484A, G496S, N501Y, Q498R, and D614G are all mutations that potentially affect the virus's behavior. The N terminal region of the spike is typically targeted by NABs or neutralizing antibodies, immunologic polypeptides that prevent viruses from infecting cells. If the target region of the NABs significantly alters, the viruses may be able to avoid the autoimmune response generated by initial infection and vaccination. A possible "receptor shift" wherein ACE2 is not exclusively an Omicron receptor is worrying, given the huge number of mutations within the RBD region. D614G is the most prevalent mutation discovered among the three major pandemic variants. The Omicron variant is the most divergent variation seen in large numbers thus far in the pandemic, raising concerns that it could be linked to a faster transmission rate, lower vaccine effectiveness, and a greater risk of re-infection. Since identifying the Omicron variant, various countries have made significant modifications to their vaccination programs, including the recommendation of a third injection of boosting vaccination dosages in large populations to reduce the risk of adverse effects. However, all three vaccine producers (Johnson & Johnson, BioNTech, Pfizer, and Moderna) have published statements claiming vaccines would protect against severe sickness and that variant-specific vaccinations and boosters are in the works. This review sheds insight on several genetic mutations and their evolution in distinct variations. However, further study is needed to improve our understanding of illness transmissibility, immune escape capacity, patient features and severity, and the use of further diagnostic and therapeutic techniques *(Fig. 1, Ref. 20)*. Text in PDF *www.elis.sk*
KEY WORDS: SARS-CoV-2, global vaccination, booster doses, COVID-19.

Introduction

The detection on the November 24, 2021, at South Africa of a severely altered Variants of Omicron of concern, which was also stated as VOC or B.1.1.529 (G.R./484A) of COVID-19 that is a severe acute respiratory syndrome coronavirus 2, aroused numerous worries (1, 2). The World Health Organization or WHO reported variant cases in 38 countries throughout all the six of WHO zones as of December 3, 2021, with growing tendencies in South Africa, implying a greater transmissibility (3). More than 500,000 genomic samples from all the 6 continents have been uploaded to the GISAID (Global Initiative on Sharing Avian Influenza Data) to confirm variations until December 2021. The Omicron version was discovered in Europe ten days before it had been discovered in South Africa, according to a report from the Dutch Ministry Of health; nevertheless, no link to the variant's African origin has indeed been established. Two of the instances discovered in the Netherlands came from tests taken on November 19 as well as 23, 2021, before the South African warning (4). According to the preliminary study, the Omicron variation features a number of deletion as well as huge mutations amount, many of which are similar to those identified in the α, π, β, as well as δ (DELTA) based VoCs (5). Deletions and mutations of this kind had long been recognized to increase viral risk of transmission as well as binding ability. Furthermore, these alterations are thought to increase the likelihood of immunological evasion as well as antibody release. The Omicron variation, on the other hand, is thought to be 3 times more contagious than the initial SARS-CoV-2 virus (6).

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Spike protein; a landscape for high mutations

The Omicron variation has about 50 alterations, including 26–32 amino acid substitutions, deletions, and insertions on the

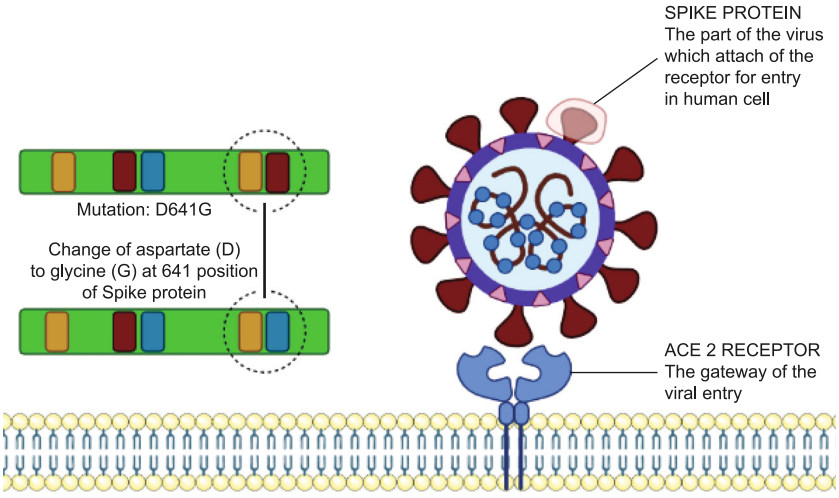

Fig. 1. SNP (single nucleotide polymorphism) mutation in the C-terminus of the Spike protein, which is responsible for the attachment to the ACE 2 Receptor on the human cell.

Spike or S protein alone. Just a few of the different mutations identified have been investigated previously. As a result, it's too early to know about the other modifications and how they could impact the virus's behavior. T478K, G339D, Y505H , S373P, S371L, S375F, N440K, K417N, S477N, G446S, Q493R, E484A, G496S, N501Y, Q498R, and D614G are the key mutations in spike protein (7). The mutations are of SNP or single nucleotide polymorphism type, where change in one aminoalkanoic acid into a different can cause a huge variation within the polypeptide structure and function (Fig. 1). The SNP process occurred at the RBD (Receptor binding domain), which is actually the outer part of the S protein that has the ability to attach on to the ACE 2 receptor on human cell (8). This variation, such as the Alpha version, which causes S gene dropouts with S gene targeting inability, has alterations identified in other variants of concern, which is constitute a delete amino acid mutation at spikes protein with location of 69 or 70, identical to the α variation. It also possesses three critical mutations, which enable immune evasion, identical to those observed in B as well as Gamma versions (9). It also features several mutations around the furin c terminus that are comparable to those seen in the δ variation. Depending on these alterations, it's considered that the Omicron variation, at least now at molecular scale, is comparable to all other variants (Fig. 1) (1).

Early data suggests that the Omicron as well as Alpha variants contain the P681H mutation, that, when combined with two additional abnormalities, may make the virus easier to transfer from individual to individual. Another study found that combining the two new mutations, Q498R as well as N501Y, may improve virus's capacity in order to connect to human protein receptor, which is Angiotensin converting enzyme 2 that is ACE 2. Several amino acids are lacking from the N-terminal region of the spike (10). NABs or Neutralizing antibodies, immunologic polypeptide that inhibit virus from invading cells, frequently target this portion of the spike. The viruses may be able to circumvent the autoimmune reaction induced by natural infection and immunization if the target region of the NABs radically changes (11). It is currently too early to remark upon the variant's infectivity as well as its effects on vaccination effectiveness based on actual scientific evidence. Since the mutations within Omicron are similar to those identified in the other variations, it is expected to be highly contagious as well as transmissible (12). D614G, K417 N and N501Y spike protein genetic changes are intended to allow the virus to be quite disease causing. Similar to the H655Y as well as N679K, with P681H substitutions, the H655Y, N679K, as well as P681H mutations may boost the virus's spread (also present in α as well as δ variants) (9). Given the large number of substitutions inside the RBD area, a probable "receptor shift" in which ACE2 is no longer the Omicron receptor is concerning. One study showed that that ACE2 expression was still required for Omicron transmission. RBD as well as ACE2 retain a submicromolar level of complex formation, which is identical in B, Δ (DELTA), as well as in Omicron. Since ACE2 is required for RBD for its activity, it appears that all variations already have got the nano-molar scale, making it impossible for virus to progress anymore. Compared to the three primary pandemic variations, β or δ, and D614G, D614G is the most common (13). Interestingly, the Omicron strain possesses 12 mutations in the receptor binding motif, which also called RBM consist of amino acid from 438aa to508aa completely, half of which are situated from around N501 at C- end of the protein terminal. All of the mutations may cause substantial structural changes, enhancing antivirulence capabilities. For future investigations, further structural biology study is needed for the precise structural characterization of the Omicron RBD as well as ACE2 interaction (14).

The transfer of the Variants of Omicron throughout a confined hotel corridor between two fully vaccinated people has emphasized the possible risk involved with variants of Omicron. Nevertheless, it's clear that for a few weeks, it'll be unclear whether Omicron is likewise capable of resisting vaccine-induced protection (15). The Omicron variation is by far the most divergent variant observed in large quantities thus far in epidemic, prompting worries so it might be connected to higher rate of transmission, decreased vaccination efficacy, and a higher risk of re - infection. A number of other countries experiencing SARS-CoV-2 Omicron VOC illnesses continues to go up across the world. It's unclear whether the Omicron SARS-CoV-2 strain is more contagious or deadly than that of the δ (DELTA) version. The study identified the binding affinity of SARS_CoV-2 δ (DELTA) and variants of Omicrons along with ACE 2, and evaluated the binding ability of Wuhan/Hu-1 with δ as well as variants of Omicron, utilizing a range of computational techniques showing that it has more potential to bind in a covalent manner hence is more susceptible to a high rate of transmission (16).

The future of virulent disease

Since the discovery of the Omicron strain, some nations have made substantial changes to their vaccination program, including the suggestion of a 3rd injection of boosting dosage of vaccination in huge populations to minimize some negative consequences. COVID-19 admissions in hospitals could be decreased with immunity increasing injections held under current levels for the at least 2 years, per modelling research by Keeling and his coworkers (17). Vaccine boosters may be necessary every 6–12 months if indeed the protection goes off quicker than planned, preventing an upsurge in hospitalizations and mortality. It's important to remember that administering vaccines to people, who have never received a particular dose is more important than implementing immunization program. The un-vaccinated population comprises a lot of individuals within Africa, where vaccination ratios are significantly lower compared to the other parts of globe, allowing variations to arise. For months, experts have warned that vaccination distribution discrepancies might aid virus development and expand through infecting large crowds of people (18). Differences in vaccination rates between nations would not put a stop to the pandemic, because countries with the lowest vaccine coverage are more likely to produce variations. Aside from boosters, the introduction of the Omicron variant needs a worldwide travel ban to avert any disastrous consequences. It is widely established that an immigration ban can provide time to reduce the devastating implications of a new variant breakout. Furthermore, while many nations' vaccination programs, particularly boosters, are all still in full gear, strong border-control measures are still essential. To provide the health care structure enough time to prepare for just any possible overloading owing to spike in cases, strong travel limits and an efficient real-time tracking mechanism are essential (19). Meanwhile, all the three vaccine manufacturers (Johnson & Johnson, BioNTech or Pfizer, as well as Moderna, have issued comments stating that vaccines even now provide protection versus severe illness and that variant-specific immunization and boosters are being developed. In even less than two weeks, BioNTech expects to get findings on vaccine efficacy against Omicron variation, allowing it to assess the necessity for a variant-specific vaccination (4, 20). More research is required, however, to enhance the knowledge about disease's transmissibility, immune escape capability, patient characteristics and severity, and the function of additional diagnostic or therapeutic strategies.

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