

Insight and Perspective on Omicron's Development, Behaviour, and Vaccine Breakthrough: Next Sequelae of COVID-19

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ABSTRACT

Background: The Severe Acute Respiratory Coronavirus (SARS-CoV-2) has emerged in a variety of forms since its first appearance in early December 2019. The Omicron variation (B.1.1.529) was recently confirmed as a relatively new Variant of Concern (VOC). There are several mutations in this S-protein, making it an exclusively lethal version of the protein. Omicron variants feature multiple mutations clustered in a region of S protein that is the principal target of antibodies, and these mutations may have an impact on the binding affinities of antibodies to the S protein, as demonstrated by structural analysis. **Materials and Methods:** Google, Sciencedirect, Web of science, and ResearchGate databases have been explored for potentially existing research to obtain the most emerging trends and up-to-date metadata on various perspectives of Omicron variants. **Conclusion:** There is evidence that the Omicron variant's mutations may interfere with antibody binding in people who have been exposed to the SARS-CoV-2

virus in the past. At the moment, there is very little information on the Omicron version. Therefore, mutation dispersion evaluations, evolutionary links to previous variants, and putative structural effects on antibody binding effects are all explored in this work. **Results:** In the current state of pandemic crises, the comprehension of Omicron will pave a path for healthcare professionals to treat infectious conditions very well.

Keywords: SARS-CoV-2 virus, Mutations, Omicron, Vaccines, Antibody.

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INTRODUCTION

There is still a lot of disquiet about the regional and multilateral effects of the SARS-CoV-2 pandemic. In some places, vaccinations for the SARS-CoV-2 virus are promising to ease this anxiety, but it is still a recurrent and low-key global public health crisis.¹ People who don't get enough vaccines; people who aren't sure about getting vaccines; and people who spread misinformation on social media all play a role in this outcome.²

COVID-19 has killed over 5 million population since the pandemic began, nearly two years ago. The world is still on high alert for COVID-19. People from the World Health Organization (WHO) have been meticulously watching and analyzing the development of SARS-CoV-2 since the beginning of 2020.³ The WHO has been working worldwide with governments, public health organizations, and researchers to do this. Since January 2020, many countries have seen many different types of the virus emerge and become the most common. The Alpha, Beta, Gamma, and Delta variants have been the utmost common so far. However, the Delta (B.1.617.2) variant of SARS-CoV-2 has been the most important in terms of how it can be transmitted and scattered.^{4,5}

When COVID-19 was first reported, it was 23 months old and there were an estimated 260 million cases and 5.2 million deaths worldwide. On Nov 24, 2021, a different and improved SARS-CoV-2 variant of concern (VOC), omicron, was found.⁶

There is still no proof that Omicron is more spread quickly from person - to - person than other variants of the virus, like Delta, so it isn't clear yet whether this is the case. This variant has caused more people in South Africa to test positive, but epidemiological data are underway to find out if it's because of Omicron or something else.⁷

In addition, it isn't yet clear if Omicron infections cause more severe illnesses than infectious diseases with other variants, such as Delta. Initial data suggests that more people are getting sick in South Africa, but this could be because more people, in general, are getting sick, not because they are getting sick with Omicron. There is no evidence that Omicron has any symptoms that are distinctive from other variants. Early infections were reported by university students, who are younger and more likely to have milder illnesses.^{5,8} It will further take several days to several weeks to figure out how bad the Omicron variant is. Covid-19 can come in many different forms, such as the Delta variant that is most common. All of them can cause serious illness or death, particularly for vulnerable people, so prevention is always important.⁹ Is to provide a comprehensive overview of various facts that highlight the structure and transmission of omicron, as well as the severity of the disease, the impact on diagnostics, and the development of vaccines, which are all covered in this review.

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MATERIALS AND METHODS

The current review has been developed by systemic assessment and exploration of distinct features of omicron and elucidated below sections.

The inception of New VOC of SARS-Cov-2: Omicron

South Africa was the first country to alert the WHO about the SARS-COV-2 VOC in 2021. On Friday, November 26, 2021, the WHO named a new variant, B.1.1.529, as a VOC and called it Omicron. On the recommendation of the WHO's Technical Advisory Group on Virus Evolution (TAG-VE), On November 30, 2021, the WHO added the new variant to its list of Variants of Concern. Omicron, a type of concern, was first called B.1.1.529. It was growing in most of South Africa's provinces, especially in Gauteng. In Gauteng, South Africa, the spread has been very fast, especially among young people.^{7,10} This has put the WHO and other global healthcare coordination on high alert.

VOC Omicron has also been found in Botswana, Hong Kong, Belgium, and Israel, as well. There have been 2382 confirmed cases in 62 countries around the world since the WHO made the announcement. These countries are Estonia, Austria, Czechia, Belgium, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Latvia, Liechtenstein, (the Netherlands, Norway, Portugal, Romania, Spain, Sweden, Argentina, Australia, Bermuda Botswana, Brazil, Chile, Canada, Hong Kong, Special Administrative Constituency, India, Fiji, Israel, Ghana, Japan, Jordan, Korea, and China.¹¹

There has been a rise in outbreaks in South Africa recently that coincided with the discovery of Omicron. The WHO classifies this as a VOC. Omicron has a lot of spike protein changes that aren't good. Some of

these changes have been linked to abridged susceptibility to monoclonal antibody treatments or shortened neutralization by convalescing and vaccine sera.⁷

Also, the European Center for Disease Prevention and Control classed this variant as a VOC because of apprehensions about "immune escape" and "steadily increasing infectivity in contrast to the Delta variant."

Because of how easily they can spread, how bad the disease is, and how much less effective treatment is, the US Government's Interagency SARS-CoV-2 Working Group also put SARS-CoV-2 variants into VBM, VIO, VOC, VHC groups based on these factors.¹² The main features of these variants, as well as some examples, are shown in Table 1.

The Emergence and Spread of Omicron

In the GISAID databases as of November 28, 2021, at 17:00 CET, there are 127 viral genomes (VOC Omicron GR/484A) that have been added to them (GSAID 2021). Several mutations in receptor binding domains (RBD) and N-terminal domains (NTD) that are thought to make people more resistant to neutralizing antibodies and more likely to spread are of concern.¹⁷

The WHO and international sequencing networks keep an eye on SARS-CoV-2 mutations, and they tell nations what they need to do to deal with the variant and stop it from spreading, where possible. Since January 2021, many countries have seen many different types of the virus emerge and become the most common. The Alpha, Beta, Gamma, and Delta variants have been the most common so far (Table 2).

Structural Characterization and Transmissibility of

Table 1: An array of identified variants of SARS-COV-2 and their distinct topographies.

Classification	Definitions	Variants Identified	References
Variant Being Monitored (VBM)	Variants that have been linked with disease severity or increased transmission but are no longer traced or are circulating at very low levels, and as such, do impart any significant risk to public health in the United States.	<ul style="list-style-type: none"> • Alpha (B.1.1.7 and Q lineages) • Beta (B.1.351 and descendent lineages) • Gamma (P.1 and descendent lineages) • Epsilon (B.1.427 and B.1.429) • Eta (B.1.525) • Iota (B.1.526) • Kappa (B.1.617.1) • 1.617.3 • Mu (B.1.621, B.1.621.1) • Zeta (P.2) 	(12-14)
Variant of Interest (VOI)	Potentially harmful variants showing evidence to change receptor binding, very low neutralization by antibodies (produced by vaccination or earlier infection), reduce efficacy of therapies, or increase in transmissibility or disease severity	None	(12-13,15)
Variant of Concern (VOC)	Viral variants that have been linked to rise transmissibility and illness severity; lower neutralization by antibodies developed during previous infection or immunization; decreased efficiency of therapies and vaccines; or detection failures.	<ul style="list-style-type: none"> • Delta (B.1.617.2 and AYlineages) • Omicron (B.1.1.529) 	(12-13)
Variant of High Consequence (VOHC)	Variants showing indication that prevention measures or medical countermeasures (given below) have significantly decreased effectiveness relative to previously circulating variants. Likely features of this variant are- Lethdown of diagnostic test targets. Noteworthy reduction in vaccine efficacy; excessive infections (in numbers) in vaccinated persons; or diminished vaccine-induced protection against severe disease Increased hospitalizations due to more severe clinical illness.	None	(12-13,16)

Table 2: WHO designated SARS-cov-2 VOC. Adapted from¹⁸.

WHO designation	Pango lineage	GISAID clade	Nextstrain Clade	Additional amino acid changes monitored	Country of origin	First documented samples
ALPHA (18/12/2020)	B.1.1.7	GRY	20I (V1)	+S:484K +S:452R	United Kingdom,	September 2020
BETA (18/12/2020)	B.1.351	GH/501Y.V2	20H (V2)	+S:L18F	South Africa	May 2020
GAMMA (18/12/2021)	P.1	GR/501Y.V3	20J (V3)	+S:681H	Brazil	November 2020
(DELTA) 11/05/2020	B.1.617.2	G/478K.V1	21A, 21I, 21J	+S:417N +S:484K	India	October 2020
(OMICRON) 26/11/2021	B.1.1.529	GR/484A	21K		South Africa, Hong Kong, Belgium, Israel	November 2021

Omicron (B.1.1.529)

As cited by NPR, the WHO reported that the first sample of the variation was obtained on November 9, although it is unclear when and where the variant originated—especially in light of the finding of Omicron in preserved European samples, according to the WHO.

Omicron’s genome has been sequenced, and it has roughly 50 mutations, along with more than 30 on the spike protein that binds to host cells, which distinguishes it from other identified variations.^{12,17}

The Omicron variant was found to have a total of 30 signature mutations when all mutations with a >50 percent occurrence were taken into consideration as signature mutations (A76V, T95I, Y145del, G339D, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F, L212I, S371L, S373P, S375E, K417N).¹⁹ These 30 distinctive mutations include 23 (bold-faced) mutations that are exclusive to the Omicron variation, meaning that they have not been detected in any of the earlier reported variants before.¹⁹

It is known as the Spike protein because it is a portion of the SARS-CoV-2 that attaches to the Angiotensin-converting enzyme 2 (ACE2) receptor of the host cell. This conformational shift allows the virus to enter host cells more easily. Mutations in this spike area may lead to the increased transmissibility of the viral infection, according to the literature.²⁰

Additional changes in the conserved non-Spike area of the B.1.1.529 variation were discovered, which are thought to be of less consequence in terms of the virus’s transmissibility and infectivity.¹⁰

The Spike area of B.1.1.529 had most mutations that were comparable to those found in the Delta variation, but some were unique, raising severe concerns at about the transmissibility of this variant (Figure 1). It is now known that genotype B.1.1.529 is now the most common COVID-19 mutation found in South African patients with COVID-19. It has also been detected in patients with COVID-19 in those other Southern African countries (Lesotho, Botswana, Namibia, Eswatini, and Zimbabwe), Belgium as well as Israel and Hong Kong.^{12,21} Figure 2 depicts the mutations in spike proteins of certain frequent forms of SARS-CoV-2 that have been identified.

The Omicron is a more transmissible variety than Delta, which raises worries that it is more transmissible than Delta. However, owing to a limited number of cases in South Africa at the time of Omicron’s emergence, it is unclear if this variant is more transmissible or not. Furthermore, because of the limited number of instances that have been reported too far, it is impossible to assess the likelihood of transmission. Analyses of differences in the spike protein have revealed that, when compared with the original SARS-CoV-2 virus, the Omicron variation is likely to have enhanced transmission; nevertheless, it has been challenging to determine if it is more infectious than the Delta version.⁵⁷

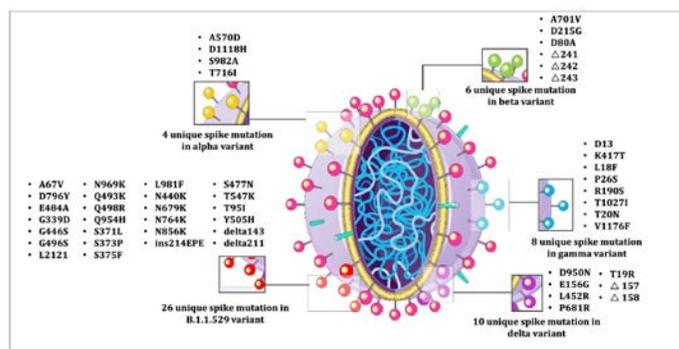


Figure 1: The mutation profile of spike protein in SARS-COV-2, from delta to B.1.1.529.

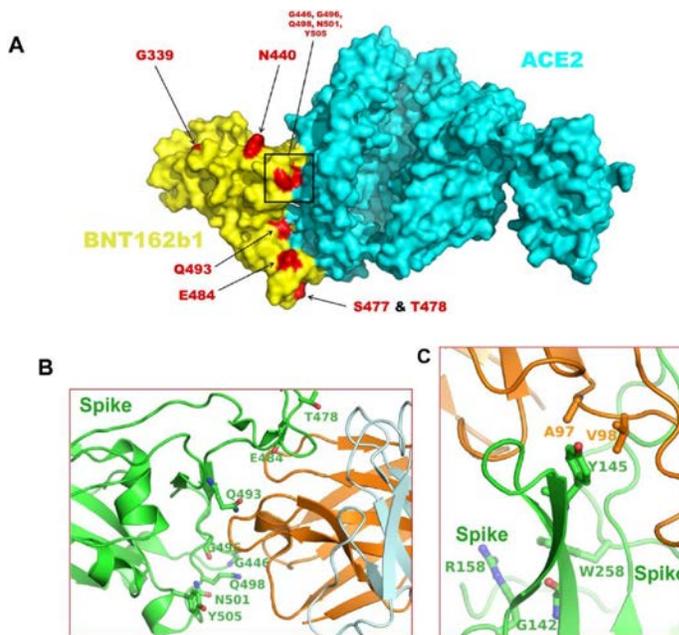


Figure 2: Spike/ACE or Spike/antibody interface: the distribution of amino acid residues at this point in time.

Part A, In this picture, you can see how the amino acid residues mutated in the Omicron variant are spread out in the complex between S-RBD, which is made by BNT162b1, and ACE2. Part B, in this picture, you can see where the mutations in the Omicron variant are found. Part C, shows how Y145 of S protein binds to antibody (1–87) residues A97 and V98 indicating that a deletion mutation, like the one in the Omicron variant, will stop these interactions. Adapted from²².

However, other changes in the Omicron spike protein should result in decreased binding to the ACE2 receptor. This might result in increased transmission. The combined effect of N501Y and Q498R may even further upsurge binding affinity; nonetheless, other changes in the Omicron spike protein should result in decreased ACE2 binding. As a result, the receptor binding affinity of the Omicron variation must be evaluated utilizing the whole range of spike protein changes present in the variant.

H655Y is located close to the furin cleavage point, and it has the potential to accelerate spike cleavage, which might facilitate transmission. N679K is positioned nearby to the furin cleavage spot and contributes to its polybasic character, which may further enhance spike cleavage and help transmission. P681H has been proven to increase spike cleavage which may help in the transfer of information. It has been discovered that this mutation is present in Alpha and that an alternative mutation at this site (P681R) is present in Delta.^{5,7,10}

Severity Concern of Omicron

According to the current knowledge, infection with the Omicron variation is not connected with a more austere form of illness. As a consequence of the limited number of instances attributable to the Omicron variation, determining the severity of the illness is challenging. The first evidence from South Africa recommends that the Omicron variant infection is not linked with any distinctive symptoms and that some individuals are asymptomatic, as is the case with other Omicron variant infections.

There is currently no information available on the capacity of sera from people who have been vaccinated or who have had a prior SARS-CoV-2 infection to neutralize the Omicron strain of the virus. In the United States, on the other hand.⁶ The Government SIG and worldwide public health cohorts are collaborating to collect this information in laboratory settings, and they will continuously monitor clinical and epidemiological indicators. The spike protein is the major target of vaccine-prompted immunity, and it has been identified as such. The Omicron variation has more mutations in the spike protein than other variants, particularly 15 alterations in the RBD, which have been detected in other variants. Depending on the number of substitutions, the position of these substitutions, and statistics from other variants with nearly identical spike protein substitutions, it is expected that sera from vaccinated or earlier infected individuals will have significantly reduced neutralizing activity, which may suggest reduced protection from infection.^{10,12}

Impact on Diagnostics

Those looking out for the most accurate guidance and statistics on diagnostic tests, which will be updated to imitate the influence of the Omicron variant, should visit the Food and Drug Administration's web page on SARS CoV-2 Viral Mutations: Impact on COVID-19 Testsexternal icon, which is updated on a regular basis.

The Omicron variant is predicted to be detected by the CDC 2019-Novel Coronavirus (2019-nCoV) Real-Time RT-PCR Diagnostics Panel and the Multiplex Assay for Flu and SARS-CoV-2, all of which are available from the CDC.

The S-gene target sensitivity of the Thermo Fisher TaqPath COVID-19 Combo Kit (3 total targets) has been drastically lowered as a result of the deletion of the H69 and V70 amino acids from the B.1.1.529 (Omicron) spike protein. Omicron may be present in specimens evaluated with the TaqPath COVID-19 Combo Kit that show an S gene target failure (SGTF). It is critical to note that every putative Omicron specimen must have been validated by DNA sequencing. Due to the fact that the TaqPath COVID-19 Combo Kit is intended to identify several genetic targets, the overall sensitivity of the test would not be affected.¹⁵

In order to better understand how readily the Omicron variation may be spread and the efficiency of already approved or permitted clinical countermeasures, for instance, diagnostic tests, vaccinations, and treatments, against this variant, scientists are attempting to learn more about it. There is a fast increase in the amount of knowledge available on the epidemiologic, virologic, and clinical aspects of the Omicron variants. The Centers for Disease Control and Prevention (CDC) and other government organisations are collaborating with international public health organizations to carefully monitor the status quo. As new information and statistics become available, the Centers for Disease Control and Prevention (CDC) will offer updates.

Vaccine Breakthrough

COVID-19 vaccination has been shown to be the most important factor in preventing and controlling the disease. There are four kinds of vaccinations: virus vaccines, DNA/RNA vaccines, protein-based vaccines and viral-vector vaccines. Virus vaccines are the most common form of a vaccine. Essentially, the COVID-19 vaccines now in use are mostly directed against the S protein. Because of the 32 amino acid alterations, which include three modest deletions and one tiny addition in the spike protein, it is possible that Omicron was generated by vaccination in humans. Therefore, these changes may have a significant impact on the variant's capacity to avoid the existing vaccinations available. The complete effect of Omicron's Spike protein mutations on existing vaccinations in use around the globe is very hard to quantify precisely in the majority of cases. At the outset, it is possible that various types of vaccines will elicit diverse immunological responses from the very same person. Additionally, different people with different characteristics based on ethnicity, age, gender, and underlying medical problems may develop distinct sets of antibodies in response to the same vaccination.^{18,20}

Many studies are being conducted to determine the efficiency of the COVID-19 vaccination against omicron viruses, which is now available.

Kannan and colleagues conducted a recent study in which they investigated the effects of Omicron S-RBD mutations on the binding of SARS-CoV-2 S-RBD to the IGHV3-53 antibody. They discovered that the sites of eight residues matching the Omicron variant fingerprint mutations (T478, E484, Q493, G496, G446, Q498, N501, and Y505),²² are at the S-RBD/ACE2 interface (encoded by BNT162b1), which is at the interface between ACE2 and S-RBD (Figure 2B). The same eight domains have also been found at the interface of the S-RBD/IGHV3-53 complex (Figure 2C). Variants with steric interference for antibody binding to the S-RBD include the following mutations: G446S, Q493R, and G496S. Variants with interaction loss for antibodies include the following mutations: E484A, Y505H, and G496S. They revealed that changes in the S-RBD may have decreased the affinity between the domain and antibodies that bind to the domain in question. As a result, they concluded that the pre-existing vaccine may not have provided the essential and optimum protection against infection by the Omicron variety.²²⁻²³

The capacity of BNT162b2 mRNA vaccination-induced antibodies to neutralize Omicron was tested by Cele and colleagues. They also investigated whether the virus still required interaction with the ACE2 receptor in order to infect cells. A live viral neutralization experiment was used to assess the capacity of plasma from BNT162b2-vaccinated study participants to neutralize Omicron vs. the ancestral D614G virus in the presence of a live virus. They observed that Omicron displayed much more escape than the samples, but the samples exhibited very high neutralization of the D614G virus. The researchers concluded that immunization or booster vaccination is to be expected to raise the neutralization level in the body and is likely to give protection against severe illness in Omicron infection.²⁴

According to, *in vitro* studies data of Wilhelm and co-workers on the neutralizing efficiency of vaccine-stimulated sera against Omicron was reported to decrease significantly when compared to the presently circulating Delta version, emphasizing T-cell mediated immunity as an imperative obstacle to avoiding severe COVID-19 infection. SARS-CoV-2 Omicron demonstrated resistance to casirivimab as well as imdevimab, indicating that genotyping of SARS-CoV-2 may be required before beginning mAb therapy.²⁵

Pharmaceutical laboratories are already evaluating the effectiveness of current vaccinations against this new variation, which is a consideration in the creation of new vaccines. Additionally, lab tests of additional COVID-19 vaccines from Johnson and Johnson (JNJ.N), AstraZeneca Plc (AZN.L), Moderna Inc (MRNA.O), and are now being conducted in this context. All of this research look at the influence of the Omicron strain on blood samples taken from individuals who have been previously infected or immunized. Furthermore, Sinovac Biotech (SVA.O), a Chinese business, is researching to assess if its deactivated viral vaccine against Omicron is effective or whether the firm has to produce additional vaccines against the virus. The Russian Sputnik V is also being tested against the Omicron.²⁶

RESULTS AND DISCUSSION

The relatively different Omicron strain of COVID-19 has been found in more than 62 nations, according to the WHO. They also have indicated that it will take several weeks to finish research on the Omicron in order to identify whether there has been a change in transmissibility, intensity, or potential ramifications for COVID vaccinations, testing, and therapies. On the other hand, the number of instances of the omicron form is growing day by day, with symptoms ranging from mild to severe. However, around 65 percent of the patients of the variation are unvaccinated, with the remaining instances being primarily partly vaccinated, according to the data. It is also important to remember that, according to statistics from the South African Department of Health, just 35.37 percent of the country's adult population has been completely vaccinated, and that the percentage of persons commencing immunization has decreased. As a result, high-income countries (HICs) should step up to assist such low-income countries (LICs) by giving COVID-19 vaccines, which would enable these nations to achieve mass immunization more swiftly. In the current state of pandemic crises, the comprehension of Omicron will pave a path for healthcare professionals to treat infectious conditions very well.

CONCLUSION

In conclusion, many countries must take immediate and stringent measures to avert the spread of the Omicron variant of SARS-CoV-2 via the deployment of policies including restrictions on international travel, increased genomic monitoring, and sequencing to diagnose the strains of the virus. According to the WHO, a significant numeral of mutations in the RBD of the Spike protein may enable the novel Omicron version to spread swiftly and restart the pandemic if it is not managed in time. The vaccine's efficacy against this recently developed variety, on the other hand, is still up in the air. As a result, strict adoption of preventative measures is required in order to keep any possible effects under check in the future.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

SARS-CoV-2: Severe Acute Respiratory Coronavirus; **VOC:** Variant of Concern; **WHO:** World Health Organization; **RBD:** receptor binding domains; **NTD:** N-terminal domains; **ACE2:** Angiotensin-converting enzyme 2.

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