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OMICRON-THE VARIANT OF CONCERN (VoC): A RAPID REVIEW

Adnan Saeed Shamsi, Mohd. Naved Ghauri, Sharique Ahmad*

*Undergraduate Student, Department of Pathology**

Era's Lucknow Medical College & Hospital, Era University, Sarfarazganj Lucknow, U.P., India-226003

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Address for correspondence

Dr. Adnan Saeed Shamsi
Undergraduate Student
Era's Lucknow Medical College & Hospital, Era University, Sarfarazganj Lucknow, U.P., India-226003
Email: adnansshamsi@gmail.com
Contact no: +91-8429155597

ABSTRACT

A new variant of coronavirus B.1.1.529. appeared on the scene, when discovered by the researchers in South Africa on Nov 24.2021. It is a heavily mutated variant of coronavirus discovered thus far with over 50+ mutations with 32 mutations over the spike protein itself. Spike proteins help the virus to bind to the bodily receptors of humans to gain entry inside. In comparison to the delta variant, which had nine mutations, it means that Omicron has better chances of evading the host immunity and is also more transmissible. And rightly so, it has been declared as a variant of concern(VoC) by the WHO. The presence of S-gene is of the determinants for the detection of the virus. But omicron seems to have missed this gene- being called as S-gene dropout or S-gene target failure (S- spike glycoprotein).

KEYWORDS: Coronavirus, mutations, Omicron, spike proteins, VOI (variant of interest), VOC (variant of concern).

INTRODUCTION

A SARS-CoV-2 VOI is a SARS-CoV-2 variant featuring-

Certain genetic changes (mutations) are known to influence or known to affect virus characteristics such as morphology, inheritance, transmissibility, disease spectrum, disease severity, immune escape mechanisms, diagnostic or therapeutic alternative pathway mechanisms.

A variant that has been identified as a potent source to cause major community transmission or numerous COVID-19 clusters, in multiple regions or nations with increasing relative prevalence alongside an increasing number of cases over time, or other apparent epidemiological impacts to suggest an emerging risk to global public health (1,2).

OMICRON TAXONOMICAL DETAILS

Severe Acute Respiratory Syndrome coronavirus 2

Genbank acronym:SARS-CoV-2

Equivalent: 2019-nCoV (novel Coronavirus)

COVID-19 virus

SARS2 (severe acute respiratory syndrome)

Human coronavirus 2019

(HCoV-19)

SARS-2

SARS-CoV2

NCBI BLAST name: viruses

Host: human vertebrates

LINEAGE

Viruses; Riboviria; Orthornavirae; Pisuviricota; Pisoniviricetes; Nidovirales; Cornidovirineae; Coronaviridae; Orthocoronavirinae; Betacoronavirus; Sarbecovirus; Severe acute respiratory syndrome-related virus (3).

Coronaviruses are enveloped, single-strand RNA viruses that can infect a wide range of hosts including avian, wild, domestic mammalian species, and humans. Coronaviruses are well known for their ability to mutate rapidly, alter tissue tropism, cross the species barrier, and adapt to different epidemiological situations (4).

Six human coronaviruses have been reported since the 1960s; four of them (OC43, 229E, NL63, and HKU1) cause mild illness similar to the common cold and gastrointestinal tract infection. The other two, severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV), have raised significant public health concerns due to their zoonotic emergence and crossing of the species barrier, causing high pathogenicity and mortality in humans (5).

OMICRON (STRAIN NO.-B.1.1.529)

WHO Label: Omicron

Pango Lineage: B.1.1.529

Nextstrain clade: 21K

The Omicron variant of the coronavirus is evidenced to have around thirty amino acid substitutions and deletions alongside one small insertion. Importantly, the major chunk of amino acid substitutions (almost 50 percent) is in the RBD (receptor binding domain). This factor single-handedly plays a key role in determining the ease of entry of the coronavirus into the host.

Amino Acid Substitutions in Spike Protein:

A67V, del69-70, T95I, del142-144, Y145D, del211, L212I, ins214EPE, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F.

Researchers estimate that Omicron can infect 3 to 6 times more people than the delta variant.

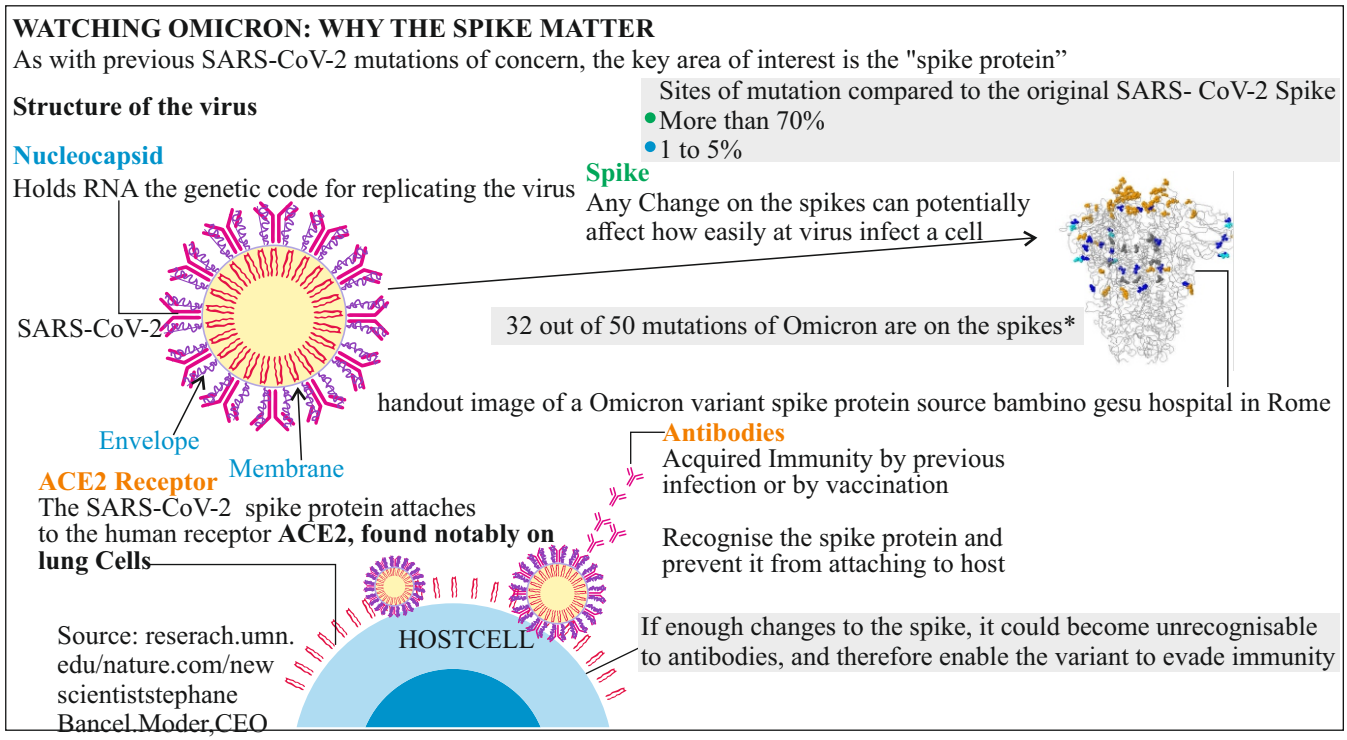

Fig.1: Below Shows Different Spike Proteins (glycoproteins) Serving as Receptor Binding Domains (mutations In Omicron)

WHO label	Lineage	Country first detected	Spike protein muatation	Evidence for impact on immunity	Evidence for impact on trnasmissibility	Severity	Transmissibility
Beta	B.1.351	South Africa	K417N, E484K N501Y,D614G A701V	YES	YES	Yes	Community
Gamma	P.1	Brazil	K417T, E484K N501Y, D614G H655Y	YES	YES	Yes	Community
Delta	B.1.617.2	India	L452R, T478K D614G, P681R	YES	YES	Yes	Dominant
Omicron	B.1.1.529	South Africa, Botswana	A67V, Δ69-70, T95I, G142D,	YES	YES	Yes	Sporadic, so far
Δ143-145, Δ211-212, Ins 214EPE, G339D, S371L, S373P, S375F, K417N, N440K, G446S, , S477N, T478K, E484A, Q493R G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, N681H, N764K, D796Y, N856K, Q954H, N969K, L981F							

Table 1: A List of Variants of Concern with Specific Information is Tabulated as Follows

	Omicron	Beta	Gamma	Delta
# Changes on Spike	37	10	12	9
# T cell Epitopes	348	125	159	108
% T cell Epitopes	27.29%	9.80%	12.47%	8.47%
# B cell Epitopes	550	231	273	198
%B cell Epitopes	30.91%	12.98%	15.34%	11.12%

Table 2: Depicting Contrasting Features Amongst Different Coronavirus Strains

(6-13)

TRANSMISSIBILITY OF OMICRON

At present, there is not enough data to support or strengthen the case of 'quicker' transmission of the variant but there has been a spike in cases of covid wherever Omicron cases have been reported. The efficiency with which the Omicron spreads is being charted wherever the cases have been identified. In South Africa, it is being reported that the Delta is being replaced by the Omicron at a quicker rate. (14)(15)Though the spike in cases is not alarming, the rise itself is a cause of concern as the spike protein substitutions in the RBD (receptor binding domain) studied and analyzed, show that the Omicron is likely to have increased transmission in comparison to its previous variants. But still, relatively small amount of cases reported-it cannot be derived that Omicron will be more transmissible than the Delta (16).

- N501Y increases binding to the ACE2 (angiotensin-converting enzyme 2) receptor, which could increase transmission, and the combination of N501Y and Q498R may increase binding affinity even more; however, other substitutions in the Omicron spike protein are expected to decrease binding to ACE2 (17). As such, receptor binding affinity needs to be assessed using the full spectrum of spike protein substitutions found in the Omicron variant.
- H655Y is proximal to the furin cleavage site and may increase spike cleavage, which could aid transmission.
- N679K is proximal to and adds to the polybasic nature of the furin cleavage site, which may also increase spike cleavage and could aid transmission(18,19).
- P681H has been shown to enhance spike cleavage, which could aid transmission. This mutation is found in Alpha and an alternate mutation at this position (P681R) is found in Delta.

DISEASE SEVERITY OF OMICRON- The Omicron variant is said to be causing a 'milder' disease. There is no reported rise in hospital admissions of severe cases or mortality in the regions where the variant is spreading. Many have been reported as 'asymptomatic' and no new symptoms have been added to the already present list of covid symptoms. Further, due to the small number of cases in these regions, commenting on disease progression, severity and prognosis will be an early call at present. Old age and individuals with comorbidities are at an added risk.

Impact on Vaccine-Induced Immunity or Immunity from Previous Infection: Currently, there are no data available to assess the ability of sera from vaccinated persons or those with previous SARS-CoV-2 infection to neutralize the Omicron variant. However, the U.S. Government SIG and global public health partners are working to generate these data in laboratory settings and will also continue to monitor epidemiological and clinical indicators.

The spike protein is the primary target of vaccine-induced immunity. The Omicron variant contains more changes in the spike protein than have been observed in other variants, including 15 in the RBD. Based on the number of substitutions, the location of these substitutions, and data from other variants with similar spike protein substitutions, significant reductions in neutralizing activity of sera from vaccinated or previously infected individuals, which may indicate reduced protection from infection, are anticipated.

Laboratory and epidemiological studies are needed to assess the impact of the Omicron variant on vaccine effectiveness and breakthrough infections, including in individuals who have received booster doses. However, vaccination is anticipated to continue to offer protection against hospitalization and death, and vaccines continue to play a critical role in controlling the COVID-19 pandemic.

IMPACT ON MONOCLONAL ANTIBODY TREATMENTS

Currently, there are no virus-specific data available to assess whether monoclonal antibody treatments will retain efficacy against the Omicron variant (20). Based on data from other variants with significantly fewer changes in the RBD, the expectation is that the Omicron variant will remain susceptible to some monoclonal antibody treatments, while others may have less potency.

Mutations within the RBD are most relevant for

monoclonal antibody therapeutics available under Emergency Use Authorization (EUA).(21) Currently, there are three monoclonal antibody treatments with EUA: Sotrovimabexternal icon, Bamlanivimab and Etesevimabexternal icon, and REGEN-COVexternal icon.

However, mutations in the monoclonal antibody binding site do not always result in a loss of binding or neutralization. Importantly, data are needed with the full spectrum of spike protein changes to understand the impact on available monoclonal antibody therapeutics (22). As data becomes available, the Department of Health and Human Services will rapidly communicate changes in treatment guidance to public health departments and health care providers, as appropriate.

In vitro Therapeutic Activity of Single RBD Substitutions found in Omicron-

Data in the table shows data available on the NCATS OpenData Portal6 that has been tested against a viral variant containing only a single amino acid substitution from a wild-type SARS-CoV-2 in an in vitro neutralization assay (23).

VACCINE AND ITS SCENARIO POST OMICRON

The efficacy of the already formulated vaccine is yet to be determined against the Omicron infection. State of vaccination, scheduling of vaccination, comorbidities, immune status of the individual and age, are namely few of the significant factors that will play a part in determining the efficacy of vaccines in this Omicron-phase. Though the numerous mutations in this variant are concerning for the healthcare professionals and vaccine manufacturers, it is too early to suggest that the vaccines could fail. Modifications to the present-formulations will be a welcome move once the researchers and scientists will have enough evidenced data to support their cause. One study conducted by Madhi, suggested that the present vaccines offered smaller quality of protection against infections of mild and moderate type in the younger population. On the other hand, a real-world analysis based in Canada depicted a promise of around eighty-percent protection against hospitalization. One study suggested that the success of the vaccines will replicate the performance of AstraZeneca-Oxford vaccine as against the Beta variant, first reported from South Africa in late 2020 (24).

OMICRON AND THE POPULATION

Early reports linked Omicron with mild disease, raising hopes that the variant might be less severe than some of its predecessors (24). But these reports — which are often based on anecdotes or scant scraps of data — can be misleading, cautions Müge Çevik, an infectious disease specialist at the University of St Andrews, UK. “Everyone is trying to find some data that could guide us,” she says. “But it's very difficult at the moment.”

DIAGNOSTIC SCENARIO OF OMICRON

Surveillance efforts in Brazil and some other countries are taking advantage of a distinctive result on particular PCR (polymerase chain reaction) tests for COVID that could allow them to pinpoint potential Omicron cases for sequencing, says a virologist, Renato Santana at the Federal University of Minas Gerais in Brazil (26). The test looks for segments of three viral genes, one of which is the gene that encodes for the spike protein. Mutations in Omicron's spike gene prevent its detection in the test, meaning that samples containing the variant will only test positive for two of the genes.

CONCLUSION

Given what information we have thus far, it is imperative for the governing authorities around the world to apply stringent laws and do not take a backseat or take the scenario otherwise with reports of 'mild' cases emerging in majority. Every nation has its own framework formulated to regulate entry and exit of its citizens over the borders. Active surveillance and testing with proper mapping are tools of immense importance. Time is crucial in all such situations which the humankind has faced from time to time. Curbing Omicron could very well be the decisive blow to the pandemic, yet it is not so much guaranteed from such an early stage. The timing of the peak alongside case burden is awaited , for the Asian nations, it is speculated to be between the phase of mid-January to early-February 2022. (based on arithematic models, might vary from factors taken into consideration from place to place). A Variant of Interest, is a concerning topic, needs to be studied and followed extensively. Mutations documented thus far from the Omicron have been studied through the microscopic lens to know all specifics pertaining to the morphology, behavior, interactions and responses- each carries its own significance.

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Orcid ID:

Adnan Saeed Shamsi - https://orcid.org/0000-0002-6313-9398

Mohd. Naved Ghauri - https://orcid.org/0000-0001-7445-3043

Sharique Ahmad - https://orcid.org/0000-0002-6313-9398

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