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Review on Omicron Variant (B.1.1.529) of SARS-CoV2

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Abstract:
The virus that causes COVID-19 is called SARS-CoV-2, and it has an Omicron variant. It is the most recent COVID-19 version. This variety, known as omicron, was initially reported to the WHO on November 24, 2021, from South Africa. The WHO's Technical Advisory Group on Virus Evolution (TAG-VE) identified PANGO lineage B.1.1.529. with the Greek letter omicron and declared it a variety of concern on November 26[1]. Omicron possesses multiple mutations that could affect its behaviour, including the degree of disease severity and its transmissibility[1]. Omicron is thought to be more contagious than its predecessors, spreading around 70 times as quickly[18]. The omicron variety is found in numerous nations worldwide[2]. Omicron will therefore not be a final variant, but it may be the final Variant Of Concern (VOC) [8]. Numerous spike protein mutations linked to enhanced infectivity and antibody evasion are also present in other variations of concern. According to computational modelling, the variation might also be able to evade cell-mediated immunity[23]. By sufficiently changing its chemical structure to avoid identification by the immune system, SARS-CoV-2 can evade the immune system[8].
(€-Variant is a viral genome that may contain one or more mutations)

Keywords: Omicron, SARS-CoV-2, Mutations, Variants

Introduction:

The omicron variant has an unusually large number of mutations, several of which are novel and a significant number of which affect the spike protein targeted by most covid-19 vaccines at the time of discover of omicron variant. The variant is first detected on 22 november 2021 in laboratories in Botswana and south Africa based on samples collected 11- 16 november [21,22] . When a virus is circulating widely and causing numerous infections, the likelihood of the virus mutating increases. The more opportunities a virus has to spread, the more opportunities it has to undergo changes[2]. We might have COVID season each winter in the same way as we have flu season now[8].

Many of the mutations to the spike protein are present in other variants of concern and are related to increased infectivity and antibody evasion. Computational modeling suggests that the variant may also escape cell mediated immunity[23]. SARS-CoV-2 can evade the immune system by mutating sufficiently that its molecular shape changes beyond the immune system's recognition[8].

All viruses including SARS-CoV-2 change over time. Most changes have little to no impact on virus properties. However, some changes may affect its properties such as disease severity, how easily it spreads, therapeutic medicines, or the performance of vaccine, diagnostic tools or other public health and social measures [27].

Epidemiology:

On 26 November 2021, the South African National Institute for Communicable Diseases announced that 30,904 COVID-test (in1day) detected 2,828 new covid infections (a 9.2% positive rate). One week later, on 3 December 2021, the NICD announced that 65,990 COVID test had found 16,055 new infections (24.3% positive rate) an that 72% of them were found in Gauteng[24,25,26].

On 13 December 2021, there were 5,006 confirmed cases of Omicron variant of concern (B.1.1.529) identified through sequencing or genotyping in England and indicates daily increase in cases in some regions of England; notably in London[12].

The omicron variant accounted for 73% of all sequenced COVID-19 cases in U.S.A.[5]

The statiscal data of confirmed Omicron variant cases is shown in figure 1.1

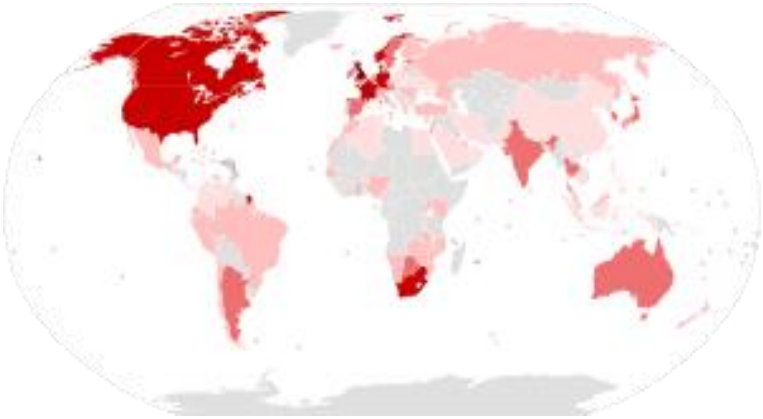

Figure 1.1

Cumulative confirmed Omicron variant cases by country and territory

10,0000-99,999	10-99
1,000-9,999	1-9
100-999	0

Source: Wikimedia- Map of countries with confirmed SARS-CoV-2 Omicron variant cases.svg

Mutations:

Compared to Wuhan variant this omicron variant has a total of 60 mutations; 50 nonsynonymous mutations, 8 synonymous mutations, and 2 non-coding mutations[3].

These mutations are identified by letters and numbers such as D614G- which means an aminoacids changed from a D (aspartate) to a G (glycine) at position number 614 of spike proteins of virus.[6]

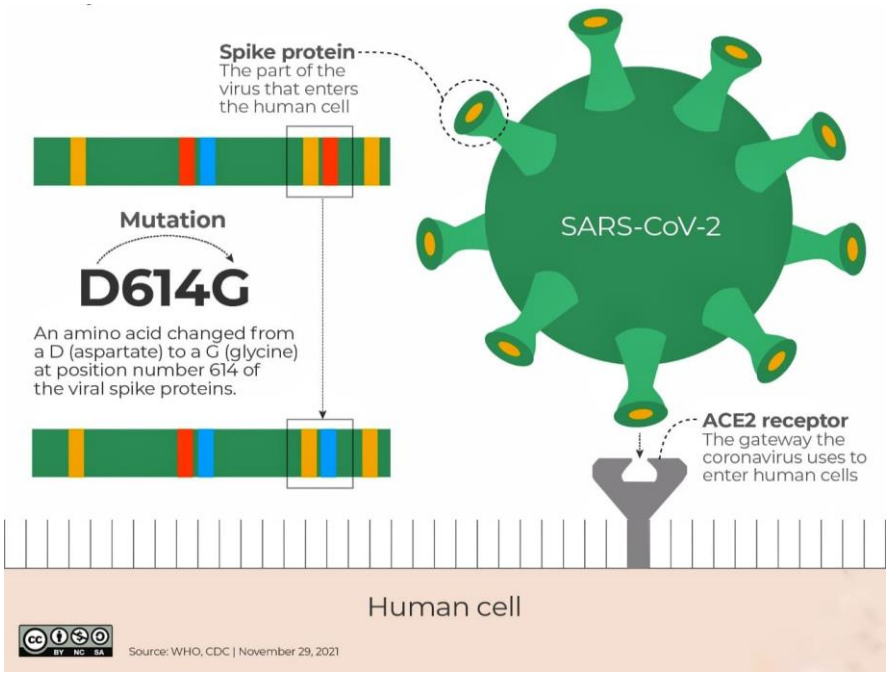

Figure 1.2

Source: *Infographic: How Omicron compares with other COVID variants*; Aljazeera.

The mutation profile includes multiple spike proteins, including in the receptor binding domain and furin cleavage site and additional mutations outside spike [of] uncertain significance. [12]

The WHO is concerned that a large number of mutations 0f COVID-19 may reduce immunity in people who were previously infected and in vaccinated people. Because of this, there is possibility of the omicron variant might be more infective in this regard than prior variants[4].

NAMING OF VARIANTS:

The WHO has identified 5 variants of concern (VOC) and 8 variants of interest (VOI). They are named after the letters of Greek alphabet.[6]

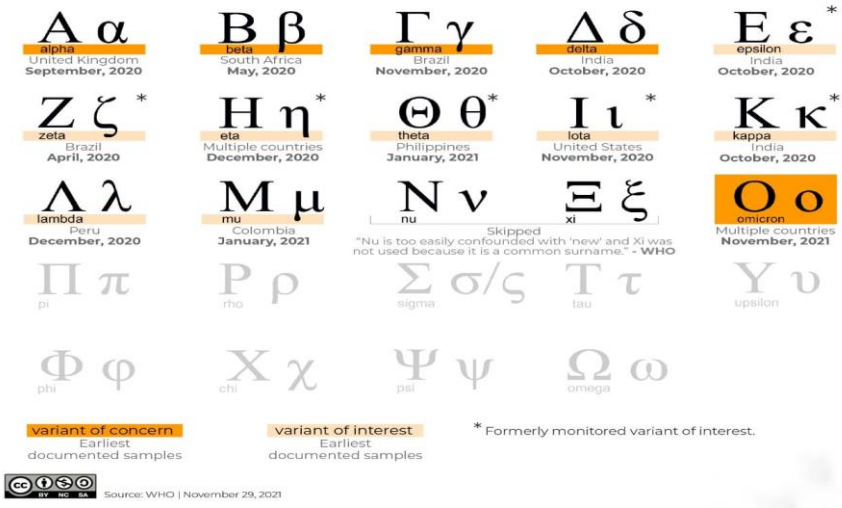

Figure 1.3

Source: *Infographic: How Omicron compares with other COVID variants*; Aljazeera.

Variants Of Concern (VOC):

There are 5 Variants Of Concern (VOC) - Alpha, Beta, Gamma, Delta, Omicron. These Variants Of Concern (VOC) has been demonstrated to be assosiciated with one or more of the following changes at the degree of public health significance.

- Increase in transmissibility
- Increase in virulence
- Change in clinical disease presentation
- Changes in COVID-19 epidemiology
- Increase in disease severity, hospitalization and death
- Decrease in effectiveness of public health and social measures
- Decrease in effectiveness of vaccines
- Decrease in effectiveness of diagnostics and therapeutics[27]

(* it is the present variant of concern)

Table 1.1 - Currently designated variants of concern (VOC)

Source: Tracking SARS-CoV-2 Variants; World Health Organization.

WHO label	Pango lineage	GISAID clade	Nextstrain clade	Additional amino acid changes monitored	Earliest documented samples	Date of designation
Alpha	B.1.1.7	GRY	20I (V1)	+S:484K +S:452R	United Kingdom, Sep-2020	18-Dec-2020
Beta	B.1.351	GH/501Y.V2	20H (V2)	+S:L18F	South Africa, May-2020	18-Dec-2020
Gamma	P.1	GR/501Y.V3	20J (V3)	+S:681H	Brazil, Nov-2020	11-Jan-2021
Delta	B.1.617.2	G/478K.V1	21A, 21I, 21J	+S:417N +S:484K	India, Oct-2020	VOI: 4-Apr-2021 VOC: 11-May-2021
Omicron*	B.1.1.529	GRA	21K, 21L 21M	+S:R346K	Multiple countries, Nov-2021	VUM: 24-Nov-2021 VOC: 26-Nov-2021

Variants Of Interest (VOI):

A variant with specific genetic marker that have been associated with changes to receptor binding, reduced neutralization with antibodies generated against previous infection or vaccination, reduced efficacy of treatment, potential diagnostic impact, or predicted increase in transmissibility or disease severity.

Possible attributes of Variants Of Interest (VOI):

- Limited prevalence or expansion

- Specific genetic marker that are predicted to affect transmission, diagnostics, therapeutics, or immune escape
- Evidence that it is the cause of an increased portion of cases or unique outbreak clusters [28].

Comparison of Omicron variant with previous variants of concern:

Compared to previous variant of concern it spreads faster, but it is less able to penetrate deep lung tissue, and perhaps for this reason there is considerable reduction in hospitalization and reduction in risk of severe disease. However, the extremely high rate of spread, ability to evade both double vaccination and body's immune system, means the total number of patient requiring hospital care at given time is still of great concern[18].

The WHO said that "there may be an increased risk of reinfection with Omicron as compared to other variants of concern, but information is limited".[1]

Omicron Variant Transmission:

Frequent sneezing and dry coughing exhibited by patient generate thousands of droplets of viral plumes per cubic centimeter and it is believed to be transmitted by aerosols and/or droplets[7].

It is not yet clear that omicron is more transmissible (more easily spread from one person to person) compared to other variants, including delta[1]. On December 15, the European Centre for Disease Prevention and Control, assessed that, even if the variant turns out to be milder than Delta, its spread will very likely to increase hospitalization and fatalities due to exponential growth in cases caused by increased transmissibilty[9.]

However, being vaccinated and taking precautions such as avoiding crowded spaces, wearing mask and maintaining social distance helps to prevent the spread of virus.

This improved spreading ability has been ascribed to mutations in spike protein- that allow it to bind more strongly to ACE2 receptors and start replicating[8].

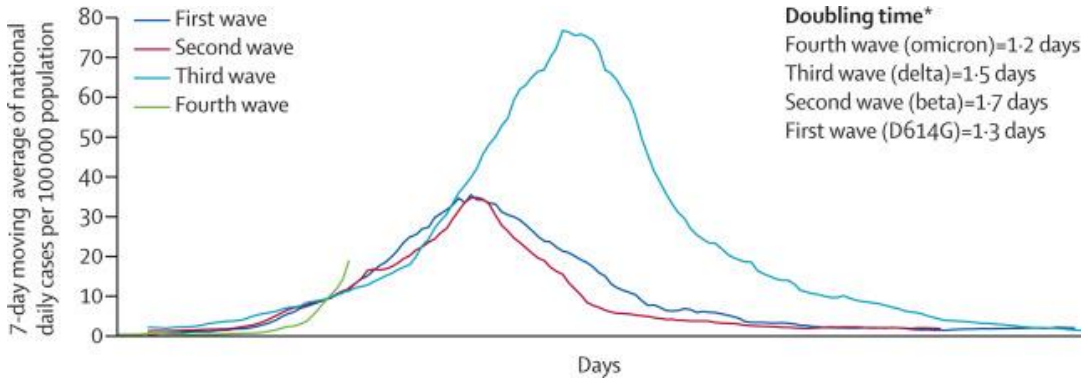

Figure 1.4 – cases in first, second, third and fourth waves, Gauteng. Province of South Africa

Source: Salim S Abdool Karim, Quarraisha Abdool Karim-Omicron SARS-CoV-2 Variant; a new chapter in COVID-19 pandemic; published- December 03, 2021. Volume 398, Issue 10317, P2126, December 11,2021.

Signs and symptoms:

The WHO's update states that "there is currently no information to suggest that symptoms associated with omicron are different from other variants "[1].

A study performed by the Center for Disease Control found that the most commonly reported symptoms were cough, fatigue, and congestions or runny nose[10].

On 25th December 2021 a research published in London suggested the most frequent symptoms states by Zoe covid app were – running nose, fatigue, headache, sneezing and sore throat. Half of those flu-like symptoms also tested positive for covid, with no clear difference in symptoms reported for delta or omicron infection[17].

Effectiveness of vaccine:

Researchers are looking into any potential impact the omicron variant has on effectiveness of COVID-19 vaccines. However, WHO reports that vaccines remain critical to reducing severe disease and death, including against the dominant circulating variant, Delta. Current vaccines are effective against severe disease and death[1].

The WHO warns the health services especially to the nations with low vaccination rate where mortality and morbidity rates are high, and urges all the nation to increase COVID-19 vaccinations[19].

Diagnosis:

The presence of mutation in SARS-CoV-2 virus in patient sample can potentially impact the test performance. And FDA has published guidelines on how PCR tests will be affected by omicron[11]. S-gene dropout or target failure has been proposed as a shorthand way of differentiating Omicron from Delta[12].

Omicron variant may also be identified by sequencing and genotyping[12].

Scientist says they have identified "stealth" version of Omicron that cannot be distinguished from other variants using the PCR test. The discovery of new version of Omicron promoted researchers to split the B.1.1.529 lineage into standard Omicron - BA.1 and newer version - BA.2[20].

The BA.1 lineage*, but not the BA.2 lineage, can be identified by S-gene target failure (SGTF) of the TaqPath assay, a trait shared with subsets of SARS-CoV-2 ALPHA variant[20].

Studies are ongoing to determine whether there is any impact on other types of test, including rapid antigen detecting tests[1].

(*lineage- A lineage is a group of closely related viruses with a common ancestor. SARS-CoV-2 has many lineages; all causes COVID-19[28].)

Treatment:

Patients with the earlier strains of COVID-19 are treated with corticosteroids such as dexamethasone and IL6 receptor blockers such as tocilizumab[1].

Pfizer CEO Albert Bourla said he has confidence that the company's COVID treatment pill, Paxlovid is effective against Omicron variant. And on 29th November 2021, Pfizer has submitted its application to FDA to authorize the pill Paxlovid for emergency use[13].

Research is ongoing relating to monoclonal antibodies (mAbs) treatment for Omicron variant[3]. Current data suggest omicron variant cause significant humoral immune evasion, while neutralizing antibodies targeting the sarbecovirus conserved region remain most effective. Impairment of NAbs of different epitope group can be seen due to various single mutations of Omicron variant Omicron pseudovirus neutralization showed that single mutation tolerating NAbs could also be escaped due to multiple synergetic mutation on their epitope. In total, over 85% of the tested NAbs are escaped by Omicron. Regarding Nab drugs, the neutralizing potency of LY-CoV016/LY-CoV555, REGN10933/REGN10987, AZD1061/AZD8895, and BRII-196 were greatly reduced by Omicron. Due to this, instruction for developing Nab drugs and vaccines against Omicron and future variants are offered [14].

Marked reduction of plasma neutralizing activity was observed against Omicron compared to ancestral pseudovirus for convalescent and vaccinated individual. Indeed, most receptor binding motif (RBM)-directed monoclonal antibodies lost in vitro neutralizing activity against omicron, with only 3out off 29

mAbs retaining unaltered potency. Furthermore, a fraction of broadly neutralizing sarbecovirus mAbs neutralized omicron through recognition of antigenic sites outside the RBM, including sotrovimab (VIR-7831) S2X259 and S2H97[15].

Prevention:

WHO recommended people to keep a physical distance of atleast 1 meter from others; wear a well-fitting mask; open windows to improve ventilation; avoid poorly ventilated or crowded spaces; keep hands clean; cough or sneeze into a bent elbow or tissue; get vaccinated when it is your turn- WHO approved COVID-19 vaccines are safe and effective[1]. Self isolate if you develop symptoms.

On December 7, 2021, researchers reported that preliminary research from a laboratory test conducted at the Africa Health Research Institute in Durban 12 people who received the Pfizer-BioNTech vaccine found a 41- fold reduction in neutralizing antibody activity against the variant in some of the samples. This is a reduction, but it doesn't mean that the variant escape vaccine completely, so vaccination with current vaccine is recommendable[16].

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