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The evolution of the SARS-CoV-2 virus, Pango lineage B.1.1.529

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Abstract

On November 24, 2021, the WHO reported the B.1.1.529 pangolinage of SARS-CoV-2 for the first time. In South Africa, there were 3 reported peaks of COVID-19 cases, one of the reported variants was the Delta variant, subsequently there was an increase in infections, which coincided with the detection of the B.1.1.529 pangolinage. The omicron variant of this B.1.1.529 pangolinage has numerous mutations, some of which are considered of concern. Initial tests indicate a higher risk of reinfection by this variant than by others. Tests to diagnose SARS-CoV-2 are by PCR and sequencing, by detecting the S protein gene, one of the 3 target genes for the virus. Using this molecular technique, the B.1.1.529 variant has been detected more frequently than with other outbreaks, indicating that it probably has a greater growth. The omicron variant of the pango lineage B.1.1.529 presented changes that affected the epidemiology of COVID-19, which is why the technical advisory group on the evolution of the SARS-CoV-2 virus recommended to the WHO that it be designated as a variant of concern. The WHO named it omicron and designated it as a variant of concern. WHO instructions to countries: Maintain surveillance and sequencing to better understand the SARS-CoV-2 variants that are circulating. Sending the complete genome sequences and related metadata to a publicly available database, such as GISAD.

Keywords: Pangolinage; SARS-CoV-2; Omicron; Variants; Mutations; COVID-19

1. Introduction

On November 24, 2021, the WHO reported for the first time the pangolinage B.1.1.529 omicron variant of SARS-CoV-2. By that date, 260 million cases of COVID-19 had been reported globally and 5.2 million deaths (WHO, 2021). In South Africa, there were 3 reported peaks of COVID-19 cases, one of the reported variants was the Delta variant, subsequently there was an increase in infections, which coincided with the detection of the B.1.1.529 omicron variant. The pangolinage B.1.1.529 omicron variant presented numerous mutations, some of which are considered of concern. Initial tests indicate a higher risk of reinfection by this variant than by others. Tests to diagnose SARS-CoV-2 are by PCR and sequencing, through the detection of the S protein gene, one of the 3 target genes for the virus. Using this molecular technique, the omicron variant of the pango lineage B.1.1.529. has been detected more frequently than with other outbreaks, which indicates that it probably has greater growth (WHO, 2021), (CDC, 2021). The omicron variant of the pango lineage B.1.1.529. presented changes that affected the epidemiology of COVID-19, which is why the technical advisory group on the evolution of the SARS-CoV-2 Virus recommended to the WHO that it be designated as a variant of concern. The WHO gave it the name omicron and designated it as a variant of concern or VOC for its acronym in English. WHO guidance to countries: Maintain surveillance and sequencing to better understand the SARS-CoV-2 variants that are circulating. Submit complete genome sequences and associated metadata to a publicly available database, such as GISAD. Notify WHO of cases or clusters of cases of infection with variants of concern, through the mechanism of the International Health Regulations. If sufficient capacity is available and in coordination with the international community, conduct field studies and laboratory analyses to better understand the effects of the variants

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of concern on the epidemiological characteristics of COVID-19, the severity of the symptoms they produce, the effectiveness of social and public health measures, diagnostic methods, immune response, antibody neutralization and other relevant issues. As well as reminding the population that to reduce the risk of contracting COVID-19, social and public health measures of proven effectiveness should be applied, such as the use of a well-fitting mask, hand hygiene, physical distancing, good ventilation of indoor spaces, avoidance of crowded spaces and vaccination (WHO, 2021). WHO has established some references on SARS-CoV-2 variants of interest and concern. SARS-CoV-2 variants of interest (VOI). Variants of interest (VOI) exhibit genome changes that have been shown or anticipated to affect characteristics of the virus including its transmissibility, disease severity, and ability to evade immune response, detection by diagnostics, or drug attack, and have been shown to result in significant transmission in non-healthcare settings, or cause multiple clusters of COVID-19 across countries with increasing relative prevalence and increasing numbers of cases over time, or appear to have other characteristics that indicate they may pose a new risk to global public health. SARS-CoV-2 variants of concern (VOC) (WHO, 2021), (CDC, 2021). These meet the criteria for variants of interest as demonstrated through comparative assessment to be associated with one or more of the following changes that are significant to global public health. They present an increase in transmissibility or a detrimental change in the epidemiology of COVID-19; or an increase in virulence or a variation in the clinical symptomatology of the disease; or a decrease in the effectiveness of social and public health measures or of the diagnostic means, vaccines and available treatments. The SARS-CoV-2 omicron variant has produced many changes around the world. The omicron variant contains emerging characteristics that are of importance to public health, which is why it is important to continue monitoring the biological and clinical behavior of the new SARS-CoV-2 omicron variants globally. Among the characteristics that have been found is its rapid transmission. The new SARS-CoV-2 variants have shown diverse epidemiological and biological characteristics, making it more contagious than other SARS-CoV-2 variants (WHO, 2021).

2. Mutations detected in the SARS-CoV-2 Omicron variant.

A phylogenetic analysis of SARS-CoV-2 sequences revealed that the Omicron variant has two subtypes, BA.1 and BA.2. BA.1 was responsible for the initial outbreak and was the predominant subtype worldwide in 2022. In the complete genome analysis of the BA.1 and BA.2 subtypes, more than 60 non-synonymous mutations were found, including substitutions, deletions and insertions. Omicron emerged in November 2021, the first reports indicate infections that occurred in South Africa, the detection of this variant is of great importance due to its characteristics, its mutations are associated with the Omicron spike protein, which is characterized by substitutions in at least 30 amino acids, 3 small deletions and a small insertion. Interestingly, 15 of the 30 substitution amino acids are in the RBD domain-binding receptor. These are also a series of changes and deletions in other genomic regions. Within the key amino acids of the spike protein substitutions (RBD): they are A67V, del69-70, T951, del142-144, Y145D, del211, L2121, ins214EPE, G339D, S371L, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F (CDC, 2021) (Zhou et al., 2022) (Willett et al., 2022). Based on analysis of changes in the spike protein, the omicron variant is likely to have an increase in transmission compared to the original SARS-CoV-2 virus. For example, N501Y increases binding to the ACE2 receptor, which could increase transmission, and the combination of N501Y with Q498R can increase binding by 90% more, however, other substitutions in omicron in the spike protein are expected to decrease binding to ACE2. H655Y is located proximal to the furin binding and binding site and may increase spike binding, which could increase transmission. N679 is located proximal to and adds to the polybasic nature of the furin cleavage site, it may increase binding to the spike protein, which may increase transmission. P681H has been shown to enhance spike binding, which could aid transmission. This mutation is located in Alpha and an alternative mutation at this position (P681R) is located in Delta (CDC, 2021). These mutations that have occurred in omicron have contributed to increased transmissibility, evasion of the immune system, and greater affinity to the ACE2 receptor. It shares 2 mutations with the VOC Alpha variant and 26 specific mutations which have been detected by the Sanger method. The Mu VOI emerged in early 2021, which was more frequent in Colombia. This variant has mutations that are also found in VOC and VOI, such as S: T951, S: E484K, S: N501Y, S: P681H and S: D95N. The S: R346 mutation had been considered specific to the Mu variant, although it was also found in the Omicron variant. As already mentioned, the characteristics exhibited by the Omicron variants of SARS-CoV-2 are: The mutations detected in the Omicron variants of SARS-CoV-2 have shown greater infectivity, can evade vaccine protection, greater transmissibility, evasion of the immune system, severity of symptoms in some cases, and increased binding affinity to the viral receptor. Some deletions and more than 30 mutations have been presented (example: 69–70del, T95I, G142D/143–145del, K417N, T478K, N501Y, N655Y, N679K, and P681H). The first mutations were detected in the S protein, in the omicron variant. Later, 39 mutations were revealed in the S protein, 27 of them with some alterations. Of the 39 mutations, 15 mutations were found in the RBD region, which accounts for around 38% of the total mutations in the omicron variant. In one study, the omicron variant exhibits a reduced binding capacity to the ACE2 receptor compared to the wild-type strain of SARS-CoV-2 (GISAID, 2021). It is very evident that the Omicron variant has a large number of mutations compared to the other variants Figure 1, (Ao et al., 2022).

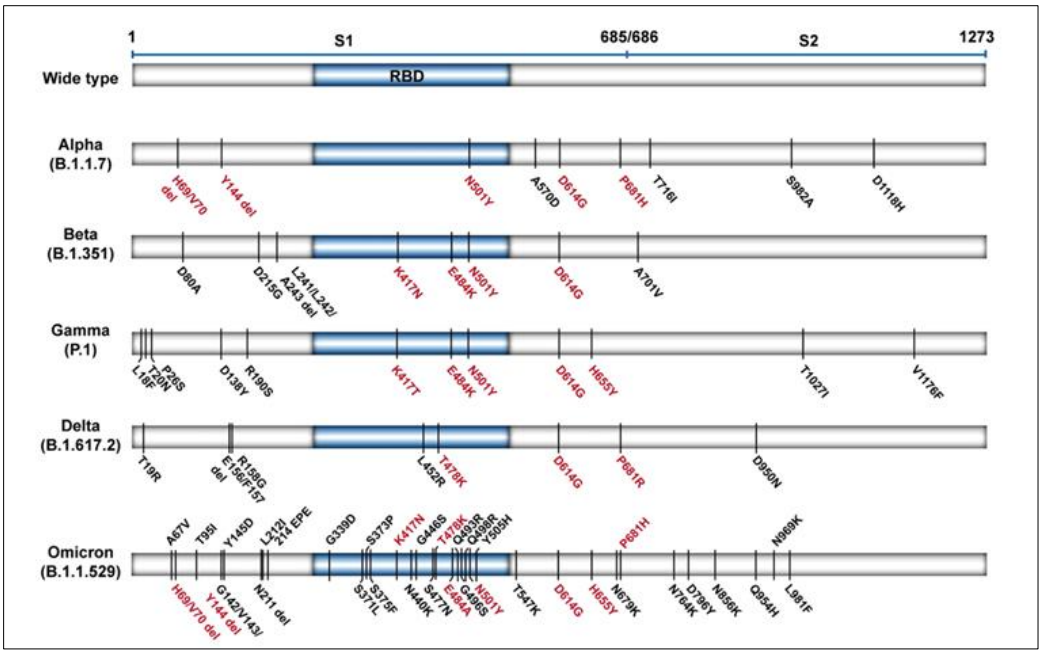

Figure 1 Schematic representation of spike protein mutations of SARS-CoV-2 variants. Mutations of the 21K BA.1 omicron variant in RBD. Taken from (Ao et al., 2022)

The fourth wave of COVID-19 in Southern Africa was associated with BA.1 and BA.2 lineages. In South Africa in April 2022, BA.4 and BA.5 rapidly replaced BA.2 and initiated the fifth wave of COVID-19, accounting for more than 50% of sequenced cases (Zhou et al., 2022). In a comparison of the BA.1, BA.1.1, BA.3, BA.4, and BA.5 lineages, the BA.2 lineage was missing the 69-70, 38, and 39 deletions which are associated with the S gene. Structural changes at positions 143-145 from deletions in BA.2 allowed it to have a high potential for electrostatic attraction on the surface, which may facilitate the interaction between BA.2-RBD and hACE2, compared to BA.2, BA.4, and BA.5 having additional mutations in the spike protein 69-70 L452R, F486V, and R493Q reversing the mutation. It was very evident that the F486V mutation led to reduced receptor affinity in BA.4 and BA.5 as well as reduced hydrophobic interactions. On the other hand, R493Q mutation reversal restored hydrogen bonds with H34 and it avoided the repulsion charge by K3, and increased the affinity between BA.4 and BA.5 RBD and hACE2 (Zhou et al., 2022). The omicron variant has not only accumulated a large number of mutations in the spike protein, but also in the open reading frame 1ab (ORF1ab), the nucleocapsid (N) protein, the envelope (E) protein, and the membrane (M) protein. Including NSP1-S135R; PLpro-T241, G489S; NSP4-L264F, T327I, L438F, T492I; 3CL-P132H; NSP6-del105-108, F108L; NSP12-P323L; 189V; NSP13-R392C; NSP14-142V; NSP15-T112I; ORF3a-T223I; E-T91; M-Q19E; N-P13L, del31-33, R203K, G204R, S413R. https://www.nicd.ac.za/latest-confirmed-cases-of-covid-19-in-south-africa/).

According to the above, the omicron variant and subvariants have been considered a public health threat, because the variant presents various mutations in its genome, which causes changes in its infectivity, reducing the effectiveness of existing infection control measures (Sreekanth et al., 2022).

3. Vaccine protection against the Omicron B.1.1.529 variant of SARS-CoV-2.

In general, SARS-CoV-2 vaccines had some protection coverage against the virus with the Delta variant, presenting an immunization effectiveness of 63% in the application of the Pfizer-BioNTech BNT162b2, 60% with the ChAdOx1 vaccine and 86% with the Moderna mRNA-1273. In one study, it was reported that the Omicron variant evades and lowers the efficiency of immunization by vaccines twice as much as other variants (Rosenberg et al., 2021). The Omicron variant showed a marked reduction in the efficacy of the main vaccines approved for emergency use such as BNT162b2 Pfizer-BioNTech with 37% efficiency, 23% with the mRNA-1273 vaccine from Moderna, and not significant for the ChAdOx1 nCoV-19 vaccine (Astra Zeneca). However, vaccination reduced COVID-19 infection, it also reduced the development of severe disease and/or mortality, factors that have been of great importance for the health sector at local, national and international levels (Ao et al., 2022). It has also been reported that the activity of the sera from the two-dose Astra Zeneca vaccine is significantly reduced, even falling below the detection limit. However, regardless of the type of vaccines a person has received, an mRNA booster dose can always cause an increase in neutralizing activity (Gruell et al., 2022). Nemet and colleagues made a similar observation when evaluating the efficacy of BNT162b2 against the

Omicron variant and found that two doses of BNT162b2 provided little protective action (Nemet et al., 2021). When the Delta variant was dominant in the United States, hospitalization rates were 12.9 times higher in unvaccinated groups. Similarly, hospitalization rates were 5.3 times higher in unvaccinated groups when the Omicron variant became dominant. This has been reflected in clinical studies in the administration of two doses of the BNT162b2 vaccine, showing an efficacy of 70% and 93% against hospitalization due to the Omicron and Delta variants, respectively. Similarly, another study in the United Kingdom showed that without having been vaccinated with Omicron infection, the hospitalization rate was 0.76, and when vaccinated with two doses of the Astra Zeneca or Pfizer vaccine, hospitalization rates were reduced by 0.37 and 0.26, respectively. This once again highlights the importance of vaccination and receiving booster doses (Ao et al., 2022). Vaccination with BNT162b and hybrid immunity, that is, by previous infection and by vaccination, increased the efficiency above 70% against severe, critical symptoms or death from COVID-19, both by BA.2 infection. However, greater protection was observed in immunity from previous infection and recent booster vaccination above 80%, and similar patterns were observed in BA.2 infection and by vaccination with mRNA-1273. In a particular analysis for BA.4 and BA.5 previously diagnosed with infection, they strongly maintained their immunity against severe hospitalization and death in 95% of those previously vaccinated with BNT162b and Ad26. CoV2 in South Africa (Ao et al., 2022) (Xu et al., 2022). Booster vaccination is essential to control the spread of omicron, public places such as schools, hospitals, restaurants, hotels, bus stations, taxis and other transportation, cinemas, theaters are places of easy transmission of SARS-CoV-2. The CDC in the US and other reference laboratories require testing within 24 hours for the detection of the virus when patients suspected of having SARS-CoV-2 infection are detected. Studies show that N95 masks can prevent infection. In a preclinical evaluation, candidate influenza vaccines were evaluated, the sarbecovirus administered intranasally has induced protective cellular and humoral immunity of the mucosa located in the lungs at the site of viral entry. These findings of post-vaccination SARS-Cov-2 infections, but not vaccination itself, inducing neutralization of the nasal mucosa, support the development and evaluation of a next generation of intranasally administered vaccines (Jun Park et al., 2022). Further laboratory and epidemiological studies are needed to understand the impact of the omicron variant on vaccination efficiency and post-vaccination infections, including booster doses. However, early vaccination continues to offer protection against hospitalization and death, as well as vaccines continue to play an important role in controlling the COVID-19 pandemic (CDC, 2021). Other therapies have been tested such as monoclonal antibodies, which are not known to be virus-specific, to see if they maintained efficacy against the Omicron variant. Comparing this to data from other variants with few significant changes in RBD, the Omicron variant is expected to remain susceptible to some monoclonal antibody treatments, while others may have less efficacy. Mutations within RBD are most relevant to monoclonal antibody therapies available for EU emergency use authorization. Sotrovimab, Etesevimab, and REGEN-COV have been used (CDC, 2021).

4. Conclusion

The Omicron lineage has been the most frequently detected variant among CoVs. The Omicron variant has had more than 50 mutations throughout its genome, more than 32 mutations in the spike protein, since August 2022, Omicron has been classified into five main lineages, BA.1, BA.2, BA.3, BA. 4, and BA.5. The management of booster doses of vaccines worldwide is important since there are inequalities in acquisition, which is why international health organizations must take measures to provide more vaccines in countries with less vaccination and greater susceptibility to SARSCoV-2 and its variants. Regarding the omicron variant and its sublineages, many questions remain, including its emergence, future evolutionary direction, and strategies for developing next-generation vaccines and therapeutics. Global surveillance and timely sequencing of new SARS-CoV-2 variants remain of great importance today for the prevention of current or future sublineages.

Compliance with ethical standards

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Disclosure of conflict of interest

The author declares that there is no conflict of interest,

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