



OMICRON THE NEW CHAPTER DURING THE PANDEMIC

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Abstract:

The variant is characterized by 30 mutations, three small deletions and one small insertion into the spike protein, of which, 15 are in the receptor binding domain. This variation was first obtained from samples collected on 11 November 2021 in Botswana and 14 November 2021 in South Africa. As of November 26, 2021, travel-related cases have been found in Belgium, Hong Kong and Israel. The Omicron variant is a very different variant found in significant numbers during the epidemic so far, raising concerns that it may be associated with increased infection, a significant reduction in vaccine efficacy and an increased risk of re-infection. As of November 26, 2021, the ECDC has listed this variant as a variant of concern (VOC) due to concerns about immune defences and potentially potent infections compared to the Delta variant.

Keywords:

Omicron variant, Delta variant, SARS-COV-2 OMICRON VARIANT, SOUTH AFRICA, COVID-19, Spike.

Introduction:

Currently, it is unknown how efficiently the Omicron variant can spread from person to person. The replacement of the Delta with Omicron as a prominent variant in South Africa raises concerns that the Omicron variant may be more contagious than the Delta, but due to the low number of incidents in South Africa where Omicron originated, it is unclear if these variations are easily transmitted. There are differences in Delta. In addition, the small number of cases documented so far makes it difficult to quantify the infection. Analysis of the mutations in the spike protein suggests that Omicron variants may increase infection compared to the real SARS-CoV-2 virus, but it is difficult to say if it is more contagious than Delta.

To examine whether reinfection risk has changed through time, it is essential to account for potential confounding factors affecting the incidence of reinfection: namely, the changing force of infection experienced by all individuals in the population and the growing number of individuals eligible for reinfection through time. These factors are tightly linked to the timing of epidemic waves. We examine reinfection trends in South Africa using two approaches that account for these factors to address the question of whether circulation of the Beta, Delta, or Omicron variants has been associated with increased reinfection risk, as would be expected if their emergence was driven by immune escape.

Emergency and the characteristics of omicron:

Since early 2020, three big waves of COVID-19 outbreaks have been recorded in South Africa in it, two are caused by the beta and delta variants respectively. The epidemiological data showed that the percentage of infections associated with the Beta variant increased to ~50% of the total daily infections within approximately 100 days since its outbreak (Figure 2). The infection percentage of the Delta variant, however, raised to ~80% during the same period of time, echoing higher transmissibility among people for Delta than for the Beta variant. In contrast, the Percentage of Omicron infection reaches to ~90% within approximately 25 days in South Africa. The early doubling time of the Beta, Delta, and Omicron variants was calculated to be about 1.7, 1.5, and 1.2 days, respectively.

These data indicate that the Omicron variant is probably more infectious than the Delta and Beta variants. It is also noteworthy that a recent retrospective study based on the population-wide epidemiological data in South Africa indicates an increased risk of SARS-CoV-2 reinfection associated with Omicron. The possibility of a new wave of COVID-19 epidemic in South Africa and even around the world therefore should not be ignored.

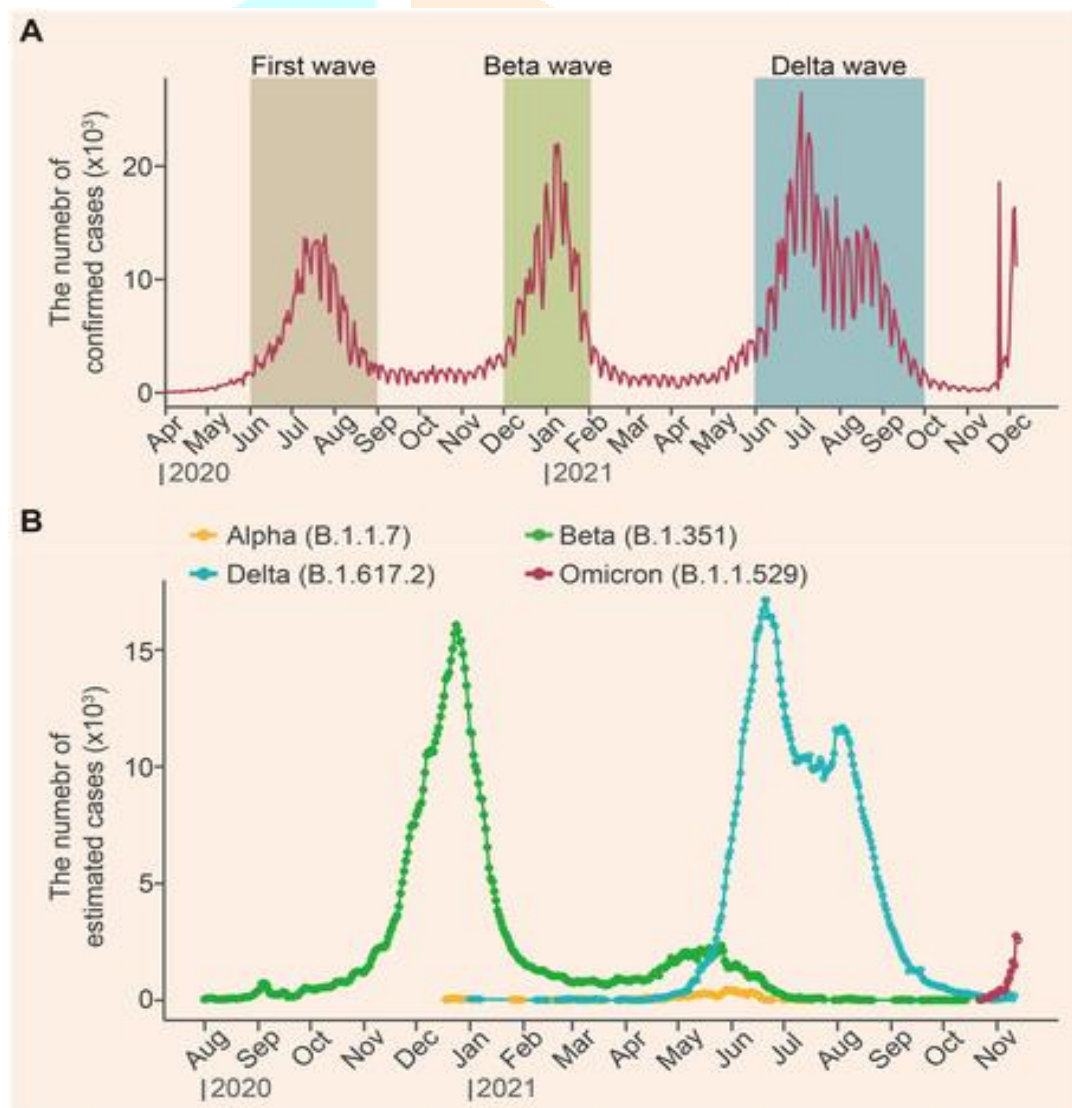


FIGURE 1

Waves of Coronavirus disease 2019 (COVID-19) epidemics recorded thus far in South Africa. (A) Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)

2) has caused three waves of epidemics in South Africa. The number of daily confirmed infection cases is plotted. Data were downloaded from the World Health Organization (WHO). (B) The number of estimated cases infected by the indicated variants of concern (VOCs) in South Africa. The original data were downloaded from global initiative on sharing all influenza data (GISAID)

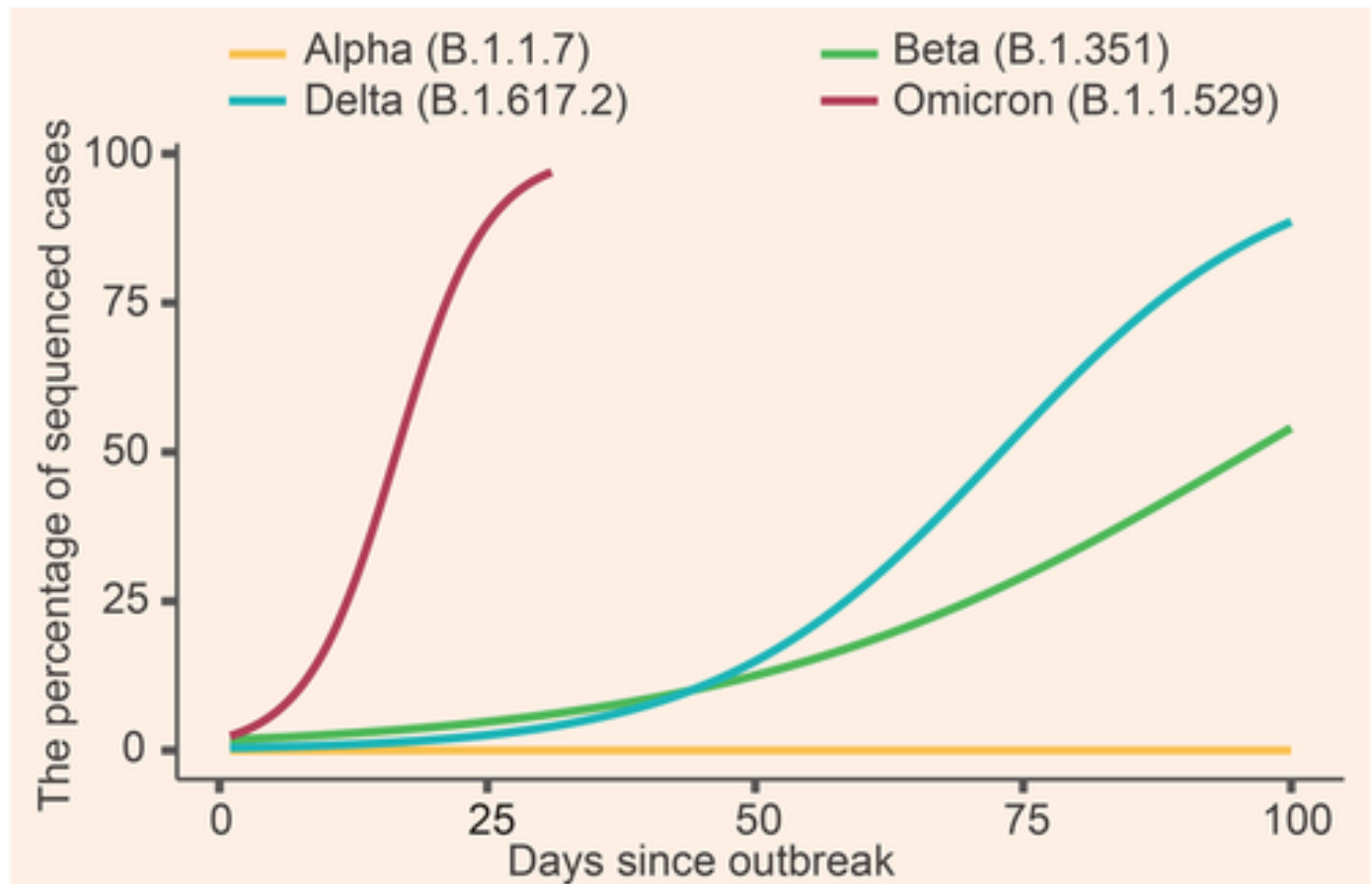


FIGURE 2

Omicron is spreading faster than other variants of concern (VOCs) in South Africa. The full genomic sequences were downloaded from global initiative on sharing all influenza data (GISAID), and the original data were processed with a logistic function.

Analysis of the genomic sequences of the Omicron variant has revealed a high number of non-synonymous mutations, including several ones in spike that have been proved to be involved in transmissibility, disease severity, and immune escape. Overall, more than 60 substitutions/deletions/insertions have been identified in the Omicron variant,¹² making Omicron a variant possessing the largest number of mutation sites of all SARS-CoV-2 variants characterized so far. Within ORF1a, the Omicron variant harbors six substitutions (K856R, L2084I, A2710T, T3255I, P3395H, and I3758V) and two deletions of in total four amino acids (amino acid 2083 and amino acids 3674–3676). Within ORF1b, the variant contains two substitutions (P314L and I1566V). In addition, a P10S substitution and a three-residue deletion at positions 27–29 are observed in ORF9b. For the structural proteins, there are one substitution (T9I) in the envelope (E), three substitutions (D3G, Q19E, and A63T) in the membrane (M), and three substitutions and a three-residue deletion in the nucleocapsid (N) proteins, respectively. While the aforementioned mutations emerge along the whole viral genome, the remaining mutations, which account for more t

han half of the total Omicron mutations identified, are accumulated in the spike. These include 30 substitutions of A67V, T95I, Y145D, L212I, 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, and L981F, three deletions of H69/V70, G142/V143/Y144 and N211, and one insertion of three amino acids (EPE) at position 214 (in some reports, the changes are described as the V143/Y144/Y145 deletion in combination with G142D and the L212 deletion in combination with N211I). In comparison to those observed in the other four VOC variants, the spike mutations identified in Omicron outnumber by about 3–

4 times (Figure 3). It is notable that all the five VOCs contain the amino acid change D614G in spike. Previous studies have clarified that D614G is associated with higher upper respiratory tract viral loads and the younger age of patients.

The Omicron variant also shares N501Y with the Alpha, Beta, and Gamma variants. This mutation is believed to enhance the binding between spike and angiotensin-converting enzyme 2 (ACE2) and to induce higher transmissibility.

When combined with the H69/V70 deletion, the transmissibility might be further increased.

Besides, Omicron also has N679K and P681H mutations near the furin cleavage site. The incorporation of basic amino acids around the furin cleavage site could facilitate the cleavage of the spike into S1 and S2, thereby enhancing fusion and virus infection. As a matter of fact, the P681H mutation was also identified in the Alpha variant (Figure 3). This mutation has been suggested to enhance SARS-CoV-2 infectivity.

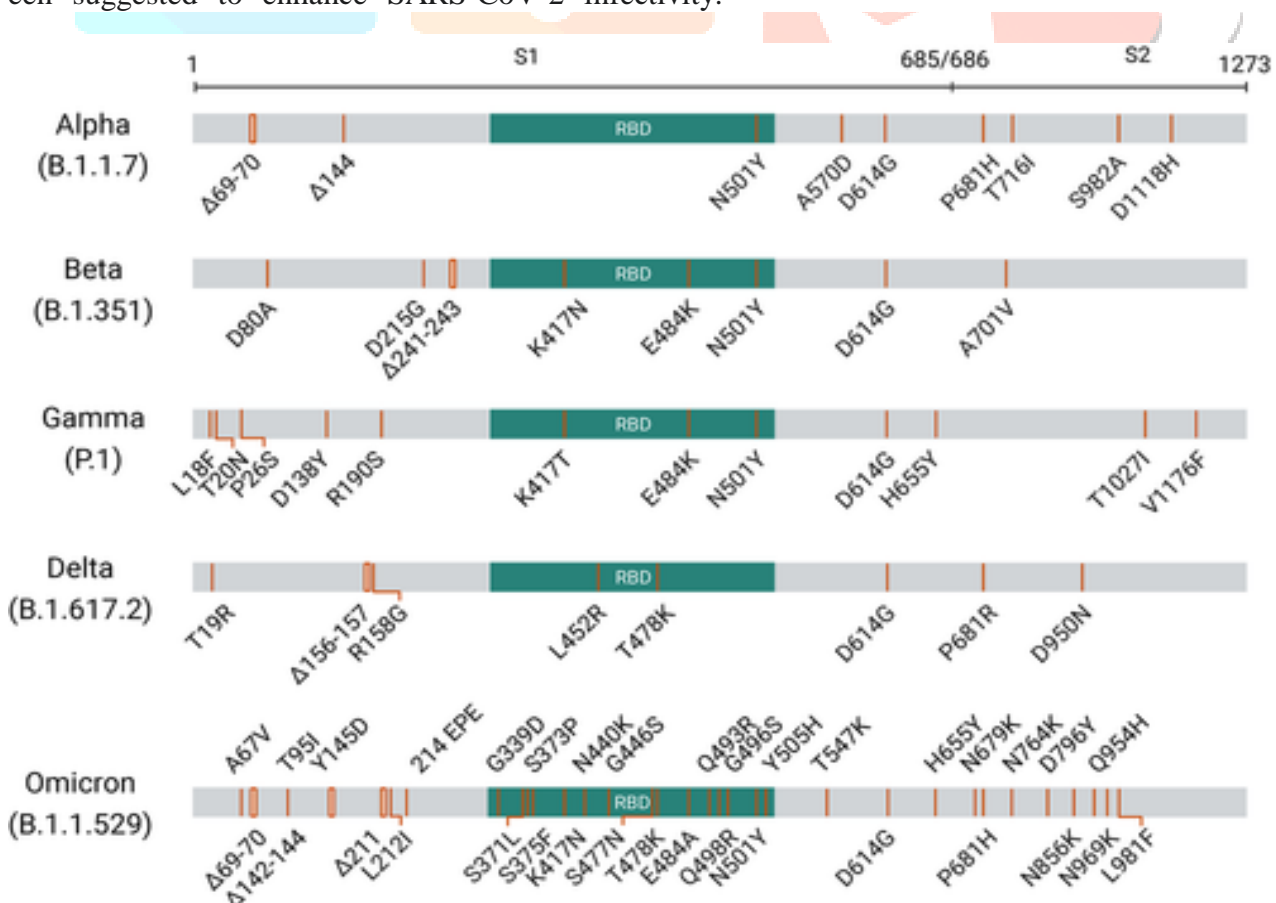


FIGURE 3

The given diagram showing the spike mutations of 5 variants of concern (VOCs). The mutations, including substitutions, deletions, and insertions, are defined based on the data from cover

variants at address <https://covariants.org> (20I for Alpha, 20H for Beta, 20J for Gamma, 21A for Delta, and 21K for Omicron, respectively)

It should also be noted that the spike receptor-binding domain (RBD) is the authentic virus entity that recognizes the ACE2 receptor to mediate virus entry.

While the currently predominant Delta variant only possesses the L452R and T478K mutations in the RBD, 15 mutations have been accumulated in the RBD of the Omicron variant (Figure 4). Among these substitutions, a bunch of residues is observed to locate nearby the bound ACE2 receptor (Figure 4). How these mutations would affect the receptor binding, however, remains to be investigated in the future.

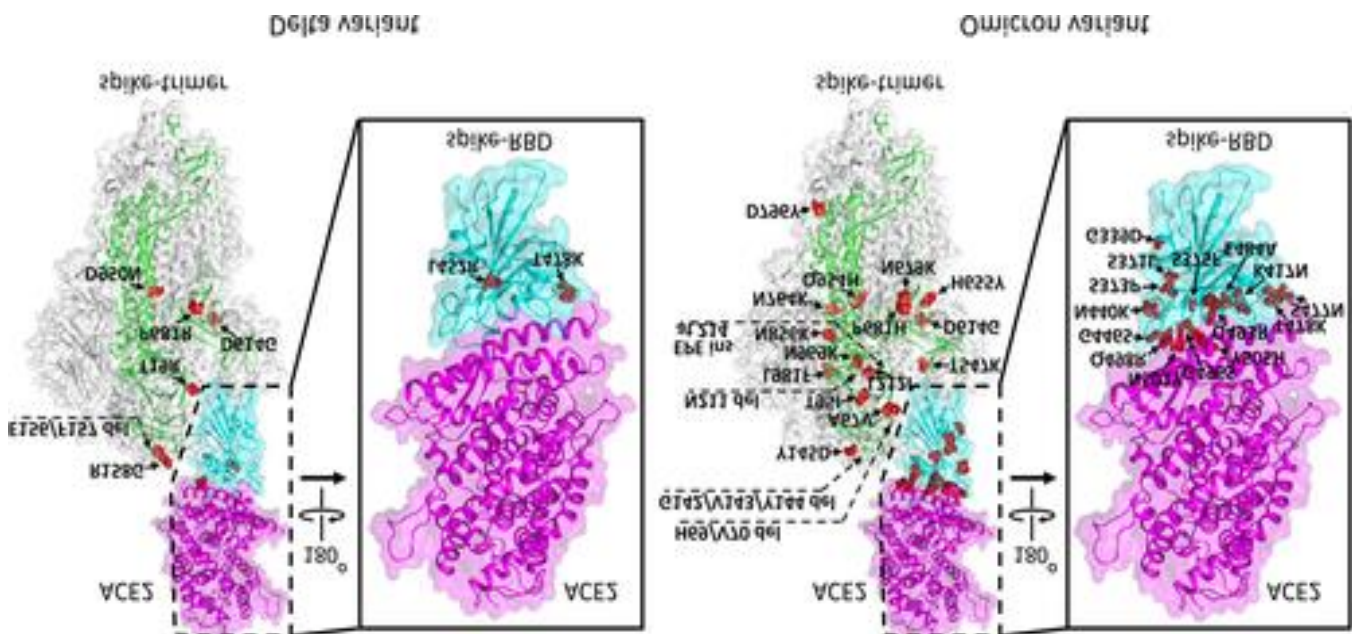


FIGURE 4

Landscape of spike mutations in the Delta (left) and Omicron (right) variants. The structures are depicted based on the cryo-electron microscopy spike trimer structure of protein data bank (PDB) code 6VYB and the crystal RBD/ACE2 complex structure of PDB code 6LZG. One protomer of the spike trimer is highlighted in green and its receptor-binding domain (RBD) in cyan. The bound angiotensin-converting enzyme 2 (ACE2) receptor is colored magenta. The mutations defined based on covariants are labeled

Whether or not and to what extent the Omicron variant can escape from immune recognition is another concern. It is notable that the spike RBD is the major target for neutralizing antibodies and that Omicron has accumulated 15 substitutions in the RBD region. We noted that multiple antigenic sites have been characterized in RBD, featured with the RBS-A, RBS-B, RBS-

C, the CR302, and the S309 sites.²¹ All the 15 mutations identified in Omicron spike RBD can be located to one or more of these antigenic sites, indicating potential resistance of Omicron to one or more of the monoclonal antibodies targeting these sites. As for the antibody treatment in clinical use, the cocktail consisting of LY-CoV555 (also known as Bamlanivimab) and LY-CoV016 (also known as Etesevimab) has been authorized for emergency use. Previous studies have revealed that the mutations at 484 and 417 positions of the spike are associated with i

immune evasion²² and that both Beta and Gamma variants could escape the neutralization of LY-CoV555 (due to E484K) and LY-CoV016 (due to K417N/T).²³ Since the Omicron variant also contains E484A and K417N mutations, it is likely that Omicron would also resist these two antibodies.

Taken together, some spike mutations of Omicron have also been identified in the other VOC variants, such as D614G, N501Y, K417N, P681H, and the residue-substitution of E484. These mutations have been indicated in higher binding affinity with ACE 2, enhanced transmissibility and pathogenicity, and reduced ability of neutralization by monoclonal antibodies and immune evasion. The functions of other mutations and whether combined effects of these mutations exist, however, are not clear, resulting in great uncertainty about how the viral behavior and susceptibility will develop

According to the WHO reports, the first known confirmed infection by Omicron could be traced back to a specimen collected on November 9, 2021.

The first Omicron sequence available, however, was from a specimen collected on November 11, 2021, in Botswana. Ever since the identification of Omicron, the variant appears to rapidly spread. A recent genomic-sequence analysis on 77 virus samples collected in Gauteng province of South Africa from November 12 to 20 showed that all the analyzed variants were actually B.1.1.529, indicating that Omicron was becoming dominant in Gauteng. Furthermore, the identification of Omicron coincides with the recent sharp increase in the number of confirmed COVID-19 cases in South Africa. The mean number of COVID-19 cases per day increased from 280 to 800 after the Omicron variant was verified. This number exceeded 2000 on November 26, 2021, and broke through 10,000 on December 3, 2021. In addition, tracing the source of COVID-19 cases revealed that B.1.1.529 had probably spread in western Europe before the first cases were detected in southern Africa.

B.1.1.529 variant was first reported by WHO on November 24, 2021. On the day after receiving the report, WHO designated it as VUM and named it as Omicron variant (B.1.1.529). Only 2 days later, WHO categorized the Omicron variant as VOC, which recorded the shortest interval period of reclassifying a variant from VUM to VOC and <https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/scientific-brief-omicron-variant.html> brought about great public concerns. A few days after the identification of Omicron in Africa, the variant has emerged in the other continents. At the time of this writing, Omicron has been reported in 34 countries and areas, including Botswana, Hong Kong, South Africa, Israel, Belgium, Italy, and the USA.⁸ Apparently, the variant has not stopped spreading to other countries and regions.

Where and how the Omicron variant evolved remains to be investigated. The analysis of sequences of SARS-CoV-2 variants reveals that Omicron is a lot different from the other SARS-CoV-2 variants such that it is difficult to identify its closest relative.

The results of phylogenetic studies shows that the Omicron variant likely has diverged early from other SARS-CoV-

2 variants rather than being developed from one of the previous VOCs. It is speculated that the Omicron variant might have been gestated in immunocompromised individuals (e.g., HIV patients co-infected by SARS-CoV-

2) for a certain period of time, or it might have evolved in a nonhuman species and is just recently spilled back into human beings

Treatment:

Does omicron is treated by covid vaccine:

Findings from a very small study involving just 12 people in South Africa, which have been released through a preprint, indicate that the efficacy of the Pfizer-BioNTech vaccine could be significantly reduced against omicron, with a 41-fold lower level of neutralising antibodies when compared with a variant of the virus that was widespread in the early stages of the pandemic (characterised by spike protein substitution D614G).

Jonathan Ball, professor of molecular virology at the University of Nottingham, said, “Whilst the amount of virus killing observed in the lab is reduced markedly—up to 40-times reduction—

there is still measurable virus neutralisation, especially in those who were vaccinated and previously infected. This group effectively mimics what we would expect in people who have had all

doses of vaccine plus a boost . . . That’s why we still need to get the message across: get vaccinated, get boosted, even if you have been infected before.”

Pfizer research said that the 3rd dose of vaccine provided same levels of neutralising antibodies against omicron as seen after two doses against the original virus

In its statement the company said that people who had had two vaccine doses exhibited “more than a 25-

fold reduction in neutralisation titers” against omicron when compared with wildtype, suggesting that two doses of the Pfizer vaccine “may not be sufficient to protect against infection with the omicron variant.” The company said “additional studies indicate that a booster with the current covid-19 vaccine increases the antibody titers by 25-fold

Pfizer and BioNTech started developing an omicron specific version of their vaccine on 25 November and said that the first batches could be ready for delivery within 100 days, pending regulatory approval. Moderna is also working on an updated version against the new variant and said it could be finished with testing and ready to file with the regulators by March 2022.

Symptoms:

The WHO states that there is no specific evidence to suggest that the symptoms related to the Omicron variant are different from the other variants. Nonetheless, the World health organization

reports that the Omicron variant could possibly increase the mortality rate in line with other COVID-

19 variants. The Omicron variant can cause the following symptoms which are similar to those of other COVID-19 variants:

- Headache
- Cough

Shortness of breath

- Fever
- Fatigue
- Sore throat
- Muscle or body aches
- A loss of taste or smell
- A runny nose

Instructions:

The following instructions noted below could help prevent the aggressive spread of the Omicron variant, as well as other variants, but further studies will be needed to clarify these factors fully -

1. Increase the number of people to administer COVID-19 testing.
2. Maintain Social distancing.
3. Wear a mask in public places.
4. Impose travel bans (if required).
5. Avoid crowded places.
6. Cough or sneeze in the bent elbow or use tissue.
7. Always keep your hands clean.
8. Make sure to receive COVID-19 vaccinations.
9. Be sure to establish and fully staff suitable treatment facilities for older patients and those with chronic comorbidities

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