

Omicron (B.1.1.529) – variant of concern – molecular profile and epidemiology: a mini review

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Abstract. Recently a new variant of SARS-CoV-2 was reported from South Africa. World Health Organization (WHO) named this mutant as a variant of concern – Omicron (B.1.1.529) on 26th November 2021. This variant exhibited more than thirty amino acid mutations in the spike protein. This mutation rate is exceeding the other variants by approximately 5-11 times in the receptor-binding motif of the spike protein. Omicron (B.1.1.529) variant might have enhanced transmissibility and immune evasion. This new variant can reinfect individuals previously infected with other SARS-CoV-2 variants. Scientists expressed their concern about the efficacy of already existing COVID-19 vaccines against Omicron (B.1.1.529) infections. Some of the crucial mutations that are detected in the receptor-binding domain of the Omicron variant have been shared by previously evolved SARS-CoV-2 variants. Based on the Omicron mutation profile in the receptor-binding domain and motif, it might have collectively enhanced or intermediary infectivity relative to its previous variants. Due to extensive mutations in the spike protein, the Omicron variant might evade the immunity in the vaccinated individuals.

Key Words:

Omicron variant, B.1.1.529, SARS-CoV-2, COVID-19, Molecular profile, SARS-CoV-2 variants.

(B.1.351), Gamma (P.1), and Delta (B.1.617.2)⁸. On 11th November 2021, a new variant was discovered in Botswana. Later many parts of South Africa reported this variant. World Health Organization (WHO), on 26th November 2021 classified this mutant as a variant of concern and named it as Omicron (B.1.1.529) (<https://www.who.int/en/activities/tracking-SARS-CoV-2-variants>).

New clinical cases of COVID-19 in South Africa due to Omicron (B.1.1.529) are being identified after its discovery (DOI: <https://doi.org/10.1038/d41586-021-03552-w>). This new variant had undergone significant mutations when compared to its previous variants. The Delta variant (B.1.617.2) has 8 mutations whereas Omicron (B.1.1.529) had undergone 32 mutations of the spike protein. It is to be noted that with eight mutations, Delta variant had created havoc in India and other countries early this year in 2020⁸. Scientists are worried about Omicron (B.1.1.529) variant since it had too many mutations relative to its previously evolved variants and it might be more notorious than the Alpha and Delta variants. Virologists have also expressed their concern that Omicron variant may have increased virulence and pathogenicity. In this review, we are focusing on the molecular aspects and epidemiology of SARS-CoV-2 variant, Omicron.

Introduction

COVID-19 due to SARS-CoV-2 was first declared as a pandemic on 11th March 2020^{1,2}. COVID-19 pandemic is responsible for huge mortality and severe morbidity in both developing and developed nations³⁻⁵. SARS-CoV-2, a coronavirus has the natural ability to undergo mutation and antigenic variation over a period of time^{6,7}. Four variants of concern (VOC) SARS-CoV-2 have been identified between December 2020-May 2021. They are Alpha (B.1.1.7), Beta

Molecular Profile

Omicron mutant has been identified to possess 32 amino acid changes in the spike (S) protein. Some of the mutations that are present in the receptor-binding domain (RBD) of the Omicron variant have been shared by other SARS-CoV-2 variants that evolved previously. These mutations are K417N, E484K, N501Y, D614G and T478K (ecdc.europa.eu). In the spike protein, RBD is composed of 319-541 residues of the S1 subunit.

The K417N mutation (lysine to asparagine substitution) is shared between Omicron and Beta variants. The mutation at residue 484 in which the glutamic acid is substituted to lysine (E484K) is found in both Beta and Gamma variants⁸. Whereas in Omicron the mutation at 484 is E484A, the residue glutamic acid is mutated to alanine. The E484A mutation in the Omicron might be an important mutation that was present as E484K (Figure 1) in the Beta and Gamma variants. In the Gamma variant the E484K mutation had the ability to cause reinfection⁹. This might be perhaps due to the substitution of a negatively charged, hydrophilic residue (glutamic acid) with a positively charged and relatively high hydrophilic amino acid (lysine). In the Omicron variant, the mutation of a hydrophilic amino acid (glutamic acid) to a hydrophobic amino acid (alanine) might alter the interaction between RBD and human angiotensin converting hACE2. The N501Y mutation (asparagine to tyrosine) present in the Omicron variant was also detected earlier in the Alpha, Beta and Gamma variants. N501Y was identified to have a stronger binding affinity

to hACE2 since it is one of the contact residues in RBD. The D614G mutation (substitution of aspartic acid to glycine) located in the S1 subunit of the Omicron variant is shared by Alpha, Beta, Gamma, and Delta variants¹⁰. Relative to Alpha, Beta, and Delta SARS-CoV-2 variants Omicron has a 5.5 to 11 times higher mutations rate in the receptor-binding motif (RBM). Among all the mutations, the crucial mutations in the RBM of the Omicron variant are T478K, E484A, Q493R and N501Y. Yi et al¹¹ showed that substitution of the residues at five different positions P499, Q493, F486, A475 and L455 of the SARS-CoV-2 spike RBM increases the affinity to receptor binding¹¹. Therefore, the Q493R might increase the affinity to bind the hACE2. The T478K mutation (threonine to lysine) found in Omicron is shared by Delta variants. Several crucial mutations in the S protein of RBD and S1 subunit of the Omicron variant are shared by other SARS-CoV-2 variants. Henceforth, the virulence and infectivity features of the Omicron variant might be either surpassing the Alpha, Beta and Delta variant reciprocally or in a transitional phase between the variants.

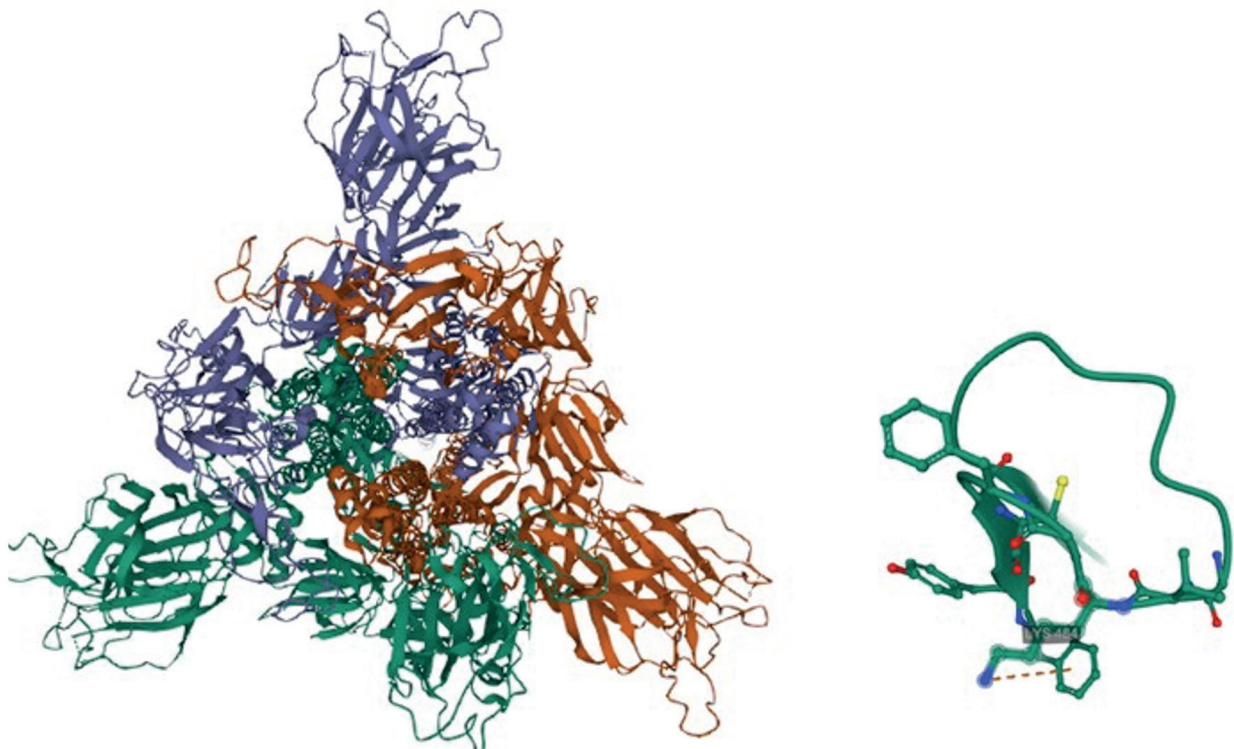


Figure 1. SARS-CoV-2 Beta variant spike protein in open state along with E484K (7VX1 – Wang, Y.F., Xu, C., Wang, Y.X., Hong, Q., Cong, Y. Conformational dynamics of the Beta and Kappa SARS-CoV-2 spike proteins and their complexes with ACE2 receptor revealed by cryo-EM. doi: 10.1093/nar/gkab314).

Epidemiology

Very recently, in November 2021, there was an alarming increase in COVID-19 cases in South Africa due to Omicron. This variant was suspected of having an enhanced immune evasion with a questionable capability of evading antibodies produced against existing vaccines. The notable feature of this variant is that they expressed enhanced transmissibility. Very quickly this variant spread to nearby provinces of South Africa. Simultaneously neighboring countries such as Botswana, Namibia, Zimbabwe, Swaziland, and Mozambique were alerted. Many countries have given travel restrictions for passengers from South Africa. Israel, Hong Kong, Egypt, Belgium, Malaysia, India and Sri Lanka reported the new cases due to the Omicron variant (<https://www.cdc.gov/media/releases/2021/s1126-B11-529-omicron.html>).

The reason for immune evasion, increased transmissibility and escape from neutralizing antibodies of already vaccinated individuals might be due to several mutations, specifically on the S-protein of the Omicron variant. This strain might be deadlier than the Delta variant that caused several thousands of deaths in India alone this year. Delta variant showed only eight mutations on the spike protein whereas Omicron variant exhibited over 30 amino acid changes. With a large number of mutations in the Omicron variant it was speculated that the widely used PCR might not detect this variant. However, it was detected by S-gene drop out or S-gene target failure¹².

Omicron variant with a high reinfection capacity may affect previously infected COVID-19 patients. Moreover, many patients infected with the Omicron variant were found to be young patients who were school students (<https://www.who.int/news/item/28-11-2021-update-on-omicron>). There are no detailed studies available on the Omicron variant about the pathogenesis, virulence, and mutational profiles (<https://www.who.int/groups/technical-advisory-group-on-sars-cov-2-virus-evolution>). Further research studies should be conducted on these areas for a better understanding of this variant.

Conclusions

With an unprecedented crisis faced by the world due to COVID-19, the next challenge to bring down the cases of COVID-19 could possibly be posed by the Omicron variant. Due to its

numerous mutations and transmissibility rate, it has the capability to spread rapidly throughout the world. Though no new precautionary measures are advised, strengthening the existing health measures and public health steps are advised to curb its spread.

Conflicts of Interest

The authors declare no conflict of interest.

References

- 1) Kannan S, Shaik Syed Ali P, Sheeza A, Hemalatha K. COVID-19 (Novel Coronavirus 2019) - recent trends. *Eur Rev Med Pharmacol Sci* 2020; 24: 2006-2011.
- 2) Acuti Martellucci C, Flacco ME, Cappadona R, Bravi F, Mantovani L, Manzoli L. SARS-CoV-2 pandemic: An overview. *Adv Biol Regul* 2020; 77: 100736.
- 3) Singh AK, Misra A. Impact of COVID-19 and comorbidities on health and economics: Focus on developing countries and India. *Diabetes Metab Syndr* 2020; 14: 1625-1630.
- 4) Elliott J, Bodinier B, Whitaker M, Delpierre C, Vermeulen R, Tzoulaki I, Elliott P, Chadeau-Hyam M. COVID-19 mortality in the UK Biobank cohort: revisiting and evaluating risk factors. *Eur J Epidemiol* 2021; 36: 299-309.
- 5) Wang Y, Xu C, Yao S, Zhao Y, Li Y, Wang L, Zhao X. Estimating the prevalence and mortality of coronavirus disease 2019 (COVID-19) in the USA, the UK, Russia, and India. *Infect Drug Resist* 2020; 13: 3335-3350.
- 6) Singh PK, Kulsum U, Rufai SB, Mudliar SR, Singh S. Mutations in SARS-CoV-2 Leading to Antigenic Variations in Spike Protein: A Challenge in Vaccine Development. *J Lab Physicians* 2020; 12: 154-160.
- 7) Pachetti M, Marini B, Benedetti F, Giudici F, Mauro E, Storici P, Masciovecchio C, Angeletti S, Ciccozzi M, Gallo RC, Zella D, Ippodrino R. Emerging SARS-CoV-2 mutation hot spots include a novel RNA-dependent-RNA polymerase variant. *J Transl Med* 2020; 18: 179.
- 8) Kannan S, Ali PSS, Sheeza A. Evolving biothreat of variant SARS-CoV-2 - molecular properties, virulence and epidemiology. *Eur Rev Med Pharmacol Sci* 2021; 25: 4405-4412.
- 9) Resende PC, Bezerra JF, Teixeira de Vasconcelos RH, Arantes I, Appolinario L, Mendonça AC, Paixao AC, Duarte Rodrigues AC, Silva T, Rocha AS, Pauvolid-Corrêa A, Couto Motta F, Teixeira DLF, de Oliveira Carneiro TF, Freire Neto FP, Herbster ID, Leite AB, Riediger IN, do Carmo Debur M, Naveca FG, Almeida W, Livorati M, Bello G, Siqueira MM. Spike E484K mutation in the first SARS-CoV-2 reinfection case confirmed in Brazil, 2020 - SARS-CoV-2 coronavirus / nCoV-2019 Genomic Epidemiology - Virological. *Virological.org* 2021.

- 10) Weissman D, Alameh MG, de Silva T, Collini P, Hornsby H, Brown R, LaBranche CC, Edwards RJ, Sutherland L, Santra S, Mansouri K, Gobeil S, McDanal C, Pardi N, Hengartner N, Lin PJC, Tam Y, Shaw PA, Lewis MG, Boesler C, Şahin U, Acharya P, Haynes BF, Korber B, Montefiori DC. D614G Spike Mutation Increases SARS CoV-2 Susceptibility to Neutralization. *Cell Host Microbe* 2021; 29: 23-31.e4.
- 11) Yi C, Sun X, Ye J, Ding L, Liu M, Yang Z, Lu X, Zhang Y, Ma L, Gu W, Qu A, Xu J, Shi Z, Ling Z, Sun B. Key residues of the receptor binding motif in the spike protein of SARS-CoV-2 that interact with ACE2 and neutralizing antibodies. *Cell Mol Immunol* 2020; 17: 621-630.
- 12) Ganesan M, Renganathan J, Vasuki V, Joseph R. S gene drop-out predicts super spreader H69del/V70del mutated SARS-CoV-2 virus. *Asian Pac J Trop Med* 2021; 14: 236-237.