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REVIEW ARTICLE

OMICRON (B.1.1.529) SARS-CoV-2 variant-Latest addition in the battle ground!!!

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ABSTRACT

Background: Fungal colonisation of airways in Post TB patients, can lead to a spectrum of diseases based on the immune response of the host. This study was aimed at studying the different entities of this spectrum. **Methods:** A cross sectional observational study was conducted over 100 patients of post TB patients to make an observation of the diseases of the spectrum of Aspergillus infections. **Results:** Of the 100 patients who were studied, IPA was found in 24 (48%), ABPA in 13 (26%), CPA in 5 (10%) patients out of the 50 diabetics. ABPA in 23 (46%) patients, Simple colonization, CPA in 11 (22%) and 4 (8%) patients showed IPA out of the 50 non-diabetics. **Conclusion:** Chronic pulmonary Aspergillosis was the most common disease from Aspergillus among Post TB patients. Diabetes was associated with invasive forms of Aspergillosis, Invasive Pulmonary Aspergillosis (IPA) and subacute invasive pulmonary aspergillosis (SAIA).

Keywords: Aspergillus, Post Recent emergence of the SARS-CoV-2 variant as OMICRON has become a global concern.

This short note highlights the identification and global spread of OMICRON which has spread over 77 nations by now, which resulted in many hypotheses about its origin and degree of infectivity. The detection of mutations in the RBD region of Spike protein is a concern by surpassing vaccine immunity. Here we will discuss its transmission potentiality, infectivity, disease morbidity as well as its effect on COVID-19 vaccines.

Recently a new variant of SARSCoV-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[1]. 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[4]. The Omicron (B.1.1.529) variant might have enhanced transmissibility and immune evasion[2]. This new variant can re infect 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[3]. Some of the crucial mutations that are detected in the receptor-binding domain of the Omicron variant have been shared by previously evolved SARSCoV-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[2]. Due to extensive mutations in the spike protein, the Omicron variant might evade the immunity in the vaccinated individuals.[6]

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Molecular Profile

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. In the spike protein, RBD is composed of 319-541 residues of the S1 subunit [4].

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 variants. Whereas in Omicron the mutation at 484 is E484A, the residue glutamic acid is mutated to alanineThe E484A mutation in the Omicron might be an important mutation that was present as E484K in the Beta and Gamma variants[3]. In the Gamma variant the E484K mutation had the ability to cause reinfection . 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[4] .

Relative to Alpha, Beta, and Delta SARS-CoV-2 variants, Omicron has a 5.5 to 11 times higher mutation 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. The 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 binding[11]. 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[6].

Epidemiology

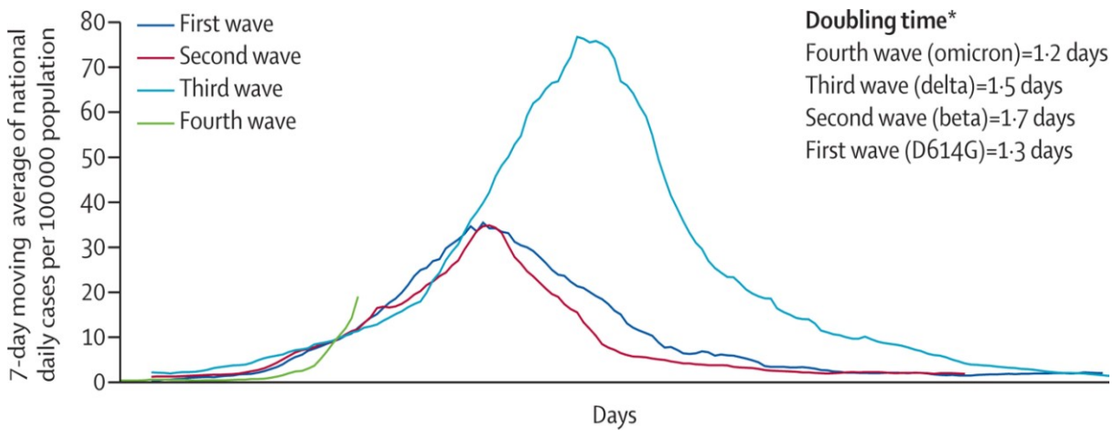
The first sequenced omicron case was reported from Botswana on Nov 11, 2021, and a few days later another sequenced case was reported from Hong Kong in a traveller from South Africa.[8] Several sequences from South Africa followed, after initial identification that the new variant was associated with an S-gene target failure on a specific PCR assay because of a 69–70del deletion, similar to that observed with the alpha variant.[9] The earliest known case of omicron in South Africa was a patient diagnosed with COVID-19 on Nov 9, 2021, although it is probable that there were unidentified cases in several countries across the world before then. In South Africa, the mean number of 280 COVID-19 cases per day in the week before the detection of omicron increased to 800 cases per day in the following week, partly attributed to increased surveillance.[10] COVID-19 cases are increasing rapidly in the Gauteng province of South Africa; the early doubling time in the fourth wave is higher than that of the previous three waves[12].

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 neighbouring countries such as Botswana, Namibia, Zimbabwe, Swaziland, and Mozambique were alerted.[5]

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[5]. 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[8] .

Transmissibility*:* The impact of omicron on transmissibility is a concern. If the overlapping omicron mutations maintain their known effects, then higher transmissibility is expected, particularly because of the mutations near the furin cleavage site[7]. Omicron has some deletions and more than 30 mutations, several of which (eg, 69–70 del, T95I, G142D/143–145del, K417N, T478K, N501Y, N655Y, N679K, and P681H) overlap with those in the alpha, beta, gamma, or delta VoCs.[4] These deletions and mutations are known to lead to increased transmissibility, higher viral binding affinity, and higher antibody escape.[10, 11] Some of the other omicron mutations with known effects confer increased transmissibility and affect binding affinity.[11,12] . Importantly, the effects of most of the remaining omicron mutations are not known, resulting in a high level of uncertainty about how the full combination of deletions and mutations will affect viral behaviour and susceptibility to natural and vaccine-mediated immunity[9].

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[9]. 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 the Omicron variant exhibited over 30 amino acid changes[3].



Severity of disease*:* It is not yet clear whether infection with Omicron causes more severe disease compared to infections with other variants, including Delta.[1]Preliminary data suggests that there are increasing rates of hospitalization in South Africa, but this may be due to increasing overall numbers of people becoming infected, rather than a result of specific infection with Omicron. There is currently no information to suggest that symptoms associated with Omicron are different from those from other variants.[4]Initial reported infections were among university students—younger individuals who tend to have more mild disease—but understanding the level of severity of the Omicron variant will take days to several weeks. All variants of COVID-19, including the The delta variant that is dominant worldwide, can cause severe disease or death, in particular for the most vulnerable people, and thus prevention is always key.[5]

Clinical Presentation: At this stage, the available anecdotal data from clinicians suggest that patients with omicron are younger people with a clinical presentation similar to that of past variants.[3] Although no alarming clinical concerns have been raised thus far, this anecdotal information should be treated with caution given that severe COVID-19 cases typically present several weeks after the initial symptoms associated with mild disease. [2]Preliminary evidence suggests there may be an increased risk of reinfection with Omicron (ie, people who have previously had COVID-19 could become reinfected more easily with Omicron), as compared to other variants of concern, but information is limited. More information on this will become available in the coming days and weeks.[5]

Effectiveness of vaccines: Due to extensive mutations in the spike protein, the Omicron variant might evade the immunity in the vaccinated individuals[1]. Extrapolations based on known mutations and preliminary observations, which should be interpreted with caution, indicate that omicron might spread faster and might escape antibodies more readily than previous variants, thereby increasing cases of reinfection and cases of mild breakthrough infections in people who are vaccinated. [6]

Although there are conflicting reports on whether COVID-19 vaccines have consistently retained high efficacy for omicron, clinical trials have reported lower efficacy for some vaccines in transmission settings in which the beta variant is dominant[6]. Previous variants have lowered vaccine efficacy; for example, the ChAdOx1 vaccine was 70% effective in preventing clinical infections for the D614G variant in the UK, but this efficacy decreased to 10% for the beta variant in South Africa. However, the efficacy of the BNT162b2 vaccine in preventing clinical infections was retained across both the D614G and beta variants.[7] Observational data from the state of New York, USA (n=8834604) indicated high vaccine efficacy in preventing severe disease in people older than 65 years, with varying levels of protection conferred by different vaccines—95% for BNT162b2, 97% for mRNA-1273, and 86% for Ad26.COV2.S17—with minimal declines in protection 6 months after vaccination[7].

Effectiveness of current tests: The widely used PCR tests continue to detect infection, including infection with Omicron, as we have seen with other variants as well. [6]In terms of diagnostics, the omicron variant is detectable on widely used PCR platforms in South Africa 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 failure[6].

Current SARS-CoV-2 PCR diagnostics continue to detect this variant. Several labs have indicated that for one widely used PCR test, one of the three target genes is not detected (called S gene dropout or S gene target failure) and this test can therefore be used as marker for this variant, pending sequencing confirmation. Using this approach, this variant has been detected at faster rates than previous surges in infection, suggesting that this variant may have a growth advantage.[4] Studies are ongoing to determine whether there is any impact on other types of tests, including rapid antigen detection tests.

Effectiveness of current treatments: Corticosteroids and IL6 Receptor Blockers will still be effective for managing patients with severe COVID-19[1]. Other treatments will be assessed to see if they are still as effective given the changes to parts of the virus in the Omicron variant[10]. There is no reason to believe that current COVID-19 treatment protocols and therapeutics would no longer be effective, with the possible exception of monoclonal antibodies, for which data on the omicron variant's susceptibility are not yet available[5]. Importantly, existing public health prevention measures (mask wearing, physical distancing, avoidance of enclosed spaces, outdoor

preference, and hand hygiene) that have remained effective against past variants should be just as effective against the omicron variant[7]

***Studies Underway**:* There are no detailed studies available on the Omicron variant about the pathogenesis, virulence, and mutational profiles. Further research studies should be conducted on these areas for a better understanding of this variant. At the present time, WHO is coordinating with a large number of researchers around the world to better understand Omicron[2]. Studies currently underway or underway shortly include assessments of transmissibility, severity of infection (including symptoms), performance of vaccines and diagnostic tests, and effectiveness of treatments.[9]

Conclusion

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.

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