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Omicron Transmissibility, Severity, Vaccines, and Future Perspectives

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ABSTRACT

SARS-CoV-2 Omicron is the next possible version of the COVID-19 virus that will spread globally after the D614G, Beta/Gamma, and Delta waves. Among all the VOCs studied to date, the virus has the highest mutation rate, making it more likely to spread and more resistant to the vaccine's protective effects. To respond effectively, getting people thinking about the issue without going overboard is necessary. The emergence of new COVID-19 variations like Omicron serves as a sobering reminder that this pandemic is far from over. Until the vaccine is widely distributed, people should remain isolated from one another, use protective gear such as masks and wash their hands frequently and ventilate their homes to reduce the spread of the infection. Access to vaccines and other preventative health care is a global need.

Keywords

Omicron, COVID-19, SARS-CoV-2, Vaccines.

Introduction

Exactly 110 countries confirmed the Omicron on December 23, 2021. Initial findings were made in the middle of November 2021 in Gauteng province, South Africa's economic hub and home to the cities of Tshwane and Johannesburg.

From that point on, it quickly became the dominant form there. Moreover, an increase in the prevalence of SGTF was seen alongside this trend in positive cases, a pattern previously recognized for the Alpha variant due to the presence of a similar deletion in amino acids 69 and 70 in the spike protein.

Since Alpha was uncommon in South Africa, the researchers quickly analyzed the whole genome of the SGTF samples, and the results showed that they had different ancestry from the previous samples. However, the Gauteng region continued to see the highest weekly incidence rate.

However, data showed a dip at December's end. With the exception of Zimbabwe, the number of incidents was noted to rise in neighboring countries of South Africa between the 13th and 19th of December. Lesotho, Namibia, eSwatini, and Mozambique all had very small gains. [1].

As of the second part of December 2021, 71.5% of samples from COVID-19 patients with known S gene status have SGTF, making Omicron the most common variant in the U.K. and hence the European area. With a case rate of almost 73% by December 18, Omicron dominated the U.S. [2]. But as of December 2021, the Omicron version has been spread to Germany, Denmark, Australia, France, the Netherlands, Belgium, Norway, India, Portugal, Israel, and Belgium [3]. Evidence from neutralization tests, early estimates of vaccination's efficacy against symptomatic

sickness, and reinfection investigations have all converged to show that Omicron is more prevalent than Delta, most likely because of immune evasion. However, further information is required to determine Omicron's generation time relative to the other variations and determine whether Omicron possesses properties that make it more transmissible.

Evolution of Omicron Strain

Since the discovery of this variation in South Africa, researchers have been looking for information about its genesis and potential course of the undiscovered pandemic. Researchers hypothesized that Omicron appears to have developed in conjunction with other SARS-CoV-2 variants and most likely separated from other strains relatively early, potentially around mid-2020 [4].

Two distinct Omicron sub-clades were identified by analysis of the receptor-binding domain (RBD). Moreover, phylogenetic analysis of 3590 SARS-CoV-2 genomes demonstrated that Omicron diverged from B.1.1.519 ancestry (clade 20B) [5]. Identifying the majority of mutations in the Omicron variant within the body of an immunocompromised HIV-infected individual raises the possibility of adaptations occurring within the bodies of chronically infected COVID-19 patients. It's possible that South Africa's high HIV prevalence rate (19%) is one of the contributing factors to Omicron [6,7].

There is also the possibility that non-human species might come into being or that the circulation and evolution of a distant population could occur as a result of tremendous evolutionary pressure. It is possible that low vaccination rates or immunization discrepancies between industrialized and impoverished nations contributed to the creation of an environment that was conducive to the formation of the variation. In spite of this, the origin of the Omicron is still largely a mystery due to the absence of strong experimental data.

Delta vs. Omicron variants

The modification power of the Omicron version is much higher than that of the Delta variant. This does not, however, make it any more hazardous than it previously was. The omicron variation has not yet been associated with any new symptoms, but because of the mutations it carries, it may spread more swiftly than other variations. The COVID-19 virus, which is caused by the SARS-CoV-2 virus, is the virus with the highest rate of mutation [8].

There are nine different versions of the spike protein, which is a protrusion on the surface of the virus that helps the virus stick to human tissues. The spike protein is responsible for the virus's ability to cling to human tissues. There are two of these in the part of the molecular hook that is referred to as the "Receptor-Binding Domain" (RBD). Because of this, its capacity to attach to cells is improved [8,9].

It is a mutant beast whose spike protein has been changed at least 30 times, with half of those changes happening at the RBD. The first SARS-CoV-2 virus usually spread to 2 or 3 more people after it had infected 6 people. A significant impact came from Delta. Delta's four-day incubation period is shorter than the original virus's six-day period. This means that people are more likely to get sick sooner. Both the Omicron's rate of communication and how long it takes to reproduce are unknown. With time, more information about the growth rates of the omicron variant in other places will be available [10].

Omicron Mechanism of Cell entry

A novel method of entry into the host has been discovered by Omicron, and it does not need the transmembrane serine protease 2 (TMPRSS2). The Omicron utilizes the endocytic route rather than the TMPRS22 pathway for viral entry and replication in contrast to the Delta variant. This might help to explain the disparity between the illnesses brought on by exposure to the Omicron and Delta versions. Alveolar lung cells express TMPRS22 extensively. However, because Omicron does not rely on the TMPRS22 route for reproduction, lung involvement following exposure may not occur or only occur in small amounts [11]. Additionally, the Omicron variant has less fusion power than the Delta version, which makes it more difficult to construct syncytia (a structure formed by the fusion of several cells). Clinical symptoms and tissue tropism become less severe after an Omicron infection because the potential to produce syncytia becomes less strong [12].

Diagnosis of Omicron and Other Variants

SARS-CoV-2 was diagnosed using a reverse transcriptase-polymerase screening test (RT-PCR), high-throughput genome sequencing, antiviral immunoglobulin M (IgM) and G (IgG) antibody serology, and a lung X-ray [13].

The polymerase chain reaction is a laboratory method used in the COVID-19 test to identify the virus' DNA (PCR). An infected individual may be swabbed in the nose or throat to collect a sample of fluid, or they could spit into a tube to collect saliva. The results might be produced more quickly if the job was done on-site or over a few days. The processing delays can be investigated away from the site if the tests are transferred to a different lab. When performed by a qualified specialist, the test is most accurate, but the rapid findings may miss a few cases [14].

The COVID-19 assay looks for proteins produced by the virus. It took less time to get the findings as a nose swab was employed to capture a sample of the fluid. A lab may be called to conduct testing on some of these. When the right steps are performed, a positive antigen test result is considered reliable. Furthermore, false-negative tests are more common, meaning that illness may be present despite the absence of obvious symptoms. To confirm whether a person is positive or negative on an antigen test, a doctor may, depending on the context, require a PCR test [15].

Transmissibility of Omicron Variant

According to what we now understand, the Omicron form is far more infectious than the others and spreads at an unheard-of

rate. According to certain research, the Omicron variation may infect people who are immune to the Delta variety and infects 3-6 times as many people as the Delta variation. As of December 12, Omicron is known to exist in 77 countries [16].

In South Africa's Gauteng region in the month of November, Omicron cases spread quickly, especially in educational institutions and among young people. Two hundred and forty-nine samples were sequenced after November 25; 183 of these samples were positive for the Omicron variant [17]. But on November 26, 2021, South Africa recorded 3,402 instances, and on December 1, 2021, there were 8,561 cases documented. Additionally, in the middle of November, several hundred new cases were reported every day. [17].

Before any instances were found in South Africa, the Omicron form was already established in the Netherlands. Actually, the Dutch health department had received reports of this disease as far back as November 19, 2021 [18]. November 26, 2021, Belgium announced the first instance of the Omicron variant in Europe. In the year 2021, on November 24, two Omicron instances were reported by German authorities at Munich Airport. When compared to the previous variant's record of 1,000 cases per day, Norwegian health authorities predict that Omicron infections will grow to 300,000. [19,20].

The capacity of the Omicron strain to avoid being recognized by the body's immune system is largely to blame for its fast spread since it has allowed it to infect both previously infected and previously vaccinated people [21]. In addition, the Omicron variant's altered cell entrance and cellular tropism may contribute to its high rate of spread [22]. In addition, the Omicron strain is associated with a higher rate of asymptomatic infections compared to the other forms; this might facilitate the virus's covert dissemination. Omicron infection has been linked to greater viral loads; however, this is still debatable [23].

Omicron and its clinical severity

Fewer severe symptoms and a reduced likelihood of hospitalization have been demonstrated in studies compared to the Delta version; however, further research is needed. Since the beginning of the Omicron wave, hospitalization rates in South Africa have been falling, with a little uptick in the fourth phase, especially in the province of Gauteng. Research-based on serological surveys in this province confirmed that there had been an uptick in the prevalence of Omicron infections compared to the Delta variation, despite generally lower rates of hospitalization and mortality [24].

A recent study found that the omicron variation of COVID-19 was associated with a 50%-70% lower risk of hospitalization compared to the Delta version of COVID-19 [25].

Omicron infections are said to be less severe, but people with preexisting conditions, those who are immune-compromised, and those who haven't been vaccinated may react differently, putting them at risk for complications or severe COVID-19. This is backed by Malik et al., who observed that patients with comorbidities, those who are immunocompromised, and the elderly are the main causes of ICU admissions and mortality [26]. Even for the Omicron variety, those with preexisting conditions are at a higher risk of SARS-CoV-2 infection.

Vaccine Effect on Omicron

The Omicron variant's heavy spike protein mutation contributes to both higher infectivity and antibody avoidance. According to Saxena et analysis of the mutations found in the spike of the Omicron variant of SARS-CoV2, currently known entry inhibitors may not be effective against newly developing variants [27]. The quantity of neutralizing epitopes that polyclonal antibodies target in SARS-CoV-2 convalescent or immunized individuals is a strong predictor of the genetic barrier to viral escape. Monoclonal antibody combinations that target non-overlapping epitopes are more resistant to escape mutations than those that target overlapping epitopes alone [28].

The computational method also showed that the Omicron variant's antigenic characteristics are alarming and related to its mutations [29]. The development of novel VOCs has generated doubts about the efficacy of neutralizing antibodies produced by COVID-19 vaccinations, despite the fact that numerous experiments have been carried out to develop effective vaccines. Analysis of the COVID-19 vaccine's possible effects on this novel variation is ongoing.

Two BNT vaccines that can offer over 90% immunity against serious disease when infected with the Delta version of SARS-CoV-2 may be much less effective against the Omicron variety of SARS-CoV-2 [30]. The effect of COVID19 vaccinations against prior VOCs, such as Delta, demonstrated the vaccine's potential for lowering severe sickness and death. Additionally, multiple Delta transmissions from and between completely immunized individuals were documented using genomic and epidemiological data. Contrary to Coronavac patients, only 20% and 24% of BNT162b2 recipients, respectively, had detectable neutralizing antibodies against the Omicron mutations HKU344R346K and HKU691. Great-scale vaccination campaigns have been launched in the United States and other countries, thanks in large part to the mRNA vaccines created by Pfizer/BioNTech and Moderna [31].

Both vaccinations generate potent anti-SARS-CoV-2 Spike (S) protein antibodies that are capable of neutralizing both the initial circulating SARS-CoV-2 strains and later variants that emerged following the vaccine development phase. Neutralizing antibodies produced by mRNA vaccines appear to be the main correlate of COVID-19 protection in both animal models and people. Three doses of the Pfizer-BioNTech vaccines provide excellent protection against the Omicron form, according to laboratory tests [32]. Compared to the other two dosages, only the booster dose can result in a 25-fold rise in neutralizing antibody titers. Anti-spike antibody levels can forecast when SARS-CoV-2 variants will

be neutralized. CD4 + T cell responses to SARS-CoV-2 mRNA vaccinations are potent. According to recent research, TFH cell responses are essential for the development of long-term immunity following this effective human vaccination. Strong neutralization of the Omicron variation in 44 recipients of mRNA vaccines was only 4-6 times lower than that of the wild type, suggesting greater cross-reactivity of neutralizing antibody responses [30].

Since most of the epitopes targeted by vaccine-induced T cells are not mutated in the Omicron variation, it is expected that current COVID-19 vaccinations will protect against the disease by lessening the severity of the illness in the vaccinated individuals.

Preventative public health measures

Preventative public health measures already in place should be preserved as a top priority in the fight against the spread of Omicron. Effective interruption of the transmission of the Omicron variation requires the same preventative measures that have been used to limit the spread of previous SARS-CoV-2 variants, such as wearing masks, proper ventilation, social distancing, and hand washing. Isolating and quarantining people who are suspected of having or have been diagnosed with this strain of the virus as soon as possible is also essential for containing its spread [33].

To prevent further transmission of the Omicron SARS-CoV-2 variant, it is crucial that patients infected with COVID19 receive prompt and effective treatment. Multiple studies, however, have shown that the commonly used mAb drugs, such as imdevimab, bamlanivimab, casirivimab, and etesevimab, have developed significant therapeutic resistance against various types of the disease [34]. Therefore, the FDA has restricted numerous mAbs for use in the treatment of Omicron infection in the U.S. as of January 24, 2022, based on the most recent available evidence [35]. This is because Omicron variants produce the vast majority of COVID-19 cases, whereas non-omicron variants are extremely uncommon, and these mAbs have much diminished therapeutic activity against the omicron variant.

But Destras et al. showed that Sotrovimab is still effective against Omicron infection, despite Omicron's ability to avoid most mAbs. This may be because sotrovimab targets a portion of the S protein that is conserved among closely related coronaviruses [36]. The FDA has approved several mAbs for the treatment of patients with mild to moderate COVID-19 who are at high risk of progression to severe disease, including hospitalization or death. These mAbs, including Paxlovid, remdesivir, and molnupiravir, are all expected to work against the omicron variant [35]. Compared to other versions, Omicron requires a larger dose of mAbs to achieve the same level of inhibition of viral reproduction. Therefore, the Omicron variation may be treated by developing a variant-specific mAb therapy strategy [37].

Misconceptions concerning the effects of COVID-19 on both adults and children have hindered the public's adoption of preventative measures. Adults went to work or visited with friends and family as usual, while parents continued to keep their children from being exposed to COVID-19 by keeping schools and kindergartens closed and restricting other educational or recreational activities. Moreover, parents chose telephone medical counseling or self-medicating owing to fear of getting the new SARS-CoV-2 illness or having their children admitted to a hospital, both of which may have negative effects on children during the COVID-19 pandemic. Parents, in particular, may help mitigate this crisis by adhering to the COVID-19 preventative guidelines, staying informed through open lines of communication with medical professionals, and getting vaccinated themselves [38].

Conclusions

Due to the large number of mutations that have boosted the Omicron variant's transmissibility and immune evasion capacity, it has garnered interest from scientists all around the world since its appearance. Omicron's binding capacity to ACE2 is still debatable, but its increased transmissibility has allowed it to quickly become the dominant species in a number of places. Since omicron spikes only partially employ TMPRSS2 for cell entry and instead rely on the endocytic pathway, the virus is less harmful since it is able to replicate less in the lung parenchyma and infect the upper respiratory tract. A booster immunization is necessary since neither routine vaccination nor a prior infection will give adequate protection against Omicron.

With herd immunity developed by vaccination and infection, and with the advent of targeted treatments, it was anticipated that the impact of the Omicron variation would be negligible. In addition, the identification of the Omicron variation suggests that the virus' inherent propensity for mutation may impede efforts to put a stop to the COVID-19 pandemic. Creating vaccinations and medicines effective against potential viral variations should be the primary goal of research.

Several research has been conducted since the Omicron variant epidemic to better understand its mechanism and features. Protection against Omicron can still be attained by the use of current vaccinations, social isolation, and targeted pharmaceuticals. A number of strategies have been proposed to address the failure of vaccinations, including the use of homologous or heterologous boosters, the development of novel vaccines targeting Omicron, and the potential development of new variations.

Although the omicron variation is not likely to be the last mutant, it is anticipated that its impact will decrease as immunity among the public increases as a result of vaccinations and infection. Infection with Omicron by vaccinated people, but not unvaccinated persons, boosts neutralizing activity against the Delta variation, according to prior research, suggesting that the prevalence of older versions will decline. It's true that no new mutant strain of the virus has been found, but overall, the virus is growing less severe, largely due to increased immunity.

Furthermore, it is crucial to stress equal distribution of vaccinations, particularly in undeveloped and developing countries, in order to

effectively battle the Omicron form and the pandemic in general. Although the current three-dose vaccine against Omicron is successful, some people may still become infected with lesser symptoms after the initial vaccination. The use of vaccinations requiring the fourth dose has been green-lit in several nations. Some studies have shown that a fourth dose is necessary to maintain protective antibody levels after the third dosage has worn off.

That's why it's a good idea to provide a fourth dose of the vaccines to some patients, such as the elderly and immunocompromised. Nevertheless, even if we might require extra boosters to maintain antibody levels over the long term, it is more important to complete the three doses in a larger population than the fourth dose in healthy individuals. Furthermore, it's not a good idea to reduce social contact barriers too fast because it might have unforeseen consequences.

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