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Public Health Concerns of SARS-CoV-2 Omicron Variant: What We Know So Far!

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ABSTRACT

The Omicron variant is the latest variant of the Severe Acute Respiratory Syndrome Coronavirus Type 2 (SARS-CoV-2), the virus that causes the Coronavirus Disease 2019 (COVID-19). The new variant is characterized by thirty (30) substitutions, three (3) small deletions and one (1) small insertion in the spike protein, of these, fifteen (15) are in the receptor binding domain (RBD). This new variant was first detected in samples collected on 11 November 2021 in Botswana and on 14 November 2021 in South Africa and was first reported to the World Health Organization (WHO) from South Africa on 24 November, 2021. As of 01 December, the variant has so far spread to at least twenty-five (25) countries around the world through international travels. So far, the Omicron variant is the most divergent variant that has been detected in significant numbers during the pandemic, which raises public health concerns that it may be associated with increased transmissibility, significant reduction in vaccine efficacy and increased risk for reinfections among those who have suffered COVID-19 before. This review takes a look at the public health concerns of the omicron variant and also highlight important interventions required to contain the variant.

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Introduction

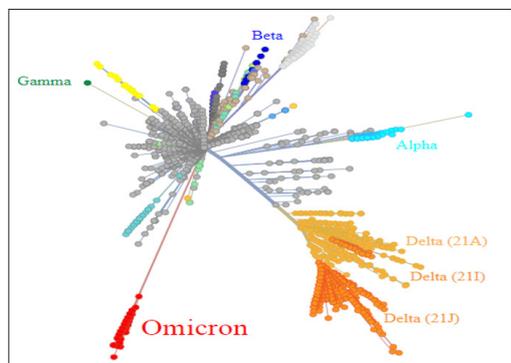
On November 11 and 14, 2021, a new strain of the Severe Acute Respiratory Syndrome Coronavirus Type 2 (SARS-CoV-2), the Omicron variant, was first detected in samples collected in Botswana and south Africa, respectively, and was first reported to the World Health Organization (WHO) from South Africa on 24 November, 2021 [1,2]. The new variant has so far spread to at least 25 countries around the world (Brazil, Canada, Australia, Israel, Hong Kong, Belgium, Japan, Norway, Sweden, United Kingdom and Nigeria among others), causing rising global concerns [3]. The United States (US) reported her first case of Omicron on December 01, 2021 in a person with recent travel history to South Africa [4]. However, a few countries, including the United States, have reported cases in individuals without travel history to South Africa. This development has resulted in new travel bans, economic uncertainties, scientific deliberations among public health experts and even panic among the general populace on the potential threats of the new variant. On the advice

of the World Health Organization's Technical Advisory Group on Virus Evolution (TAG-VE), the World Health Organization designated the Omicron variant (B.1.1.529), a variant of concern (VOC). This decision taken on November 26, 2021, was based on the evidence presented to the TAG-VE that Omicron has several mutations that may influence how it behaves, for instance, its transmissibility and the severity of illness it causes. Interestingly, significant spike protein substitutions have been observed in Omicron, some of which have been previously observed in other variants and are known to be associated with reduced susceptibility to available therapeutics including monoclonal antibody and sera from convalescent COVID-19 patients and vaccinees [4].

Genomic Diversity of Omicron

The Omicron variant (B.1.1.529) belongs to Pango lineage B.1.1.529, Nextstrain clade 21K, and is characterized by at least thirty (30) amino acid substitutions, three (3) small deletions and one (1) small insertion in the spike protein compared to the original virus (A67V, Δ69-70, Δ143-145, Δ211, T95I, G142D, G339D, S371L, L212I, ins214EPE, K417N, S373P, S375F, S477N, T478K, N440K, G446S, G496S, Q498R, E484A, Q493K, T547K, N501Y,

Y505H, N679K, D614G, H655Y, D796Y, P681H, N764K, N969K, L981F N856K, Q954H). Notably, fifteen (15) of the thirty (30) amino acid substitutions are in the receptor binding domain (RBD) (residues 319-541). There are also a number of changes and deletions in other genomic regions (V1069I, Δ1265, NSP3 – K38R, NSP4 – T492I; L1266I, A1892T; NSP6 – Δ105-107, NSP5 – P132H; NSP14 – I42V; A189V; NSP12 – P323L; Q19E, E – T9I; M – D3G, Δ3133, A63T; N – P13L, G204R, R203K) [3, 5]. According to the latest report by Bambino Gesu hospital in Rome, the Omicron variant (Figure 2) has many more mutations than the Delta variant [6].



(Image credited to: Soupvector - Own work, CC BY-SA 4.0, <https://commons.wikimedia.org/w/index.php?curid=112983798>)

Figure 1: Omicron variant and other major or previous variants of concern of SARS-CoV-2 depicted in a tree scaled radially by genetic distance, derived from Nextstrain on 1 December 2021.

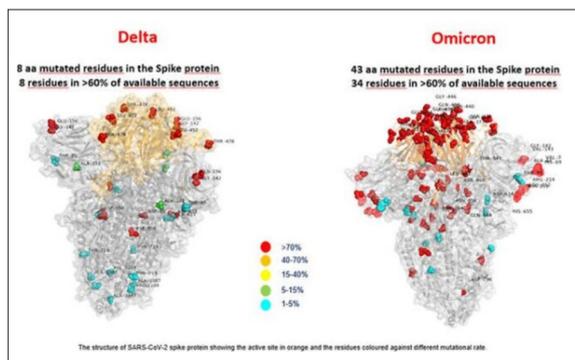


Figure 2: A first image of the Omicron variant, compared to the Delta variant, made by the Bambino Gesù Hospital in Rome [6].

Public Health Concerns of Omicron

The Omicron variant is the most divergent variant that has been detected in significant numbers during the pandemic so far, which raises public health concerns that it may be associated with increased transmissibility, significant reduction in vaccine effectiveness and increased risk for reinfections.

The emergence of the Omicron variant came has no surprise. It would be recall that SARS-CoV-2 has been previously reported to acquires at least one new mutation in its genome every two weeks [7, 8]. The potential implications of this observed mutations in terms of diagnostics, therapeutics and vaccine development is being investigated some of which include:

Ability to spread more quickly in humans

The current emergence of Omicron as the predominant variant in South Africa raises worries that the Omicron variant may be more transmissible than Delta variant, but due to the low number of cases in South Africa when Omicron emerged, it is unclear if

this variant is more transmissible than the Delta variant. Further, the relatively small number of cases documented to date makes it difficult to estimate transmissibility. Analysis of the changes in the spike protein indicates that the Omicron variant is likely to have increased transmission compared to the original SARSCoV-2 virus, but it is difficult to infer if it is more transmissible than Delta [4, 5]. Investigations in South Africa using S-gene target failure (SGTF) of the PCR assays as a proxy for the variant have shown that there is a very sharp increase in incidence across most provinces since mid-November, with the most pronounced increase in the Gauteng province, where SGTF is observed for more than 50% of all tested specimens in the last few days. Sequencing of 77 selected SGTF samples from Gauteng collected between 12 and 20 November 2021 confirmed all of them as Omicron. These findings presented in a press conference held by the South African Ministry of Health on 25 November 2021 suggest that the Omicron variant is already dominant in Gauteng and is present in significant magnitudes in most parts of South Africa. Overall, COVID-19 case numbers are rapidly increasing in Gauteng, albeit from low levels, and it is likely that this increase is driven by the presence of Omicron [5]. The reporting of sequencing results in the African region is low overall. Only Botswana and South Africa have reported sequences from samples collected within the last 30 days to a level that allows for detection of community transmission of Omicron. This means that ongoing transmission of this variant cannot be excluded for other countries. Since the variant is spread across regions in South Africa and has been detected in Botswana, some circulation in other countries is likely [5]. According to a BBC News report [1], daily infections in South Africa were averaging between 200 and 300 in mid-November, until the emergence of Omicron. Some 8,500 new COVID-19 infections were registered in the latest daily figures. That is almost double the 4,300 cases confirmed the previous day. This is suggestive of increased transmissibility and call for concerns. The number of Omicron reported to GISAID EpiCoV from samples collected since 26 October 2021 from all countries and territories in Africa is presented in Table 1. A total of 100 sequences were reported, of which 59 were confirmed cases of Omicron.

Table 1. Frequency of Omicron sequences in Africa [5]

Country or territory	Number of Omicron sequences	Total sequences reported
Botswana	6	98
Kenya	0	5
Mayotte	0	10
Democratic Republic of the Congo	0	11
Rwanda	0	4
Senegal	0	8
Seychelles	0	10
South Africa	59	100

Ability to cause either milder or more severe disease in humans

So far, the Omicron variant has shown signs of high frequency of mutation and transmissibility. However, clinical manifestation associated with it appear to be very mild. Scientists in South Africa and around the world are conducting research to better understand the dynamics of the new variant and will continue to share the findings of these studies as they become available. Initial findings suggest that there may be an increased risk of re-infection with Omicron (*i.e.*, people who have previously suffered COVID-19 could become re-infected more easily with this new variant), as compared to other variants of concern, but the information is scanty [3]. Currently, it is unclear if infection with the Omicron variant causes the severe type of COVID-19 or not. More number of cases will be needed to associate the Omicron variant with disease severity. Initial findings from South Africa indicates that there are no unusual symptoms associated with Omicron variant infection, and as with other variants. So far, some patients have been reported to be symptom free [5].

Ability to evade detection by specific diagnostic tests

Existing SARS-CoV-2 PCR diagnostics have continue to detect this variant. Several laboratories 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 [3]. The current Food and Drug Agency (FDA)'s analysis has identified the following EUA authorized molecular tests whose performance may be impacted by other SARS-CoV-2 viral mutations: Xpert Xpress SARS-CoV-2 DoD, Xpert Xpress SARS-CoV-2, Xpert Omni SARS-CoV-2 (Cepheid), Linea COVID-19 Assay Kit (Applied DNA Sciences, Inc.), TaqPath COVID-19 Combo Kit (Thermo Fisher Scientific, Inc.), Accula SARS-CoV-2 Test (Mesa Biotech Inc.), among others. However, the CDC 2019-Novel Coronavirus (2019-nCoV) Real-Time RT-PCR Diagnostic Panel and the Multiplex Assay for Flu and SARS-CoV-2 are expected to detect the Omicron variant. Meanwhile, the Thermo Fisher TaqPath COVID-19 Combo Kit (3 total targets) has significantly reduced S-gene target sensitivity due to the deletion at H69 and V70 in the B.1.1.529 (Omicron) spike protein. Specimens being tested using the TaqPath COVID-19 Combo Kit that yield an S gene target failure (SGTF) could be Omicron. Importantly, any possible Omicron specimen must be confirmed by sequencing. It is expected that since the TaqPath COVID-19 Combo Kit is designed to detect multiple genetic targets, the overall test sensitivity should not be affected negatively [9, 10].

Decreased susceptibility to therapeutic agents

Nearly all lineages designated as Delta remain susceptible to available monoclonal antibody therapeutics and are preventable by the current vaccines. Currently, there are no virus-specific data available to assess whether monoclonal antibody treatments will retain efficacy against the Omicron variant. Based on data from other variants with significantly fewer changes in the RBD, the expectation is that the Omicron variant will remain susceptible to some monoclonal antibody treatments, while others may have less potency [4, 11].

Ability to escape vaccine-induced immunity

At the moment, there are no data available to assess the Omicron neutralizing ability of sera from vaccinees or convalescent patients with previous SARS-CoV-2 infection [4]. Laboratory and epidemiological studies are needed to assess the impact of the Omicron variant on vaccine efficacy and breakthrough infections, including individuals who have received booster doses. Experts are highly optimistic that vaccines will continue to play a critical role in controlling the COVID-19 pandemic, particularly to offer protection against hospitalization and death. Among the possibilities mentioned above, the ability to escape vaccine-induced immunity— would likely be the most worrisome because once a large proportion of the population is vaccinated, there will be immune pressure that could favor and accelerate emergence of such variants by selecting for “Escape mutants” [12-14]. We however, hope this is not the case with the Omicron variant.

Other concerns include: Omicron will place more pressure on COVID-19 vaccine inequity in Africa (where under 7% of the population is vaccinated). Besides, unless drastic measures are taken, another broad-based lockdown is already looming with potential economic, social and educational impacts. Nobody want this to happen, hence the need for urgent public health interventions to contain the new variant.

Public Health Interventions to contain Omicron

Measures to slow down or contain the virus will include among others travel restrictions. Active epidemiological surveillance, early detection, isolation and case management. Vigorous testing of travelers regardless of vaccination status. Airport Surveillance Post-Arrival Testing and Sequencing (COVID-19 viral test should be conducted for all travelers 3-5 days after arrival. Travelers who are yet to receive the booster dose should self-quarantine for 7 days, even if their test is negative. It is also important for Travelers to self-isolate if they test positive or become symptomatic). Continuous strengthen of the health systems, especially in resource-limited countries is very critical. Enforcement of non-pharmaceutical measures including mask mandate on Planes and public places. Robust contact tracing of suspected cases. Acceleration of vaccine coverage for high-priority groups, especially the booster doses. Prioritization of laboratory studies to support field findings (Laboratory data and clinical findings are needed to ascertain if those who are vaccinated and boosted are less likely to be infected with Omicron or not. Health care professionals including the Clinical laboratory staff should be: 1) aware that genetic variants of SARS-CoV-2 arise regularly, and false negative test results can occur, 2) Molecular tests that use multiple genetic targets to determine a final result are less likely to be impacted by increased prevalence of genetic variants and 3) consider negative results in combination with clinical observations, patient history, and epidemiological information and consider repeat testing with a different EUA authorized or FDA cleared molecular diagnostic test (with different genetic targets) if COVID-19 is still suspected after receiving a negative test result.

International cooperation and solidarity with global partners including WHO should be sustained especially in the area of information sharing according to the IHR agreement. Continuous provision of technical supports to resource-limited countries to enable early response to this variant, as well as to aid access to diagnostics, vaccines, and therapeutics.

Highlights of Existing knowledge

So far we now know that a new variant (Omicron) with more significant numbers of mutation than the Delta variant is currently ravaging the world with a likely higher transmissibility rate.

- Degree of associated severity is yet to be known.
- Existing SARS-CoV-2 PCR diagnostics have continue to detect this variant.
- Decreased susceptibility to existing therapeutic agents should be anticipated.
- Data to support the ability of the variant to escape vaccine-induced immunity is being anticipated.
- The variant will continue to place a strain on the already overwhelmed fragile health care system, especially those of the developing countries. In addition, infection with COVID-19 does not confer a long lasting immunity (Immunity to COVID-19 does not involve long-term memory cells).
- Serum therapy is useful in less severe cases.
- Adequately treated cases do not become seronegative as quickly as possible.
- A lot of likely surrogates for the diagnosis of COVID-19 are still being investigated.

Patients who had recovered from COVID 19 can be re-infected by the Omicron variant with potential for high fatality depending on the immune status.

Highlights of knowledge gaps

Identified knowledge gaps include: 1) Virological characterization, including in-vitro infectivity studies and neutralization studies evaluating both vaccinee and convalescent sera are still under way. 2) Lack of sequencing and screening using S-gene target failure in many of the likely affected countries means that the true prevalence of this variant is likely underestimated. 3) The severity of this strain particularly with reference to impact on hospitalization and fatality is yet to be determined. 4) Epidemiological analyses to estimate growth rates and secondary attack rates is also not known. 5) Analyses of the vaccine effectiveness for different vaccines against Omicron (direct and indirect effects) are currently being investigated. 6) Cross-protection of natural immunity from other SARS-CoV-2 variants is also not known.

Conclusion

No doubt, Omicron is here to stay with us like other variants, enhanced genomic and epidemiological surveillances is important to stay one-step ahead of the virus in the molecular-arm-race. At the moment, research efforts are ongoing to learn more about the variants to better understand how easily it might be transmitted and whether currently authorized vaccines will protect people against it. Information regarding the virologic, epidemiologic, and clinical characteristics of the new variant will be emerging in the coming days.

Competing Interests

The authors have declared that no competing interests exist.

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