Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Omicron: A highly transmissible SARS-CoV-2 variant

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1. The COVID-19 pandemic

More than two years ago, an unexpectedly high number of patients were reportedly hospitalized with an atypical pneumonia in Wuhan, Hubei Province, China. Weeks later, the causative agent of the respiratory illness was identified as an enveloped betacoronavirus named 2019-nCoV, later called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Lai et al., 2020). Rapid spread of the disease (later named COVID-19) and high transmissibility of the virus convinced WHO to announce, initially, an epidemic of public-health emergency and then a pandemic (Cucinotta and Vanelli, 2020). Almost two years later, on 16 January 2022, the number of positive cases and casualties due to COVID-19 reached 327,003,651 and 5,554,854, respectively (Worldometer, 2022). Furthermore, the COVID-19 pandemic has been unpredictable, notably due to the emergence of new variants as is normally expected of viruses. Since the beginning of the pandemic, distinct rises in the numbers of infected cases have coincided with emergence of new, mutated SARS-CoV-2 variants, for example, Gamma, Beta, and Alpha (Pung et al., 2021; Tang et al., 2021; Tao et al., 2021). In turn, peaks of cases infected with the variants have coincided with high rates of hospitalizations, especially of the nonvaccinated and immunocompromised individuals (Angius et al., 2021; He et al., 2020). Comparisons of the two viral lineages, B.1.1.7 (Alpha variant) and Wuhan/A-lineage (Wuhan variant), show that mutations have increased the viral transmissibility by up to 90%, especially in Europe (Cantón et al., 2021).

Here, we discuss the implications of the Omicron SARS-CoV-2 variant that was first reported from South Africa.

2. Emergence of the Omicron variant (B.1.1.529 strain) in South Africa

WHO routinely tracks and surveys the potential public-health threats posed by the emergence and circulation of SARS-CoV-2 variants of concern (VOCs), variants of interest (VOIs), or variants under monitoring (VUMs), enabling updating of the public-health recommendations. The WHO classification system attempts to prioritize global dissemination of information and monitoring of any new variant with potential to change the COVID-19 epidemiology drastically. In November 2021, the South African National Institute for Communicable Diseases confirmed discovery of a new SARS-CoV-2 variant, initially named B.1.1.529. Initial cases infected with this variant were detected in early November in Botswana, with travelers spreading the variant farther to Hong Kong and South Africa. On 26 November 2021, the Technical Advisory Group on SARS-CoV-2 Virus Evolution designated B.1.1.529 as a VOC, named Omicron (World Health Organization, 2021a). According to recent data available through GISAID (https://www.gisaid.org/hcov19-variants/), Omicron was detected in Botswana (hCoV-19/Botswana/R42B90_BHP_000842207/2021), Hong Kong (hCoV-19/Hong Kong/VM21045145/2021), and South Africa (hCoV-19/South Africa/CERI-KRISP-K032250/2021). All the 77 clinical specimens obtained during November 2021 belonged to young patients positive with Omicron (Sample, 2021). From 30 November 2021 to the second week of January 2022, the global number of new COVID-19 cases rose by 55% whereas the case numbers decreased in the African region to 11% (World Health Organization, 2022). Until 16 January 2022, more than 365,742 genetic sequences were recorded, with approximately 42% originating from the UK. According to the recorded sequencing data, 119 countries from all the continents have reported the Omicron variant (https://www.gisaid.org/hcov19-variants/) by mid-January 2022.

Preliminary evidence indicated that Omicron carries a high number of mutations that could associate with immune evasion (Sample, 2021). Detection of more than 30 mutations only in the Spike protein of Omicron has alarmed the clinicians, scientists, and the authorities (Callaway, 2021) who consistently recommended vaccination as the best tactic against the COVID-19 pandemic. Moreover, deletion of the non-structural protein 6 (NSP6), similar to that seen in Alpha, Gamma, Lambda, and Beta variants, could significantly affect the host innate immunity, indirectly affecting viral transmissibility. Additionally, R203K and G204R (also seen in Alpha and Gamma) could increase infectivity by the variant. Another collection of mutations, including P681H, H655Y, and N679K, could modulate viral entry into its target host cells, altering its infectivity and transmissibility. Two sister-clades of Omicron, 21K and 21L, share clusters of mutations (Fig. 1 and https://covariants.org/variants/21L.Omicron). The 21K variant, however, carries six more mutations than 21L in the Spike protein: S:R408S, S:D405N, S:T19I, S:T376A, S:S371F, and S:V213G. Such mutations may also increase the risk of reinfection leading to more-severe clinical

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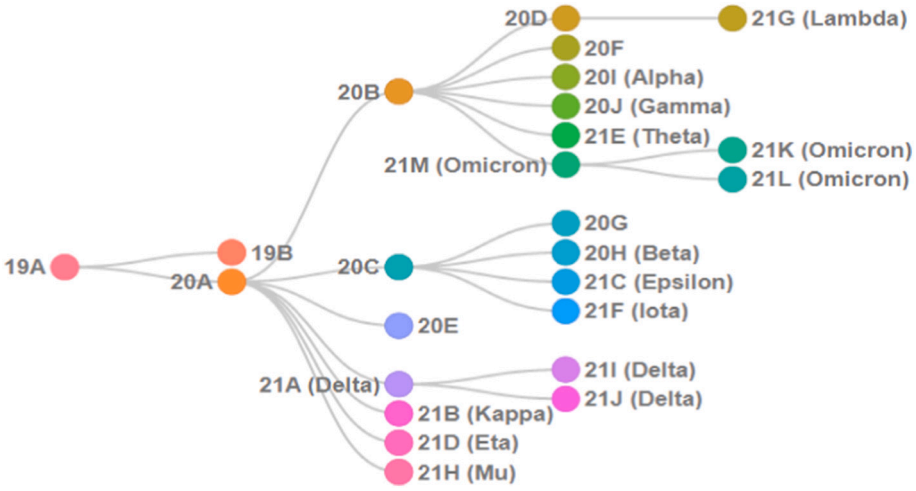

Fig. 1. Phylogenetic relationships among SARS-CoV-2 Nextstrain clades (https://covariants.org/).

manifestations in naïve subjects, at least in comparison with previous VOCs.

New variants could expectedly emerge from the existing variants under natural pressure. Therefore, global, equitable vaccination campaigns along with other countermeasures, including frequent hand hygiene, correctly donning of appropriate type of facemasks, physical distancing, and banning of indoor crowded activities, are still profoundly pertinent, despite the vaccination status of any country.

3. Future perspective

Accurate tracing of Omicron by sequencing in South Africa and other countries is highly recommended before clear decisions can be made based on the corresponding epidemiological data. This VOC may potentially evade the immune responses acquired following vaccination or previous natural infection. Research is warranted to elucidate the effects of the mutated variants on the effectiveness of the available vaccines and the dynamics of the pandemic. BioNTech recently announced that at least two weeks were required to reassess the vaccine effectiveness against infection with the Omicron variant (Gonultas, 2021).

Researchers were highly cautious following the rise of the new COVID-19 cases in Gauteng, South Africa, where Omicron was first reported. However, the infection rate started to subside mid-January 2022 in Gauteng. A similar scenario unfolded in other countries where the COVID-19 case numbers are rising rapidly when this manuscript was being written. The recent profile of the COVID-19 epidemiology shows rapid distribution of Omicron with the Delta variant decreasing (Fig. 2). Negligible distribution of Gamma, Alpha, and Beta variants has been reported in various countries (Fig. 2). Omicron presents in 60% of new reported cases, hence rapidly dominating the pandemic globally, whereas the former dominant Delta variant is subsiding.

Indeed, Omicron has a faster doubling time than previous variants at least by twofold, thus providing an advantage to the variant (Brandal et al., 2021; Karim and Karim, 2021). Clinical evidence indicates that Omicron causes a less severe disease than the previous variants (Abdullah et al., 2021; Jassat et al., 2021); however, hospitalizations and death rates due to Omicron have been rising. Therefore, the message about the severity of the disease by Omicron must be relayed cautiously particularly because some preconditions still increase the vulnerability to the virus. For example, in Australia in the wake of the Omicron wave, on 21 January 2022, 5147 were hospitalized with 424 requiring ICU care. Although many countries had already banned travel from South Africa, the Omicron crisis has not been controlled while 119 countries have reported the variant within a relatively short period after its detection (Brandal et al., 2021; Petersen et al., 2022). Initial reports indicate that the titers of neutralizing antibodies against Omicron in double-vaccinated subjects or those with previous natural infection by SARS-CoV-2 may be insufficient for protection. Rapid propagation of Omicron in new regions indicates that new formulations of prophylactic vaccines are required. The rising trend of reinfection of partially or fully immunized individuals in some European countries highlights the risk of immune evasion by Omicron.

We have learnt from previous peaks of COVID-19 cases in many countries that Omicron can be the newest but not the last SARS-CoV-2 variant. Sooner or later, the world will host another VOC or VOI, probably more (or less) infectious than Omicron, generating a new wave of the COVID-19 cases. The third, fourth, or probably the fifth

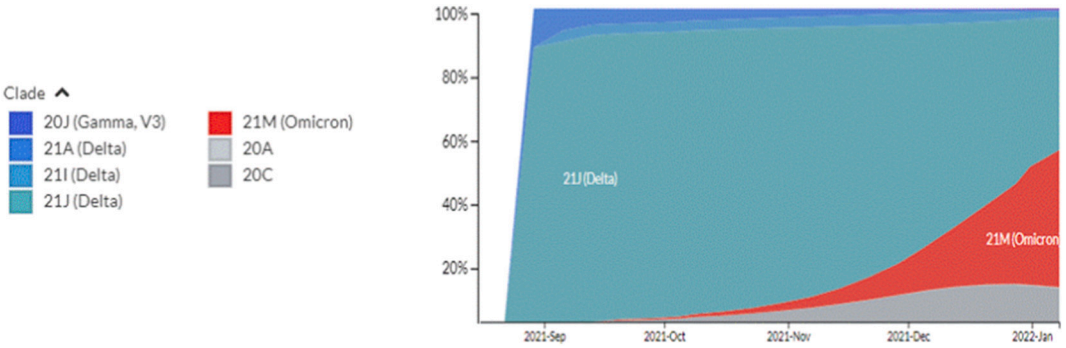

Fig. 2. Rising frequency of Omicron in comparison with other SARS-CoV-2 variants in the world (Date of access: 20 January 2022, available from nextstrain.org/sars-cov-2.)

vaccination doses may be necessary to enforce the neutralizing immunity against the highly variable SARS-CoV-2 variants (Garcia-Beltran et al., 2021). WHO maintains that the extent of waning of immunity differs among different vaccines and target populations. Circulating viral VOCs, the extent of previous natural infection in a community at the same time as the first vaccination, first-dose schedule and inter-dosing intervals, and the exposure intensity all likely affect reversion of protection (World Health Organization, 2021b). Rapid distribution of Omicron from Africa to other continents reflects regionally unequitable global vaccination (Petersen et al., 2022). Undoubtedly, equitable, consistent global vaccination by using effective vaccine formulations is important to prevent emergence of the viral mutants. Indeed, a 90% double-vaccinated population in the North America or Australia cannot be fully protected by emergence of a variant from the African continent with 5% vaccination status because the world will remain interconnected. Consistent adherence to hygiene protocols is necessary to prevent another surge of the COVID-19 cases and a high mortality rate due to this VOC or other potentially emerging variants.

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Declaration of competing interest

None.

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