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Editorial

Emergence of new SARS-CoV-2 Variant of Concern Omicron (B.1.1.529) - highlights Africa's research capabilities, but exposes major knowledge gaps, inequities of vaccine distribution, inadequacies in global COVID-19 response and control efforts

Introduction

Nearly two years since the start of the SARS-CoV-2 pandemic, which has caused over 5 million deaths, the world continues to be on high COVID-19 alert. The World Health Organization (WHO), in collaboration with national authorities, public health institutions and scientists have been closely monitoring and assessing the evolution of SARS-CoV-2 since January 2020 (WHO 2021a; WHO 2021b). The emergence of specific SARS-CoV-2 variants were characterised as Variant of Interest (VOI) and Variant of Concern (VOC), to prioritise global monitoring and research, and to inform the ongoing global response to the COVID-19 pandemic. The WHO and its international sequencing networks continuously monitor SARS-CoV-2 mutations and inform countries about any changes that may be needed to respond to the variant, and prevent its spread where feasible. Multiple variants of the virus have emerged and become dominant in many countries since January 2021, with the Alpha, Beta, Gamma and Delta variants being the most prominent to date. (Table 1).

Announcement of new SARS-CoV-2 Variant of Concern - Omicron

On Friday 26 November 2021, the WHO announced (WHO 2021c) that a new SARS-CoV-2 Variant of Concern, named Omicron (initially named B.1.1.529), appeared to be increasing in almost all of South Africa's provinces, particularly Gauteng. The rapid spread, especially among the younger age group, in Gauteng, South Africa, has placed WHO and global health systems on high alert. The SARS-COV-2 VOC was first reported to the WHO from South Africa on 24 November, 2021. Cases of VOC Omicron had also been identified in Botswana, Belgium, Hong Kong and Israel. On 29 November, 2021, three days after the announcement by WHO, cases of VOC Omicron have been detected in Austria, Australia, Belgium, Canada, Czech Republic, Denmark, France, Germany, Italy, the Netherlands and the United Kingdom.

The global public health community applauds scientists in South Africa and other countries which have reported the new VOC for the speed with which they have identified, sequenced and characterized SARS-CoV-2 strains, and their transparency and openness in reporting quickly to WHO (WHO 2021c). Their SARS-CoV-2 sequencing work has been exemplar (Wilkinson et al. 2021; Tao et al. 2021). As of November 28, 2021, 17:00 CET, 127 viral genomes (VOC Omicron GR/484A) have been entered into the GISAID databases (GSAID 2021). Several receptor binding domains (RBD) and N-terminal domains (NTD) mutations hypothesised to be associated with resistance to neutralizing antibodies and increased transmissibility are of concern.

Travel bans to and from southern African countries – are they necessary?

Immediately following announcement by WHO of VOC Omicron, the European Union, Australia, Bahrain, Brazil, Canada, India, Iran, Israel, Japan, Kuwait, Oman, Saudi Arabia, Switzerland, Thailand, Turkey, the United Arab Emirates, the United States and others, imposed travel bans or travel restrictions to and from countries in southern Africa reporting the Omicron variant, even including neighbouring countries. There is also the danger of the whole of Africa being lumped together in the same basket with a ban all travel links. These political 'knee-jerk' decisions have generated widespread dismay and anger that South Africa and other African countries are being unfairly treated. While throughout Africa there is pride that South Africa has been able to identify VOC Omicron and rapidly share information, the South African scientists have felt the wrath of those within who anticipate another lockdown, turndown of the economy and further hardship, which they experienced under previous COVID-19 lockdowns. This is extremely unfortunate. The consequential vilification of scientists in South Africa due imposition of these travel bans is unwarranted.

Are Travel bans to limit global spread of VOC Omicron justified?

Travel bans go against WHO COVID-19 recommendations (WHO 2021d; Petersen et al. 2020). In light of the huge air traffic between countries and continents, it is rather simplistic and naïve to assume that by imposing travel bans and travel restrictions on a few countries reporting the new VOC Omicron, will prevent importation of the virus, or limit establishment of significant clusters of

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Table 1
WHO designated SARS-CoV-2 Variants of Concern (VOCs): (Adapted from WHO https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/)

WHO designation (Date of Designation)	Pango lineage	GISAID clade	Nextstrain Clade	Additional amino acid changes monitored	Country of origin of first documented samples
ALPHA (18 Dec 2020)	B.1.1.7	GRY	20I (V1)	+S:484K +S:452R	Sept 2020 United Kingdom,
BETA (18 Dec 2020)	B.1.351	GH/501Y.V2	20H (V2)	+S:L18F	May 2020 South Africa
GAMMA (11 Jan 2021)	P.1	GR/501Y.V3	20J (V3)	+S:681H	Nov 2020 Brazil
DELTA (11 May 2020)	B.1.617.2	G/478K.V1	21A, 21I, 21J	+S:417N +S:484K	Oct 2020 India
OMICRON (26 Nov 2021)	B.1.1.529	GR/484A	21K		Nov 2021 South Africa, Hong Kong, Belgium, Israel

GISAID = Global initiative on sharing all influenza data

the Omicron VOC. The travel bans will no doubt have negative direct and indirect economic and social consequences on health systems of African countries which are only just starting to recover from the devastating effects of several COVID-19 lockdowns over 2 years. This is all the more important where the economy is fragile, suffering inflation, currency deflation and their hospitals lack funds to operate efficiently. In many of these African countries there is little evidence to show that they are contributing to the global burden of SARS-CoV-2 infections, but this could change. It is likely that the VOC Omicron variant has already spread across the world, and will continue to be detected in more countries across continents.

The WHO recommends that countries continue to apply a risk-based and scientific approach when implementing specific travel measures and recommendations for reducing risk of acquisition or spread (WHO 2021d). However, over the past few months, in lieu of extensive roll out of COVID-19 vaccines, and reducing numbers of COVID-19 cases and deaths, many countries have over the past few months relaxed basic WHO recommended infection control measures to reduce SARS-CoV-2 transmission, and communities are becoming increasingly relaxed about the disease. With the emergence of Omicron VOC these countries now need to seriously consider re-introducing WHO recommended basic public health and social infection control measures such as wearing well-fitting masks, hand hygiene, physical distancing, improving ventilation of indoor spaces, avoiding crowded spaces if unvaccinated. Countries should also accelerate the COVID-19 vaccination programs.

Major Knowledge gaps on VOC Omicron

Since its first appearance in November 2019, thousands of SARS-CoV-2 mutations have been identified from across the world (GISAID 2021), including Africa (Inzauale et al. 2021; Martin et al. 2021; Tao K et al. 2021; Wilkinson et al. 2021). These have had no major impact on protection induced by vaccines. Sequencing of VOC Omicron shows approximately 50 mutations in its genome, including more than 30 on the spike protein used to bind to host cells setting it apart from other known variants. This is a cause for concern since antibodies induced by vaccine or natural infection which neutralize the virus primarily target the spike protein. These may be potentially significant mutations which could alter responses to vaccines, treatments and transmissibility. Other mutations appear similar to changes seen in other variants associated with enhanced transmissibility. Whether VOC Omicron spreads faster, makes vaccines and drugs less effective, or whether it leads to more severe disease and deaths remains to be defined urgently.

Many other questions arise regarding VOC Omicron and major gaps in knowledge need to be filled. In South Africa, secondary cases from the epicentre in Gauteng need to be traced and followed up and the epidemiology, transmissibility, pathogenesis, immune responses, and vaccine escape require urgent study. It remains to be proven that existing COVID-19 vaccines might be effective at preventing serious disease due to VOC Omicron. Further information on the levels and types of antibodies and the role of T-cells in preventing infections, reducing serious disease or deaths in vaccinated individuals requires definition. In many parts of the world, HIV infection and other infections can synergize with the SARS-CoV-2 influencing COVID-19 management outcomes potentially influencing both pathogenesis of COVID (Karim F et al. 2021; Nachega et al. 2021b; Nachega et al. 2021c). *Plasmodium falciparum* infection induces cross-reactive antibodies to carbohydrate epitopes on the SARS-CoV-2 Spike protein (Lapidus et al. 2021) and could influence pathogenesis of COVID and perceptions of herd immunity (Ansumana et al. 2020) in many African countries. This requires further study.

Low rollout of COVID-19 vaccines in Africa

The explosive global spread of COVID-19 pandemic in 2020 generated international consensus in principle, between the WHO, vaccine developers, governments, funders, donors and industry, with agreement on the need to develop an effective COVID vaccine and plans for fair and equitable rollout to all countries. During the Covid-19 pandemic, these programs provided a model for the WHO and global partners to rapidly establish the COVID-19 Vaccines Global Access (COVAX) initiative to bridge the vaccine gap and ensure rapid and equitable access to vaccines in both high-income countries and low- and middle-income countries (WHO 2021e). The African Vaccine Acquisition Task Team of the African Union and the WHO-led COVAX consortium with its global partners had hoped to secure millions of doses of COVID-19 vaccines to achieve 60% coverage in Africa by June, 2022 (WHO 2021e; 2021f; Nkengasong et al. 2020). This has been a major disappointment (WHO 2021g). Richer nations focused on being the first to develop and roll out COVID-19 vaccines to their own populations, rather than focus on what was best for all of humanity. The statistics for rollout of COVID-19 vaccines in Africa are appalling. Whilst in Europe an average of 60% of the population have received COVID vaccines, in Africa only 5-10% (24% in South Africa) of the population have received the first dose (WHO 2021g). Vaccine acceptance rates have also been low in some African countries. Tragically, concerns regarding access to COVID-19 vaccines in Africa are similar to those raised during the HIV pandemic in the mid-1990s and early 2000s, when highly active antiretroviral treatment (HAART) was accessible in high-income countries but was too expensive for rollout in African countries (Nachega et al. 2021a) - a disparity that resulted in many preventable deaths in these high-burden settings.

Addressing inequities

Less than a fifth of people in Africa have been fully immunized against COVID-19, including millions of health workers and vulner-

able populations. There remain many unvaccinated vulnerable populations around the world, and every month thousands of people are still dying of COVID-19. The more SARS-COV-2 circulates and transmits, the more VOCs evolve and further evolution of variants may eventually lead to variants resistant to vaccines. One of the contributing factors to emergence of VOCs is the low vaccination rates in parts of the developing world, particularly Africa. There remains an urgent need to get adequate and regular supplies of COVID-19 vaccines rolled out to, and accepted by all the peoples of Africa through strategic community education to increase vaccination rates and prevent severe disease and death.

Given the continuing circulation of SARS-CoV-2 and emergence of VOC Omicron in Africa and elsewhere, vaccine development must adapt and evolve over time. It is re-assuring that in light of the emergence of VOC Omicron, vaccine manufacturers such as Moderna, Pfizer, AstraZeneca and Novavax, have indicated that they have plans to adapt their current COVID-19 vaccines and modify them accordingly. African governments also need to take leadership and ownership of the emerging and re-emerging infections agenda and invest more into developing their own capabilities for manufacturing affordable and easily scalable vaccines.

The emergence the VOC Omicron variant and its rapid spread reflects the legacy of wealthy nations' failure to equitably distribute COVID-19 vaccines globally. This failure also contributes to prolonging the pandemic, and has placed the whole world at continued risk of COVID-19 and continuing impact on their economies. Whether VOC Omicron, will turn out to be 'a storm in a teacup' or 'a lethal evolving threat to global health security', its appearance nearly two years after its first discovery, is a stark reminder that the COVID-19 pandemic is far from over. Richer countries need to take heed of the WHO slogan that 'none of us is safe until all of us are safe' which has been highlighted *ad nauseam*.

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