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Editorial

The African Lag in COVID-19 Pandemic; An Editorial to Volume 18 of EC Microbiology

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In Africa, there has been a lag in cases and responses to the coronavirus disease 2019 (COVID-19), which could prolong the pandemic. This editorial to Volume 18 of EC Microbiology will present progress made so far in combating the ongoing COVID-19 pandemic, highlighting observed lags in Africa and making reference to articles published in this volume on the subject and other topics.

According to recent updates as of 31st of March 2022, from both John Hopkins University (https://coronavirus.jhu.edu/map.html) and Worldometer (https://www.worldometers.info/coronavirus/) show that nearly half a billion cases of COVID-19 with six million (6M) deaths have been recorded worldwide since the pandemic began in December 2019, with USA, India and Brazil having 81M, 43M and 29M cases occupying the first, second and third positions respectively. Europe (177M) recorded the highest cases followed by Asia (138M), North America (96M) and South America (56M), with Africa (11.7M) and Oceania (5.3M) being the least. Cases in only three countries, namely South Africa (3.7M), Morocco (1.1 M) and Tunisia (1.0M) accounted for over 50% of cases in Africa. The total cases in Africa compared with the 11.5M cases in Spain, which ranked 11th position globally. Deaths tend to follow the same pattern within the four continents (South and North America, Europe, Asia) accounting for 93% of global deaths. USA recorded the highest death of one million followed by Brazil (0.6M) and India (0.5M). Of the 252K deaths in Africa, three countries, namely South Africa (100K), Tunisia (28K) and Morocco (16K) accounted for 57 %. The total death in Africa was slightly higher than the 212K deaths recorded in Peru, but lower than the 368K deaths recorded in Russia. About 46 of Africa's 54 countries belong to Sub-Saharan Africa (SSA) region, which have a population of 1.1 billion, which accounted for 14% of world population of 7.9 billion in 2021. Total cases in SSA was 8.5M, which accounted for just 1.75% of global cases. South Africa cases accounted for nearly half of the total cases in SSA. Total deaths in SSA is 168K, of which nearly 100k death occurred in South Africa alone. SSA accounted for 2.8% of global deaths. Because of the weak health infrastructure, it was feared that SSA would be worst hit, but this prediction has not happened. The reason why Africa especially SSA was relatively spared is unknown, but there are several speculations such as limited testing and underreporting, climatic differences, pre-existing immunity to coronaviruses, dominance of the population by healthy youths, genetic factors and behavioural differences. There were speculations that about 86% of cases in Africa go unreported, about six of every seven infections unnoticed and that the actual number ought to be about seven times more than reported cases. High titres of cross-reactive anti-SARS-CoV-2 antibodies have been observed in some countries including Kenya, Malawi, Mozambique and Cameroon, which scientists believed could be responsible for protection in SSA. It is also possible that the frequent exposure to infectious diseases might have trained the immune system to counter emerging pathogens, including SARS-CoV-2. Some scientists have also speculated that the widespread use of antimalaria drugs in Africa could have ameliorated the disease in Africa.

When the disease started, it took the world by surprise, because there were no available licensed testing kits, vaccines, drugs, antibodies for the disease. Hence, response was limited to hand hygiene, physical distancing, ban on mass gathering, masking. As the pandemic progressed, lockdowns and other forms of restrictions followed. Notwithstanding, the scientific community rose to the challenge by researching on the repurposing of existing drugs, testing methods and kits, developed and tested novel drugs, antibodies and vaccines. Vaccines were prioritized as a way to quickly bring the pandemic to an end.

As of July 2020, i.e. about seven months into the pandemic, World Health Organization (WHO) announced 166 candidate vaccines in development, most of which were in preclinical stages. However, six vaccine candidates rapidly advanced onto Phase III clinical trials. These are ChAdOx1 nCoV-19/ AZD1222 (University of Oxford/AstraZeneca, UK), BNT-162b2 mRNA (Pfizer/BioNTech, USA/Germany), mRNA-1273 (Moderna and the National Institute of Allergy and Infectious Diseases (NIAID)), PiCoVacc (Sinovac Biotech, China), Ad5-nCoV vaccine (CanSino Biologics/Beijing Institute of Biotechnology, China), and BBIBP-CorV inactivated vaccine (Sinopharm, China). Apart from the vaccine that was produced via the traditional inactivated whole virus (Sinovac Biotech, Sinopharm), the other leading vaccines were produced via innovative technologies including adenovirus vector (AstraZeneca, CanSino) and mRNA (Moderna and Pfizer). The is the first time that mRNA technology was used for the production of vaccines. The Pfizer mRNA vaccine got regulatory approval within a year, which is unprecedented. As soon as the virus sequence was released in January 2020, Pfizer developed their vaccines and commenced preclinical studies within the same month. They carried out overlapping clinical trials, Phase I/II in April, Phase II/III in July and obtained approval (US, EU, UK, WHO) for emergency use in December. As research continued, the landscape of vaccines increased and by December 2020, at least 10 vaccine candidates have commenced Phase III clinical trials. Mass vaccination commenced on 8 December 2020. As of June 2021, only 10% of the world was fully vaccinated with any of the approved 20 vaccine candidates, while vaccinations in Africa was less than 1%. At this same time, China was vaccinating a staggering 20 million people a day and successfully administered more than 1 billion doses cumulatively.

The vaccine strategy was faced with several challenges. Rich nations particularly UK, EU, US, Canada, Australia and Japan pre-ordered most of the available doses ahead of licensure. There was vaccine nationalism causing unequal distribution, with Africa lagging behind. Lack of cold chain infrastructure in SSA limited the use of vaccines especially the mRNA vaccines that require ultra-freezers. Moderna mRNA vaccines require -20^{o}C while Pfizer vaccines require -70^{o}C for storage. This is where other vaccines have the advantage of storage at fridge temperatures including Oxford/AstraZeneca, Sputnik V, Johnson and Johnson, Novavax. Because of huge research costs, researchers in Africa were unable to develop home-grown vaccines. The WHO coordinated COVID-19 Vaccine Global Access Facility (COVAX), which comprise of 172 nations in a public-private vaccine partnership initiative, helped to pool resources that led to the supply of vaccines to poor countries including Africa. Ghana became the first country that received AstraZeneca vaccine via COVAX followed by Ivory Coast in February 2021. Other shipments followed subsequently. Conspiracy theories and antivaxx movements rose early into the pandemic, which fuelled vaccine hesitancy. Therefore, as of Sept 2021, less than 3% of the population of 12 countries in Africa (Benin, Burkina Faso, Cameroon, Democratic Republic Congo, Ethiopia, Ghana, Liberia, Mali, Nigeria, Sierra Leone, Somalia, Sudan) have received only one dose. As of 1st of April 2022, when about 65% of the world had received at least one dose of COVID-19 vaccine, only about 15% have received a dose among low-income countries. Only 11% of Africans were fully vaccinated in February 2022. For instance, Nigeria, which is the most populous country in Africa, with a population of about 200m, only 4.5% was fully vaccinated as at 1st of April 2022. It was therefore suggested that Africa requires six-fold vaccination to be able to catch up wit the rest of the world.

The situation in Seychelles was somewhat different. As of May 2021, Seychelles was among the most vaccinated country in the world with about 61.4% of the country fully vaccinated. But COVID-19 continued to increase in the following months causing deaths even among vaccinated persons, most of which we linked to pre-existing conditions. Breakthrough infections were also recorded among persons without pre-existing conditions. Vaccine induced immunity waned within six months. It became doubtful if vaccines alone are sufficient to end the pandemic. Natural immunity following infection also waned, hence reinfection cases occurred. Hence, herd immunity seems unattainable with COVID-19. Recent studies have shown that hybrid immunity is stronger than either vaccine-induced or natural immunity.

Variants emerged early in the pandemic, which undermined countermeasures including vaccines, antibodies, drugs and diagnosis. Thus, posing increased risks to public health. Variants that significantly affected countermeasures, increased transmissibility and/or disease severity were classified by WHO and Centers for Disease Control and Prevention (CDC) into Variants of Interest (VOIs) or Variants of Concern (VOCs), for purpose of global monitoring, research attention and response. Variants that have potential to undermine countermeasures or previous VOI and VOC were designated as Variants Under Monitoring (VUM) and Variants Being Monitored (VBM) by WHO

and CDC respectively. The WHO used Greek letters for the naming the variants for ease and to avoid stigmatization. For instance, the Beta variant, which was first detected in South Africa, was previously declared as VOC, is now downgraded to VUM. Current circulating variants of global importance are mostly Delta and Omicron. Sub-variants of Omicron have also been reported including BA.1, BA.2, BA.3, BA.4, BA.5 and XE. Omicron, which appears to have originated from Botswana, but first detected in South Africa, is fast becoming the dominant variant in circulation globally.

Most of the first-generation vaccines especially the vector and mRNA vaccines targeted the spike protein of the coronavirus. Hence, significant mutation of the spike protein of the virus, decreased the effectiveness of vaccines. This is an aspect, where inactivated vaccine produced from whole virus seems to have advantage over other vaccines. But superiority of inactivated vaccines in countering variants have not been established. Sinopharm and Sinovac are about to commence clinical trials for Omicron-specific COVID vaccine candidates.

Apart from the Johnson and Johnson vector vaccine that required a single dose to be fully vaccinated, most other vaccines required two doses. However, due to the problem of waning immunity and emerging variants, it became obvious that vaccine boosters will be necessary. While the rest of the world took first booster jab, which is the third dose and currently considering second boosters, SSA was again left behind.

The mRNA vaccines have a rare side effects of heart inflammation called myocarditis especially among young men, while the vector vaccines are associated with blood clots potentially causing thrombosis. But the benefits of the vaccine were assessed to outweighed their risks. But it is uncertain if this risk assessment is applicable to SSA, where the cases are relatively low. Studies carried out in Israel, UK, Singapore and US show that fully vaccinated people can become infected and can easily transmit Delta variant of the virus like unvaccinated persons. Notwithstanding, vaccination is considered critical for preventing severe disease and further mutations of the virus potentially leading to the emergence of deadlier variants. Scientific efforts are now focused on the development of universal coronavirus vaccines that could be effective in neutralizing all the variants currently in circulation and possibly future variants.

This volume of EC Microbiology featured interesting articles focusing on COVID-19 and other aspects of microbiology. Tackling emerging variants is key to ending the pandemic. Vinod Nikhra discussed the effects of mutations and variants on the management of the pandemic, especially with respect to transmissibility of the virus, disease severity, immunity and countermeasures including vaccination and therapeutics. The article listed some properties of some variants in circulation, most of which have now been downgraded except Delta and Omicron. The paper also listed some therapeutics that have been found to be effective in the treatment of COVID-19. The paper argued that the pandemic be deescalated to endemicity. Xu and others demonstrated how Brilacidin (PMX-30063) prevented infection by blocking entry of Gamma and Alpha variants of SARS-CoV-2. There is the need to check the efficacy of this molecule against current circulating variants i.e. Delta and Omicron, which could be a game changer in ending the pandemic.

Other articles in this volume focused on other viral, protozoa, bacteria and fungi infections. Using a 4-year cross-sectional study, Adeola and others focused on hepatitis B virus (HBV) infection among pregnant women and provided epidemiological data that could inform policy decisions. Ghazvini and others investigated the effects of Silymarin on HBV infected hepatocytes *in vitro* and found that Silymarin had no significant effects on HBV activity but damaged hepatocellular cells. Through literature studies, Hamad et al discussed the possible role of *Toxoplasma gondii* in the protection from the malaria parasite, *Plasmodium* species among immune competent persons. Veretennikova and Chang showed how *Chlamydia trachomatis* but not *Lactobacillus* species enhances HIV infection in Non-Activated peripheral blood mononuclear cells. This study provided important clues to the management of HIV infections. Ahmad Aliyu., *et al*. carried out a systematic review of literature on onychomycosis and found that 60% of finger nail and 80% of toe nail onychomycosis in tropical countries are caused by *Trichophyton rubrum* and *T. mentagrophytes*. Constantin et al discussed the importance of surface microbiology in the monitoring and control of production in the food industry.

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