

COVID-19 pandemic complexities on endemic infectious disease management and diagnosis in poor countries

Emenike Onyebum Irokanulo¹, Eugene Ayeni², Charles Nwonuma³, Dolapo Orotayo¹, Benita Agbaso¹

¹Department of Microbiology, Landmark University, Omu-Aran Kwara State, Nigeria

²Department of Medical Microbiology and Parasitology, College of Medicine, University of Ibadan, Nigeria

³Department of Biochemistry, Landmark University, Omu-Aran Kwara State, Nigeria

ABSTRACT

The persistence and frequency of prevalent infectious diseases continue to be a major problem on the African continent. Malaria, TB, and HIV/AIDS are the most common infectious diseases in Sub-Saharan Africa. Malaria and tuberculosis have had a considerable negative impact on poor nations' health, resulting in high mortality and morbidity. Fortunately, the World Health Organization's introduction of the RTS, S/AS01 malaria vaccine may soon put an end to the lingering difficulties in malaria eradication, barring new contagious disease outbreaks like COVID-19. The literature reviewed looked at the current condition of endemic infectious illnesses in low-income countries from 2018 to 2022. Improvements in disease management and other mitigating strategies were evaluated alongside the resurgence of malaria, and particularly tuberculosis, the deadliest infectious disease of considerable global health concern in recent decades. The study's focus was the destructive effects of COVID-19 on the treatment and prevention of infectious illnesses. PubMed, Web of Science, and Google Scholar were used as relevant databases. The COVID-19 pandemic had a significant global impact on Africa, but not because the continent was directly impacted by the scourge and its fatal effects; rather, it did so by successfully forcing resource reallocation and diverting medical personnel to COVID-19 treatment, which in turn made TB, malaria, and HIV/AIDS-related problems worse. To halt the endemicity of these diseases and their potential intensification if a new pandemic like COVID-19 emerges in the future, enhanced efforts from all stakeholders, particularly in poorer climes, are required to be more inward looking and less reliant on foreign support.

Keywords: diagnosis, infectious diseases, tuberculosis, multi-drug resistant tuberculosis, malaria, HIV/AIDS, low-income countries

INTRODUCTION

Several infectious diseases of public health significance that have continued to dominate the landscape of poor countries, now appear to be native to the African continent due to their endemic character. These have had a very negative impact on Sub-Saharan Africa in a wide range of economic and social sectors.

Among the three most widely identified endemic infectious diseases, tuberculosis (TB) is the world's deadliest and continues to be a leading cause of

death, owing primarily to its antimicrobial resistance. In 2019, approximately 1.4 million people died from the disease worldwide [1]. Prevalence of these diseases is high in African countries such as Nigeria, Kenya, and Ghana, amongst others. Aside from the economic implications, African populations have been negatively impacted by the region's poorly developed environment as well as by the region's temperate climate, which allows infectious agents to thrive thus exposing individuals to avoidable communicable diseases.

Disregard for what are often regarded as common infectious diseases in some parts of the world may have its roots in weak governance aided by poor economy, conflicts, poor health-care system, and scarcity of medical supplies. Crimean-Congo hemorrhagic fever, Lassa fever, yellow fever, Dengue fever, HIV/AIDS, malaria, and tuberculosis are among these diseases with HIV/AIDS, malaria, and tuberculosis, as the three most common. These continue to be serious public health threats, killing approximately 3 million people each year [2].

As an infectious disease, tuberculosis (TB), regarded as the oldest disease of man [3], has become chronic, difficult to treat, and can be considered a global disease, infecting approximately 10 million people globally each year. The disease is more prevalent in Asia and Africa: in 2019, the Southeast Asia Region accounted for 44 percent of the global TB burden; Africa, 25 percent; the Western Pacific, 18 percent; the Eastern Mediterranean, 8.2 percent; the Americas, 2.9 percent; and Europe, 2.5 percent. India, Indonesia, China, the Philippines, Pakistan, Nigeria, Bangladesh, and South Africa account for approximately 67 percent of the global TB burden [4]. Several reports, however, show a not too steady decline in both incidence and deaths. While some reports indicate a gradual drop in incidence and mortality [5], others – such as the Southeast Asia report, which recorded a 43% burden of TB incidence – noted a minor but rising trend in incidence [6] suggesting that increased action is required to halt the disease's spread.

Like tuberculosis, estimates show that cases of malaria worldwide have remained high. This is in spite of reports of a decline in the malaria burden for sub-Saharan Africa [7,8].

Malaria cases rose from 218 million to 232 million, and fatalities increased from 544 000 to 599 000 in the WHO African Region between 2019 and 2020, and in 2021, cases increased to 234 million, with deaths decreasing to 593 000 [9]. During this time span, Africa accounted for around 95% of cases and 96% of deaths worldwide, a very concerning scenario.

The prevalence of mixed malaria may explain why, despite advanced therapy, public health control, and management, malaria remains one of the leading causes of sickness and death globally.

While we savor the good news about malaria control efforts, a number of endemic infectious illnesses have persisted and others have evolved, with malaria, TB, and HIV/AIDS being widespread in Sub-Saharan Africa. The recent emergence of COVID-19 has significantly stretched Africa's health sector, aggravating, and intensifying the problem in the continent's already deplorable health-care system. Because of the high mortality rate of COVID-19, other recognized infectious diseases were virtually disre-

garded to focus more attention on containing the pandemic [10].

The picture as painted by the WHO report shows that in 2020, close to half of the world's population stood at risk of malaria; about 247 million cases in 2021, and mortality of about 619 000 [9]. In all of this, Africa WHO Region carries a high proportion of the global malaria burden, for instance, in 2020, Africa accounted for 95% and 96% of malaria cases and deaths, respectively [11].

Current Status on TB Diagnosis in Poor Resource Nations

The influence of COVID-19 on tuberculosis and malaria is particularly noticeable in the diagnosis and treatment of these two long-standing infectious diseases, as well as the halting of eradication programs.

While certain low and middle-income countries, such as Pakistan [10] are working to improve tuberculosis diagnosis, the situation remains uncertain in other low-income countries including those in Africa.

Diagnosis and multidrug resistance of tuberculosis in low-income countries is fraught with difficulties of limited resources which are heightened by TB in HIV-infected patients and additionally by the COVID-19 pandemic that swept through the world like a tsunami.

Due to a lack of infrastructure and experienced personnel, the most innovative strategies for diagnosing tuberculosis in HIV-positive people may face the difficulty of poor or ineffective use, which is exacerbated by resource diversion due to highly infectious diseases such as COVID-19 in most poor nations' settings.

In resource-poor countries where smear microscopy is still being used as the principal diagnostic option, there are problems of understaffing, poor maintenance of diagnostic equipment, lack of consistent water and electricity supply. Furthermore, programs for quality assurance and external quality assessments (EQAs) are often not in place. For an enhanced productivity in diagnosis, more sensitive as well as specific TB point-of-care tests (POCTs) should be developed [11].

Another source of concern is a lack of funding for research and development of new drugs and vaccines to combat drug-resistant tuberculosis and malaria as well as for newer diagnostics.

In some regions, such as India that was adversely hit by the ravages of COVID-19, previous major challenges include a lack of public awareness, poverty and malnutrition, poor infrastructure, an increase in drug-resistant cases, and inadequate surveillance [12]. In Indonesia, diagnosis is mainly by clinical evaluation of patients, sputum smear microscopy and chest radiography, which are, low in specificity.

Underdiagnoses and underreporting of diagnosed cases are still serious issues in African and Asian countries. According to the Global TB report [13] the large gap between the number of newly diagnosed patients and the number of people estimated to have developed TB in 2019 occurred more in Africa and Asia, specifically in India, Nigeria, Indonesia, Pakistan, and the Philippines, which contributed to two-thirds of global TB cases in 2019.

Most developed countries implemented social protection schemes such as insurance, food assistance, among other things and offer free TB treatment to those who are infected with the disease, yet TB patients are still subjected to significant medical and non-medical costs. It is always a mammoth task for individuals and governments to cover these costs in the absence of a pandemic, let alone with COVID-19's disastrous effects.

TB Diagnosis under COVID-19

Until the COVID-19 epidemic, HIV/AIDS was the most important multidrug-resistant TB issue in low-income nations. Following the COVID-19 pandemic outbreak, several serious concerns were expressed in a report that looked at the impact of COVID-19 and HIV on TB in a few Eastern European and Central Asian countries. This is particularly of concern for HIV-infected TB patients due to the synergy between the two diseases. In addition, all the countries investigated between 2020 and April 2021, including Moldova, Georgia, Bosnia and Herzegovina, Kyrgyzstan, and Ukraine (lower-middle income countries), had reduced HIV testing and TB detection, as well as patient-physician contact [14]. As a result of the COVID-19 pandemic and lockdowns, inadequate social protection services were pervasive, particularly among TB communities and persons living with HIV. Pulmonologists shifted their attention from TB to COVID-19 care, affecting the availability of personnel for TB patient care. There was also an HIV/TB drug shortage in countries such as Ukraine [14].

The true impact of COVID-19 has yet to be determined. Tuberculosis diagnosis and treatment, particularly in Africa and other developing countries, stands to suffer significantly given the rate at which other health-care issues, and in particular infectious diseases of global importance, were put on hold, albeit temporarily. This is because most low-income countries still do not have pandemic emergency plans that follow science-based governance [15].

Effect of Covid-19-Related Disruptions on Prevention-Control of Infectious Diseases

Pre-COVID-19 pandemic, infectious disease outbreaks and endemicity in Sub-Saharan Africa, which kill over 3 million people annually and referred to as "humanity's health burden" [2] have persisted in

the population despite improvements in the treatment programs. On February 14, 2020, Egypt confirmed Africa's first case of COVID-19. Other African countries followed suit, with Nigeria reporting the first case of SARS-CoV-2 on February 27, 2020 [16]. This spread was rapid and unabated and sparked widespread concern throughout the world [17]. From then on, up until the middle of 2022, incidences of the disease continued to occur in a rather sporadic manner [18].

Africa's reliance on other countries for pharmaceuticals and other critical resources for drug development became hampered as COVID-19 confirmed cases and mortality rose, presumably because developed countries were themselves battling the plague as well. The emergence of new strains, the Delta and latter Omicron variants, further exacerbated Africa's already dire infectious disease control situation. Not done, BA.2, a relative of the major Omicron variant – BA.1, started displacing its sibling in countries all over the world as observed in countries like Denmark, the Philippines, and South Africa. Worryingly, Africa, which has far fewer resources to deal with this pandemic, started becoming increasingly embroiled in outbreaks of new variants while the rest of the world struggled to deal with the initial surge.

A critical area where infectious diseases have had an impact is the economy of many nations. In 2017, Sub-Saharan Africa spent about 5.17 percent of its total GDP on health, according to the World Bank. The percentage of GDP spent on health care is much lower than the national average, potentially reversing recent achievements in human development. One of the resultant effects of COVID-19 on the African economy, is high inflation in African markets, according to indications. The impact on small-scale traders in developing economies was huge; local commodity prices rose, and most countries resorted to budgetary adjustments to deal with the situation, with little success in averting economic downturns. Low revenue creation correlating to reduced tax rates, became evident on Africa's fiscal results, as demonstrated in the African mining and tourism industries [19]. COVID-19's negative impact on the global community and on people's lives extended to, not only in terms of public health, but also in terms of politics, the economy, and government services. To make matters worse, the African health-care system pre-COVID was quite vulnerable, resulting in a more disastrous impact from the pandemic.

The agricultural sector was also impacted by the COVID-19 disease on a global scale. While the pandemic persisted, a rise in agricultural produce prices was experienced and was believed to be linked to a lack of labor due to restrictions on movement, as well as a lack of operational activities by companies

involved in food production and processing. Africa experienced disruptions in livestock supply chains due to factors such as limited access to inputs and services, transportation and roadblocks, restricted labor movements, and increased credit financing or poor liquidity, which resulted in higher food prices [20].

COVID-19 caused a shift in focus, with donor-nation aid cuts, travel restrictions, and lockdowns all exacerbating the issue. Its far-reaching consequences in Africa, was not because of the high number of cases or fatalities, but because of its implications for other common diseases, poverty, food security, and economic growth. This is so because, even without COVID-19, quantifying the potential impact of various intervention approaches on mortality caused by malaria, TB, and HIV is challenging. A pandemic, such as COVID-19, should be contained quickly; otherwise, it could result in significant increases in tuberculosis and malaria mortality, with estimates ranging from 10% to 20% to 36% over a 5-year period in high-burden environments [21], as the already overburdened health-care system will be overworked, resulting in significant disruptions in healthcare services. COVID-19-related disruptions in everyday operations and services have the potential to undo years of hard-won successes in tuberculosis and malaria control and eradication programs in infectious disease-endemic countries.

According to Hogan et al., [21] mitigation strategies implemented in response to the COVID-19 pandemic have resulted in a reduction in certain activities and care-seeking; decreased health-care capabilities due to an overwhelmingly high demand for COVID-19-related care; and commodity supply disruptions due to effects on both domestic and international supply chains.

This is in spite of the fact that progression of the COVID-19 disease in Africa was relatively slow in comparison to other continents [22]. The shift in attention is evidenced by the vigorous and sustained global efforts made to contain the disease through the processes of prevention, diagnostics, management, and treatment, but which has resulted in lower healthcare costs in malaria interventions [23]. The long-term consequences of this neglect, no matter how brief, can be huge. For instance, mutant Poliovirus Type 2, a new strain of poliovirus, emerged in the wake of the COVID-19 pandemic. The strain, known as Circulating Vaccine-Derived Poliovirus type 2, was allegedly derived from the Oral Poliovirus Vaccine (OPV) that was detected in countries such as Pakistan, Sudan, Chad, Nigeria, and Somalia. Immunization gaps, characterized by a period of sensitivity during which the host's antibody levels are low in the relevant populations are thought to be the cause of the emergence of this mutant strain [24].

Because other highly endemic infectious diseases, particularly malaria and tuberculosis, were almost entirely ignored in Africa's current COVID-19 pandemic control measures, patients increasingly turned to self-help, with the potential to result in the evolution and spread of drug-resistant pathogens, as well as a reduction in expected outcomes such as in patient productivity due to increased morbidity from endemic infectious diseases like HIV/AIDS, TB, and malaria [22]. Evidence-based data gathered in countries where the Global Fund invests shows that the number of persons treated for drug-resistant TB in those countries decreased by roughly 19% between 2019 and 2020. According to the findings, people receiving treatment for extensively drug-resistant tuberculosis had a higher decline (37%). In 2020, the number of HIV-positive TB patients receiving antiretroviral therapy as well as TB treatment declined by 16%, with about one million fewer persons receiving TB treatment than in 2019 [10].

With the tangle of new mutations, one hopes that poorer nations do not become reservoirs for the SARS-CoV-2 virus, as has become the case with malaria and tuberculosis. Following discoveries on mutations and the numerous variants that emerged during the COVID-19 pandemic, a bleak image for the world's poorest countries when it comes to combating new and emerging infectious illnesses was portrayed.

CONCLUSION

Clearly, Africa's high death rate from infectious diseases, which is believed to be approximately 3 million people each year, is concerning.

Tuberculosis, malaria, and HIV/AIDS are concentrated in low-income resource-depleted settings, as opposed to high-income countries where living standards are high, and deprivation is minimal or non-existent. Low living standards, malnutrition, and poverty, as well as a lack of political will, influence, and strategy on the part of governments to reduce disease occurrence in low-income countries, all contribute to their sustained prevalence. Multidrug resistance, and the seemingly never-ending sporadic surge of new-emerging and re-emerging infectious diseases that tend to divert the attention of low-income governments away from dealing with the three main contending diseases – tuberculosis, malaria and HIV/AIDS are among the many other challenges confronting low-income countries and exacerbating the situation. During the first phase of the COVID-19 pandemic, a lack of will to do what was necessary to contain its spread by some economically less endowed countries that are TB endemic, resulted in many deaths as well as a tremendous economic and psychological strain on their

populations. COVID-19 has had a terrible impact on the battle against HIV, TB, and malaria among peoples, with apparent negative implications on highly regarded support groups and organizations whose core program successes regressed. One can only imagine the degree to which COVID-19 outcome impacted poor countries' efforts to combat other infectious diseases.

At its peak, the COVID-19 pandemic cast a pall over the diagnosis and treatment of most other serious infectious and non-infectious diseases worldwide, particularly in the less economically endowed countries, many of which are found in Sub-Saharan Africa. Continued disregard for other diseases, such as tuberculosis, in the event of an outbreak of a highly contagious illness with a high mortality risk, will almost certainly have severe consequences for the region's life expectancy and economic growth; a consequence that will become apparent sooner rather than later if an effective cure for this fatal disease, tuberculosis, is not discovered immediately.

Even though the progression of COVID-19 in Africa was relatively slow in comparison to other continents, it was evident that its emergence put additional strain on poor countries already failing health systems. The World Health Organization has made strident efforts in selecting the first six African countries: Egypt, Kenya, Nigeria, Senegal, South Africa, and Tunisia, which earlier applied, as recipients of the technology required to produce mRNA vaccines on the African continent. It is therefore hoped that whatever little attention is still paid to malaria, tuberculosis and other infectious diseases

will not be completely lost as attention shifts to the production of COVID-19 vaccine in Africa, in view of a likely diversion of scarce resources.

Notwithstanding the apparent setbacks highlighted, we anticipate that with renewed efforts, particularly stakeholder interventions that prioritize TB, malaria and HIV/AIDS care, well-planned policies and strategies, good follow-up on plans, a motivated health workforce with available support and resources, and patients' adherence to treatment, a more rapid progress toward achieving a tuberculosis-free world will be possible sooner rather than later. Even though clinical studies have yet to be finished, the current roll out of Oxford University's R21 malaria vaccine in Africa; Ghana and Nigeria being the first recipients, is significant and a positive news. Despite competing odds such as COVID-19, this ambitious attempt shows that Africa may be on the verge of a new dawn in infectious disease control and management.

There is also a need to focus on diagnosing childhood tuberculosis and improving reporting and documentation to ensure prompt data availability in Africa, as this will undoubtedly help to reverse current endemicity in parts of Africa, Asia, and South America.

Improvements in the health sector, as well as ensuring that the country's GDP leans more strongly towards the health sector, are viable answers to the experiences gained by African countries because of the effects of COVID-19. This should be done on purpose, in anticipation of future epidemics and pandemics. To minimize drug shortages, African governments must invest in medical security.

Conflict of interest: none declared
Financial support: none declared

REFERENCES

1. Fukunaga R, Glaziou P, Harris JB, Date A, Floyd K, Kasaeva T. Epidemiology of Tuberculosis and Progress Toward Meeting Global Targets - Worldwide, 2019. *MMWR Morb Mortal Wkly Rep.* 2021;70(12):427-30. Epub 20210326. doi: 10.15585/mmwr.mm7012a4. PMID: 33764960. PMCID: PMC7993552.
2. Muller FL, Song W, Liu Y, Chaudhuri A, Pieke-Dahl S, Strong R et al. Absence of CuZn superoxide dismutase leads to elevated oxidative stress and acceleration of age-dependent skeletal muscle atrophy. *Free Radic Biol Med.* 2006;40(11):1993-2004. Epub 2006/05/24. doi: 10.1016/j.freeradbiomed.2006.01.036. PMID: 16716900.
3. Saleem A, Azher M. The next Pandemic-Tuberculosis: The oldest disease of mankind rising one more time. *BJMP.* 2013;66:21.
4. Organization WH. Meeting report of the WHO expert consultation on the definition of extensively drug-resistant tuberculosis, 27-29 October 2020. 2021.
5. Chakaya J, Petersen E, Nantanda R, Mungai BN, Migliori GB, Amanullah F et al. The WHO Global Tuberculosis 2021 Report - not so good news and turning the tide back to End TB. *Int J Infect Dis.* 2022;124(Suppl 1):S26-s9. Epub 20220320. doi: 10.1016/j.ijid.2022.03.011. PMID: 35321845. PMCID: PMC8934249.
6. Narain JP, Dawa N, Elo O. Eliminating malaria, tuberculosis & HIV/AIDS in South-East Asia: Why cross-border is so critical. *Medknow;* 2022.
7. Snow RW, Sartorius B, Kyalo D, Maina J, Amratia P, Mundia CW et al. The prevalence of *Plasmodium falciparum* in sub-Saharan Africa since 1900. *Nature.* 2017;550(7677):515-8.
8. Organization WH. Interim recommendations for use of the inactivated COVID-19 vaccine, CoronaVac, developed by Sinovac: interim guidance, first issued 24 May 2021, updated 21 October 2021, updated 15 March 2022. World Health Organization, 2022.
9. Organization WH. World malaria report 2022: World Health Organization; 2022.
10. Yaqoob A, Hinderaker SG, Fatima R, Shewade HD, Nisar N, Wali A. Diagnosis of childhood tuberculosis in Pakistan: Are national guidelines used by private healthcare providers? *Int J Infect Dis.* 2021;107:291-7. Epub 20210422. doi: 10.1016/j.ijid.2021.04.055. PMID: 33895413.
11. Seki M, Kim CK, Hayakawa S, Mitarai S. Recent advances in tuberculosis diagnostics in resource-limited settings. *Eur J Clin Microbiol Infect Dis.* 2018;37(8):1405-10. Epub 20180419. doi: 10.1007/s10096-018-3258-y. PMID: 29675788.
12. Thakur G, Thakur S, Thakur H. Status and challenges for tuberculosis control in India—Stakeholders' perspective. *Indian J Tuberc.* 2021;68(3):334-9.
13. Organization WH. Global tuberculosis report 2021: supplementary material. Global tuberculosis report 2021: supplementary material2022.

14. Organization WH. Report of the Regional Director: the work of the WHO Regional Office for Europe in 2020–2021. World Health Organization. Regional Office for Europe, 2021.
15. Cloeckaert A, Kuchler K. Grand Challenges in Infectious Diseases: Are We Prepared for Worst-Case Scenarios? *Front Microbiol.* 2020;11:613383. Epub 20201130. doi: 10.3389/fmicb.2020.613383. PMID: 33329504. PMCID: PMC7734098.
16. Mennechet FJ, Dzomo GRT. Coping with COVID-19 in sub-Saharan Africa: what might the future hold? *Viral Sin.* 2020 Dec;35(6):875-84. doi: 10.1007/s12250-020-00279-2.
17. Osseni IA. COVID-19 pandemic in sub-Saharan Africa: preparedness, response, and hidden potentials. *Trop Med Health.* 2020;48:48. Epub 20200617. doi: 10.1186/s41182-020-00240-9. PMID: 32550822. PMCID: PMC7298917.
18. WHO Guidelines Approved by the Guidelines Review Committee. Clinical management of COVID-19: Living guideline. Geneva: World Health Organization; 2022.
19. Lone SA, Ahmad A. COVID-19 pandemic—an African perspective. *Emerging microbes & infections.* 2020;9(1):1300-8.
20. Ejeromedoghene O, Tesi JN, Uyanga VA, Adebayo AO, Nwosisi MC, Tesi GO et al. Food security and safety concerns in animal production and public health issues in Africa: A perspective of COVID-19 pandemic era. *Ethics Med Public Health.* 2020;15:100600. Epub 20200929. doi: 10.1016/j.jemep.2020.100600. PMID: 33015275. PMCID: PMC7523516.
21. Hogan AB, Jewell BL, Sherrard-Smith E, Vesga JF, Watson OJ, Whittaker C et al. Potential impact of the COVID-19 pandemic on HIV, tuberculosis, and malaria in low-income and middle-income countries: a modelling study. *Lancet Glob Health.* 2020;8(9):e1132-e41. Epub 20200713. doi: 10.1016/s2214-109x(20)30288-6. PMID: 32673577. PMCID: PMC7357988.
22. Teboh-Ewungkem MI, Ngwa GA. COVID-19 in malaria-endemic regions: potential consequences for malaria intervention coverage, morbidity, and mortality. *Lancet Infect Dis.* 2021;21(1):5-6. Epub 20200921. doi: 10.1016/s1473-3099(20)30763-5. PMID: 32971007. PMCID: PMC7505551.
23. Nghochuzie NN, Olwal CO, Udoakang AJ, Amenga-Etego LN, Amambua-Ngwa A. Pausing the Fight Against Malaria to Combat the COVID-19 Pandemic in Africa: Is the Future of Malaria Bleak? *Front Microbiol.* 2020;11:1476. Epub 20200618. doi: 10.3389/fmicb.2020.01476. PMID: 32625198. PMCID: PMC7314964.
24. Macklin GR, Goel AK, Mach O, Tallis G, Ahmed JA, O'Reilly KM et al. Epidemiology of type 2 vaccine-derived poliovirus outbreaks between 2016 and 2020. *Vaccine.* 2023;41 Suppl 1:A19-a24. Epub 20220822. doi: 10.1016/j.vaccine.2022.08.008. PMID: 36008232.