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COVID-19: A unique opportunity to improve laboratory capacity for neglected tropical diseases in sub-Saharan Africa

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While many public health and university laboratories have become involved in COVID-19 testing during the pandemic, these laboratories now run the risk of being underutilized as COVID-19 testing wanes. This is particularly true of established COVID-19 laboratories in many low- and middle-income countries (LMICs). In this article, we make a case for repurposing many of these laboratories to support control programs for neglected tropical diseases (NTDs) in endemic countries as they contemplate how to strengthen laboratory capacity for all endemic and emerging epidemiological diseases.

KEYWORDS

NTDs, COVID-19, laboratory capacity strengthening, diagnosis, onchocerciasis

Introduction

The COVID-19 pandemic has tested the strength of the most developed health systems and created a global economic and health crisis. After a prolonged period of trying to control different variants of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), there have been unprecedented achievements in the development and production of COVID-19 vaccines. Approximately 66.8% of the world population have received at least one dose of a COVID-19 vaccine (as of April 2022) and 60% are fully vaccinated (1, 2), although there are concerns about the equality of vaccine coverage (3, 4).

Non-pharmaceutical interventions (NPIs), intended to halt the rate of transmission and reduce mortality, were the principal control strategies at the initial stage of the pandemic (5). This included the rapid identification of cases and isolation of confirmed and probable cases, with the primary aim of maintaining health systems' capacity to identify, isolate, and treat as many cases as possible. Central to this control strategy was

the capacity of laboratories to diagnose samples of suspected cases quickly and correctly. This strategy necessitated a global ramping up of molecular diagnostic capacity including in Africa where such capacity was hitherto limited. The African Centre for Disease Control and Prevention (Africa CDC) led the mobilization of resources and coordinated with partners to scale up testing capacity in member countries. Ethiopia established 65 testing centers-up from zero-with molecular testing capability for COVID-19, with at least one center in every regional state within 10 months (6). A similar observation was recorded in Nigeria where the number of laboratories with COVID-19 testing capacity increased from an initial 3 to 28 throughout 18 states as of May 2020 (7). Currently, all 36 states and the Federal Capital Territory of Nigeria have COVID-19 diagnostic capabilities, and 28 states across the 6 geopolitical regions have polymerase chain reaction (PCR) diagnostic capabilities. The COVID-19 diagnostic capacity of the Ghanaian health services increased from 2 to 16 centers within 7 months (8). However, as countries contemplate how to consolidate these gains in laboratory capacity for all endemic and emerging epidemic diseases, we are making a case for repurposing COVID-19 laboratories to support the control programs for neglected tropical diseases in endemic countries given the current status of the pandemic, with lockdowns being lifted and the need for established laboratories is decreasing.

Diagnosis of neglected tropical diseases and the 2030 roadmap targets

Neglected tropical diseases (NTDs) are a group of diseases mostly affecting those in poverty and imposing a devastating human, social, and economic burden on more than 1 billion people worldwide. Mainly prevalent in tropical and subtropical areas, sub-Saharan Africa accounts for 40% of all global NTD cases, burden, and atrisk populations (9). The World Health Organization (WHO) recently released a 10-year NTD elimination roadmap to accelerate the control and elimination of these diseases targeting to reduce the burden of these diseases and eliminate such diseases in endemic countries by 2030 (10). The roadmap sets disease-specific targets, provides milestones to measure progress toward achieving the targets, and highlights gaps that need to be addressed to achieve the targets. Diagnostics has been identified as one of the critical gaps that would impede progress toward achieving the 2030 targets for multiple NTDs (11). Accurate and reliable diagnosis is an essential component of the monitoring and evaluation (M&E) of NTDs programs. Confirmation of interruption of transmission and elimination of diseases, treatment decisions that include frequency change or mass treatment stoppage, post-treatment, and postelimination disease surveillance are all decisions in disease control that are based on information available only from diagnostics.

Despite the critical role of diagnosis in the different phases of disease control and elimination, it is an inadequately emphasized component of many national NTD masterplans, such as the national roadmap recommended by WHO to bring NTDs under control and some toward elimination. For instance, there is no strategic plan for the development of diagnostic capacity for endemic NTDs in the NTD masterplans of Nigeria, Malawi, Rwanda, and Ethiopia (12-15). Furthermore, the NTD community has traditionally underinvested in the development of diagnostic tools and capacity-building in endemic countries. This precarious situation has only been further exacerbated by the COVID-19 pandemic with indications of reprioritization of resources toward the control of SARS-CoV-2 (16). The overarching NTD investment strategy is delivering mass drug administration (MDA) or treatment costing US 63 cents, considered a best buy in global health (17). Prioritization of resource allocation toward MDA for preventive chemotherapy is somewhat justified given that fewer resources are available to programs in NTD endemic settings. However, progress toward disease elimination warrants a shift in focus toward other critical elements of the elimination program, and instances of missed opportunities to address challenges should be avoided. Expeditiously strengthening the less developed components of these programs is important because delays in identifying and addressing problematic areas will unnecessarily slow the interruption of transmission, delay neighboring areas or countries from completing post-treatment or post-elimination surveillance, and prolong the program (18). Inadequate laboratory capacity is an increasingly significant obstacle to meeting global control and elimination targets for many NTDs in the 2030 WHO-NTD roadmap. This issue is evidenced by specimen backlogs from surveillance activities that have not been analyzed due to limited laboratory capacity in number of endemic sub-Saharan African countries (19), causing delays in programmatic decision-making.

Opportunities for capacity strengthening

Despite an obvious dearth in laboratory infrastructure and capacity in Africa, a unique opportunity for strengthening specific components of diagnostic and laboratory capacity needs for disease control on the continent was capitalized on since the onset of the COVID-19 pandemic. The rapid scale-up of the decentralized capacity to diagnose SARS-CoV-2 throughout the continent despite the resource challenges posed by the pandemic exemplified what can be achieved with the right political will and unity of purpose. These were crucial to the success accomplished by the efforts to control the pandemic on the continent amidst the many dire predictions of deaths on the continent (20). Nucleic acid amplification tests (NAATs),

including PCR and rapid diagnostic tests (RDTs), were central to SARS-CoV-2 diagnostics and are also commonly used for NTD diagnostics. Nevertheless, the increasing curtailment of quarantine measures and testing requirements, for international travelers as well, against the backdrop of increased vaccinations (21) and the slowing of new and symptomatic cases will likely result in less of a need for the established COVID-19 testing centers and infrastructure in lowand middle-income countries (LMICs). While surveillance for SARS-CoV-2 and emerging variants will be ongoing in most countries, the scaling-down of the resources put in place to combat COVID-19 is inevitable due to high maintenance costs, especially in LMICs. For example, it costs three times as much to procure a similar set of reagents for COVID-19 diagnosis in Nigeria as it costs in developed countries (Christian Happi, Personal Communications). However, making these resources available for NTD programs in endemic countries will ameliorate some of the challenges of in-country NTD diagnostics, reduce disparity in investment in NTD diagnostics (11), and contribute to long-term cost efficiency. Our experiences have shown that laboratory diagnostics account for more than one-third of the cost of essential programmatic surveys such as the onchocerciasis elimination mapping (OEM) surveys (22). Access to a dedicated laboratory by NTD programs would likely help in cost reduction by enabling bulk purchasing of consumables at competitive pricing and by facilitating the inclusion of imported diagnostics on the Ministry of Health (MoH) exemption list, effectively removing or reducing importation and customs costs. Furthermore, programs would benefit from the laboratory space provided for longer-term storage of basic laboratory reagents, sample storage, and an avenue for the standardization and quality assessment of NTD diagnostics.

NTD diagnostics can be broadly grouped into NAATs, RDTs, enzyme immunoassays (EIAs), and microscopy (23). Classical clinical and microscopic techniques are employed and largely adequate for mapping disease distribution and monitoring the progress of most NTD interventions (11). RDTs employed in M&E surveillance have shown improved performance when used in laboratories rather than in field settings (24, 25), and routine utilization of NAATs and EIAs is increasingly being required to advance elimination objectives (26). These methods require laboratory infrastructure that is often not easily accessible to NTD control programs given that NTDs are typically found in settings with fragile health care systems with weak laboratory infrastructure. Furthermore, newly-developed and promising diagnostic techniques for addressing programmatic needs in low-prevalence settings are often NAATs, which emphasize the importance of PCR and molecular testing capabilities to the control and elimination of NTDs.

The evidence needed to prove the interruption of transmission and to confirm the elimination of diseases such

as onchocerciasis is a confirmed negative PCR test result of the blackflies vectors in endemic regions for the Onchocerca volvulus parasites (27). The detection of DNA from the microfilariae of lymphatic filariasis (LF) in human blood and mosquito vectors using PCR is a potential diagnostic method for the disease. In fact, post-MDA surveillance for LF elimination verification after transmission assessment surveys (TAS) requires an entomological assessment of parasites in mosquito vectors using PCR to inform transmission interruption or recrudescence (28). PCR molecular methods are also used for the diagnosis of NTDs other than onchocerciasis, such as Buruli ulcer, leishmaniasis (29), human African trypanosomiasis (30), schistosomiasis (31), dengue (32), chikungunya (33) and soiltransmitted helminths (34). These methods are often unavailable for programmatic use in LMICs where NTDs are endemic mostly because of a lack of laboratory infrastructure and capacity. The upfront cost of providing thermocyclers and qPCR equipment for the different NAATs can be offset by using a repurposed COVID-19 laboratory.

Discussion

Strategically repurposing COVID-19 infrastructure could be the catalyst for a global NTD laboratory network. NTD programs currently lag behind other global health programs that have globally connected networks of laboratories and systems for externally validating laboratory data as recommended by the World Health Assembly (35). Strong NTD laboratory systems will be able to address both research and program needs. Reliable and accessible laboratory services that produce quality-assured results in a timely manner are critical for any country's surveillance capacity (36) and are an essential component of disease control programs. Laboratories would still need adequate support to improve their capacity with respect to specific NTD diagnostics and protocols to provide high-quality laboratory data for informed decision-making. The operational capacity of laboratory technicians to perform adequate, quality-assured laboratory analysis in the context of NTD diagnosis can be improved through a formal training program. Established laboratory networks with infrastructure and capacity are better positioned to access support and global health equity from diagnostics manufacturers.

Establishing a formal NTD laboratory network that can provide quality assurance and referral functions for NTD programs has been a priority of the WHO Strategic and Technical Advisory Group (STAG) (37). Likewise, it has been a point of discussion at NTD management meetings for quite some time (19). Despite the prioritization and discussion efforts, little has been achieved in getting this off the ground. NTD laboratory expertise in endemic low-resource settings is often fragmented and uncoordinated, with no formal referral system or network to provide the required support for quality assurance of NTD testing (38). Shott et al. (39) described a framework for establishing a laboratory network for onchocerciasis diagnosis and identified the standardization of protocols, QA systems, supply chains, and communication systems as essential components. These are pronounced and thoroughly utilized components of the laboratory coordination deployed to produce a daily national overall COVID-19 data in all sub-Saharan African countries and can be adapted for use in NTDs. Embarking on a strategic plan to repurpose some of the COVID-19 infrastructure and capacity for NTD control could be a critical moment in solving the infrastructure and supply-chain logistics challenges associated with NTD diagnostics, given that control programs would have hitherto not been able to command such resources. Alternatively, frameworks of extant networks such as that of the Buruli ulcer laboratories can also be adapted to establish a sustainable NTD laboratory network (40).

Whatever existing infrastructures can be leveraged or created, establishing an NTD laboratory network that is interconnected and in which individual laboratories can rely on each other for mutual support will require deliberate resource commitment. Laboratory networks should build on the momentum created by the WHO's global genomic surveillance strategy for pathogens with pandemic and epidemic potential to sustain the gains made during the COVID-19 response and to strengthen capacities (36). Support will be needed to establish an NTD diagnostics external quality assessment (EQA) program that allows participating laboratories to assess their capabilities by comparing their results to those obtained via the laboratory network through panel testing, blinded rechecking, on-site supervision, and mentoring. The EQA program can facilitate the definition of standard operating procedures for diagnostics, data flow, and protocols; establish a robust QA/QC system and coordinate the supply-chain management of participating laboratories by forecasting the diagnostic needs for each country's control programs, which may be at different stages. Furthermore, an EQA program provides the advantage of deviating from the current practice of strategic decisions about program implementation being based on laboratory data generated by laboratories working in isolation that are not enrolled in any external quality assurance scheme (38).

Conclusion

The increased availability of molecular technical capacity in LMICs due to COVID-19 has provided an opportunity that should be capitalized on to scale-up existing international networks of NTD laboratories such as the NTD Laboratory Coordinating Bureau, African Research Network for NTDs, and Centre for NTDs. Alternatively, the described frameworks for the establishment of an NTD laboratory network should be adopted (39, 40); and WHO resources such as the WHO's Stepwise Laboratory Improvement Towards Accreditation (WHO-

SLIPTA) tool and the African Society of Laboratory Management's (ASLM) Strengthening Laboratory Management Towards Accreditation (SLMTA) program can be used to enhance the quality assurance process of potentially repurposed COVID-19 testing laboratories. Tools such as those described by Njelesani et al. (41) can be used to monitor achievable progress. An early success of this initiative, if implemented, could be the clearance of the backlogs of NTD specimens, which resulted from limited technical and personnel capacity in a *quid pro quo* for earlier support NTD programs provided to COVID-19 control efforts.

Summarily, the described opportunity to improve NTD diagnostics can be approached by (1) revising the national NTD masterplans to include the adaptation of established COVID-19 laboratories as a strategy to improve local NTD diagnostic capacity; (2) training COVID-19 laboratory technicians on NTD diagnosis; (3) providing supply-chain support for essential NTD laboratory supplies; (4) establishing an international network of NTD laboratories; (5) establishing a QA/QC framework *via* any of the extant models, and; (6) establishing a general laboratory quality management framework.

However, repurposing COVID-19 laboratories to support NTD programs in LMICs will require initial funding support that would be cheaper, more cost-effective, and more sustainable than establishing new vertical laboratories. Having the WHO lead and provide centrally coordinated technical oversight of multi-organizational efforts will ensure full accountability, better resource utilization, and stronger support in overcoming some of the diagnostics challenges identified in the 2030 WHO-NTD roadmap.

Authors contributions

AA and LH conceptualized the study. AA wrote the first draft. All authors read and approved the final version of the article.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as potential conflicts of interest.

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