Improving Laboratory Capacity; A necessity towards elimination of malaria in Nigeria

Obunge O. K[1], Oboro I. L[1], Chijioke-Nwauche I.N[2]

[1]Department of Medical Microbiology, Faculty of Basic Medical Sciences, University of Port Harcourt, Port Harcourt, Nigeria

[2]Department of Clinical Pharmacy and Management, Faculty of Pharmaceutical Sciences, University of Port Harcourt, Port Harcourt, Nigeria

ABSTRACT

The quest to achieve malaria elimination requires that all the steps leading to its achievement should be strengthened. One of the key areas of focus is assessment of diagnostic capabilities. Strengthening diagnostic testing will reduce mortality through administration of the exact recommended treatment. The article addresses the challenge of diagnosis within the context of the current concerted drive to achieve malaria elimination in Nigeria. One of the key facts emphasized is the need for the establishment of Reference laboratories in various parts of the country with the required facilities, expertise, supply chain, funding, political and administrative support.

Key Words: Elimination, diagnosis, molecular techniques, reference laboratories.

Malaria is caused by Plasmodium parasites that are transmitted to people through the bites of infected female Anopheles mosquitoes. Though it is a life-threatening disease, it is preventable and curable. The WHO African Region where Nigeria lies, continues to bear a disproportionately high share of the global malaria burden, accounting for 93% of cases and 94% of deaths from malaria in 2018 [1].

In line with the World Health organization's vision of achieving malaria elimination in various regions of the world and its eradication ultimately, the Nigerian government launched the National malaria elimination program (NMEP), domiciled in the Federal and State Ministries of health, through which various efforts have been made towards achieving malaria elimination in Nigeria. In 2015, the director of the NMEP shared the National malaria strategic plan in which the goal was to reduce malaria burden to pre-elimination levels and bring malaria-related mortality to zero by 2020 [2].

Elimination defined as Interruption of local transmission (reduction to zero incidence of indigenous cases) of a specified malaria parasite species in a defined geographical area as a result of deliberate activities implies zero transmission of malaria in a geographical region because only after transmission of all human Plasmodium parasites is interrupted is a certificate of elimination issued [3].
In the past decade, 10 countries (including Algeria) were certified by WHO to have eliminated malaria[1]. This proves that elimination is possible, however; it is a task that requires a well-coordinated approach, which should be designed after critically appraising the various factors that determine transmission of malaria in Nigeria.

The steps to elimination starts from malaria control through pre-elimination and elimination phases before finally working to prevent reintroduction. Key considerations and thus areas of focus should include unique transmission dynamics of local settings (effects of seasonal variations, weather pattern and differing topography), diagnostic capabilities, therapeutic options and control efforts including surveillance systems. Post- eradication management is also critical to prevent a re-introduction of malaria. Hence, long-term strategic planning has to be made.

Thankfully, a lot of progress has been made as incidence and mortality rates in Nigeria and globally, continues to drop; most of these gains being attributed to the increased use of insecticide treated bed nets and indoor residual spraying, and the global push to test and treat [1,3].

With regards to diagnosis, the World Health

Organization (WHO) Global malaria program's framework for malaria elimination which provides guidance for countries as they work towards elimination, buttresses the need to optimize currently and commonly available laboratory techniques such as malaria microscopy and the use of rapid diagnostic tests (RDTs) for diagnosis and monitoring of infections reiterating that these are veritable tools as evidenced in regions that have successfully achieved elimination [3].

Molecular method is a tool that plays a role both in the area of clinical diagnosis and malaria epidemiology. This approach questions the use of microscopy as the gold standard for malaria diagnosis being of higher sensitivity and specificity while molecular epidemiology leverages on genetic information to study risk factors and transmission dynamics [4].

The need for molecular methods such as polymerase chain reaction (PCR) arises due to but not limited to the identification of asymptomatically infected persons with low parasite density who serve as reservoirs of the plasmodium parasite [3, 4]. The PCR is also useful for the identification of molecular markers of malaria parasites that are resistant to treatment. These markers have been proven to be tools for surveillance of resistance, provide additional data that compliment clinical observations of the *in vivo* efficacy of a drug and has been instrumental to policy making with regards to control of malaria epidemic[6].

Also, following treatment of symptomatic infected persons, treatment failures versus re-infection can be elucidated more effectively using molecular methods to determine the genetic relatedness of the parasite before and after treatment[7].

Understanding the genetic diversity and structure of malaria parasite populations is the key for predicting the emergence and spread of phenotypes of interest, such as new antigenic or drug resistance variants[8, 9]. Sequencing is aimed to better understand the diversity of a gene under consideration as a vaccine candidate or because it harbors mutations linked to drug resistance[10, 11].

As part of the integrated vector approach, molecular identification of species and sibling species of Anopheline mosquitoes is an important tool to appreciate divergence of vector siblings and early detection and monitoring of insecticide resistance in local vectors[11].

In molecular characterization of progress made during pre and post-elimination, measures such as the complexity of infection, genetic relatedness of parasites causing infection, sources and sinks of outbreaks as well as anti-malarial drug resistance genes can be monitored effectively using genetic toolkits such as genetic barcodes and sequencing among others[7, 11]. This would certainly prove beneficial in sustenance of elimination

The major limitation associated with the use of molecular techniques would be their application to large numbers of specimens principally because of the associated high cost implication and technical expertise required [4], which at present is limited in Nigeria. It is therefore most effective to maximally apply them from the pre-elimination phase where we have fewer numbers of infections, however, we must invest in preparation now. To overcome PCR limitations, a more field-friendly and cost-effective diagnostic tool, the loop-mediated isothermal amplification (LAMP) which has no major capital equipment requirement, simplified DNA extraction methods, was developed[12]. The technique facilitates running amplification reactions in difficult test environments, enabling use outside of a high-tech laboratory and requires minimal training in addition to requiring less time compared to PCR[13].

One of the key roles of a reference laboratory as detailed in the WHO elimination framework is coordinating the referral of samples from district laboratories and providing confirmatory testing and special testing services (e.g. molecular and serological tests, expert microscopy) [3].

Therefore, in the move towards elimination, there is need to build capacity across the span of the country for ease of access, reduced turnaround time and better control. Reference laboratories with the required facilities, expertise, supply chain, funding and political and administrative support must be

established and equipped adequately. There should be a network for collaboration and easy exchange/ sharing of information necessary for technical development in requisite areas so all centers in the country progress at a similar pace.

Most importantly, these should be decentralized because failure of elimination in some parts of the country could strongly undermine elimination achieved in other regions of the country.

The combination of conventional and molecular techniques is helpful to ascertain how malaria incidence is affected by parasites, vectors, and human host populations and therefore contribute significantly in the elimination phase of malaria in Nigeria[7, 11].

REFERENCES

1. World Health Organization. Malaria Fact Sheet (2019). Available at https://www.who.int/news-room/fact-sheets/detail/malaria. Accessed November 5th, 2019.
2. Ezeigwe N. Nigeria's Road to Malaria Elimination by 2020. National Malaria Elimination Programme; 2015. Available at http://www.gbchealth.org/wp-content/uploads/2015/07/NC_NMEP_CAMA_2015_Final.pdf. Accessed October 2nd, 2019.
3. World Health Organization. A framework for malaria elimination (2017). Geneva: Licence: CC BY-NC-SA 3.0 IGO. Available at https://apps.who.int/iris/rest/bitstreams/1081424/retrieve. Accessed October 15th, 2019
4. Santana-Morales MA, Afonso-Lehmann RN, Quispe, MA, Reyes F, Berzosa P, Benito A. Microscopy and molecular biology for the diagnosis and evaluation of malaria in a hospital in a rural area of Ethiopia. *Malar J.* 2012; 11: 199. https://doi.org/10.1186/1475-2875-11-199
5. Djimde A, Doumbo OK, Steketee RW & Plowe CV. Application of a molecular marker for surveillance of chloroquine-resistant falciparum malaria. Lancet, 2001; 358, 890-1.
6. Mugittu K, Ndejembi M, Malisa A, Lemnge M, Premji Z, Mwita A, et al. Therapeutic efficacy of sulfadoxine-pyrimethamine and prevalence of resistance markers in Tanzania prior to revision of malaria treatment policy: Plasmodium falciparum dihydrofolate reductase and ihydropteroate synthase mutations in monitoring in vivo resistance. Am J Trop Med Hyg, 2000; 71, 696-702.
7. Conway DJ. Molecular epidemiology of malaria. ClinMicrobiol Rev. 2007; 20:188–204.
8. Arnott A, Wapling J, Mueller I, Ramsland PA, Siba PM, Reeder JC, Barry AE. Distinct patterns of diversity, population structure and evolution in the *AMA1* genes of sympatric *Plasmodium falciparum* and *Plasmodium vivax* populations of Papua New Guinea from an area of similarly high transmission. Malar J. 2014;13:233
9. Mascorro CN, Zhao K, Khuntirat B, Sattabongkot J, Yan G, Escalante AA, Cui L. Molecular evolution and intragenic recombination of the merozoite surface protein MSP-3α from the malaria parasite *Plasmodium vivax* in Thailand. Parasitology. 2005; 131:25–35.
10. Chenet SM, Branch OH, Escalante AA, Lucas CM, Bacon DJ. Genetic diversity of vaccine candidate antigens in *Plasmodium falciparum* isolates from the Amazon basin of Peru. Malar J. 2008; 7:93.
11. Gholizadeh S, NaseriKarimi N, Zakeri S, DinparastDjadid N. The Role of Molecular Techniques on Malaria Control and Elimination Programs in Iran: A Review Article. *Iran J Parasitol*. 2018; 13(2):161–171.
12. Notomi T, Okayama H, Masubuchi H, Yonekawa T, Watanabe K, Amino N, et al. Loop-mediated isothermal amplification of DNA. Nucleic Acids Res. 2000; 28 (12): E63. pmid:10871386
13. Polley SD, Gonzalez IJ, Mohamed D, Daly R, Bowers K, Watson J, et al. Clinical evaluation of a loop-mediated amplification kit for diagnosis of imported malaria. J Infect Dis, 208, 637-44.