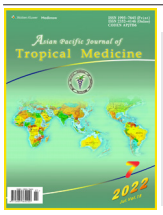

Perspective

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Hurdles in achieving the goal of malaria elimination by India

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India is a major contributor to the malaria burden in Southeast Asia, with 83% estimated cases and 82% estimated deaths reported in 2020[1]. As per the National Center for Vector-Borne Disease Control (NCVBDC) estimates, around 0.19 million cases and 93 deaths occurred in the country due to malaria in 2020. Since 2002, India has made impressive progress in malaria control with an approximately 90% reduction in malaria cases over the last two decades and is on the road to malaria elimination by 2030.

India detailed its elimination strategy in the National Framework for Malaria Elimination (NFME), launched in February 2016[2]. The critical approaches listed in NFME for nationwide malaria control include early diagnosis and radical treatment, case-based surveillance and integrated vector management supported by indoor residual spray, durable insecticidal nets and larval source management. Although a considerable reduction in malaria burden has been achieved using the existing interventions, there are several impediments to disrupting indigenous transmission. Malaria in India is mainly caused by two *Plasmodium* species-*Plasmodium (P.) falciparum* and *P. vivax*. Interestingly, India accounts for 50% of global *P. vivax* malaria cases and *P. vivax* causes nearly 40% of the country's malaria cases. To disrupt *P. vivax* transmission, the NFME advocates expansion of bivalent rapid diagnostic test (RDTs), an efficient detection of all *P. vivax* infections through microscopy and total compliance with the 14-day radical treatment by affected individuals.

In order to achieve the goal of malaria elimination within the defined time limit, it is essential to clear *P. vivax* malaria from communities completely. However, the unique biological characteristics of *P. vivax* render its elimination challenging. *P. vivax* forms hypnozoites in the liver of infected individuals that allow it to survive for weeks or months and cause relapses. To date, primaquine is the only recommended drug in India for a radical cure of *P. vivax* malaria that requires a 14-day regimen for adequate clearance of hypnozoites. Adherence to an extended treatment regimen is difficult if not supervised completely. Studies reported that drug compliance could be as low as 30% for radical cure in case of unsupervised treatment[3]. Therefore, the national program should implement direct-observed therapy to ensure complete *P. vivax* clearance. Furthermore, primaquine is known to induce hemolysis in G6PD deficient patients, which can be potentially life-threatening. Therefore, G6PD screening is also essential. However, point-of-care diagnostics for G6PD are not available. Moreover, primaquine is also contraindicated in infants and pregnant women, and treatment guidelines for clearance of hypnozoites in such patients are clearly lacking. In this context, tafenoquine might be helpful due to its single-dose regimen, but G6PD deficiency in the community will be a challenge[4]. Appropriately, point-of-care tests for determining the G6PD status of individuals before drug treatment need to be developed. Mapping G6PD deficiency across the nation, especially in *P. vivax* dominant regions, should be done to identify vulnerable subsets of the population. Detection of submicroscopic/asymptomatic malaria reservoirs in low transmission settings is another challenge for elimination. Sub-microscopic parasitemia is challenging to capture with routine microscopy and/or RDTs and plays a vital role in perpetuating malaria transmission. Successful detection of such infections is possible only by adopting molecular methods like polymerase chain reaction (PCR). A recent review on relapse in malaria reported that nearly half of the infections were missed by microscopy compared to PCR[5]. But PCR requires technical expertise, which is relatively expensive and difficult to

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conduct in field conditions. This could be overcome by developing easy, rapid and cheap techniques for molecular detection of the parasite, which can be handled by technicians at the primary health centre level (Figure 1). The current pandemic of COVID-19 has dramatically strengthened the country's infrastructure for molecular detection of the virus at multiple sites/levels. On similar lines, innovations should be encouraged and prioritized for developing high-sensitivity molecular diagnostic techniques capable of detecting parasites in field conditions with minimum expertise. Disease spread through migration further imposes difficulty in disruption of disease transmission. There are many uncontrolled movements of people from malaria-endemic areas like Odisha, Chhattisgarh, and Jharkhand to non-endemic areas resulting in reporting malaria cases from such non-endemic regions. Screening of such population is essential, but it is also a cumbersome task and will require the involvement of a lot of funding and human resources. However, the challenge can be addressed through inter-sectoral collaboration between government departments of labour employment and NCVBDC. Such associations will facilitate the screening of labour migrants for malaria enrollment in industry, construction sites, *etc*. Border malaria in the northeastern states of India, having international borders with Bangladesh, Myanmar and Bhutan, is also a significant concern. A recent study highlighted the role of malaria along the international borders in sustaining malaria in the adjoining districts of Tripura, Mizoram and Meghalaya. Low surveillance in most border districts, favourable climatic conditions for perennial malaria transmission, and movement of potential parasite carriers because of the porous borders are major reasons that promote disease transmission in these states[6]. Strengthening epidemiological surveillance through cross-border collaborations could be key to mitigating the importation or exportation of malaria cases in these areas.

In addition to the highlighted obstacles, the development of drug resistance and insecticide resistance by the parasite and vector respectively poses a big threat to the goal of malaria elimination which can only be resolved by the development of new drugs and insecticides[7]. The widespread use of long lasting insecticidal nets (LLIN) by the communities may have promoted outdoor malaria transmission, which needs to be identified and resolved. As India has deployed all the available control measures, therefore, evidence for residual malaria should also be gathered, and strategies should be modified accordingly to push through the last mile of elimination. Further, India should adopt new tools for malaria control which have proven effective elsewhere. The use of attractive toxic sugar baits (ATSB), endectocides (mass drug administration of population with ivermectin), zooprophylaxis are some of these innovative tools which have shown good results for malaria control in other countries[8,9]. We also need to be watchful of the strategies being adopted by other countries, which are also in the elimination phase and update/modify ours accordingly.

It seems that eliminating malaria from the country by 2030 is an uphill task. Addressing underscored issues will escalate the journey towards the goal of malaria elimination.

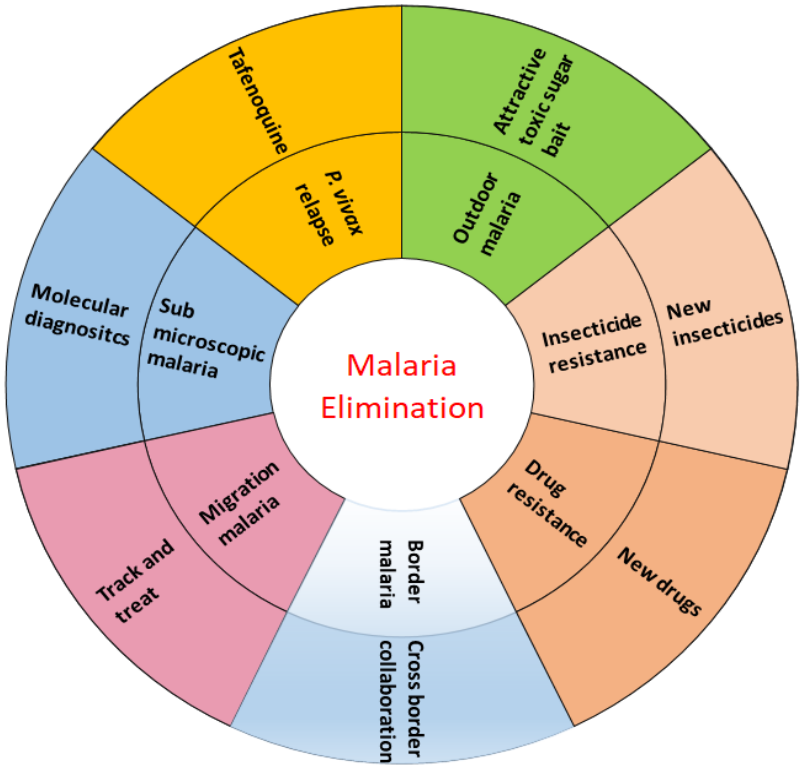

Figure 1. Major hurdles along with the possible solutions for the elimination of malaria in India.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

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Authors' contributions

GK and SP conceptualized and drafted the manuscript. GK, SP and JK reviewed the manuscript and finalized it.

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