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Short Commentary Open Access

A Short Commentary on Temporal Dynamics of Subclinical Malaria in Different Transmission Zones in Myanmar

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Abstract

The role of ultrasensitive Polymerase Chain Reaction (usPCR) in detecting low-density infections compared to conventional Rapid Diagnostic Tests (cRDT) amid the doubtful field applicability of advanced molecular laboratory methods in resource poor settings. The article demonstrated the vital role of testing in border areas and identifying high risk groups and hot spots by point-of-care diagnostics. Moreover, Glucose 6-phosphate dehydrogenase deficiency is alarming when using primaquine for radical cure of *P.vivax* infections. The hsRDT is capable of detecting subclinical malaria in low transmission settings but is limited by the controversial issue of its cost-effectiveness.

Keywords: Cost effectiveness; *P. vivax*; Subclinical malaria; Surveillance system

About the Study

Reaching the global malaria elimination goal by 2030 faces many challenges in the Greater Mekong Subregion (GMS). Myanmar remains the country with the highest malaria burden in the GMS linked with the high prevalence of artemisinin partial resistance associated with PfKelch13 mutations alongside persistent transmission of malaria [1]. Egger , et al., in their recent publication in the "American Journal of Tropical Medicine and Hygiene" highlighted the temporal dynamics of subclinical malaria in low endemic areas of Myanmar

The Authors discussed the role of ultrasensitive Polymerase Chain Reaction (usPCR) in detecting low-density infections compared to the conventional Rapid Diagnostic Tests (cRDT) in the study cohort, their evidence suggested a more or less similar transmission pattern of subclinical, low-density malaria amid temporal dynamics in three epidemiologically distinct sites particularly among older age groups, those with significant outdoor exposure and travellers [2].

Subclinical malaria

usPCR is a novel diagnostic tool which was able to identify the dominance of *P. vivax* compared to P. *falciparum* (6% vs. 1.5%) at the cross-sectional time point, and was able to identify the significant reservoir of subclinical malaria which is left undetected by standard cRDTs. The Limit of Detection (LOD) of usPCR is approximately 16 parasites/mL for P. falciparum and 49.5 copies/mL for *P. vivax*, more than 5,000-fold more sensitive than cRDT. The authors confirmed that blood samples could be collected by trained village volunteers using Dry Blood Spot (DBS) without any cold chain requirement. Still the field applicability of advanced molecular laboratory methods in resource poor settings remains unresolved [3]. A systematic review of 18 studies in 2022 revealed that the pool prevalence of malaria in asymptomatic populations was 46% higher using a hsRDT compared to a cRDT, although that varied by concentration and parasite density in the peripheral blood. The hsRDT had a higher sensitivity (64.1%) compared to microscopy and cRDT (59% and 53.8% respectively) [4]. hsRDT is a reliable, low cost, point-of-care test which detects asymptomatic infections in targeted populations [5]. t (< $1.00 USD), uses uncomplicated technology, portable testing and provides immediate results [6].

Cross-border infections

The article importantly included the border areas of Myanmar, China, and India as study sites. Without addressing the cross-border problem, malaria elimination in the GMS will not be possible by 2030. In this connection, China has piloted and successfully implemented a 3+1 strategy to reduce border malaria between Myanmar and Yingjian County of China [7]. In recent years, conflict affected sites with a high degree of internal displacement have become a focus of persistence of subclinical malaria which could lead to outbreaks in hot spots along border areas [8]. An integrated approach is needed to malaria surveillance and control through strong political leadership leading to collaborative activities including epidemiological data sharing along border regions, joint vector control, foci management and capacity building. Further implementation research is needed to gain insight on how effective partnership driven strategies can combat cross border malaria particularly aimed at strengthening the active surveillance system and the notification of the movement of cases along the borders [9].

Attention to *P. vivax*

The article identifies *P. vivax* as the dominant species compared to *P. falciparum* (6.0% vs. 1.5%). *P. vivax* has particular challenges to control measures. Pregnant women and children are particularly vulnerable to the adverse consequences of vivax malaria [10]. A higher risk of *P. vivax* infections was found following the treatment of *P. falciparum,* leading to relapse [11]. From 1995 to 2016, *P. vivax* became the leading cause of malaria infection along the Thailand - Myanmar border [12]. Radical cure of *P. vivax* is the primary solution; however treatment adherence to the 14-day primaquine regimen is the major challenge in the community. Directly-Observed Therapy (DOT) proved to prevent relapse of *P. vivax* within the 90-day period following treatment [13]. Glucose 6-Phosphate Dehydrogenase (G6PD) deficiency plays a critical role in the use of primaquine for radical cure. The high prevalence of G6PD deficiency is preventing primaquine use [14]. G6PD deficiency is prevalent in 10% of Chin and Rakhine national groups [15] and 20% of the ethnic populations in upper Myanmar [16]. Reduction of *P. vivax* malaria needs to be addressed by strong support of G6PD testing among the national groups [15]. A cost-effectiveness analysis of the use of G6PD testing has shown reduction of recurrences and a lower risk of haemolytic anaemia in G6PD deficiency patients at low cost [17].

Conclusion

Identifying high risk group and their locations (hot spots) by applying the practical use of point-of-care diagnostics is vital for eliminating residual malaria. Adequate supplies of commodities are critical. Strengthening the malaria surveillance system is a challenge for resource limited scenarios, especially for low transmission settings in Myanmar. Innovative intervention strategies are required to fight against malaria particularly for conflict affected areas and point-of-care testing is critical for detecting subclinical malaria. Despite their limited temperature stability and shorter shelf-life, hsRDT could be capable of detecting subclinical malaria for a focal test and treat approach to targeted populations in low transmission setting. Demonstrating the cost-effectiveness of hs-RDT is challenging for resource limited national programs in reaching vulnerable populations under difficult circumstances, when targeting malaria elimination by 2030.

Authors Contribution

Both authors have conceptualized, wrote this Short Commentary, reviewed and approved for publication.

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