Policy | Brief

Detection of the exposure to malaria parasites as a viable means for malaria elimination: Evidence from serological assay

Summary

Ethiopia has realized a sustained decline in malaria burden comparing to most malaria endemic countries. Nevertheless, there is a need to foster dialogue and decisions that are practiced by the best available evidence in the malaria prevention and control endeavors.
A combination of methods including microscopy, molecular assays and serology were used to examine the current burden of malaria and history of malaria transmission among 1,144 samples, 46 – 128 per village, in Babile district, Ethiopia.

The study supported that Serology can be adapted as an alternative tool to monitor malaria elimination effort of the malaria program with relatively less technical demand. Thus, district-based serological surveillance is suggested to predict receptive areas at risk of malaria outbreaks in low transmission settings. The aim of this policy brief is to foster dialogue and decisions that are practiced by the best available evidence in the malaria prevention and control endeavors.

Brief Background of Malaria

Malaria epidemiology in Ethiopia differs from most of the sub-Saharan Africa with generally lower prevalence coupled with higher spatial and temporal heterogeneity characterized by frequent epidemics, exceptionally Plasmodium Vivax most common in various parts of the country [1]. Following the policy change in malaria control and intervention since 1998 which further intensified at the Millennium Development Goal (MDG), Ethiopia achieved a substantial reduction in mortality from malarial infection and recently embarked on the Sustainable Development Goals (SDGs), which the country is in appreciable stride to realize a 40% reduction in malaria incidence by 2020 [1, 2].

Evidence reveals that the country has realized a sustained decline in malaria burden against most malaria endemic countries reported to have considerable surge in its magnitude [2]. In line with the global commitment, the government of Ethiopia has set an ambitious plan to eliminate malaria by 2030. The aim of this policy brief is to foster dialogue and decisions that are practiced by the best available evidence in the malaria prevention and control endeavors.

Important Findings

The current and past burden of malaria was examined among 1,144 samples, 46 – 128 per village, in Babile, one of the districts selected for elimination by the Ministry of Health, Ethiopia. We used a combination of methods including microscopy, molecular assays and serology to examine the current burden of malaria and history of malaria transmission. Microscopy detected 1.3% Plasmodium falciparum and 0.4% Plasmodium vivax infections; whereas molecular assays detected 5.1% Plasmodium falciparum and 3.6%) Plasmodium vivax infections.

Antibodies were detected in 11.2% and 13.0% of study participants against Plasmodium falciparum and Plasmodium vivax respectively. Parasite prevalence estimates varied between villages significantly for microscopy (range, 0% - 6.2%), molecular assay (range, 1.1% - 24.5%) and antibody responses to Plasmodium falciparum (range, 0% - 38.4%) and Plasmodium vivax (range, 0% - 75.7%).

A significant decline in malaria transmission happened in the study area 15 years prior to the study for Plasmodium falciparum and 11.5 years for Plasmodium vivax with continuing heterogeneity, but measurable local transmission. A similar rate of decline was reported by another group in another serological study, in northwestern Ethiopia [4].
The trend in incidence and prevalence of malaria in the district since 2005 and the variation in age seroprevalence curves in malaria transmission is displayed in figure 1 [5], annexed.

Major points extracted

- The study indicated that serological analysis can be used to monitor malaria control/elimination in Ethiopia, through tracking long period programmatic performance.

- The method accelerates both data (sample collection) and laboratory analysis and gives efficient estimate of programmatic performance in elimination settings for tailored intervention.

Improved and new tools to support malaria elimination

Despite significant decline in malarial transmission intensity, finding, quantifying, and treating the sparse and heterogeneously distributed remaining infection results in operational challenges. This necessitates the need for improved and validated tools to estimate the level of disease transmission, for appropriately allocating interventions, quantifying their impact to help achieve transmission interruption.

Traditional approaches such as parasitological and entomological measures which were keys during the control phase for high transmission settings will no longer suffice to guide intervention for elimination approaches in low transmission settings because numbers of positive observations (infected mosquitoes or humans) are low. Moreover, these measures are affected by environmental changes, vary rapidly and affected by season. Utilization of antibody responses to malaria antigens can alternatively serve as an indirect and low-cost approach for malaria transmission intensity measurement in low-endemic settings [3].

When combined with age, seroconversion rates reflect cumulative malaria exposure in a population and can be used as a robust measure of malaria transmission intensity. Serological responses to parasite antigens are informative tools to reflect history of malaria, monitor malaria control program, and have the potential to uncover heterogeneity in the effectiveness of malaria control interventions.

Policy Implications

- The current findings support evidence for a decline in malaria burden and demonstrate that malaria transmission is still ongoing in the study area, arguing in favor of continued and tailored control efforts to accelerate the stride towards elimination efforts. Whilst importation of malaria is possible, and an important source of infection in several low-endemic settings, our findings of detectable serological responses in children, often accompanied by PCR-detected infection, suggest that there is still non-negligible local transmission.

- Novel tools that can interrupt transmission and improved strategies on enhanced community case management to find the sparse remaining infections that plausibly maintain the infectious parasite reservoir play paramount importance in accelerating the stride towards elimination.

- The striking variation in malaria indicators between village highlights, the need for better understanding of variation in the uptake of interventions and potentially tailor interventions to the local needs to accelerate elimination efforts in the region.
- Serology can be adapted as an alternative tool to monitor malaria elimination effort of the malaria program with relatively less technical demand.

Policy/Intervention

- Implement serological analysis as an alternative option to monitor malaria control/elimination in Ethiopia, through tracking long period programmatic performance
- Conduct district-based serological surveillance to predict receptive areas at risk of malaria outbreaks in low transmission settings.
- Serology may play a relevant role in low transmission settings for (micro) stratification, for identification and classification of clusters of lower and higher exposure areas to help strategically allocate resources and guide interventions.

Future directions

The limited number of examined villages and villagers is a limitation of this study. Future larger studies might help generate high resolution evidence on village level heterogeneity. Although AMA1 is a well-characterized marker of historical exposure at the population level [6], malaria exposure might have been missed by only measuring responses to single antigen in the present study. Further information could be generated by measuring other antigens and also short-lived antibodies to indicate recent exposure to infection across all ages [7].

In order to preserve and build on the control milestones achieved in the last two decades and accelerate the progress to elimination, the need for innovation to achieve malaria elimination is greater than ever. Above all, robust research is critical for the country to be able to build evidence-based policies and guidelines in locally tailored manner.

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Key references

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Annex

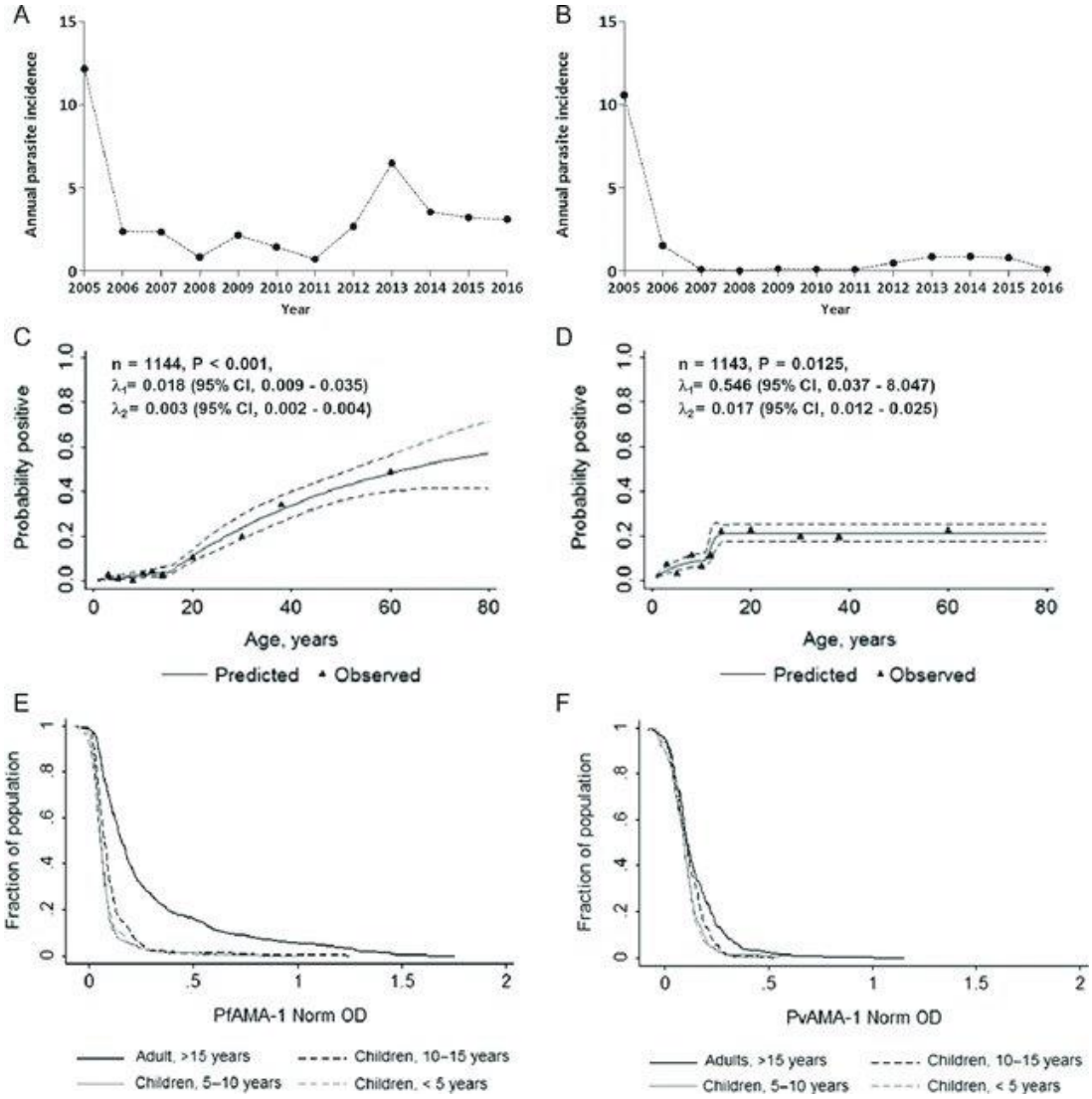

Figure 1. Annual parasite incidence, age seroprevalence plots and trends in antibody titres. Retrospective data from the district health bureau between 2005 and 2016 is presented for (A) P. falciparum and (B) P. vivax. Indicated on the y-axis is annual parasite incidence per 1000 population with the years indicated on the x-axis. Seroconversion curves are presented for (C) Pf-AMA (n=1144) and (D) Pv-AMA (n=1143) using a simple reversible catalytic model fitted by maximum likelihood. Triangles represent observed data and black lines represent predicted values. Dotted black lines represent upper and lower 95% CIs for the predicted seroprevalence by age. A likelihood ratio test was used to determine if a model with a change in transmission fitted the data best. Associated p-values as well as seroconversion rate estimates pre-and post-change are shown on the plots. Numbers indicate pre-change (λ 1) and post-change (λ 2) seroconversion values. Reverse cumulative distribution plots for age groups are indicated for (E) Pf-AMA and (F) Pv-AMA for the four age groups (adults >15 y of age, black lines; children 10-15 y of age, black dotted lines; children 5-10 y of age, grey lines; children <5 y of age, dotted grey lines). Shown in (E) and (F) are log 10 -transformed normalized OD values on the x-axis and the percentage of individuals having the indicated values or higher on the y-axis.