The Journal of Infectious Diseases

MAJOR ARTICLE

Use of an *Anopheles* Salivary Biomarker to Assess Malaria Transmission Risk Along the Thailand-Myanmar Border

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Background. The modalities of malaria transmission along the Thailand-Myanmar border are poorly understood. Here we address the relevance of using a specific *Anopheles* salivary biomarker to measure the risk among humans of exposure to *Anopheles* bites.

Methods. Serologic surveys were conducted from May 2013 to December 2014 in 4 sentinel villages. More than 9400 blood specimens were collected in filter papers from all inhabitants at baseline and then every 3 months thereafter, for up to 18 months, for analysis by enzyme-linked immunosorbent assay. The relationship between the intensity of the human antibody response and entomological indicators of transmission (human biting rates and entomological inoculation rates [EIRs]) was studied using a multivariate 3-level mixed model analysis. Heat maps for human immunoglobulin G (IgG) responses for each village and survey time point were created using QGIS 2.4.

Results. The levels of IgG response among participants varied significantly according to village, season, and age ($P<.001$) and were positively associated with the abundance of total *Anopheles* species and primary malaria vectors and the EIR ($P<.001$). Spatial clusters of high-IgG responders were identified across space and time within study villages.

Conclusions. The gSG6-P1 biomarker has great potential to address the risk of transmission along the Thailand-Myanmar border and represents a promising tool to guide malaria interventions.

Keywords. Thailand-Myanmar border; malaria vectors; transmission; human antibody response; Salivary Biomarker; gSG6-P1.

In Thailand, malaria displays geographical heterogeneity and is exemplified by the so-called border malaria type, with most of the malaria cases concentrated along the borders with Myanmar [1]. Malaria transmission along the Thailand-Myanmar border is high because of extensive population movement across the border, especially mobile and forest workers, who make a substantial contribution to the regional malaria burden [2]. The forest area along the border presents very efficient vectors species, including *Anopheles minimus sensu lato, Anopheles maculatus sensu lato*, and *Anopheles dirus sensu lato* [3, 4]. The vectorial capacity and relative importance of these vector species in malaria transmission are, however, poorly understood, hence representing a threat to the success of malaria control and elimination in the region [2].

The emergence of artemisinin-resistant *Plasmodium falciparum* is a threat to malaria control. Given the paucity of new antimalarials, the only viable option is elimination of the parasite. Eliminating malaria requires accurate tools for monitoring local malaria transmission intensity [5]. The gold standard for estimating malaria transmission is the entomological inoculation rate (EIR), which is defined by the number of infected bites received per human per unit of time [6]. The EIR is estimated by human-landing collection events that are strongly dependent on the density of human-biting mosquitoes in a given time [5]. However, the density of vectors has been shown to greatly vary according to collection site and season and seems to be insensitive within small geographical areas [7–9]. Moreover, mosquito collections are time-consuming, costly, difficult to sustain for the long term, and pose ethical challenges in areas of endemicity for vector-borne diseases [10]. In settings of low malaria transmission, where people received generally <1 infected bite per person per year [11], the EIR may lack sensitivity because the number of *Plasmodium*-positive samples is inadequate to estimate of the sporozoite index [12–14]. Effectively using limited resources for malaria elimination and evaluating interventions require new measurements of the risk of being infected with *Plasmodium* at both population and individual levels [15, 16].

Recently, alternative serological methods for monitoring human-vector contact by measuring the intensity of antibody response to mosquito bites have been developed [17]. Positive

Received 23 August 2016; editorial decision 31 October 2016; accepted 15 November 2016; published online 7 December 2016.

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The Journal of Infectious Diseases® 2017;215:396–404

DOI:10.1093/infdis/jiw543