MACEPA PATH
Malaria Control and Elimination Partnership in Africa

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Malaria parasitemia and serological prevalence in near-zero transmission settings in Ethiopia

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Background

Ethiopia has made enormous progress in the fight against malaria and is close to elimination in certain regions.

Passive incidence of malaria cases is the main metric used in near-zero transmission settings; other methods to assess potential interruption of transmission are needed.

We conducted two surveys in areas with zero reported malaria incidence to:

- Assess exposure to malaria infection in the population using serology, PCR, and a rapid diagnostic test (RDT) for malaria.
- Describe secular trends in malaria transmission using serological conversion rates (SCR).
- Identify the best operational sampling strategy for malaria elimination scale-up by comparing a community vs. a convenience survey.

Methods

Study design

The study was conducted in Amhara National Regional State from December 2015–February 2016 (Figure 1). Four health post catchment areas with the following criteria were selected:

- Zero malaria incidence: 0 confirmed, locally acquired malaria cases (i.e., with no travel history) reported in the last two years.
- Data quality quality audit showing complete and accurate surveillance data.

Primary endpoint: sero-prevalence of malaria antibodies in children aged 12–59 months old.

Sampling methods

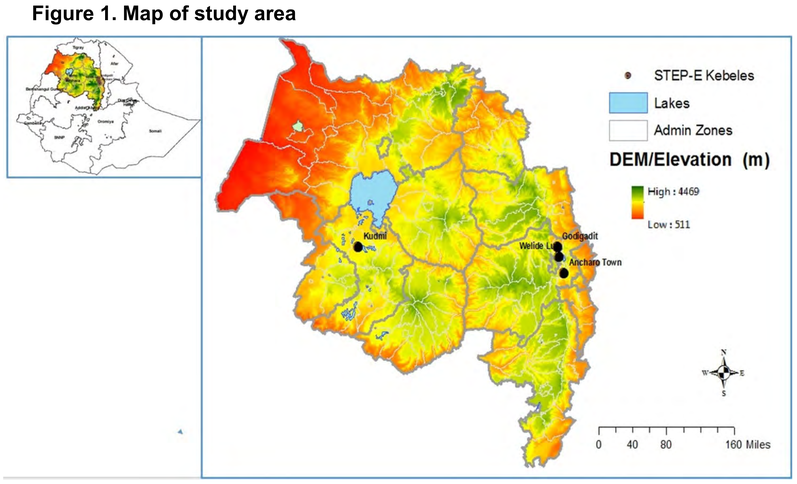
Two surveys were conducted:

- A community-based cross-sectional study was conducted in 1,649 households randomly selected from an existing census. All consenting children aged 1–9 years and a subsample of randomly selected individuals ≥10 years old were included.
- A convenience sample of approximately 400 children 12-59 months old recruited at health facilities and during community health outreach activities in the same areas was identified to assess whether this "easy-access" survey yielded similar results to the community sample.

Data collection and analysis

Standardized questionnaires using Open Data Kit on smartphones were employed. A finger-prick blood sample was collected for blood smear, dried blood spots (DBS) on filter paper, and RDT. SCR was estimated for *P. falciparum* for the community survey through simple reverse catalytic models fitted to sero-prevalence and age data using maximum likelihood methods.

Figure 1. Map of study area



Methods continued

Laboratory methods

Samples were assayed at the Amhara Regional Health Research Laboratory Center. Blood smears were read by two independent microscopists.

DBS samples were assayed for anti-malarial IgG antibody responses to *Pf* and *P. vivax* merozoite surface protein (MSP-1_{19}) and apical membrane antigen 1 (AMA-1) recombinant protein by enzyme-linked immunosorbent assay (ELISA).

DBS samples were assayed by real-time PCR using a photo-induced electron transfer (PET)-PCR. Samples that were *Pf* positive or genus positive were considered positive for this analysis.

Results

Prevalence of infection

1,207 individuals participated in the community survey (455 12–59 months old, 382 5-9 years old and 430 >=10 years), and 391 children 12-59 months old participated in the convenience survey.

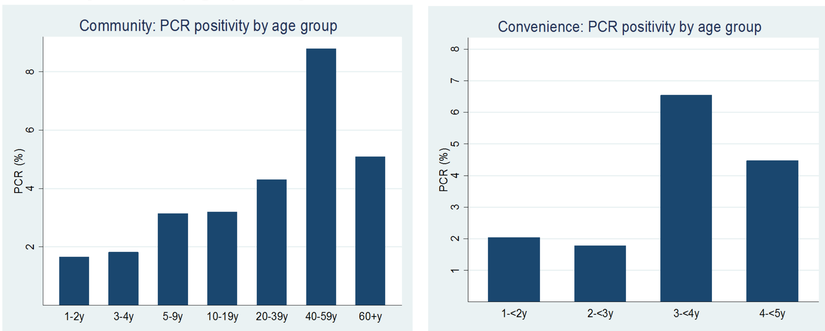
In the community survey, prevalence of infection by RDT and microscopy was 0.08% (95% CI:0.01-0.6), with only one *Pf* infection by RDT and microscopy, confirmed by PCR. This was in a 3-year-old child with no travel history who lived in the same household as an adult with travel history.

In the easy-access survey there were no positives by RDT or microscopy.

Infection prevalence by PCR was 3.3% (95% CI: 2.5–4.5) in the community survey and 4.3% (95% CI: 2.7–6.9) in the easy-access survey. Prevalence increased with age, with the highest prevalence in those 40–59 years old (Figure 2).

33.3% of PCR-positive cases versus 6.9% of PCR-negatives (p=0.02) travelled in the previous month.

Figure 2. Prevalence of infection by PCR by age group in the community (left) and easy-access (right) surveys



Serology

In the community survey, sero-prevalence for *Pf* was very low (range: 0.5–5.7%) in children 12–59 months and increased with age. Sero-prevalence for *Pv* was zero in individuals <20 years old and very low in those ≥ 20 years old (range: 1.1–6.1%) (Figure 3).

In the easy access survey, sero-prevalence of *Pf* was 0.9% (1 positive in a 3-year-old) and there were no positives for *Pv*. Sero-prevalence results among children 12–59 months old were similar in the community and convenience surveys, although more positives for *Pf* were found in the community survey (Figure 4).

Among children 12–59 months, none of sero-positives had moved or lived in another area or travelled; 0.9% of sero-negatives moved or lived in another area and 2.7% travelled.

The serological conversion rate for *Pf* shows that transmission dropped around ten years ago (Figure 5). In the community survey, *Pf* sero-prevalence was 6.7% in PCR-positive vs. 12.8% in PCR-negative individuals (p=0.48); in the convenience survey, *Pf* sero-prevalence was 0% in PCR-positive vs. 0.2% in PCR-negative (p=0.9).

Figure 3. Sero-prevalence by age group in the community survey

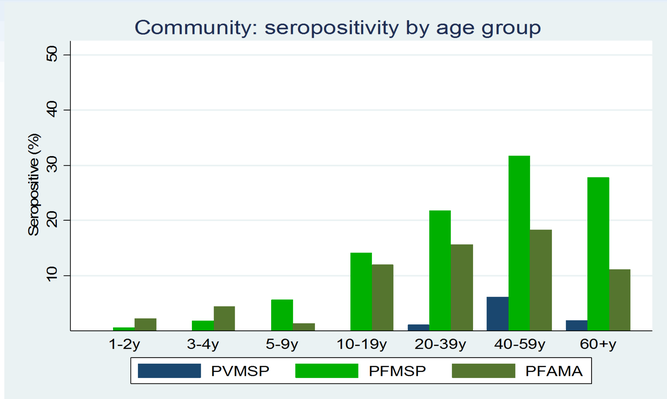


Figure 4. Sero-prevalence in children 12–59 months old in the community (left) and convenience (right) surveys

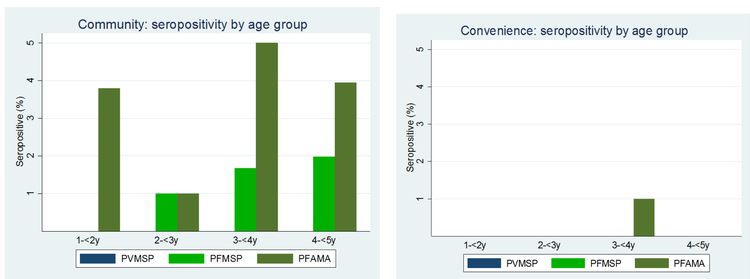
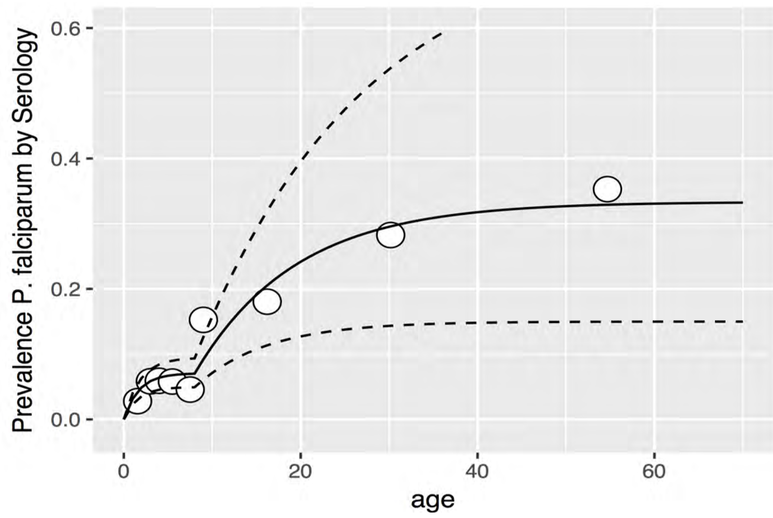


Figure 5. Age-seroconversion plots for antibody responses to *P. falciparum* antigens



Conclusions

Even though there were zero reported passively-detected local cases in the previous two years, sero-prevalence in children 12–59 months old and PCR-prevalence in all age groups show that there is still some residual transmission in the area. However, importation might play an important role in transmission.

Serological conversion rates suggest there has been a drop in *P. falciparum* in the last decade, coinciding with the scale up of malaria control tools.

Sero-prevalence in young children is very low but shows some exposure to malaria has occurred in children who were born after transmission decreased. Thus, sero-surveys in young children might be an appropriate complement to clinical surveillance data to assess interruption of transmission at a sub-national level.

The PCR and sero-prevalence data from the easy-access survey in children provided similar conclusions to the community-based survey, ie there is still some residual transmission. Those surveys are operationally easier and might be a good alternative to the more expensive community surveys.