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

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Background

Senegal has made enormous progress in the fight against malaria and is close to elimination in some regions in the north.

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

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

- Assess exposure to malaria infection in the population using sero-prevalence and infection prevalence.
- Describe historical changes in malaria transmission using serological conversion rates (SCR).
- Identify the best operational sampling strategy for scale-up by comparing a community versus an easy-access survey.

Methods

Study design

The study was conducted in Richard Toll district, Northern Senegal (Figure 1) from January–March 2016. Four health post catchment areas with the following criteria were selected:

- Zero or almost zero malaria incidence: ≤3 confirmed, locally acquired malaria cases (i.e., with no travel history) reported in the last 2 years.
- Data quality audit showing complete and accurate surveillance data.

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

Sampling methods

A census of the selected areas was conducted prior to study start. Two surveys were conducted:

- A community-based cross-sectional study was conducted in an age-stratified sample of 1,200 individuals randomly selected from the census: 400 12–59-month-olds, 400 5–9-year-olds, 400 ≥10 years old.
- A survey in an "easy-access" (convenience) sample of 400 children 12–59 months old recruited at health facilities and during community health outreach activities in the same areas was conducted to assess whether this easy-access survey yielded similar results to the community survey.

Data collection and analysis

Standardized questionnaires were employed using Open Data Kit on smartphones.

Finger-prick blood was used for a blood smear, dried blood spots (DBS) on filter paper, and rapid diagnostic test (RDT).

Figure 1. Map of study area

Serological conversion rates were estimated for the community survey through simple reverse catalytic models fitted to sero-prevalence and age data using maximum likelihood methods.

Methods continued

Laboratory methods

Samples were assayed at the parasitology laboratory of Le Dantec Hospital, Université Cheikh Anta Diop.

Blood smears were read by two independent microscopists.

DBS samples were assayed for anti-malarial IgG antibody responses to *P. falciparum* 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.

Results

Prevalence of infection

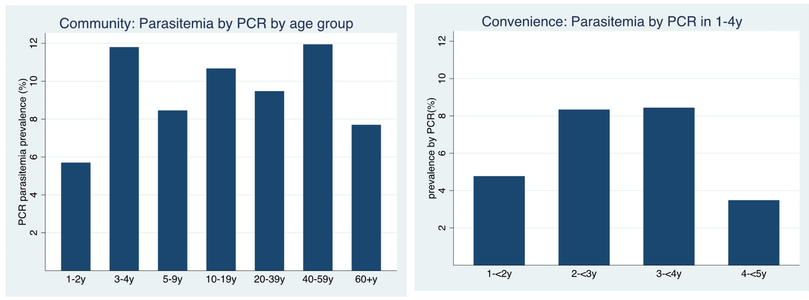
1,216 individuals participated in the community survey (404 12–59 months old, 406 5-9 years old, and 406 ≥10 years); 442 children 12–59 months old participated in the easy-access survey.

There were zero *P. falciparum* infections by RDT and microscopy in both surveys.

Infection prevalence by PCR was 9.4% (95% CI: 7.7–11.3) in the community and 5.9% (95% CI: 3.8–8.9) in the easy-access survey. In both surveys, prevalence wasn't significantly different by age group (Figure 2).

In the community survey, 4.1% of PCR-positive cases vs 6.0% of PCR-negatives (p=0.44) travelled in the previous month. In the easy-access survey, it was 4.4% and 0% (p<0.0001) respectively.

Figure 2. *P. falciparum* parasitemia prevalence by PCR by age group in the community (left) and easy-access (right) surveys



Serology

Sero-prevalence increased by age group in the community survey both for AMA-1 and MSP-1 (Figure 3). Antibody titers for both antigens also show a significant increase with age (data not shown).

Among children aged 12–59 months old, sero-prevalence was <5% for MSP-1 and AMA-1 in both surveys, although it was slightly higher in the easy-access survey (Figure 4).

Among children 12–59 months in both surveys, there were no significant differences in reporting having lived in another area between the sero-positives and the sero-negatives.

Serological conversion rates for *P. falciparum* show that transmission dropped around 15 years ago (Figure 5).

P. falciparum sero-prevalence was 2.9% in PCR-positive and 1.3% in PCR-negative individuals respectively (p=0.43) in the community survey. In the easy-access survey the percentages were 13.0% and 3.3% (p=0.019), respectively.

Results continued

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

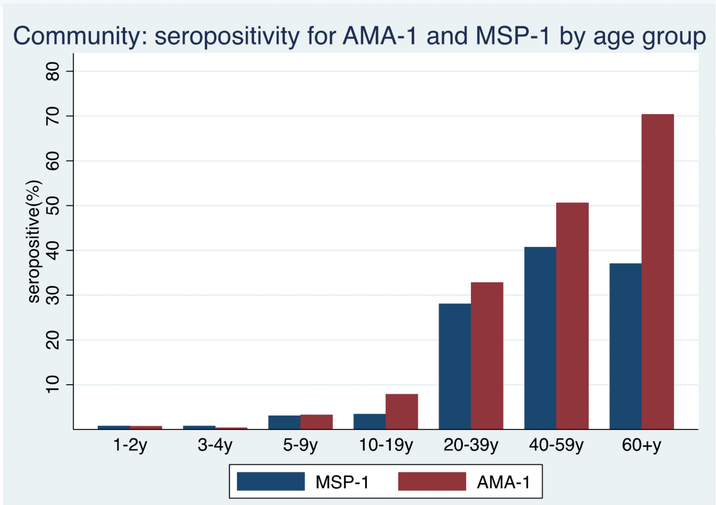


Figure 4. Sero-prevalence in children 12–59 months old in the community (left) and easy-access (right) surveys

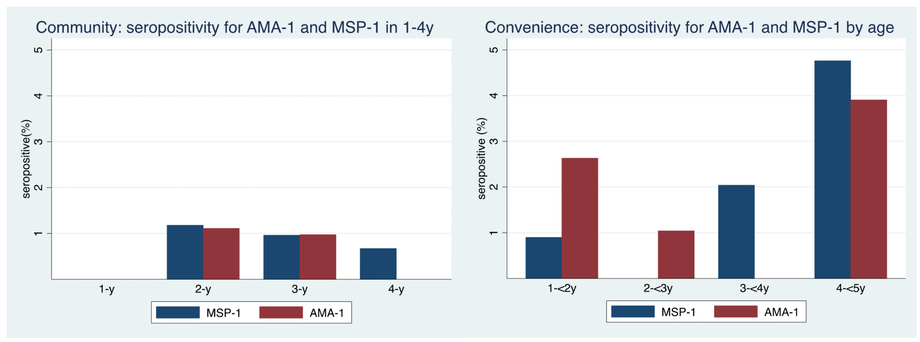
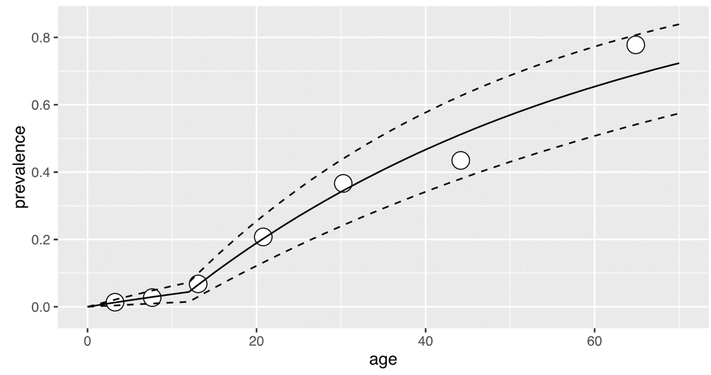


Figure 5. Age-seroconversion plots for antibody responses to *P. falciparum* antigens



Conclusions

Even though there were zero reported passively detected local cases in the previous two years, PCR prevalence in all age groups shows that there might still be some residual transmission in the area. Importation from other areas might play a role in transmission but does not seem to be responsible for all of it.

Serological conversion rates suggest there was a drop in *P. falciparum* around 15 years ago, coinciding with the scale-up of malaria control tools.

Sero-prevalence in young children is extremely low, reflecting the almost-zero transmission in the area. Low antibody titers in those children suggest that some of these might be false positives.

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 (i.e., there is still some residual transmission). Those surveys are operationally easier and might be a good alternative to the more expensive community surveys.