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Continuing Intense Malaria Transmission in Northern Uganda

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Abstract. Recent reports of reductions in malaria transmission in several African countries have resulted in optimism that malaria can be eliminated in parts of Africa where it is currently endemic. It is not known whether these trends are global or whether they are also present in areas where political instability has hindered effective malaria control. We determined malaria parasite carriage and age-dependent antibody responses to Plasmodium falciparum antigens in cross-sectional surveys in Apac, northern Uganda that was affected by political unrest. Under-five parasite prevalence was 55.8% (115/206) by microscopy and 71.9% (41/57) by polymerase chain reaction. Plasmodium ovale alone, or as a co-infection, was detected in 8.6% (12/139) and Plasmodium malariae in 4.3% (6/139) of the infections. Age seroprevalence curves gave no indication of recent changes in malaria transmission intensity. Malaria control remains a tremendous challenge in areas that have not benefited from large-scale interventions, illustrated here by the district of Apac.

INTRODUCTION

Despite reported reductions in malaria transmission intensity in several African regions, malaria remains one of the most important public health problems in sub-Saharan Africa with an estimated 863,000 deaths annually. Widespread use of insecticide-treated nets (ITNs), effective vector control, increased urbanization, and treatment of uncomplicated falciparum malaria with artemisinin-based combination therapies (ACT) have all been assumed to contribute to the reported reductions in malaria incidence, although in some areas these reductions were observed before control measures were scaled up. This widespread decline in the burden of malaria has resulted in optimism that malaria can be eliminated in parts of Africa where malaria is currently endemic. However, reports of reductions in malaria transmission mostly originate from areas that have been involved in intensive and effective malaria control programs and sustained implementation of health care, with some valuable findings from less well-controlled settings. It is uncertain if trends of declining transmission intensity are evident across Africa or whether they are apparent in areas where political instability and economic arrest have hindered effective control and surveillance of infectious diseases. Conflict and human insecurity pose considerable challenges by causing a breakdown in health delivery systems and a loss of human and financial resources for health programs. In those areas, malaria control is likely to have been less efficiently implemented and maintained and, as a result, malaria transmission intensity may have remained unaltered, or malaria may have re-emerged in areas where it was previously under control.

In this study, we determined the current level of malaria transmission intensity in the Apac district in northern Uganda, a remote region that was previously described as holoendemic for malaria. Northern Uganda has been involved in conflict since the early 1980s with the Lord’s Resistance Army as the main rebel group that continues to be a threat to the region up to the present day. This conflict hindered economic development in northern Uganda and resulted in a lower access to healthcare compared with other regions in Uganda. The area of Apac was affected by political unrest in the early 1990s. Although health facilities remained functioning throughout the conflict, serious supply shortages affected the quality of care.

The aim of this study was to determine the current prevalence of Plasmodium falciparum parasite carriage by microscopy and polymerase chain reaction (PCR) and to use age-dependent antibody responses to P. falciparum circumsporozoite (CSP) antigen and blood-stage antigens apical membrane antigen-1 (AMA-1) and merozoite surface protein-1 (MSP-1) to look for evidence of recent changes in transmission intensity.

METHODS

The study was conducted in Apac Sub-County, a rural district in Northern Uganda located between Kwania Lake and the Victoria Nile (latitude 1.985; longitude 32.535). Apac District covers an area of 6,684 square kilometers and ranges in altitude between 1,350 and 1,500 meters above sea level. The rainfall pattern is bimodal with a dry season from November to February and two short rainy seasons from April to May and from September to October. According to surveys conducted in 2001–2002, this area experiences perennial holoendemic malaria with parasite prevalence rates of 70–90% in children <10 years of age. The entomological inoculation rate was estimated at >1,500 infective bites per person per year and the major vector responsible for transmission is Anopheles funestus. Plasmodium falciparum is the dominant parasite species, Plasmodium malariae being responsible for ~3% of the infections and Plasmodium ovale was previously not observed. Ethical approval was obtained from the ethical review committee of the London School of Hygiene and Tropical Medicine (no. 5539), the ethical committee of the Medical Biotech Laboratory, and the national ethical committee of Uganda.

Data collection. Subjects were recruited in October 2009 in four parishes. Sampling was done in Apac District Hospital, two health facilities in the parishes of Abedi and Akere, and a primary school in the parish of Atopi. Before the sampling days, community meetings were organized to explain the purpose of the study and to invite people to attend sampling points.

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At the health facilities and the hospital, all individuals attending the facilities for clinical care, antenatal visits, or who came specifically to benefit from the screening offered by this study were selected for enrollment together with accompanying family members or guardians. This approach was previously shown to provide an estimate of malaria-specific antibody prevalence that is comparable to that obtained through community surveys. Before sampling at the school in Atopi, a community meeting was organized and parents were informed of the survey through the school’s pupils. All inhabitants of Atopi who attended the sampling point, including pupils and their parents or guardians, were eligible for enrollment and people were sequentially enrolled until the sample size was reached. We aimed to recruit 200–300 individuals per parish of whom half were <15 years of age. This sample size was based on a previous study where this number of participants was found to be sufficient for a reliable determination of transmission intensity by serological markers of malaria exposure. To ensure a balanced representation of all age groups, essential for determining the age-dependent seroconversion rates (SCRs), seven age categories were defined per parish (1–2 years, N = 45; 3–5 years, N = 45; 6–10 years, N = 40; 11–15 years, N = 40; 16–25 years, N = 40; 26–55 years, N = 40; and >30 years, N = 50) and questionnaires were printed in pre-defined quantities in different colors for each age group. Questionnaires contained clinical information, demographic data, information on the use of antimalarial drugs, and protective anti-mosquito measures. As soon as the sample size for an age category was reached, no further individuals were enrolled for this category but enrollment continued for other age categories.

Written informed consent or, in case of illiteracy, consent by thumb print, was obtained from each participant ≥15 years of age and from parents or guardians of younger individuals. Each individual enrolled in the study underwent a clinical examination, during which axillary temperature was measured twice using a digital thermometer and the higher of the two values was recorded. A single blood sample was obtained by finger prick (~0.3 mL) for thick and thin blood films, for filter paper blood collection (Whatman 3 mm, Maidstone, UK) and for Rapid Diagnostic Tests (RDT; Paracheck Orchid Biomedical Systems, Goa, India) for malaria. This RDT has an estimated detection rate of 97.5% for parasite densities >2,000 parasites/μL and 54.4% for parasite densities of 200–400 parasites/μL. Filter papers were air-dried and stored in plastic bags with silica desiccant gel type III (Sigma, Dorset, UK), stored at ~20°C in the field, transported at room temperature, and again stored at ~20°C in the laboratory until further processing. Thick blood films were Giemsa-stained in the field and read after completion of the study. Clinical diagnosis was based on the result of the RDT; RDT-positive individuals with (reported) fever were treated with artemether-lumefantrine (Lomart; Bliss Gvs Pharma Ltd., India) according to national guidelines. The first dose was given under supervision; the remaining five doses were given to the participant/guardian for treatment at home.

**Parasite detection by microscopy and PCR.** Microscopic slides were examined for the presence of parasites in 100 high-power fields by two experienced microscopists; the average parasite density of the two readings was recorded and a third microscopist consulted in case of disagreement. Asexual parasites were counted against 200 white blood cells and converted to parasites/μL by assuming a density of 8,000 white blood cells/μL blood. We explored the value of PCR for parasite detection in a single parish. Abedi. DNA was extracted from all filter paper blood spots from Abedi, using the chelex method and tested for the presence of P. falciparum, P. vivax, P. malariae, and P. ovale in the nested PCR approach originally described by Snounou and others and Padley and others. Samples that were negative by PCR were rescreened by PCR using as a template DNA extracted using QIAamp DNA Mini Kit (QIAGEN, Hilden, Germany).

**Enzyme-linked immunosorbant assay (ELISA).** Antibodies were eluted from filter paper blood spots and assayed by ELISA, as described in the online protocol by Corran and others. Briefly, a 3.5-mm circle was cut from the spot and placed into 300 μL of phosphate buffered saline with 0.5% Tween 20 (PBS-T) and 0.05% sodium azide, approximately equivalent to a 1/200 serum dilution. Immunoglobulin G (IgG) antibodies against circumsporozoite protein (CSP), apical membrane antigen (AMA-1), and merozoite surface protein 1 (MSP-1) were detected by ELISA using standard methodology. Recombinant MSP-1 (Wellcome genotype), AMA-1 (3D7 genotype), and a synthetic peptide CSP (NANP4) were coated onto ELISA plates overnight at 4°C at a concentration of 0.5 mg/mL, respectively. Plates were washed using PBS plus 0.05% Tween 20 (PBS/T) and blocked with 1% (w/v) skimmed milk powder (Marvel, UK) in PBS/T. Samples were added in duplicate to each plate at a serum dilution of 1:200 for CSP, 1:2000 for AMA-1, and 1:750 for MSP-1 in 1% bovine serum albumin (BSA) in PBS/T. A positive control of pooled hyper-immune serum collected from adults resident in a malaria-endemic area was included in duplicates on each plate to allow standardization of day-to-day and plate-to-plate variation; serum from malaria-naive Europeans was included in each assay as negative controls. After overnight incubation at 4°C the plates were washed and horseradish peroxidase-conjugated rabbit anti-human IgG (Dako Ltd., High Wycombe, United Kingdom) (1/5,000 in PBS/T) was added to all wells. All plates were developed using OPD/H2O2 substrate solution and reactions were stopped with 2 M H2SO4. Plates were read immediately at 492 nm and optical density (OD) values recorded.

**Data analysis.** All data were double entered and validated in Microsoft Access (Redmond, WA); inconsistencies were verified against the original questionnaire. Data were imported into Stata 11.0 (Stata Statistical Software, StataCorp, College Station, TX) for statistical analysis. Fever was defined as a temperature ≥37.5°C, submicroscopic parasitemia was defined as parasitemia by PCR in the absence of microscopically confirmed parasite carriage. Parasite density was presented as geometric mean in microscopically positive parasite carriers only with the 25th and 75th percentile (interquartile range, IQR). Duplicate OD results in ELISA assays were averaged and normalized against the positive control sample on each plate. A cut-off above which samples were deemed antibody positive was defined using a mixture model as previously described. Briefly, the distribution of normalized OD values was fitted as the sum of two Gaussian distributions (a narrow distribution of seronegatives and a broader distribution of seropositives) using maximum likelihood methods. The mean OD of the Gaussian corresponding to the seronegative population plus three standard deviations was used as the cut-off for seropositivity. The seroconversion rate (SCR or γ) was estimated by fitting a simple reversible catalytic model to the measured seroprevalence, stratified into yearly age groups, using maximum likelihood methods. For
these models only individuals’ ≥ 1 year of age were included to avoid the effect of maternally derived antibodies in infants. Evidence for temporal changes in SCR was explored by fitting models in which the SCR is allowed to change at a single time point.23,24 The significance of the change was identified using likelihood ratio tests against models with no change, and profile likelihoods were plotted to determine confidence intervals (CIs) for the estimated time of the change.23 The titer and profile likelihoods were plotted to determine confidence using likelihood ratio tests against models with no change, 

Plasmodium falciparum

Fever, % (n/N)  

Age, median (IQR)  

Parasite prevalence by RDT, % (n/N)  

P. falciparum parasite prevalence by microscopy, % (n/N)  

P. falciparum parasite density, GM (IQR)  

P. falciparum parasite prevalence by PCR, % (n/N)  

Table 1  

Characteristics of enrolled individuals*  

Abedi Akere Atopi

N 251 217 213 202

Age, median (IQR) 15 (5.3–25) 13 (4.3–29) 19 (5.5–32) 13 (5.6–30)

Fever, % (n/N)  

< 5 years 30.0 (18/60) 27.1 (16/59) 46.9 (23/49) 14.3 (6/42)

5–14 years 12.9 (8/62) 17.7 (9/51) 36.6 (15/41) 9.1 (6/66)

≥ 15 years 6.5 (8/124) 3.9 (4/102) 9.5 (11/116) 3.4 (3/88)

Parasite prevalence by RDT, % (n/N)  

< 5 years 56.7 (34/60) 73.3 (44/60) 71.4 (35/49) 81.0 (34/42)

5–14 years 59.4 (38/64) 44.2 (23/52) 51.2 (21/41) 64.2 (43/67)

≥ 15 years 16.8 (21/125) 17.3 (18/104) 14.1 (17/121) 15.4 (14/91)

P. falciparum parasite prevalence by microscopy, % (n/N)  

< 5 years 54.4 (31/57) 50.9 (29/57) 59.6 (28/47) 63.4 (26/41)

5–14 years 59.7 (37/62) 42.0 (21/50) 51.3 (20/39) 65.7 (44/67)

≥ 15 years 20.2 (25/124) 22.0 (22/100) 11.3 (12/106) 23.3 (21/90)

P. falciparum parasite density, GM (IQR)  

< 5 years 6,063 (480–77,880) 2,844 (400–32,640) 8,102 (1,380–43,720) 2,874 (520–11,120)

5–15 years 753 (120–3,320) 1,235 (440–2,120) 1,404 (460–3,740) 918 (310–2,740)

≥ 15 years 215 (80–520) 453 (80–1,520) 232 (60–540) 456 (160–800)

P. falciparum parasite prevalence by PCR, % (n/N)  

< 5 years 66.7 (38/57) ND ND ND

5–15 years 69.4 (43/62) ND ND ND

≥ 15 years 42.6 (52/122) ND ND ND

* IQR = interquartile range; RDT = rapid diagnostic test; GM = geometric mean; ND = not done; PCR = polymerase chain reaction.
15,000–80,000 parasites/μL, the prevalence of fever was 65.9% (29/44), OR = 5.98 (95% CI = 2.93–12.21, P < 0.001). The association between parasite density and fever prevalence did not improve when fever was defined as a temperature ≥ 38.0°C and/or if children who reported using antipyretics were excluded.

**Malaria-specific antibody responses.** Antibodies against CSP, AMA 1, and MSP-119 were measured in 825 individuals. The overall seroprevalence was 25.2% (95% CI = 22.2–28.3) for CSP, 63.8% (95% CI = 60.4–67.0) for AMA-1, and 44.2% (95% CI = 40.8–47.7) for MSP-119. Seroprevalence generally increased with age (P < 0.001) for all the antigens (Figure 3) and this increase was most pronounced for AMA-1 where antibody prevalence rapidly rose to 74.3% (95% CI = 65.1–82.2) in children aged 5–10 years and 81.7% (95% CI = 72.9–88.6%) in children aged 10–15 years, and gradually decreased with age in older age groups (OR = 0.92; 95% CI = 0.96–0.99, P = 0.001). This decrease in older age groups may reflect a reduction in immune boosting by blood-stage infections in individuals with effective anti-parasite immunity. The age-seroprevalence curves did not indicate more than one force of infection over time; this was checked by allowing the SCR to differ at a single time point. For none of the antigens did multiple SCRs improve the fit of the age-seroprevalence curves. The overall SCR rate (λ) was estimated at 0.025 (95% CI = 0.019–0.033) for CSP, 0.260 (95% CI = 0.208–0.326) for AMA 1, and 0.056 (95% CI = 0.044–0.072) for MSP-119 (Figure 3). Microscopically confirmed parasitemia was associated with a higher odds of being AMA-1 seropositive for children 1–5 years of age (OR = 3.2, 95% CI = 1.54–6.61, P = 0.002) but not for older individuals (P = 0.46), after adjustment for age within the age strata (Table 2). A similar trend of a higher odds of being seropositive for parasitemic compared with non-parasitic children < 5 years of age was seen for CSP (OR = 3.25; 95% CI = 0.67–15.8, P = 0.14) and MSP-119 (OR = 1.62; 95% CI = 0.79–3.32, P = 0.19), although not statistically significant. The titer of AMA-1 antibodies was also higher in the presence of microscopically confirmed infections (1.92-fold increase; 95% CI = 1.38–2.66, P < 0.001, after adjustment for age). A similar association was observed for CSP antibody titer (1.25-fold increase; 95% CI = 1.00–1.57, P = 0.05), whereas this trend was not significant for MSP-119 (1.26-fold increase; 95% CI = 0.88–1.83, P = 0.20). The presence of submicroscopic infections did not significantly influence the prevalence of AMA-1 (OR = 1.45; 95% CI = 0.32–6.60, P = 0.63), MSP-119 (OR = 0.37; 95% CI = 0.04–3.17, P = 0.37), or CSP (OR = 2.47; 95% CI = 0.23–26.25, P = 0.45) antibody responses in children 1–5 years of age compared with uninfected children of the same age. Similarly, antibody titer was not significantly elevated for AMA-1 (1.08-fold increase; 95% CI = 0.54–2.15, P = 0.83), MSP-119 (0.47-fold decrease; 95% CI = -0.17–0.76, P = 0.12), or CSP (0.11-fold decrease; 95% CI = -0.44–0.45, P = 0.64) in the presence of a submicroscopic infection in children < 5 years of age. These estimates will have been affected by small numbers, only 11 children < 5 years of age carried parasites at submicroscopic densities.

**DISCUSSION**

In this work, we describe the current malaria situation in Apac, northern Uganda. *Plasmodium falciparum* parasite prevalence was high, ≥ 50% by microscopy in children
<5 years of age, and infections with *P. malariae* and especially *P. ovale* were common. Parasite carriage often occurred asymptptomatically, at densities ranging from submicroscopic concentrations to densities > 5,000 parasites/μL. These parameters are consistent with continuing holoendemic malaria transmission and, unsurprisingly, the age-dependent prevalence of malaria-specific antibodies did not indicate recent changes in transmission intensity.

In our surveys, *P. falciparum* parasite prevalence in children 2–9 years of age was 58%. This was slightly lower than the previously reported parasite prevalence of 70–90% in the same age group living in neighboring parishes in Apac District in 1995–1999, but within the 50–100% range reported in world malaria maps. When PCR was used for parasite detection, overall *P. falciparum* parasite prevalence was 55.2% in all age groups (37.5% by microscopy) and 69.3% in children 2–9 years of age (57.3% by microscopy). The prevalence of submicroscopic parasite carriage is in perfect agreement with the recent meta-analysis by Okell and colleagues, who reported a median PCR parasite prevalence of 58.6 (IQR = 51.4–74.0%) for areas where the microscopical parasite prevalence is 25–50%. The relative proportion of parasite carriers that harbored parasites at submicroscopic densities increased with age; this is likely to be a reflection of acquired immunity that allows adults to control infections more effectively. However, even in the youngest age group a substantial proportion of infections were not detected by microscopy, as was previously shown in areas of intense and low endemicity. Microscopy will be sufficiently sensitive to detect clinically relevant parasite densities, although our data clearly indicate that not every episode of parasitemia with fever equals clinical malaria. One-quarter of children <10 years of age presented with fever in the absence of parasites and the proportion of febrile children did not change considerably until malaria parasite densities exceeded 10,000 parasites/μL. Our data were insufficient to define a pyrogenic threshold density or malaria-attributable fraction of fever episodes; only 77 children had a parasite density ≥10,000 parasites/μL.

**Figure 3.** Age-seroprevalence plots for circumsporozoite protein (CSP), merozoite surface protein-1, and apical membrane antigen-1. Dots indicate the observed antibody prevalence for different age groups, the solid line the best fit based on age as a continuous variable, the dotted line the upper and lower limit of the 95% confidence interval (CI). The serocconversion rate λ was estimated at 0.025 (95% CI = 0.019–0.033) for CSP, 0.056 (95% CI = 0.044–0.072) for MSP-119, and 0.260 (95% CI = 0.208–0.326) for AMA 1.

**Table 2.** Antibody prevalence and density in relation to parasite carriage by microscopy.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Parasite-neg</th>
<th>Parasite-posit</th>
<th>1–5 years</th>
<th>7.8 (8/103)</th>
<th>37.9 (21.4–61.5)</th>
<th>44.7 (46/103)</th>
<th>552.7 (167.9–1,429.3)</th>
<th>27.1 (32/118)</th>
<th>64.0 (25.5–167.1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥15 years</td>
<td>Parasite-neg</td>
<td>36.4 (112/308)</td>
<td>93.0 (51.3–147.2)</td>
<td>67.7 (216/319)</td>
<td>1,063.6 (608.1–1,561.2)</td>
<td>62.3 (198/318)</td>
<td>248.2 (94.1–478.8)</td>
<td>27.1 (32/118)</td>
<td>64.0 (25.5–167.1)</td>
</tr>
</tbody>
</table>

* Median titer includes all individuals, also seronegatives. The prevalence or (log-10-adjusted) titer were compared between parasite-positive and parasite-negative individuals by microscopy; these analyses were done for different age categories and adjusting for age within that category.

† *P < 0.05.*

‡ *P < 0.01.*
malaria-attributable fraction, because the density of peripheral parasitemia within a single individual can fluctuate widely between times of the day and between days.\textsuperscript{39}

The prevalence and density of antibody responses was influenced by microscopically detectable parasite densities.\textsuperscript{20,41} This was only apparent in children < 5 years of age and suggests that immune responses are less stable in this age group, fluctuating with concurrent infections.\textsuperscript{42} In older age groups immune responses were not influenced by concurrent parasitemia. Contrary to previous studies, we did not find evidence for a boosting of immune responses by submicroscopic parasite carriage.\textsuperscript{43,44} We observed few submicroscopic infections in children 1–5 years of age (N = 11), which will have affected our power to detect such an immune-boosting effect. These findings confirm previous indications that parasitization status can be an important consideration in longitudinal assessments of the protective role of immune responses.\textsuperscript{41,45}

Age-seroprevalence plots can reveal recent reductions in transmission intensity when the age-seroprevalence curve shows an improved fit to the data when more than one SCR rate is assumed for specific time periods.\textsuperscript{3,24} We did not find any evidence for more than one force of infection and therefore have no reason to conclude a reduction in transmission intensity since the last surveys in the area.\textsuperscript{17} The used methods may not have picked up a steady, gradual decline in transmission intensity,\textsuperscript{25} but this was not suggested by our findings in relation to previous surveys. Our approach of convenient sampling at health facilities and a school where surrounding villagers were mobilized for screening has some drawbacks. Although it was previously shown that this approach is valid in obtaining an estimate of antimalarial antibody prevalence,\textsuperscript{25} it may have resulted in an overestimation of parasite carriage because of a selection of symptomatic or overly exposed individuals. Although this implies that some caution is required in extrapolating the results to the general population, we feel that the asymptomatic nature of the vast majority of infections makes it likely that our estimates are informative for the general population. The observation of persisting intense transmission are in agreement with a recent review that concluded that reductions in transmission intensity are not evident in all African settings\textsuperscript{8} and that transmission intensity may have remained unchanged or even increased in northwestern Uganda\textsuperscript{46} and neighboring countries in East and Central Africa.\textsuperscript{47–49} The failure to reduce the burden of malaria could reflect sub-optimal implementation of malaria control measures. Even in areas of intense malaria transmission intensity, considerable gains can be achieved by vector control and effective antimalarial treatment, as was illustrated by successful malaria control on Bioko island.\textsuperscript{50} Malaria control efforts in Apac were not reliably monitored in the last decade and affected by political unrest in preceding years. The ACTs were officially available in Apac from 2006, but especially the smaller health facilities were still profoundly needed in areas in Africa where transmission remains intense and malaria control continues to be a tremendous challenge.

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REFERENCES


