A Cross-Sectional Population Study of Geographic, Age-Specific, and Household Risk Factors for Asymptomatic *Plasmodium falciparum* Malaria Infection in Western Kenya

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Abstract. The burden of *Plasmodium falciparum* (Pf) malaria in Kenya is decreasing; however, it is still one of the top 10 causes of morbidity, particularly in regions of western Kenya. Between April 2015 and June 2016, we enrolled 965 apparently healthy children aged 0–15 years in former Nyanza and Western Provinces in Kenya to characterize the demographic, geographic, and household risk factors of asymptomatic malaria as part of an epidemiologic study to investigate the risk factors for endemic Burkitt lymphoma. The children were sampled using a stratified, multistage cluster sampling survey design. Malaria was assessed by rapid diagnostic test (RDT) and thick-film microscopy (TFM). Primary analyses of Pf malaria prevalence (pfPR) are based on RDT. Associations between weighted pfPR and potential risk factors were evaluated using logistic regression, accounting for the survey design. *Plasmodium falciparum* malaria prevalence was 36.0% (27.5%, 44.5%) by RDT and 22.3% (16.0%, 28.6%) by TFM. *Plasmodium falciparum* malaria prevalence was positively associated with living in the lake-endemic area (adjusted odds ratio [aOR] 3.46; 95% confidence interval [95% CI] 1.63, 7.37), paternal occupation as peasant farmer (aOR 1.87; 1.08, 3.26) or manual laborer (aOR 1.83; 1.00, 3.37), and keeping dogs (aOR 1.62; 0.98–2.69) or cows (aOR 1.52; 0.96–2.40) inside or near the household. *Plasmodium falciparum* malaria prevalence was inversely associated with indoor residual insecticide spraying (IRS) (aOR 0.44; 0.19, 1.01), having a household connected to electricity (aOR 0.47; 0.22, 0.98), and a household with two (aOR 0.45; 0.22, 0.93) or ≥ three rooms (aOR 0.41; 0.18, 0.93). We report high but geographically heterogeneous pfPR in children in western Kenya and significant associations with IRS and household-level socioeconomic factors.

INTRODUCTION

Plasmodium falciparum (Pf) malaria exerts substantial morbidity and mortality worldwide and accounted for an estimated 216 million cases and 445,000 deaths in 2016, mostly among children living in sub-Saharan Africa, including Kenya.^{1,2} Although the burden of malaria in Kenya has been decreasing, mirroring global trends,³ malaria still ranks among the top 10 causes of morbidity and was estimated to cause between 3.5 and 9.6 million clinical cases in 2016.⁴ The malaria burden in Kenya varies by geography, with areas neighboring Lake Victoria having the highest reported prevalence (~42.4% by rapid diagnostic test [RDT]) and designated the lake-endemic malaria zone.^{5,6} Malaria transmission in the adjacent western Kenya highlands is lower (prevalence ~4.9%), tends to be seasonal, and is characterized by epidemics, whose magnitude vary from year to year; hence, this zone is designated as highland-epidemic malaria zone.⁶ The well-demarcated malaria-epidemiologic zones in Kenya lend themselves to targeted malaria control,⁷ but there are challenges about how to deal with > 75% of malaria infections, which are usually asymptomatic.^{8–10} People who are asymptotically infected constitute a major source of new infections^{11,12} because they are more likely to be bitten by mosquitoes than parasite-free individuals,¹³ they are

usually not detected or treated, and are often mobile,^{10,14} which increases their potential to establish foci of transmission in distant areas.¹⁵

A better understanding of the dynamics of asymptomatic malaria in western Kenya may help design interventions to efficiently target high malaria burden regions.¹⁶ Our interest in the dynamics of asymptomatic malaria in Kenya had an additional motivation. *Plasmodium falciparum* malaria is suspected to be causally related to endemic Burkitt lymphoma (eBL),¹⁷ but the evidence remains incomplete. Previous research on malaria in Kenya has been conducted in a few relatively small geographical areas,^{15,18} in children of a restricted age range,¹⁹ and in clinical cases²⁰ or children attending school^{21,22}; therefore, those data are imperfect for eBL studies. This study aimed to generate baseline data to enable precise evaluation of malaria patterns in healthy eBL-age children in the regions of western Kenya where eBL incidence is high. Specifically, we were interested in measuring household- and individual-level risk factors of *P. falciparum* malaria in children enrolled from representative villages in western Kenya.

MATERIALS AND METHODS

Setting of the study. Between April 2015 and June 2016, we conducted a stratified, multistage cluster design cross-sectional survey to enroll healthy children aged 0–15 years in 100 randomly selected villages (Figure 1) in two administrative regions of Kenya, formerly known as Nyanza and Western Province (Figure 2A). Children enrolled in the cross-sectional survey will serve as controls in a case-control study of eBL called EpideMiology of Burkitt Lymphoma in East African

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FIGURE 1. Diagram of sampling scheme used in the recruitment of apparently healthy children aged 0–15 years between April 2015 and June 2016 from the Western and Nyanza provinces of Kenya. *No child was enrolled from one of the 34 selected villages in the EA far from water and low population density.

Children and Minors (EMBLEM).²³ The two regions wrap around Lake Victoria, which is about 3,700 ft. above sea level and extend inland into the Great Rift Valley that rises to about 4,600 ft. above sea level. The study area was divided into the lake-endemic and highland-epidemic areas, based on definitions used by the Kenya National Malaria Control Program.⁶ The lake-endemic area was further subdivided into lakeshore districts, defined as districts with a lake shoreline, except for Kuria West and East, which are at a higher altitude, and inland districts, defined as districts separated from the shoreline by one or more districts (as shown in Figure 2B). The climate is warm (18–31°C), wet (48–250 mm of rainfall per month, with two rainfall seasons), and humid and, therefore, conducive to perennial malaria transmission in the lakeshore area, but drier (27–250 mm per month) and cooler (10–25°C), and thus not conducive to malaria transmission in the adjacent highlands.^{6,24}

Ethics approval and consent to participate. The Moi University Institutional Research and Ethics Committee (000536) and the National Cancer Institute Special Studies Institutional Review Board reviewed and approved the study (10-C-N133). Written informed consent was obtained from the parents or guardians of the children and written informed assent was obtained from children aged seven years or older prior to enrollment.

Sampling design. A stratified multistage cluster design (Figure 1) was implemented to enroll a representative sample of children.²⁵ In the first stage, 100 census enumeration areas (EAs) were selected from a national census list,²⁶ grouped into four strata, namely, “low population density,” “high population density,” “near water,” and “far from water.” These were the areas we expected to be associated with malaria transmission.^{24,25} Enumeration areas were defined as low-density stratum (rural) when they had fewer than 2,235 children aged 0–15 years (i.e., below the average EA childhood population in western Kenya); otherwise the EAs were classified as high-density EA stratum (urban). Based on distances estimated from geographical information system maps of Kenya, EAs with a boundary next to or within 500 m of an all-season surface water body (swamp, river, or lake) were defined as near-water stratum; otherwise they were classified as far-from-water EA stratum. Thus, 50 EAs were sampled from the “far-from-water” stratum and 50 from the “near-water” stratum, both with probability proportional to size, in such a way that 34 of the EAs were from the low-density stratum EAs and 16 of the EAs were from the high-density stratum. In the second stage, one village per EA was randomly selected. In the third stage, all households in a village were counted, listed, and 22–25 households randomly selected per village. Finally, 1–20 children in the selected households were enrolled at their

FIGURE 2. (A) Map showing the study area in Kenya. The location of the study area is marked by a rectangular box, and the details of study area are shown in the zoom out including regions named Western Province and Nyanza Province, based on the old administrative names present before the Constitutional change of 2013. Details include the provincial, district, and sublocation, which is also the census enumeration area (EA), boundaries. The selected EAs are color coded to indicate their distribution and stratification: rural or urban status and proximity to surface water (see Methods and Materials). (B) This figure shows *Plasmodium falciparum* prevalence (pfPR) in the study region divided into malaria-epidemiological zones (see Introduction). The lake-endemic area is divided into a lakeshore area (lighter shade of red, labeled lake-endemic) and a more inland area (darker shade of red, lake-endemic intermediate), and the highland-epidemic (lime green). (C) Age-specific patterns of geometric mean parasite density (GMPD), parasites/μL. Data for the lake-endemic area are plotted. The solid square represents the GMPD and short horizontal bars connected by a vertical line represent 95% confidence bands of the GMPD. Because of sparse data, GMPD results for the highland-epidemic area are not graphed but tabulated below the graph. The numbers shown in the graph are for children who were positive on TFM with quantified parasites. The total number of children tested by thick film microscopy (TFM) is similar to those shown in Figure 3B, except for the 6- to 8-year age group in which 18 children were tested by TFM. This figure appears in color at www.ajtmh.org.

homes, based on a predetermined age and gender distribution of typical eBL cases in western Kenya and invited to take part. Enrollment was implemented such that about half of the villages were enrolled during the dry season and the other half during the wet season. Children aged 0–15 years old who were usual residents of the household and did not report any symptoms of malaria or another illness requiring medical treatment on the day of interview were eligible.

Participant enrollment and malaria testing. Study activities involved a one-time cross-sectional contact with participants. Following written consent of a parent/guardian and assent of children older than 7 years, experienced field teams administered structured questionnaires to record demographic and household information (Tables 1, 3, and 4). Venous blood specimens for research (10 mL) and clinical tests (4 mL) were collected from each child in ethylenediaminetetraacetic acid (EDTA) tubes. Research blood specimens were transported in cold boxes to local EMBLEM field laboratories within 2 hours of collection; centrifuged for 15 minutes at 1,300 g to separate plasma, buffy coat, and red cell fractions; and all samples were stored in barcoded cryovials at -80°C . Clinical specimens were immediately tested for human immunodeficiency virus (HIV) using commercial RDTs and for malaria parasitemia using thick-film microscopy (TFM) and RDT. As per guidelines, three approved commercial HIV

test kits were used, namely, Determine HIV1/2, Stat Pack, and Unigold. Determine HIV1/2 was used as the screening test, Stat Pack was used as the confirmatory test for a Determine positive test, and Unigold was used as the tie breaker, in case Determine and Stat Pack results disagreed. A positive HIV test result was based on at least two positive test results. No child aged < 1 year was found to be HIV-positive, so the issue of positivity from maternal antibodies did not arise. Rapid diagnostic test was based on the *P. falciparum* malaria histidine-rich protein 2 (HRP2) antigen (CareStart™ MALARIA HRP2 (Pf); ACCESSBIO, Somerset, NJ), which has a false-positive rate of 1.5% for *P. falciparum*.²⁷ Thick-film microscopy was performed on thick-film slides stained with 10% Giemsa for 10 minutes. Visualized asexual malaria parasite forms were counted against 200 white blood cells (WBCs) and standardized to the WBC count/μL. Thin-film smears were examined to identify *Plasmodia* species. *Plasmodium falciparum* was seen in ~98% of the samples; therefore, this species is assumed in this report. Rapid diagnostic tests have high sensitivity and specificity in different evaluations when compared with conventional light microscopy,²⁸ the gold standard for confirming malaria parasitemia²⁹ and are gaining popularity for malaria surveillance in endemic areas.^{30,31} The RDTs proved easy to perform, interpret, and robust under field conditions. Furthermore, because malaria

TABLE 1
Characteristics of 965 asymptomatic children aged 0–15 years surveyed between April 2015 and June 2016 in western Kenya

Characteristic	N = 965*	Weighted%† (95% confidence interval)
Demographics		
Age, years		
0–5	334	31.1 (27.2, 35.1)
6–10	401	41.0 (36.8, 45.2)
≥ 11	230	27.9 (23.6, 32.2)
Gender		
Female	448	47.8 (43.7, 52.0)
Male	517	52.2 (48.0, 56.3)
Stratification variables		
Proximity to water		
Far (> 500 m)	500	34.1 (25.4, 42.7)
Near (≤ 500 m)	465	65.9 (57.3, 74.6)
Population density of children 0–15 years		
Low (< 2,235)	652	47.7 (38.9, 56.6)
High (≥ 2,235)	313	52.3 (43.4, 61.1)
Geographical variables		
Region		
Nyanza Province	648	52.6 (38.1, 67.1)
Western Province	317	47.4 (32.9, 61.9)
Malaria endemicity		
Highland epidemic	60	17.1 (4.5, 29.7)
Lake endemic	905	82.9 (70.3, 95.5)
Season of enrollment‡		
Dry	267	26.7 (15.4, 37.9)
Wet	698	73.3 (62.1, 84.6)
Parental characteristics		
Mother's education		
Up to standard 4	182	20.4 (14.5, 26.3)
Standard 5–7	456	45.4 (39.9, 50.9)
≥ Senior secondary school	316	32.8 (26.8, 38.8)
Father's education		
Up to standard 4	151	17.7 (12.6, 22.8)
Standard 5–7	371	36.4 (30.7, 42.1)
≥ Senior secondary school	414	43.1 (36.3, 49.8)
Mother's occupation		
Trader/sales	254	27.3 (21.3, 33.3)
Peasant farmer	570	60.0 (52.6, 67.4)
Manual laborer	133	11.6 (8.3, 15.0)
Father's occupation		
Trader/sales	243	24.2 (18.2, 30.3)
Peasant farmer	422	45.8 (38.2, 53.5)
Manual laborer	291	28.8 (23.2, 34.4)
Mother's income\$, Kenyan shillings		
≤ 5,703	856	85.5 (81.0, 89.9)
> 5,703	109	14.5 (10.1, 19.0)
Malaria prevention		
Slept under mosquito net the night before		
No	363	34.4 (27.8, 41.1)
Yes	591	63.5 (57.1, 69.9)
Indoor residual insecticide sprayed in house		
No	880	90.8 (86.3, 95.3)
Yes	71	7.2 (2.7, 11.7)
Don't know	4	0.1 (0.0, 0.3)
History of malaria treatment		
Inpatient		
Yes, past 12 months	95	8.6 (6.1, 11.1)
Yes, > 12 months	117	14.5 (10.7, 18.2)
Never	743	75.0 (70.6, 79.5)
Outpatient		
Yes, past 12 months	539	55.3 (49.4, 61.3)
Yes, > 12 months	64	6.7 (4.3, 9.1)
Never	352	36.1 (30.0, 42.2)

* The column shows the unweighted frequencies for each category of the characteristics examined.

† The column shows the weighted percent for each variable. The weighted percentages may not add up to 100% for some variables because of missing data. The weighted population was estimated to be 1,663,200 with a coefficient of variation of 1.2.

‡ January to March and July to August were classified as dry season months, whereas April to June and September to December were classified as wet season months.

§ Income categorized based on the international poverty line of \$1.90 per a day, which is approximately equal to 5,703 Kenyan shillings for the average 30-day monthly income. Total household income or father's income was not analyzed because the results for these were considered unreliable.

antigens appear in blood before asexual parasites and remain in blood for several weeks after asexual parasites have been cleared from blood,³² individuals who are RDT positive but TFM negative can be considered as malaria positive, although without visualized parasites and not as false positives. Only eight (0.6%) children were deemed to have clinical malaria, based on reporting a fever that was verified ($\geq 37.5^{\circ}\text{C}$) and having $> 2,500$ parasites/ μL at the time of interview.³³ These children were not excluded from the study but referred for evaluation and treatment as per National Treatment Guidelines.

Data management. Questionnaires and laboratory forms were reviewed for completeness, accuracy, and clarity and then computerized by DataFax. Consistency checks were performed on the electronic data and corrections applied, in consultation with field staff.

Statistical analysis. The results were weighted by the inverse probability of children in the two regions (approximately 1,663,200 children aged 0–15 years) being sampled into the study.²⁵ Weights were trimmed by replacing the value of the weights in the highest 5th percentile of the weight distribution with the value of the weight at the 95th percentile to minimize the impact of outlier weights. The variance estimation took sampling weights and the clustering of children in the village into account. The performance of RDT to detect asexual parasites was validated by calculating sensitivity and specificity against TFM performed by experienced local microscopists.^{28,30} Because malaria antigens appear in blood before asexual parasites and remain in blood for several weeks after asexual parasites have been cleared from blood,³² our primary analyses of *Pf* prevalence (pfPR) are based on RDT, which captures both current and recent infection. The geometric mean parasite density (GMPD) was calculated in participants with asexual parasites visualized by TFM. Associations between pfPR and study covariates were assessed by odds ratios (ORs) and associated Wald-type 95% confidence intervals (95% CIs) using Proc Survey logistic (SAS version 9.4, Cary, NC). The independent association between pfPR and 10 uncorrelated variables with a $P < 0.10$ in the unadjusted analysis or those selected a priori as risk factors for malaria or eBL was assessed using multivariate models. As the goal of this study was hypothesis generation, these results were not corrected for multiple comparisons, such as with a Bonferroni method, and a two-sided $P \leq 0.05$ was considered statistically significant.

RESULTS

Characteristics of study population. Overall, 965 (98.6%) of 979 children invited were enrolled, representing 7,851 eligible children living in 2,696 selected households in 99 of

100 selected villages. One village from which one child was selected to be enrolled was dropped because one parent insisted that the other parent be present to give permission, but it was not possible to arrange a second visit to this village because this happened toward the end of the fieldwork, which ended shortly thereafter.

The weighted population distribution is shown in Table 1 and Supplementary Table 1: 41.0% of children were aged 6–10 years, 52.2% were males, 52.3% lived in high-density villages, 65.9% lived in villages near (within 500 m) surface water, and 52.6% were from Nyanza Province. Most (82.9%) children were from the lake-endemic malaria area, with 44.2% living in subareas abutting Lake Victoria and 38.7% in more inland areas, and 17.1% lived in the highland-epidemic malaria area (as shown in Figure 2B). Most mothers and fathers had attained standard 5 or higher education (78.2% and 79.5%, respectively); occupation was peasant or subsistence farmer for 60.0% of the mothers and 45.8% of the fathers; and 85.5% of mothers had a monthly income $\leq 5,703$ Kenyan shillings (equivalent to US\$ 1.90 per day, based on the poverty index by the World Bank). Ownership of long-lasting treated mosquito bed nets was 69.7%, and 63.5% of the children were reported to have slept under a treated net the night before the interview. By contrast, only 7.2% of households were reported to have received indoor residual insecticide spraying (IRS). History of inpatient malaria treatment was reported for 23.1% of the children, including 8.6% with inpatient treatment in the past 12 months and 14.5% more than 12 months before interview. Outpatient malaria treatment was reported for 62.0% of the children, including 55.3% in the past 12 months and another 6.7% in the period more than 12 months before the interview. HIV infection was positive in 1.1% ($n = 15$; youngest HIV-positive child was age 2 years) of the children.

Weighted *P. falciparum* malaria prevalence and density.

The weighted cross-sectional pfPR was 36.0% (95% CI: 27.5%, 44.5%) by RDT and 22.3% (16.0%, 28.5%) by TFM performed by experienced local technicians (Table 2). The sensitivity of RDT to detect parasitemia was 82.0% (75.1%, 89.0%) and the specificity was 76.8% (69.4%, 84.1%), as compared with TFM performed by experienced local technicians. Following the rationale described in the Materials and Methods, the 157 individuals who were RDT positive but TFM negative (18.1%; Table 2) were considered as having malaria antigenemia but not visualized parasites rather than as false positives.

The weighted GMPD, among those with visualized parasites on TFM, was 901 parasites/ μL (95% CI: 460, 1,767). Geometric mean parasite density was higher in the TFM-positive/RDT-positive group than the TFM-positive/RDT-negative group (1,122 versus 179 parasites/ μL ; $P < 0.001$).

TABLE 2

Weighted results showing the validation of RDT to detect parasitemia using thick-film microscopy by experienced local microscopists, among children 0–15 years surveyed between April 2015 and June 2016 in western Kenya

TFM by experienced local technicians			
	Negative weighted % (n)	Positive weighted % (n)	Total weighted % (n)
Rapid diagnostic test			
Negative	59.6 (532)	4.0 (39)	63.6 (571)
Positive	18.1 (157)	18.3 (206)	36.4 (363)
Total	77.7 (689)	22.3 (245)	100.0 ($N = 934^*$, N weighted = 1,612,821)

RDT = rapid diagnostic test; TFM = thick film microscopy. The sensitivity of detecting parasitemia by RDT was 82.0% (75.1%, 89.0%) and the specificity was 76.8% (69.4%, 84.1%) as compared with TFM by experienced local technicians.

* Results do not include 31 children not successfully tested: two missing RDT results, 15 missing TFM results, and 14 missing both.

Geometric mean parasite density was higher among children in the lake-endemic area than those in the highland-epidemic area (1,046 versus 132 parasites/ μ L; $P = 0.04$) and peaked in children aged < 6 years compared with older children (2,917 versus 554 parasites/ μ L; $P < 0.001$). These GMPD patterns were driven by results in the lake-endemic but could not be assessed in the highland-epidemic area because only five children were TFM positive (Figure 2C). No differences in GMPD by gender were seen ($P = 0.36$).

Geographical, demographical, and seasonal pfPR patterns. The pfPR was higher in the lake-endemic area than the highland-epidemic area (40.7% versus 13.8%, $P < 0.001$). However, within the lake-endemic area, pfPR was not different in children living in areas abutting the lakeshore versus those living more inland but sharing similar climate (39.9% versus 41.7%; Figure 2B). Age-specific pfPR in the lake-endemic area was 39.0% in children aged 0–2 years old, slightly higher (43.0–44.0%) in children aged 3–8 years old and peaked (47.0%) in children aged 9–11 years, then moderately lower (30.0%) in those aged 12–15 years (Figure 3A). The age-specific pfPR patterns in the highland-epidemic area children were low (0.0–10.0%) in children aged 0–11 years and spiked in those aged 12–15 years (46.8%), although these results are based on small

numbers (Figure 3B). Thus, the age-specific pfPR patterns differed from the age-specific GMPD patterns described previously.

Pf malaria prevalence was perennial (unrelated to season) in the lake-endemic areas (Figure 3C) but it was high only in the wet season in the highland-epidemic areas (Figure 3D), although this interpretation is based on only three children enrolled in the dry season.

Factors associated with asymptomatic malaria infection.

The unadjusted associations between pfPR and studied covariates are shown in Tables 3 and 4. An increased pfPR was associated with living in the lake-endemic (versus the highland-epidemic area: OR 4.29; 95% CI: 2.06, 8.95) and with having a father whose occupation was reported as peasant farmer (OR 2.53; 95% CI: 1.31, 4.87) or manual laborer (versus trader or sales: OR 1.94; 95% CI: 1.15, 3.29; Table 3). An increased pfPR was associated with keeping pigs (OR 2.73; 95% CI: 1.07, 6.92), dogs (OR 1.66; 95% CI: 1.05, 2.63), and, to a lesser extent, cows inside or near the house (versus not: OR 1.52; 95% CI: 0.96, 2.40; Table 4).

Pf malaria prevalence was inversely associated with male gender (versus female: OR 0.74; 95% CI: 0.53, 1.05) and with reporting IRS application to the household (versus not: OR 0.49; 95% CI: 0.22, 1.08; Table 3). *Plasmodium falciparum*

FIGURE 3. Multipanel figure showing bar graphs of weighted age group *Plasmodium falciparum* prevalence (pfPR) in children aged 0–15 years in western Kenya in the lake-endemic (A) and highland-epidemic (B) areas and seasonal pfPR patterns in the lake-endemic (C) and highland-epidemic (D) areas. The dry season was defined as January to March and July to August; the wet season was defined as April to June and September to December. The results from the early and late dry and wet season months were combined for the highland-epidemic areas because of sparse data. The horizontal bars connected by a vertical line represent 95% confidence bands for the pfPR. This figure appears in color at www.ajtmh.org.

TABLE 3

Unadjusted ORs of factors associated with *Plasmodium falciparum* parasite infection among children aged 0–15 years surveyed between April 2015 and June 2016 in western Kenya

Characteristics	N = 949*	Unadjusted		
		Weighted %	OR (95% confidence interval)	P†
All subjects	949	36.0		
Demographics				
Age, years				0.14
0–5	325	36.3	Ref	
6–10	398	39.9	1.17 (0.77, 1.75)	
≥ 11	226	29.9	0.75 (0.39, 1.43)	
Gender				0.09
Female	441	39.6	Ref	
Male	508	32.8	0.74 (0.53, 1.05)	
Design variables				
Proximity to water				0.74
Far (> 500 m)	494	34.0	Ref	
Near (≤ 500 m)	455	37.1	1.15 (0.51, 2.57)	
Population density of children 0–15 years				0.90
Low (< 2,235)	637	36.6	Ref	
High (≥ 2,235)	312	35.5	0.96 (0.46, 1.98)	
Geographical				
Region				0.60
Nyanza Province	637	38.2	Ref	
Western Province	312	33.6	0.82 (0.39, 1.72)	
Malaria endemicity				< 0.001
Highland epidemic	60	13.8	Ref	
Lake endemic	889	40.7	4.29 (2.06, 8.95)	
Season of enrollment‡				0.47
Dry	265	40.5	Ref	
Wet	684	34.4	0.77 (0.38, 1.58)	
Parental characteristics				
Mother's education				0.21
Up to standard 4	180	40.7	Ref	
Standard 5–7	450	38.9	0.93 (0.47, 1.83)	
≥ Senior secondary school	308	29.0	0.64 (0.29, 1.41)	
Father's education				0.32
Up to standard 4	150	41.5	Ref	
Standard 5–7	363	38.2	0.87 (0.37, 2.01)	
≥ Senior secondary school	408	31.1	0.64 (0.29, 1.41)	
Mother's occupation				0.28
Trader/sales	251	28.8	Ref	
Peasant farmer	560	39.7	1.63 (0.88, 2.99)	
Manual laborer	131	33.2	1.23 (0.62, 2.45)	
Father's occupation				< 0.01
Trader/sales	237	22.7	Ref	
Peasant farmer	418	42.6	2.53 (1.31, 4.87)	
Manual laborer	285	36.3	1.94 (1.15, 3.29)	
Mother's income§, Kenyan shillings				0.63
≤ 5,703	841	36.7	Ref	
> 5,703	108	32.2	0.82 (0.36, 1.87)	
Malaria prevention				
Slept under mosquito net the night before				0.45
No	358	39.3	Ref	
Yes	580	34.6	0.82 (0.48, 1.38)	
Indoor residual insecticide sprayed in house				0.08
No	865	37.2	Ref	
Yes	70	22.4	0.49 (0.22, 1.08)	
History of malaria treatment				
Inpatient				0.59
Yes, past 12 months	95	41.4	Ref	
Yes, > 12 months	117	38.6	0.89 (0.35, 2.24)	
Never	727	35.1	0.77 (0.41, 1.42)	
Outpatient				0.13
Yes, past 12 months	531	39.9	Ref	
Yes, > 12 months	64	23.4	0.46 (0.22, 0.98)	
Never	344	33.0	0.74 (0.43, 1.29)	

OR = odds ratio.

* Results are based on children with complete rapid diagnostic results. Children with missing results (N = 16) are excluded.

† The P value is for heterogeneity.

‡ January to March and July to August were classified as dry season months, whereas April to June and September to December were classified as wet season months.

§ Income categorized based on the international poverty line of \$1.90 per a day, which is approximately equal to 5,703 Kenyan shillings for the average 30-day monthly income. Father's income was not estimated because of concerns about reliability of data.

TABLE 4

Unadjusted ORs of additional factors associated with *Plasmodium falciparum* parasite infection among children aged 0–15 years surveyed between April 2015 and June 2016 in western Kenya

Characteristics	N = 949*	Unadjusted		P†
		Weighted %	OR (95% confidence interval)	
Home characteristics				
Distance of home from main road				0.17
Far from the main road	508	33.2	Ref	
Near the main road	330	46.0	1.71 (0.85, 3.45)	
In town or city	104	24.6	0.66 (0.27, 1.62)	
Distance to water source				0.73
Near (≤ 500 m)	351	34.7	Ref	
Far (>500 m)	591	36.7	1.09 (0.67, 1.79)	
Source of drinking water				0.20
Unprotected spring/well	562	38.9	Ref	
Protected spring/well	170	38.7	0.99 (0.58, 1.70)	
Public tap/piped household	207	26.8	0.57 (0.30, 1.11)	
Connected to electricity grid				0.01
No	822	38.9	Ref	
Yes	115	19.6	0.38 (0.18, 0.80)	
Number of rooms in house				0.04
1 room	138	55.9	Ref	
2 rooms	389	34.7	0.42 (0.21, 0.83)	
≥ 3 rooms	415	31.1	0.36 (0.15, 0.85)	
Number of people sleeping in the same room as child				0.04
1–2 people	383	32.2	Ref	
3 people	255	28.8	0.85 (0.49, 1.47)	
≥ 4 people	304	45.3	1.74 (0.84, 3.61)	
Number of usual children residents				0.95
1–2 people	346	37.0	Ref	
3 people	228	35.1	0.92 (0.50, 1.69)	
≥ 4 people	368	35.2	0.93 (0.55, 1.56)	
Number of usual adult residents				0.63
1–2 people	565	35.1	Ref	
3 people	181	39.7	1.22 (0.79, 1.89)	
≥ 4 people	196	34.5	0.98 (0.56, 1.71)	
Other malaria prevention				
Owns treated mosquito bed net				0.20
No	315	41.3	Ref	
Yes	623	34.2	0.74 (0.46, 1.18)	
Regularly uses mosquito insecticide sprays				0.25
No	908	36.8	Ref	
Yes	24	21.8	0.48 (0.14, 1.70)	
History of fevers and hospital admission				
Has fever at enrollment				0.40
No	820	36.6	Ref	
Yes	120	30.6	0.76 (0.40, 1.44)	
Reported ≥ 1 fever in the last 12 months				0.90
No	312	37.2	Ref	
Yes	509	36.5	0.97 (0.64, 1.48)	
Reported ≥ 1 fever due to malaria in the past 6 months				0.34
No	281	31.9	Ref	
Yes	659	37.6	1.29 (0.76, 2.17)	
Reported ≥ 1 fever not due to malaria in the last 6 months				0.59
No	761	36.6	Ref	
Yes	176	32.9	0.85 (0.46, 1.55)	
Reported ≥ 1 hospital admission				0.71
No	682	35.7	Ref	
Yes	254	37.6	1.08 (0.71, 1.66)	
Animals kept near or inside house				
Chicken				0.31
No	111	28.2	Ref	
Yes	831	37.1	1.50 (0.68, 3.34)	
Pigs				0.04
No	883	34.4	Ref	
Yes	59	58.8	2.73 (1.07, 6.92)	
Goat				0.46
No	648	34.8	Ref	
Yes	294	38.8	1.19 (0.75, 1.89)	

(continued)

TABLE 4
Continued

Characteristics	N = 949*	Weighted %	Unadjusted	P†
			OR (95% confidence interval)	
Sheep				0.36
No	748	35.2	Ref	
Yes	194	39.9	1.23 (0.79, 1.90)	
Cows				0.07
No	365	29.9	Ref	
Yes	577	39.3	1.52 (0.96, 2.40)	
Birds				0.39
No	881	36.6	Ref	
Yes	61	26.5	0.63 (0.21, 1.84)	
Dogs				0.03
No	298	29.1	Ref	
Yes	642	40.5	1.66 (1.05, 2.63)	

OR = odds ratio.

* Results shown do not include children with missing rapid diagnostic test results (N = 16).

† The P value is for heterogeneity.

malaria prevalence tended to be inversely associated with higher educational attainment by parents, but the trend results did not reach statistical significance (Table 3). In addition, pfPR was inversely associated with living in a household connected to electricity (versus not: OR 0.38; 95% CI: 0.18, 0.80) and with living in a house with two rooms (OR 0.42; 95% CI: 0.21, 0.83) or more than two rooms (versus one room: OR 0.36; 95% CI: 0.15, 0.85; Table 4).

Pf malaria prevalence was not associated with sleeping under a mosquito bed net the night before the interview, a history of inpatient or outpatient malaria treatment, proximity of village to surface water, population density, season, fever at the time of enrollment, reported fevers due to malaria or other illnesses, the number of lifetime hospital admissions, or HIV status (Tables 3 and 4).

In the adjusted analysis, pfPR was positively associated with living in the lake-endemic area (adjusted OR [aOR] 3.46; 95% CI: 1.63, 7.37) and with the father's occupation reported as peasant farmer (aOR 1.87; 95% CI: 1.08, 3.26) or manual laborer (aOR 1.83; 95% CI: 1.00, 3.37; Table 5). Keeping dogs and cows inside or near the house was associated with a higher pfPR, albeit not statistically significant. *Plasmodium falciparum* malaria prevalence was inversely associated with living in a house connected to electricity (aOR 0.47; 95% CI: 0.22, 0.98), living in a house where IRS was applied (aOR 0.44; 95% CI: 0.19, 1.01), and living in a house with two rooms (aOR 0.45; 95% CI: 0.22, 0.93) or more than two rooms (aOR 0.41; 95% CI: 0.18, 0.93), but the relationship was not monotonic. The inverse association between pfPR and male gender tended to persist in the adjusted analysis (aOR 0.70; 95% CI: 0.48, 1.02; Table 5), albeit not statistically significant.

DISCUSSION

Our study was conducted to generate population-level data about low-grade, mostly asymptomatic, malaria in the western regions of Kenya that also has a high incidence of eBL.³⁴ This aggressive childhood cancer has been linked to perennial malaria transmission,^{35,36} it shows a strong ecological correlation with malaria transmission zones in western Kenya,³⁴ and peaks in children aged 6–9 years who are more likely to be asymptomatic parasite carriers.³⁷ Thus, our comprehensive analysis of household- and individual-level exposures in healthy children of an age typical of eBL cases in western

Kenya³⁸ provides baseline data about malaria patterns in this region relevant to malaria public health authorities and eBL researchers.^{23,25}

Our study found high but geographically heterogeneous pfPR in children in the eBL age range in western Kenya. We observed strong inverse associations between pfPR and IRS application in the household and with characteristics indicative of high socioeconomic status (a house with two or more rooms, or connected to electricity), and positive associations with characteristics indicative of low socioeconomic status (having a father employed as a peasant farmer or manual laborer). Age-specific pfPR peaked in older children, particularly in the lake-endemic area, mirrors the patterns observed in eBL cases,³⁷ whereas GMPD peaked in younger children, consistent with the notion that younger children have lower antiparasite immunity³⁹ and that high GMPD might not be a risk factor for eBL.³⁹ Further research on pfPR/GMPD patterns could shed new insights about the role of malaria in eBL.^{37,40}

We confirm the high ownership and use of insecticide-treated bed nets, as reported by 69.7% of the population.⁴¹ However, in contrast to the expected reduction in pfPR associated with bed net use, as was shown in a community trial conducted in two districts of western Kenya in 2005–2007,⁴² bed net use the night before was not associated with significant reduction in the odds of malaria infection in our study. Our results confirm the strong protective effect of IRS against malaria infection, as reported previously in Kenya⁴³ and elsewhere.^{25,44} Our findings that pfPR was elevated in children with fathers engaged in peasant or manual laborer jobs and decreased in children living in bigger houses and those connected to electricity reaffirm the important role socioeconomic environment of the child plays in influencing malaria risk.⁶ These results highlight the potential to enhance malaria control through greater use of IRS and policies that improve income and housing construction.⁴⁵

Our finding of high pfPR in the lake-endemic area is not surprising because Lake Victoria is the main geographical factor influencing the warm, wet, and humid climate that is conducive for perennial malaria transmission.⁵ However, our finding that pfPR was similar in the areas abutting the lake than those that were more inland (39.3% versus 40.9%) suggests that breeding sites located closer to people's homes, such as slow-flowing streams, rain ponds, and vegetation, play an

TABLE 5

Adjusted ORs of factors associated with *Plasmodium falciparum* parasite infection among children aged 0–15 years surveyed between April 2015 and June 2016 in western Kenya

Characteristics	OR* (95% confidence interval)	P†
Demographical		
Age, years		0.22
0–5	Ref	
6–10	1.22 (0.77, 1.95)	
≥ 11	0.85 (0.40, 1.80)	
Gender		0.06
Female	Ref	
Male	0.70 (0.48, 1.01)	
Geographical		
Malaria endemicity		< 0.01
Highland epidemic	Ref	
Lake endemic	3.46 (1.63, 7.37)	
Parental characteristics		
Father's occupation		0.05
Trader/sales	Ref	
Peasant farmer	1.87 (1.08, 3.26)	
Manual laborer	1.83 (1.00, 3.37)	
Malaria prevention		
Indoor residual insecticide sprayed in house		0.05
No	Ref	
Yes	0.44 (0.19, 1.01)	
Home characteristics		
Connected to electricity grid		0.04
No	Ref	
Yes	0.47 (0.22, 0.98)	
Number of rooms in house		0.08
1 room	Ref	
2 rooms	0.45 (0.22, 0.93)	
≥ 3 rooms	0.41 (0.18, 0.93)	
Animals kept near or inside house		
Pigs		0.36
No	Ref	
Yes	1.52 (0.62, 3.75)	
Cows		0.09
No	Ref	
Yes	1.60 (0.92, 2.78)	
Dogs		0.06
No	Ref	
Yes	1.61 (0.97, 2.68)	

OR = odds ratio.

* All variables in the table are adjusted for one another (see Methods).

† The P value is for heterogeneity.

important small-area role in maintaining high malaria transmission patterns in both lakeshore and inland areas.⁴⁶ This reasoning is consistent with the observation that most mosquito vectors tend to breed near sites of human habitation⁴⁷ and that most fly relatively short distances (< 3 km) to find blood meals,⁴⁸ which is considerably shorter than the average distance across districts used to define lakeshore versus more inland areas. Our finding of high GMPD (~1,000 parasites/μL) among asymptomatic children in the lake-endemic area may have public health relevance if we consider that GMPD > 1,000 parasites/μL may be a surrogate of carrying gametocytes.⁴⁹ Conversely, a lower GMPD, such as that observed in asymptomatic children in the highland-epidemic area (mean < 200 parasites/μL) may indicate a lower likelihood of carrying gametocytes.⁴⁹ Given the public health interest in suppressing malaria, public health authorities could stress the potential for high GMPD carriers establishing foci for new infections during short-term visits to low endemicity areas.¹⁴

We found that keeping certain animals inside or near the house was associated with higher pfPR. These associations may be relevant because animals may divert mosquitoes either

away from human hosts, which is also termed zoophylaxis, or they may attract mosquitoes and incidentally increase mosquito bites for humans tending or in close proximity with the animals, leading to the so-called zoopotential.⁵⁰ Although these mosquito–animal–human interactions are plausible, their directionality is also influenced by the feeding preference of prevalent mosquito vectors, either for humans, also called anthropophilic, or for animals, also called zoophilic.⁵¹ In view of the potential animal-related risk for pfPR to households,^{52,53} further research is needed to understand the human–animal–vector interactions around households and their impact on malaria risk.⁵⁴

The strengths of our study include using a general population sample of healthy children in western Kenya to study malaria patterns. Our results complement those from studies that enrolled children in clinics⁵⁵ or schools.⁵⁶ The limitations of our study include having only cross-sectional data based on a one-time contact with the participant, which may overestimate asymptomatic malaria, and the use of RDT to estimate asymptomatic malaria, which may miss some cases. We also lacked data on the number, proximity of animals in relation to humans, and any recent changes in livestock,^{57,58} or housing design.^{47,59} In addition, we did not collect data about specific vectors prevalent in the different areas or the quality of the bed nets.⁶⁰ We acknowledge that the sample size was relatively small and many comparisons were performed; thus, the results should be considered exploratory.

CONCLUSION

This study confirmed high but geographically variable asymptomatic malaria prevalence in children with low-grade GMPD in eBL-age children in two provinces in western Kenya. Age-specific pfPR and GMPD patterns were discordant (pfPR high in older children, GMPD high in younger children), supporting the hypothesis that chronic carriage of parasites at older ages occurs in children with malaria immunity, which may be relevant for malaria biology in eBL. Our findings about IRS and measures of high socioeconomic status, including house design, highlight approaches that could be implemented to enhance malaria control in Kenya.

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