Environmental, socio-demographic and behavioural determinants of malaria risk in the western Kenyan highlands: a case–control study

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Summary

OBJECTIVE—To identify risk factors for uncomplicated malaria in highland areas of East Africa at higher risk of malaria epidemics, in order to design appropriate interventions.

METHODS—Prospective, population-based, case–control study in the Nandi Hills, a highland area of western Kenya, to identify environmental, sociodemographic and behavioural factors associated with clinical malaria. Data were collected using field observation, a structured questionnaire, and a global positioning system device.

RESULTS—We interviewed 488 cases of slide-confirmed malaria and 980 age-matched controls. Multivariate analyses associated higher malaria risk with living <250 m of a forest [OR = 3.3 (95% CI 1.5, 7.1)], <250 m of a swamp [2.8 (1.3, 5.9)], <200 m of maize fields [2.0 (1.2, 3.4)], in the absence of trees <200 m [1.6 (1.2, 2.2)], on flat land [1.6 (1.2, 2.2)], in houses without ceilings [1.5 (1.1, 2.2)], in houses with a separate kitchen building [1.8 (1.4, 2.3)] and in households where the female household head had no education [1.9 (1.1, 3.1)]. Travelling out of the study site [2.2 (1.2, 4.1)] was also associated with increased risk.

CONCLUSIONS—In this East African highland area, risk of developing uncomplicated malaria was multifactorial with a risk factor profile similar to that in endemic regions. Households within close proximity to forest and swamp borders are at higher risk of malaria and should be included in indoor residual spraying campaigns.

Keywords

highland malaria; *Plasmodium falciparum*; case–control; risk factors; environmental; household-level

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Introduction

Historically, malaria transmission in the East African highlands (>1500 m) has been low and unstable but notable increases have occurred in the past few decades. Transmission is spatially focal in the highlands. Cases and anopheline mosquitoes cluster in low-lying valley bottoms, often in close proximity to swamps or rivers (Brooker *et al.* 2004; Minakawa *et al.* 2004; Zhou *et al.* 2004, 2007; Ernst *et al.* 2006; Githeko *et al.* 2006). Although overall risk may be higher in these areas, behavioural, micro-environmental and socioeconomic factors likely modify the relationship between malaria risk and environmental suitability for transmission. Little research has been conducted to examine household-level environmental and behavioural factors that mediate risk in the East African highlands. Studies have been restricted to children despite significant incidence of clinical malaria in adults in these areas (Ghebreyesus *et al.* 2000; Brooker *et al.* 2004), and were conducted during an epidemic when risk factors may have differed from those during normal seasonal transmission (Brooker *et al.* 2004). The clinical malaria age distribution, climate, agricultural activities, cultural practices and biophysical environments in highland regions differ from the endemic lowlands, potentially resulting in a different risk profiles.

To identify risk factors for malaria in the highlands that differ from the lowlands, a prospective, population-based, case–control study was conducted in a highland area of western Kenya. Living close to swamps and forests and at lower elevations was associated with greater malaria risk (Ernst *et al.* 2006) in this area but did not fully explain malaria risk. Accordingly, additional environmental factors that may influence vector abundance, density or activity, as well as sociodemographic and behavioural factors potentially related to developing clinical malaria were investigated.

Methods

Study sites

The study was conducted in Kipsamoite and Kapsisiywa (sub)locations (pop. ~7000) in Nandi District, western Kenya (Figure 1), at elevations of 1887–2100 m. North Nandi forest borders Kipsamoite's western side. Kimondi swamp borders much of the remaining study area (Ernst *et al.* 2006 for details). Primary occupations are subsistence farming and animal husbandry.

Study design

A prospective, population-based, case–control study design was used. Cases were identified as individuals with *Plasmodium* species identified in thick or thin blood smears who had presented to either of the two local health centres with symptoms consistent with malaria (fever, chills, headache or severe malaise).

Quarterly demographic surveillance was conducted in a concurrent study during which residents were assigned permanent unique study identification numbers. Using the enumerated population, malaria cases were frequency-matched to two controls by site (Kispsamoite or Kapsisiywa) and age category (<5, 5–14, 15–44, or >45 years old). Three visits on three separate days, at different times of day, were made to homes of potential controls to determine eligibility and request participation. Exclusion criteria for selected controls were (1) prior malaria diagnosis during the study period, (2) symptoms of malaria in the preceding month, or (3) moved or primary residence out of study area. Controls deemed ineligible or refusing to participate were replaced. Controls that later became cases were reinterviewed and replaced.

Exposure measurements

Environmental data were collected for cases and controls from direct household observations, Global Positioning System (GPS) measurements (Trimble Navigation, Sunnyvale, CA, USA), and a questionnaire. The dwelling in which the participant normally slept was assessed and distances (GPS corrected 1 m resolution) to mapped forest edge, swamps, rivers, roads, and health centres were calculated using ordinary Euclidean distance in ArcGIS V 9.0 (Redlands, CA, USA). Distances from the perimeter of the sleeping place to agricultural fields and penned livestock within a radius of 200 m were measured using steel tape. Type of vegetation within 200 m of the house was recorded (Earth Institute 2005).

A questionnaire was orally administered to cases and controls in the local language, Kalenjin, to ascertain sociodemographic and behavioural characteristics such as number of occupants, travel history, malaria prevention practices, and presence of livestock and other assets.

Variables

Bednet use was defined as sleeping under a net each day of the previous week. Individuals who reported using mosquito coils (at least three times a week), taking malaria medication as prophylaxis (at least once a month) and clearing brush (at least once a month) were classified as exposed to those factors. Distances from household to swamp, forest, river and roadsides were divided into four categories <250, 250–500, 500–1000, >1000 m [average flight range of *Anopheles gambiae* (Costantini *et al.* 1996)]. Elevation and distance from the household to the nearest clinic were divided into equal quartiles. Tea, maize, trees and bushes were classified as present if located within 200 m of the structure where the participant slept. Exposure to channelled swamp water was defined as participants who lived within 250 m of a swamp and reported channelling swamp water. Geographic slope was categorized by the field assistants into four classes (flat land, gentle slope, medium slope, and steep slope). The final variable for slope was dichotomous; sloped, including any grade of slope, or flat. Similarly, field assistants used a model illustration to determine if there were no trees, few trees, some trees or many trees within 200 m of the house. The final variable was also dichotomous; no trees *vs*. trees. Overnight travel was restricted to people sleeping outside the home 7–21 days prior to interview, adjusting for the average incubation period of malaria. Travel to any area outside the study sites was included.

Household Wealth Index

Principal component analysis (PCA) was conducted using sas V 9.1 (Cary, NC, USA) to estimate a relative household wealth index from a combination of household and asset variables (Filmer & Pritchett 2001). Household characteristics included building materials used for wall, floor, separate kitchen and roof. Assets included television, radio, bicycle, pressure lamp, car, sofa set, and charcoal cooking stove. The first component accounted for 30% of the total variance. A linear combination of the original asset variables (standardized to mean = 0 and variance = 1) multiplied by their respective standardized scoring coefficients (Table 1) was used to create the household wealth variable which was then divided into quartiles.

Statistical analyses

Bivariate analyses, logistic regression, and then backwards stepwise regression with generalized estimating equations (GEE) were used to create multivariable models using sas V 9.1. All explanatory variables were initially included in the model and variables making the smallest contribution were sequentially dropped until all variables included in the model were $P < 0.10$. Matching variables, site and age were kept in the model with week of

interview which was used to control for the average 2-week time difference in interviews for controls *vs*. cases. An exchangeable correlation matrix was used to adjust for correlation among members of the same household. People from different households were considered independent of each other. Model residuals were assessed for spatial autocorrelation using Moran's I statistics (ArcGIS ver. 9.1, ESRI, Redlands, CA, USA).

Ethical considerations

All cases and controls, or the guardians of subjects <18 years old, provided written, informed consent before participation. Approval to undertake this study was obtained from the Institutional Review Board (IRB) committees at the University of Michigan (Ann Arbor, MI, USA), Kenya Medical Research Institute (KEMRI, Nairobi, Kenya), and U.S. Centers for Disease Control and Prevention (CDC, Atlanta, GA, USA). Approval for the demographic and malaria surveillance in this study was obtained from the IRB committees at Case Western Reserve University (Cleveland, OH, USA), CDC, University of Michigan and KEMRI.

Results

Study population characteristics

From March through September 2004, 492 malaria cases were identified, of whom 99.1% (*n* = 488) agreed to be in the study. Participation was similarly high (98.9%, *n* = 980) for the 990 eligible controls. Malaria cases were equally distributed between the sexes (M:F = 251:237) and were identified in all age groups [<5 years of age, *n* = 100 (20.5%); 5–14 years, *n* = 163 (33.4%); 15–44 years, *n* = 182 (37.5%); >45 years, *n* = 43 (8.8%)].

Associations with sociodemographic and environmental variables

In bivariate analyses, increased malaria risk was associated with various sociodemographic and behavioural factors (Table 2) including low education levels of female household heads, overnight travel, living near channelled swamp water and keeping livestock near the house at night. Living in a house with a metal roof, no ceiling or separate kitchen also were related to higher risk, while open eaves and uncovered windows did not appear to have an effect. Environmental risks included living on flat land, living close to forests, and having bushes but not trees <200 m from the house (Table 2).

The final multivariable model included many of the same variables, indicating that greater malaria risk was associated with lower levels of education of female household heads, recent overnight travel, living near channelled swamp water and near forests, lack of ceiling in the house, a separate kitchen and having goats in the compound. External environmental influences such as living on flat land, in close proximity to maize fields, and on land lacking nearby trees also increased malaria risk (Table 3).

Discussion

Previous analyses of passive malaria surveillance data from Kipsamoite suggested 'hotspots' of transmission associated with distance from swamps and forests (Ernst *et al.* 2006). Even in these apparent hotspots, there were malaria-free households. Although shared bio-physical environments can produce clusters of higher transmission, other factors at the individual and household levels can mediate this risk. Accordingly, associations between malaria risk and environmental, socio-demographic, and behavioural variables were explored.

Environment around the home was important. Closer proximity to swamps and forest border was associated with increased malaria risk and is consistent with findings in other highland areas (Lindblade *et al.* 2000; Staedke *et al.* 2003; Brooker *et al.* 2004; Minakawa *et al.* 2004; Zhou *et al.* 2004, 2007). These habitats may represent enhanced *Anopheles* breeding sites or microclimates that prolong adult vector survival. Our analyses also demonstrated a 500-m threshold for these relationships. Absence of trees and presence of maize near dwellings also were associated with increased risk. *Anopheles gambiae* s.s. prefer breeding in open areas (Minakawa *et al.* 2004) and exposure to sunlight increases water temperatures potentially speeding up the development rate of the aquatic stages of *An. gambiae* s.s. (Bayoh & Lindsay 2003). Maize pollen is a good nutritional source for *An. gambiae* larvae (Ye-Ebiyo *et al.* 2003) and has been related to higher malaria incidence (Kebede *et al.* 2005). The presence of many mixed vegetation classes within 200 m of the house may have obscured further relationships.

Living on flat ground, where water is most likely to accumulate, was associated with increased risk corroborating results found by Cohen *et al.* (2008) that demonstrated topography, when used as a predictor of wetness, is highly correlated with malaria risk. Absolute elevation, however, was not associated with risk. This is counter to results from a study by Brooker *et al.* (2004), who found a significant relationship between malaria risk and elevation. The narrower range of elevation across this study area (213 m) as compared to theirs (400 m) may have prevented a similar association.

Similarly to the study by Brooker *et al.* (2004), we found no association between household wealth and malaria risk. Our index may not have accurately differentiated levels of household wealth or variation may have been too limited to impact risk. Having a kitchen separate from the sleeping area was strongly associated with increased malaria odds, perhaps because smoke repels vector mosquitoes, although sleeping in a smoky room was not associated with risk in another study in the Kenyan highlands (Brooker *et al.* 2004). Many relatives and older children reported sleeping in the kitchen area and there was a tendency to keep fires burning at night for warmth in this study area which may differ from other highland communities. House construction also influences mosquito access to people sleeping inside and we found that having a ceiling in the home was associated with decreased risk of malaria. Open eaves have been associated with increased risk in some past studies (e.g. Ghebreysus *et al.* 2000) but not by Brooker *et al.* (2004) or in our study.

The education level of female heads of household was inversely associated with malaria risk. Other studies have shown that use of malaria prevention measures has been consistently related to higher maternal education (e.g. Keating *et al.* 2005; Noor *et al.* 2006), yet we saw no notable associations between use of preventive measures, including bednets, and malaria risk except for a modest decreased risk among those using mosquito coils. In our study, as in that by Brooker *et al.* (2004), practice of preventive measures was quite low. Environmental control (removal of tins and brush) was the most commonly reported activity, indicating effective environmental management techniques could be well-received. Prevalence of bednet use was low and we did not test the nets for insecticide or examine them for holes, potentially obscuring their true association with malaria risk. Although people expressed interest in bednets, anecdotal evidence suggests that even those who owned bednets did not use them, primarily because vector density, hence perceived risk, was low. Some believed that only those living near the swamps were at risk of malaria. Education regarding the importance of net use, even when vector density is low, could improve effectiveness of bednets in this area.

In our study, like others (e.g. Shanks *et al.* 2005), overnight travel increased malaria risk, even though such movement was primarily to neighbouring highland communities.

Increased malaria risk may be related to increased vector-human contact in such settings. Indeed, some interviewees informally reported that when attending funerals it was common to sleep in the open air. The relationship between malaria risk and travel should be interpreted with caution, however, as frequency of travel was low and positive bias could have arisen if residents temporarily living outside the study area were included as cases (perhaps at home on holiday and seen at the clinic) versus controls (replaced if residing out of area for work or school).

This study had both strengths and potential entries of bias. High participation rates and a fully enumerated population permitting strata-specific random selection of controls created a highly representative sample. Recall bias, a concern in case–control studies, was minimized by interviewing shortly after case and control identification. The need to replace ineligible and unavailable controls put their interview times an average of 2 weeks later than cases; however, week of interview was adjusted for in the multivariable model. Although all cases were slide-confirmed, logistical constraints precluded the testing of controls and asymptomatic cases may have been misclassified as controls, thus biasing associations. Past studies, however, demonstrated that the level of asymptomatic malaria in this region is low (John *et al.* 2005). The large sample size required multiple field assistants, potentially resulting in differential information bias particularly for subjectively measured variables such as slope and tree cover. To minimize such bias, an intensive training program was combined with spot checks of 10% of all questionnaires by the study coordinator and by dichotomizing highly subjective variables (tree cover and slope).

Results of our study underscore the complexity of highland malaria transmission. Prior studies have assessed some of the factors that we evaluated, but our investigation adds to these earlier reports by assessing multiple environmental, social and behavioural factors in a single multivariate model. The report by Brooker *et al.* (2004) is the only other study of this nature from the east African highlands, but their study focused on children during an epidemic and a different set of variables. Although our results indicate that malaria risk may cluster near specific land covers, considerable time and resources are needed to identify such high risk areas, and only some of the malaria cases are included. Moreover, predictors of high risk may vary among regions. The resources needed to map high risk areas may be better allocated, for example, toward achieving universal coverage of indoor residual spraying. Workers administering the spraying should keep in mind that not all members of the household sleep in the main house and spraying of outbuildings, particularly kitchen buildings, may be necessary to ensure complete coverage.

Acknowledgments

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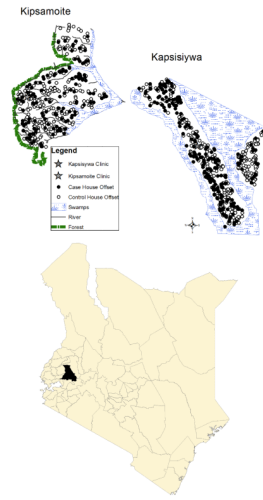
Figure 1.
Nandi District in western Kenya with map of study site (Kipsamoite Sublocation and Kapsisiywa Location).

Table 1

Standardized scoring coefficients

Variable	Pressure lamp	Stove	Sofa	Lantern	Bike	Radio	TV	Cement Floor	Mud Walls	Metal Roof	No Separate Kitchen
Standardized Scoring Coefficient	0.17	0.23	0.09	0.26	0.36	0.37	0.17	0.17	−0.17	0.02	−0.10

Table 2

Bivariate analysis of association between malaria risk (cases/controls) and various demographic, social and environmental variables in Kipsamoite and Kapsisiywa, Kenya, March–September 2004

Potential risk factors	No. cases (n = 488)	No. controls (n = 980)	Crude odds ratio (95% CI)	P
Socio-demographics				
Female Household Head Education				
None	78 (16)	155 (16)	1.85 (1.09, 3.13)	0.02
Primary/some secondary	386 (79)	737 (75)	1.92 (1.20, 3.07)	0.006
Completed Secondary +	22 (5)	84 (9)	1	
Household Wealth Index				
First quartile (poorest)	123 (25)	244(25)	0.85 (0.62, 1.16)	0.31
Second quartile	146 (26)	253 (30)	0.95 (0.70, 1.30)	0.75
Third quartile	115 (24)	240 (24)	1.14 (0.85, 1.54)	0.37
Fourth quartile	104 (21)	243 (25)	1	
People sleeping in room				
<3	168(35)	309 (31)	1	
3–5	271 (45)	571 (48)	0.87 (0.69, 1.11)	0.26
>5	49 (20)	100 (20)	0.90 (0.61, 1.31)	0.60
Prevention activities				
Malaria prophylaxis	4 (1)	10 (1)	0.82 (0.25, 2.56)	0.71
Mosquito coils	10 (2)	28 (3)	0.71 (0.34, 1.48)	0.36
Bednet use	15 (3)	37 (4)	0.81 (0.44, 1.49)	0.49
Clearing of bushes	167 (34)	398 (38)	0.84 (0.64, 1.09)	0.17
Burning herbs at night	55 (11)	95 (9)	1.12 (0.63, 1.99)	0.69
Travel/residential history				
Overnight travel 7–21 days prior	21 (4)	20 (2)	2.16 (1.16, 4.02)	0.02
Immigrated from outside study	22 (5)	36 (4)	1.24 (0.72, 2.13)	0.44
Agricultural and animal husbandry activities				
Channelled swamp water	50 (10)	44 (4)	2.43 (1.59, 3.70)	<0.001
Animals sleeping in compound				
Insecticide treated cattle	254 (52)	509 (52)	1.00 (0.81, 1.25)	0.97

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Potential risk factors	No. cases ($n = 488$)	No. controls ($n = 980$)	Crude odds ratio (95% CI)	P
Insecticide free cattle	84 (17)	131 (13)	1.35 (1.00, 1.82)	0.05
Goats	43 (9)	48 (5)	1.88 (1.23, 2.88)	0.003
Dogs	252 (52)	435 (44)	1.34 (1.08, 1.66)	0.01
House construction				
Metal roof	284 (58)	483 (49)	1.43 (1.15, 1.78)	0.001
Mud walls	430 (88)	867 (88)	0.97 (0.69, 1.35)	0.84
Absence of ceiling	409 (84)	771 (79)	1.40 (1.05, 1.87)	0.02
Open eaves	387 (79)	795 (81)	0.89 (0.68, 1.17)	0.41
Uncovered windows	52 (11)	119 (12)	1.06 (0.74, 1.51)	0.76
Separate kitchen	129 (74)	356 (64)	1.59 (1.25, 2.02)	0.001
Surrounding environment				
Livestock holding area <100 m	206 (42)	374 (38)	1.18 (0.95,1.48)	0.14
House on flat land	121 (25)	179 (18)	1.47 (1.13, 1.91)	0.004
Location at bottom of hill	52 (11)	85 (9)	1.26 (0.87, 1.81)	0.22
Elevation (quartiles)				
<1932 m	110(23)	260 (27)	0.95 (0.69, 1.30)	0.74
1932–1947 m	114 (23)	247 (25)	1.03 (0.76, 1.41)	0.84
1947–1983 m	151 (31)	220 (22)	1.53 (1.13, 2.08)	0.06
>1983 m	113 (23)	253 (26)	1	
Distance from forest				
<250 m	33 (7)	40 (4)	1.77 (1.10, 2.85)	0.02
250–500 m	37 (8)	50 (5)	1.58 (1.02, 2.47)	0.04
500–1000 m	55 (11)	113 (12)	1.02 (0.71, 1.45)	0.82
>1000 m	363 (74)	777 (79)	1	
Distance from swamp				
<250 m	166 (34)	263 (27)	1.36 (0.94, 1.98)	0.10
250–500 m	198 (41)	421 (43)	1.02 (0.71, 1.45)	0.93
500–1000 m	68 (14)	175 (18)	0.84 (0.55, 1.28)	0.42
>1000 m	56 (11)	121 (12)	1	
Distance from clinics (quartiles)				
1190 m	115 (23)	253 (26)	0.78 (0.57, 1.06)	0.11

Potential risk factors	No. cases (n = 488)	No. controls (n = 980)	Crude odds ratio (95% CI)	P
1190–2081 m	125 (26)	241 (24)	0.89 (0.66, 1.20)	0.44
2081–2711 m	112 (23)	253 (26)	0.76 (0.56, 1.03)	0.08
>2711 m	136 (28)	233 (24)	1	
Distance from Stream				
< 250 m	97 (19)	186 (20)	1.19 (0.92, 1.53)	0.19
250–500 m	83 (17)	113 (12)	1.79 (1.23, 2.59)	0.002
500–1000 m	6 (1)	12 (1)	1.11 (0.41, 2.97)	0.84
> 1000 m	302 (62)	669 (68)	1	
Absence of trees within 200 m	394 (81)	703 (72)	1.65 (1.27, 2.15)	0.0002
Presence of bushes within 200 m	124 (25)	194 (20)	1.38 (1.07, 1.79)	0.01
Presence of tea within 200 m	243 (50)	522 (53)	0.87 (0.70, 1.08)	0.21
Presence of maize within 200 m	445 (91)	887 (90)	1.09 (0.74, 1.59)	0.67

Table 3

Multivariate model of associations between measured variables and malaria risk in Kipsamoite and Kapsisiywa, western Kenyan highlands, March–September 2004

Potential risk factors	Adjusted* odds ratio (95% CI)	P
Female Household Head Education		
None	2.02 (1.08, 3.75)	0.03
Primary/some secondary	2.01 (1.16, 3.05)	0.01
Cmpleted Secondary +	1	
Mosquito coils	0.48 (0.21, 1.10)	0.08
Overnight travel 7–21 days prior	2.17 (1.15, 4.11)	0.02
Channelled swamp water	1.75 (0.96, 3.20)	0.07
Goats sleeping in compound	1.61 (0.95, 2.74)	0.07
Absence of ceiling	1.53 (1.08, 2.18)	0.02
Separate kitchen	1.77 (1.35, 2.32)	<0.0001
House on flat land	1.61 (1.19, 2.18)	0.002
Elevation (quartiles)		
< 1932 m	1.35 (0.60, 3.04)	0.47
1932–1947 m	1.68 (0.76,3.71)	0.20
1947–1983 m	2.02 (1.08, 3.79)	0.03
> 1983 m	1	
Distance from forest		
< 250 m	3.26 (1.49, 7.12)	0.003
250–500 m	2.23 (1.02, 4.85)	0.04
500–1000 m	1.26 (0.72, 2.20)	0.41
> 1000 m	1	
Distance from swamp		
< 250 m	2.81 (1.34, 5.89)	0.006
250–500 m	2.31 (1.15, 4.65)	0.02
500–1000 m	1.52 (0.80,2.89)	0.20
> 1000 m	1	
Absence of trees within 200 m	1.59 (1.15, 2.19)	0.005
Presence of maize within 200 m	2.02 (1.21, 3.37)	0.007

*
Model adjusted for age, site and week of interview.