Significance of Travel to Rural Areas as a Risk Factor for Malarial Anemia in an Urban Setting


Department of Epidemiology, and Department of Biostatistics, School of Public Health, University of Michigan, Ann Arbor, Michigan; Division of Parasitic Diseases, National Center for Zoonotic, Vector-Borne and Enteric Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia; Centre for Vector Biology and Control Research, Kenya Medical Research Institute, Kisumu, Kenya

Abstract. The epidemiology of malaria in urban environments is poorly characterized, yet increasingly problematic. We conducted an unmatched case–control study of risk factors for malarial anemia with high parasitemia in urban Kisumu, Kenya, from June 2002 through February 2003. Cases (n = 80) were hospital patients with a hemoglobin level ≤ 8 g/dL and a Plasmodium parasite density ≥ 10,000/μL. Controls (n = 826) were healthy respondents to a concurrent citywide knowledge, attitude, and practice survey. Children who reported spending at least one night per month in a rural area were especially at risk (35% of cases; odds ratio = 9.3, 95% confidence interval [CI] = 4.4–19.7, P < 0.0001), and use of mosquito coils, bed net ownership, and house construction were non-significant, potentially indicating that malaria exposure during rural travel comprises an important element of risk. Control of severe malaria in an urban setting may be complicated by Plasmodium infections acquired elsewhere. Epidemiologic studies of urban malaria in low transmission settings should take travel history into account.

INTRODUCTION

Of the estimated 300–500 million annual cases of acute clinical malaria worldwide, only a small fraction progress to severe illness or death.1 Severe malarial anemia (SMA) is the most frequently observed severe outcome, with an estimated 1.42–5.66 million cases and 0.19–0.97 million fatalities annually.2 Most research has focused on severe malaria in general,3 miologic patterns of severe malaria are well-documented.4,5 However, evidence of socioeconomic and environmental risk factors have been linked in various locations to cerebral malaria (CM)4,9 and severe anemia.13 Duration of symptoms and distance to hospital have in several cases been identified as risk factors for severe malaria and severe anemia.10,16 Protective effects for bed nets have been observed for anemia4,10 and cerebral malaria,15 but not for severe malaria,10,12 CM,15 or malarial anemia.13 Investigations of insecticide-treated bed net (ITN) use and severe malaria are more extensive, but also provide conflicting results. Research in Kenya, The Gambia, and the Congo found no effect of ITN use on severe malaria,10,12 CM,15 or malarial anemia.13 However, bed nets have been shown to reduce mortality and severe morbidity in a variety of contexts.17,18 Protective effects for bed nets have been observed for anemia in Malawi19 and severe anemia in Tanzania.16 Bed nets were shown to increase hemoglobin levels and reduce SMA in western Kenya20 and to reduce malaria cases in Malawi, where ITNs were socially marketed.21 Further research is needed to clarify the different effects of socioeconomic and environmental risk factors on severe malaria occurrence.

Severe malaria outcomes have rarely been examined in the context of urban environments, despite rapid urbanization in Africa.22 This is due, in part, to observed lower transmission in large urban centers relative to rural areas, decreased availability of anopheline vector breeding sites, a lower ratio of vectors to humans, and diminished range of vector dispersion.23 However, the potential for malaria outbreaks and severe malaria morbidity in sub-Saharan African urban areas is likely increased by high levels of circular rural-urban migration, frequent commerce among peripheral urban and outlying village populations, proximity of low-transmission (low-immunity) areas to high-transmission zones, and the tradition of urban agriculture, which may provide perpetual vector breeding sites and thus chronic sources of infection for urban residents.

A few studies have examined the epidemiologic profile of severe malaria and anemia in urban areas,24–29 and there is substantial research on urban behavioral factors related to malaria,30–31 on urban entomologic patterns,23,32 and on the distribution of prevalent infection in urban areas.33,34 However, few studies have attempted to quantify risk factors for severe malaria outcomes among urban residents.29,28,35 To address this need, we investigated the epidemiology of malarial anemia in the

‡ Address correspondence to Mark L. Wilson, Department of Epidemiology, School of Public Health, University of Michigan, 109 Observatory, Ann Arbor, MI 48109-2029. E-mail: wilsonml@umich.edu

multivariate, analysis,13 whereas a study in Gabon could not identify any effects of socioeconomic status factors.14 These factors have been linked in various locations to CM15 and severe anemia.16 Investigations of insecticide-treated bed net (ITN) use and severe malaria are more extensive, but also provide conflicting results. Research in Kenya, The Gambia, and the Congo found no effect of ITN use on severe malaria,10,12 CM,15 or malarial anemia.13 However, bed nets have been shown to reduce mortality and severe morbidity in a variety of contexts.17,18 Protective effects for bed nets have been observed for anemia in Malawi19 and severe anemia in Tanzania.16 Bed nets were shown to increase hemoglobin levels and reduce SMA in western Kenya20 and to reduce malaria cases in Malawi, where ITNs were socially marketed.21 Further research is needed to clarify the different effects of socioeconomic and environmental risk factors on severe malaria occurrence.

Severe malaria outcomes have rarely been examined in the context of urban environments, despite rapid urbanization in Africa.22 This is due, in part, to observed lower transmission in large urban centers relative to rural areas, decreased availability of anopheline vector breeding sites, a lower ratio of vectors to humans, and diminished range of vector dispersion.23 However, the potential for malaria outbreaks and severe malaria morbidity in sub-Saharan African urban areas is likely increased by high levels of circular rural-urban migration, frequent commerce among peripheral urban and outlying village populations, proximity of low-transmission (low-immunity) areas to high-transmission zones, and the tradition of urban agriculture, which may provide perpetual vector breeding sites and thus chronic sources of infection for urban residents.

A few studies have examined the epidemiologic profile of severe malaria and anemia in urban areas,24–29 and there is substantial research on urban behavioral factors related to malaria,30–31 on urban entomologic patterns,23,32 and on the distribution of prevalent infection in urban areas.33,34 However, few studies have attempted to quantify risk factors for severe malaria outcomes among urban residents.29,28,35 To address this need, we investigated the epidemiology of malarial anemia in the
city of Kisumu, Kenya, a hyperendemic region representative of rapidly growing urban environments in SSA. In particular, we implemented an unmatched case–control study aimed at understanding risk factors for malaria in this urban setting.

**METHODS**

**Study area.** This study was conducted in Kisumu, western Kenya (population = 326,407) on the shores of Lake Victoria. The proximity of the lake, extensive swamps, abundant rainfall (1,000–1,500 mm/year) and a year-round warm climate combine to make this region one of the most favorable for malaria transmission in east Africa. Transmission is highest in several months after the rainy seasons, which occur during April–June and October–December. In rural areas near Kisumu, exposure to infective mosquito bites is estimated to be 90–410 per year. The study site was limited to the urban area. Exposure to infective mosquito bites is estimated to be 90–410 per year.

**Survey instrument and ancillary data.** The KAP survey instrument was administered at the hospital to caregivers of cases by a study interviewer. A trained supervisor accompanied field and hospital interviewers on randomly selected occasions to ensure consistency. The survey instrument consisted of seven sections: basic demographics, knowledge of malaria, health and treatment history, malaria treatment-seeking behavior, use of malaria prevention, travel history, socioeconomic status, and environmental characteristics of the home and surroundings. Wealth was assessed by constructing an index based on ownership of specific household items using principal components analysis.

**Population data and maps.** Population data and maps were obtained from the Kenya Central Bureau of Statistics. Locations of survey households were determined using a handheld Garmin Etrex global positioning unit. Geographic data were processed with geographic information system software (ArcGIS version 9.0; Environmental Systems Research Institute, Redlands, CA), which was also used to estimate population density from digitized street maps and enumeration area boundaries. A Quickbird high-resolution multispectral satellite image (DigitalGlobe, Longmont, CO) was used to derive normalized difference vegetation index (NDVI) values for the entire study area using PCI Geomatica (PCI Geomatics, Richmond Hill, Ontario, Canada). The NDVI, which ranges from −1 to 1, was transformed to a 200-point scale by adding 1 to the value and multiplying by 200, to create a more interpretable index and to enhance comparability with other studies.

**Statistical analysis.** Observed distributions for 32 potential risk factors and confounders were compared by case status using SAS version 9.1 (SAS Institute, Cary, NC). Significant associations were identified by using chi-square or Fisher’s exact tests for categorical and Student’s t tests or Wilcoxon’s rank-sum tests for continuous variables. All significant predictors of case status were entered singly into logistic regression models for malarial anemia to produce odds ratios (ORs).

A multivariate logistic model was constructed using the LOGISTIC procedure in SAS. Variable selection for this model was guided by results of the bivariate analysis and the known epidemiology of malarial anemia. However, the limited number of cases included in the analysis resulted in wide confidence intervals for estimated ORs.
of cases (n = 80) constrained the number of variables that could be considered. Although logistic models with less than 10 events per variable should be interpreted with caution, excluding important variables can bias or invalidate results. Based on previous studies, seven variables were included in the multivariate model a priori: child age, bed net ownership (independent of whether nets were treated), mosquito coil use, housing quality, regular travel to rural area by the child (i.e., at least one night per month), household wealth, and level of urbanization. Level of urbanization comprised an index encompassing a wide range of other socioeconomic and environmental variables, including NDVI, distance to town, population density, ownership of transportation and luxury items. In addition, variables that met the Bonferroni significance criteria for multiple testing (i.e., \( P < 0.0016 \)) for 32 individual risk factors in bivariate analysis were included as potential risk factors in the multivariate model. Interaction terms were not considered because of the small sample size.

The final logistic model was produced using a forward selection method, beginning with the seven initial variables, and including other variables that again met criteria for multiple testing during multivariate analysis. Multicollinearity among predictor variables was assessed using variance inflation factors. Continuous variables were examined for nonlinearity with respect to the logit of the dependent. Multiple imputation was used to compensate for small amounts (≤ 5%) of missing data in some variables; three imputations were considered adequate based on guidelines in the literature. The Hosmer-Lemeshow goodness-of-fit test was used to assess adequacy of model fit. Residual diagnostics were used to identify significant outliers, and the model was rerun with those observations removed to test the stability of parameter estimates. A variogram of the model residuals measuring the similarity between pairs of point measurements at different geographic distances was constructed using PROC VARIOGRAM in SAS.

Protection of human subjects. Written informed consent from parents or caretakers of participants was obtained prior to all interviews. The protocol for this study was reviewed and approved by the institutional review boards of The University of Michigan (Ann Arbor, MI), CDC (Atlanta, GA), and the Kenya Medical Research Institute (Nairobi, Kenya).

RESULTS

From July 2002 through February 2003, 141 children less than 10 years of age had malarial anemia and high *Plasmodium* parasitemia at KDH. Of these children, 80 (57%) were identified and interviewed for this study. Captured cases were slightly younger, smaller, and lighter in weight than un Interviewed cases, although no differences were statistically significant. Symptoms were comparable in captured and missed cases, except that the latter had significantly lower parasitemia (mean = 35,218/μL versus 48,061/μL; \( t = 2.75, P = 0.007 \)). Over the same period, 826 controls were identified from among 4,336 interviews conducted in the KAP survey.

Not surprisingly, age was found to be a strong predictor of case status, with cases much more likely to be between six months and three years old than controls, and few cases greater than five years of age (Table 1). Various characteristics of the structure, environment and behavioral patterns of

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Bivariate analysis of categorical variables investigated as potential risk factors for severe malarial anemia in Kisumu, Kenya*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
<td>No. (%) cases, n = 80</td>
</tr>
<tr>
<td>Households head male</td>
<td>70 (87.5)</td>
</tr>
<tr>
<td>Presence of wage earner other than caregiver</td>
<td>41 (51.3)</td>
</tr>
<tr>
<td>At least one self-reported household malaria case during previous month</td>
<td>25 (31.3)</td>
</tr>
<tr>
<td>Child’s age</td>
<td></td>
</tr>
<tr>
<td>&lt; 6 months</td>
<td>8 (10.0)</td>
</tr>
<tr>
<td>6 months–3 years</td>
<td>61 (76.3)</td>
</tr>
<tr>
<td>3–5 years</td>
<td>8 (10.0)</td>
</tr>
<tr>
<td>&gt; 5 years</td>
<td>3 (3.8)</td>
</tr>
<tr>
<td>Child regularly spends ≥ 1 night/month in rural area</td>
<td>28 (35.0)</td>
</tr>
<tr>
<td>Child slept under a bed net during previous week</td>
<td>41 (51.3)</td>
</tr>
<tr>
<td>Child shares a sleeping room</td>
<td>79 (98.8)</td>
</tr>
<tr>
<td>Child was born in a rural area</td>
<td>11 (13.8)</td>
</tr>
<tr>
<td>Prior household residence was rural</td>
<td>32 (40.0)</td>
</tr>
<tr>
<td>Ownership of current residence</td>
<td>21 (26.3)</td>
</tr>
<tr>
<td>Ownership of land other than residence</td>
<td>62 (77.5)</td>
</tr>
<tr>
<td>Ownership of rural land</td>
<td>49 (61.3)</td>
</tr>
<tr>
<td>Bed net ownership</td>
<td>45 (56.3)</td>
</tr>
<tr>
<td>ITN ownership</td>
<td>20 (25.0)</td>
</tr>
<tr>
<td>Use mosquito coils for malaria prevention</td>
<td>42 (52.5)</td>
</tr>
<tr>
<td>House has open eaves or poorly covered windows</td>
<td>58 (72.5)</td>
</tr>
<tr>
<td>House wall materials (stone or brick)</td>
<td>28 (35.0)</td>
</tr>
<tr>
<td>House floor not earthen</td>
<td>61 (76.3)</td>
</tr>
<tr>
<td>Presence of windows</td>
<td>70 (87.5)</td>
</tr>
<tr>
<td>Standing or running water within 10 meters</td>
<td>32 (40.0)</td>
</tr>
<tr>
<td>Primary source of washing water is natural</td>
<td>16 (20.0)</td>
</tr>
<tr>
<td>Domestic animals kept overnight at residence</td>
<td>22 (27.5)</td>
</tr>
<tr>
<td>Level of urbanization</td>
<td></td>
</tr>
<tr>
<td>Semi-rural</td>
<td>30 (37.5)</td>
</tr>
<tr>
<td>Peri-urban</td>
<td>41 (51.3)</td>
</tr>
<tr>
<td>Urban</td>
<td>9 (11.3)</td>
</tr>
</tbody>
</table>

* CI = confidence interval; NA = not available; ITN = insecticide-treated bed net. Statistically significant values are shown in bold.
the household were significantly related to malarial anemia in bivariate analysis (Tables 1 and 2). In addition to the seven variables selected *a priori* for multivariate analysis, eight others met the significance criteria for multiple testing, and were included as candidate variables in the forward-selected logistic model including sex of household head, land ownership other than residence, rural land ownership, prior residence in rural area, close proximity to standing/running water, washing with natural water sources, domestic animals present overnight, and household size.

Despite a relatively low number of events per variable (6.7), regression diagnostics indicated a good fit to the data, no significant problems with outliers or autocorrelation (variance inflation factors for predictor variables were uniformly low, ranging from 1.03 to 1.38), and moderate predictive ability (max-rescaled $r^2 \approx 45\%$). The resulting multivariate logistic model showed that age was a strong predictor of case status when adjusting for other factors (Table 3). Bed net ownership or use of mosquito coils were not statistically protective after multivariate adjustment. Relative to those living in an urban EA, children in semi-rural and peri-urban areas were more likely to be cases, though neither association was significant, nor was there significant increased risk from poor housing quality. Other variables found to be significant risk factors in the final model included ownership of land other than the residence (OR = 4.0, 95% confidence interval [CI] = 2.1–7.6, $P < 0.0001$), presence of standing or running water within 10 meters of the household (OR = 4.8, 95% CI = 2.5–9.3, $P < 0.0001$), presence of domestic animals overnight at the household (OR = 3.9, 95% CI = 1.8–8.1, $P = 0.0004$), and number of people in the household (OR = 1.4, 95% CI = 1.2–1.6, $P = 0.0002$). Most significantly, the odds of being a case were more than nine times greater (OR = 9.3, 95% CI = 4.4–19.7, $P < 0.0001$) for children who reported typically spending at least one night per month in a rural area.

### DISCUSSION

This study characterized risk factors for malarial anemia in an urban setting surrounded by an area of high endemicity in western Kenya. The observed age range of cases was consistent with that observed for severe malaria outcomes in other highly endemic areas, as was the failure to observe any CM among admissions to KDH during the study period. Although the latter may be caused by difficulty in diagnosing CM, the age profile for cases of malarial anemia was more like that observed in rural settings than in typically lower-transmission urban contexts. We found that regular overnight travel to rural areas was a strong risk factor after adjusting for other factors in the multivariate analysis, which suggested that frequent exposure to infected mosquitoes during rural travel significantly increased risk among urban residents. Although prior residence in a rural area did not meet the Bonferroni criteria for inclusion in the multivariate model, it was a risk factor in bivariate analysis. This finding may further substantiate the idea that chronic rural exposure contributes to incidence of malarial anemia, such that children from high-exposure rural areas experience higher risk even after migrating to cities, although this was difficult to evaluate in our study. In bivariate analysis, we did not find an effect for increasing length of time spent in rural areas. However, this finding may reflect recall difficulty in accurately reporting duration of travel or monthly or seasonal variations in travel patterns.

The current data do not enable us to establish a causal link between exposure during rural travel and acute presentation with malarial anemia. Investigating such a link would have

### Table 2

**Bivariate analysis of continuous variables investigated as potential risk factors for severe malarial anemia in Kisumu, Kenya**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cases mean</th>
<th>Controls mean</th>
<th>Odds ratio (95% CI)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. persons in household</td>
<td>5.09 (4.69–5.48)</td>
<td>4.32 (4.21–4.43)</td>
<td><strong>1.3 (1.1–1.4)</strong></td>
<td>0.0001</td>
</tr>
<tr>
<td>Length of time in current residence, years</td>
<td>5.78 (4.13–7.43)</td>
<td>4.11 (3.74–4.49)</td>
<td><strong>1.2 (1.0–1.4)</strong></td>
<td><strong>0.0165</strong></td>
</tr>
<tr>
<td>Wealth percentile</td>
<td>45.9 (40.1–51.8)</td>
<td>49.8 (47.8–51.8)</td>
<td>1.0 (0.9–1.0) (10% increase)</td>
<td>0.2492</td>
</tr>
<tr>
<td>Proportion of household members sleeping under net during previous night</td>
<td>0.78 (0.68–0.88)</td>
<td>0.83 (0.81–0.86)</td>
<td>0.5 (0.2–1.4)</td>
<td>0.3161</td>
</tr>
<tr>
<td>Number of nights/month child sleeps outside Kisumu</td>
<td>0.8 (0.37–1.23)</td>
<td>0.34 (0.18–0.50)</td>
<td>1.1 (1.0–1.1)</td>
<td>0.1113</td>
</tr>
<tr>
<td>NDVI (within 25 meters of household) (scale = 0–200)</td>
<td>124.9 (121.9–129.0)</td>
<td>129.5 (128.5–130.4)</td>
<td><strong>0.8 (0.7–0.9)</strong></td>
<td><strong>0.0068</strong></td>
</tr>
<tr>
<td>Distance to lakeshore, km</td>
<td>2.01 (1.78–2.24)</td>
<td>2.08 (2.02–2.14)</td>
<td>0.9 (0.7–1.2)</td>
<td>0.5176</td>
</tr>
<tr>
<td>EA population density, 1,000/km²</td>
<td>16 (12.2, 19.9)</td>
<td>18.8 (17.3, 20.3)</td>
<td>1.0 (0.9–1.0) (increase of 5,000/km²)</td>
<td>0.1914</td>
</tr>
<tr>
<td>Distance to hospital, km</td>
<td>2.84 (2.57, 3.12)</td>
<td>2.58 (2.50, 2.66)</td>
<td>1.2 (1.0–1.4)</td>
<td>0.0526</td>
</tr>
</tbody>
</table>

*CI = confidence interval. Statistically significant values are shown in bold.

### Table 3

**Multivariate logistic regression of potential risk factors for severe malarial anemia in Kisumu, Kenya**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adjusted odds ratio (95% CI)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use mosquito coils for malaria prevention</td>
<td>0.6 (0.3–1.1)</td>
<td>0.0853</td>
</tr>
<tr>
<td>Bed net ownership</td>
<td>0.9 (0.5–1.7)</td>
<td>0.8334</td>
</tr>
<tr>
<td>House has open eaves or poorly covered windows</td>
<td>1.8 (0.8–4.1)</td>
<td>0.1297</td>
</tr>
<tr>
<td>Child regularly spends ≥ 1 night/month in rural area</td>
<td><em>9.3 (4.4–19.7)</em></td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Wealth percentile (increase of 10%)</td>
<td>0.8 (0.7–0.9)</td>
<td>0.0004</td>
</tr>
<tr>
<td>Household head is male</td>
<td>3.6 (1.6–8.1)</td>
<td>0.0017</td>
</tr>
<tr>
<td>Ownership of land other than household</td>
<td>4.0 (2.1–7.6)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Standing or running water within 10 meters</td>
<td>4.8 (2.5–9.3)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Domestic animals kept overnight at residence</td>
<td>3.9 (1.8–8.1)</td>
<td>0.0004</td>
</tr>
<tr>
<td>No. persons in household</td>
<td>1.4 (1.2–1.6)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Level of urbanization</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Semi-rural</td>
<td>1.7 (0.7–4.6)</td>
<td>0.2756</td>
</tr>
<tr>
<td>Peri-urban</td>
<td>2.0 (0.8–5.1)</td>
<td>0.1415</td>
</tr>
<tr>
<td>Urban</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Child’s age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 6 months</td>
<td><em>6.7 (1.5, 30.8)</em></td>
<td>0.0143</td>
</tr>
<tr>
<td>6 months–3 years</td>
<td>18.9 (5.0, 70.9)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>3–5 years</td>
<td>3.3 (0.8, 14.5)</td>
<td>0.1100</td>
</tr>
<tr>
<td>&gt; 5 years</td>
<td>Reference</td>
<td></td>
</tr>
</tbody>
</table>

*CI = confidence interval. Statistically significant values are shown in bold.

---

**394 SIRI AND OTHERS**
required details of recent trips (often multiple trips per house-
hold) with respect to timing, location, and participation by indi-
vidual household members, adding considerable complexity
to the survey process for interviewers and respondents. How-
ever, there was a significant correlation between reporting
typical travel to rural areas and spending at least one night
outside Kisumu in the previous month. This link needs to be
explored in more detail.

Two-thirds of cases occurred in households where the child
did not typically travel to rural areas, indicating some level of
intra-urban transmission. The magnitude of this is unclear for
various reasons: for example, some children for whom regular
travel was not reported might nevertheless have spent a recent
night in a rural area. Further research is needed to clarify the
roles of travel, rural exposure, chronic and acute infection, and
intra-urban transmission in determining severe malaria risk in
sub-Saharan African urban settings.

The effects of bed net ownership, mosquito coil use, and
house construction were all in the expected direction, but not
statistically significant. Bed nets or ITNs have been found
not to reduce SMA in some contexts, although it is gen-
erally accepted that they reduce *Plasmodium* infection and
mortality. In urban Kisumu, increased risk of malarial anemia
may have resulted if a significant fraction of exposure subse-
quently occurred during travel when nets were not being used.
Mosquito coils were found to be preventive in bivariate analy-
sis, but had a non-significant effect after multivariate adjust-
ment. Good house construction, as characterized in this study,
normally is considered to be another barrier to transmission,
and was similarly related to malarial anemia in bivariate analy-
sis, but non-significant in the multivariate model. As with nets,
good house construction would not have prevented increased
exposure during travel.

Household size was found to represent a risk factor in the
final model. However, this result is potentially an artifact of
the different sampling schemes for cases and controls. To the
extent that household size is associated with other risk factors,
this finding could bias results in either direction. Although we
were unable to include interaction terms in the final model,
the inclusion of household size should have controlled for this
effect. Moreover, we did not observe inordinately high correla-
tions between household size and other variables in the data.

The overall effect of level of urbanization on malarial ane-
mia risk was non-significant, although some individual vari-
ables comprising this index (e.g., distance to the hospital,
population density, source of water, and NDVI) were signifi-
cantly associated with disease in bivariate analysis. These rela-
tionships were in the directions expected, except that higher
NDVI, indicating more nearby vegetation, was associated
with lower risk for malarial anemia. This unexpected relation-
ship may possibly have resulted from the low NDVIIs that are
found in peri-urban zones (where residents are most likely to
travel to rural areas), or from higher socioeconomic levels that
enable greater access to malaria prevention in highly urban
zones where houses have gardens. The unexpected association
with NDVI may explain why the urbanization index was not a
significant predictor. Inclusion of interaction terms in a larger
dataset would help clarify these relationships.

The limited sample size reduced the statistical power of
this study to identify some risk factors. Nonetheless, the strict
requirements for inclusion in the final model, the consistent
direction and magnitude of observed relationships in compar-
ison with bivariate results, and the robustness of the model
to deletion of outliers and exclusion of specific variables indi-
cate that it represents a solid and conservative compromise.

A larger study over a longer period of time is needed to fur-
ther explore the multifactorial nature of risk for severe malaria
outcomes. We failed to recruit >40% of cases meeting our case
definition at KDH, but differences between identified and
missed cases were minimal and should not have biased the
analysis. Captured cases were generally sicker than those that
were missed, indicating that our results may only be applicable
to more severe cases. The reasons why cases were missed are
not clear. However, missed cases tended to cluster near the
beginning and end of the study period and during times when
caseload was high, indicating that failure to capture may have
resulted from some combination of an inability to handle the
caseload with interviewer inexperience or fatigue. We were
also unable to evaluate the effects of caregiver characteristics
because of the different methods for recruitment of cases and
controls.

These results imply that different prevention and control
strategies may be necessary for the large and growing group
of urban residents, many of whom frequently travel to rural
areas. Traditional prevention strategies may be ineffective
for urban families who use bed nets at home but fail to do so
when traveling. In particular, travel histories and their impact
on severe malaria need to be more carefully described in sub-
Saharan Africa because studies have so far been limited on
this count. At the same time, the presentation of these cases
within urban areas and the limited timeframe within which
some may experience exposure (i.e., traveling to rural areas)
present opportunities for effective and efficient prevent-
ion that are often unavailable in remote areas where access to
health facilities is limited and exposure is protracted. A better
understanding of the link between travel and severe malaria
could have direct practical benefits for public health by helping
to direct the allocation of resources among and within cities,
effectively targeting and focusing education and intervention
programs, and producing clear and informed policies for urban
public health. Likewise, a clearer picture is needed of risk fac-
tors for severe malaria for those urban residents who do not
travel. A major component of this research should focus on
descriving the urban environment and delineating the specific
elements of urbanization that may increase risk. Such efforts
should produce a better understanding of urban malaria risk
factors, thus enabling effective targeting of control strategies
to those at greatest risk of severe malaria.

Acknowledgments: We are indebted to the parents and caregivers
who agreed to participate in this project and to Kisumu government
officials who provided permission and support for the research.
The Kenya Central Bureau of Statistics and Maurice Ombok provided
census data and maps. Amos Odhacha and Frank Odhiambo contrib-
uted to the implementation of focus group discussions and coordina-
tion with local officials. The KDH staff and CDC/KEMRI workers
at KDH were instrumental in identifying and recruiting cases. The
CDC/KEMRI staff at the Kisian field station facilitated the day-to-
day functioning of the project. We also thank CDC/KEMRI interview-
ers, including Betty Odidii, Dinah Wambua, Lillian Omollo, Modrine
Alumasa, Paul Oluru, Dominic M’Njeru, Rose Ouma, and Tereza
Achieng for their participation in the study.

Financial support: This research was supported by CDC/KEMRI
and by the University of Michigan through the Rackham Graduate

Received January 25, 2009. Accepted for publication October 25,
2009.
REFERENCES


44. Pearson K, 1900. On the criterion that a given system of deviations from the probable in the case of a correlated system of variables is such that it can be reasonably supposed to have arisen from random sampling. *Philosophical Magazine Series 5*: 157–175.


