MAJOR ARTICLE

Plasmodium falciparum and Helminth Coinfection in a Semiurban Population of Pregnant Women in Uganda

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Background. Helminth infections and malaria are widespread in the tropics. Recent studies suggest helminth infections may increase susceptibility to *Plasmodium falciparum* infection. If confirmed, this increased susceptibility could be particularly important during pregnancy-induced immunosuppression.

Objective. To evaluate the geographical distribution of *P. falciparum*–helminth coinfection and the associations between *P. falciparum* infection and infection with various parasite species in pregnant women in Entebbe, Uganda.

Methods. A cross-sectional study was conducted at baseline during a trial of antihelminthic drugs during pregnancy. Helminth and *P. falciparum* infections were quantified in 2507 asymptomatic women. Subjects' socioeconomic and demographic characteristics and geographical details were recorded.

Results. Hookworm and *Mansonella perstans* infections were associated with *P. falciparum* infection, but the effect of hookworm infection was seen only in the absence of *M. perstans* infection. The odds ratio [OR] for *P. falciparum* infection, adjusted for age, tribe, socioeconomic status, HIV infection status, and location was as follows: for individuals infected with hookworm but not *M. perstans,* 1.53 (95% confidence interval [CI], 1.09–2.14); for individuals infected with *M. perstans* but not hookworm, 2.33 (95% CI, 1.47–3.69); for individuals infected with both hookworm and *M. perstans,* 1.85 (CI, 1.24–2.76). No association was observed between infection with *Schistosoma mansoni, Trichuris,* or *Strongyloides* species and *P. falciparum* infection.

Conclusions. Hookworm–*P. falciparum* coinfection and *M. perstans*–*P. falciparum* coinfection among pregnant women in Entebbe is more common than would be expected by chance. Further studies are needed to elucidate the mechanism of this association. A helminth-induced increase in susceptibility to *P. falciparum* could have important consequences for pregnancy outcome and responses to *P. falciparum* infection in infancy.

Parasitic infections represent a major cause of disease and morbidity in Africa [1]. The World Health Organization estimates that more than one billion people are chronically infected with soil-transmitted helminths, 200 million are chronically infected with schistosomes [2], and 150 million are chronically infected with filarial helminths [3]. Mortality from malaria is estimated at two million deaths per year [4].

Because helminths and *P. falciparum* infection are endemic through most of Africa, populations often endure infections with a number of different parasite species [5], and individuals are often coinfected with combinations of helminths and malaria parasites [6, 7]. The rates of coinfection may depend not only on chance, but also on the spatial distribution of environmental conditions that favor the transmission of multiple species [8], as well as on immunological interactions and common factors that affect genetic susceptibility or host behavior.

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Immunological factors would be expected to influence the rates of coinfection because helminths modulate host immune responses both to themselves and to concurrent infections [9–11]. With regard to malaria, murine models provide evidence of interactions that manifest as an altered probability of morbidity or mortality [12–16]. For example, infection with the filarial nematode *Brugia pahangi* has been found to protect against the development of cerebral malaria [14], whereas superinfection with *Schistosoma mansoni* delayed clearance and increased severity of *Plasmodium* infection [15]. With respect to interactions in humans, published studies have not led to any consensus [17–24]. Reports from Thailand suggest that hookworm, *Trichuris trichiura* and *Ascaris lumbricoides* infections may increase the incidence of *P. falciparum* infection [18], although they also suggest that *A. lumbricoides* infection protects against severe *P. falciparum* infection [19, 20]. This result agrees with the results in an earlier report and a recent trial that suggest the incidence of malaria attacks increased after treatment of severe *A. lumbricoides* infection [21, 25], but studies elsewhere have not supported these findings [16, 17, 22]. Inconsistent results have also been reported in studies of schistosome and *P. falciparum* coinfections [23, 24]. These contrasting results leave important questions unanswered about the biological associations between *P. falciparum* and helminths.

These contrasting results may be explained by a failure to assess spatial variation in exposure to parasitic infections [8]. Parasites are subject to microgeographical variation with respect to the risk of infection: for example, the risk of schistosomiasis is greater around sites where individuals have contact with water, the risk of malaria is affected by distance from a larval breeding site [26], and the risk of *A. lumbricoides, T. Trichiura,* and hookworm infection are influenced by environmental conditions [27]. Because exposure to multiple species of parasites may vary over small distances, analyses clearly need to consider residential location as a confounder of the risk of coinfection, something that few previous studies have attempted [8].

Pregnant women are an insufficiently studied group, but they are more vulnerable to infections, due to suppression of the immune system during pregnancy [28, 29]. If helminths do have a biological effect on susceptibility to *P. falciparum* infection, this may be particularly important during pregnancy, when malaria is associated with increased maternal mortality and anemia, intrauterine growth restriction, and fetal and perinatal death [30]. During pregnancy, maternal immune responses also influence the offspring's immunity and response to *P. falciparum* infection in infancy [31].

We therefore aimed to test the hypothesis that helminth infections increase susceptibility to *P. falciparum* infection in pregnant women. We examined whether helminth–*P. falciparum* coinfections among pregnant women are more common than would be expected by chance, and we also explored the spatial stratification of coinfections to determine whether environmental factors were likely to explain any associations we observed.

METHODS

This cross-sectional study used data collected at baseline (before treatment) from the "Entebbe Mother and Baby Study," a randomized, double-blind, placebo-controlled trial of antihelminthic treatment during pregnancy (International Standard Randomised Controlled Trials no. 32849447), conducted in Uganda, in the Entebbe Municipality and the adjacent Katabi subcounty. [32]. The area is a peninsula in Lake Victoria bounded by lake and swampland, which is occupied by semiurban, rural, and fishing communities that have a diverse tribal and socioeconomic makeup.

The study design and selection criteria have been described elsewhere [32]. Women were enrolled at Entebbe General Hospital antenatal clinic between April 2003 and November 2005. They were eligible if they were pregnant at the time of enrollment, a resident of Entebbe or Katabi, and in good health. They were excluded if they were severely anaemic (hemoglobin, <8 g/dL), the pregnancy was not normal, they were unwilling to receive an HIV test result (as part of the hospital program for Prevention of Mother To Child Transmission of HIV), or if they were unwell on the day of enrollment.

Recruitment took place over 2 visits to the clinic, the screening visit and enrolment visit. At the screening visit, women gave blood samples to be examined for *P. falciparum* and *M. perstans*. Socioeconomic and demographic data were collected by questionnaire. Women returned for the enrollment visit with a stool sample. All samples were collected as part of the baseline survey before treatment was given.

Stool samples were examined by using the Kato-Katz method [33] and charcoal culture for *Strongyloides stercoralis* [34]. Two Kato-Katz slides were prepared for each sample; the slides were examined within 30 min for hookworm and examined the following day for other parasites. The intensity of hookworm infection was categorized as follows: light, $<1{,}000$ eggs/gram of stool; moderate, 1,000–3,999 eggs/gram of stool; high, $\geq 4{,}000$ eggs/gram of stool. [35] Blood was examined for *P. falciparum* by using a thick film and examined for *M. perstans* by using a modified Knott's method; intensity was estimated as the number of *P. falciparum* per 200 white blood cells and the number of microfilariae per milliliter of blood [36].

The residence of each participant was georeferenced with handheld global positioning system units (Etrex Venture; Garmin) during a survey carried out in the first quarter of 2006. If the participant was found to have moved since enrollment, her address at enrollment was visited and georeferenced. Approval for the study was given by of the Uganda Virus Research Institute Science and Ethics Committee, the Uganda National Council for Science and Technology, and the London School of Hygiene and Tropical Medicine.

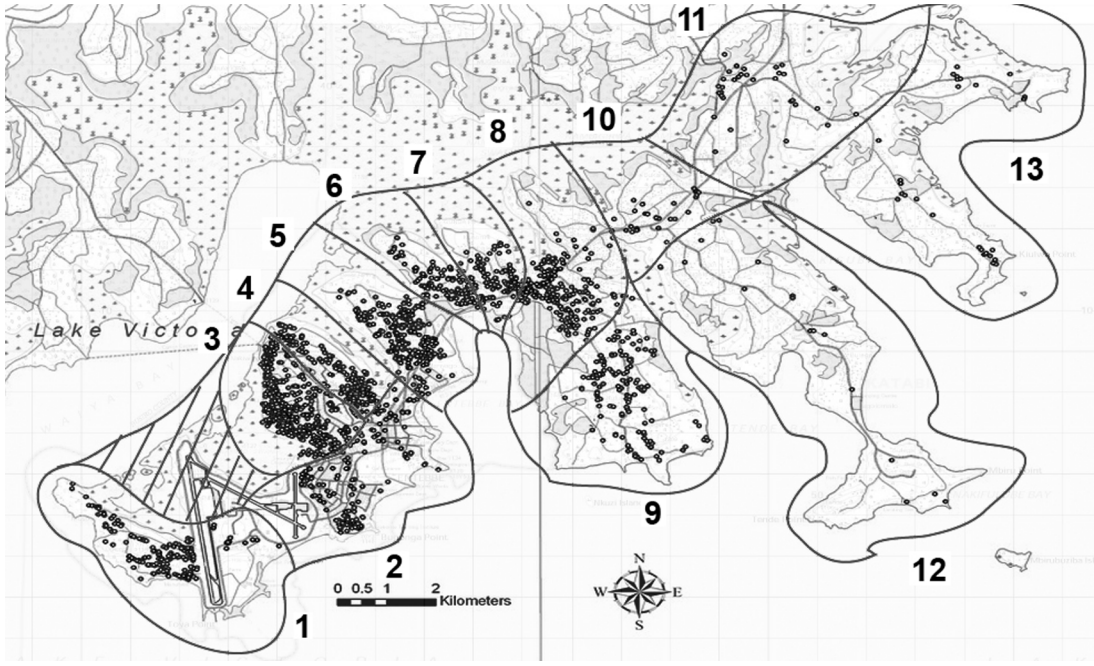

Figure 1. Map of Entebbe and Katabi showing the study area, location of women's residences, and breakdown of geographical zones for spatial stratification. The study area was situated 50 km southwest of Kampala, Uganda's capital city. *Black circles*, individual residences.

Analyses were conducted using Stata (version 7; Stata). ArcGIS Desktop (Environmental Systems Research Institute) was used to assign subjects to geographically defined zones on the basis of their coordinates. The analysis was divided into 2 parts. The first part was the analysis of coinfection by helminth species and *P. falciparum,* adjusting for maternal demographic and socioeconomic factors, as well as clinical confounding factors, and the second part was a more detailed assessment of coinfection in relation to geographical area.

Simple univariate and adjusted analysis of association with *P. falciparum* infection was performed for infection with each helminth species, by using logistic regression. The variables that were considered to be potential confounding factors, and included in the initial model, were age, tribe, the woman's socioeconomic status, household socioeconomic status, geographical zone, and HIV infection status. Two scales for socioeconomic status, each with 6 levels of scoring, were devised from the questionnaire. The woman's socioeconomic status was determined by the woman's level of education, personal income, and occupation. The household's socioeconomic status was determined by the materials from which the home was built and the number of rooms it had, as well as the items owned [37].

Geographical zones were defined before analysis with the aim of stratifying the population in an attempt to acknowledge the reality of variations in environment across a large study area, and were guided by the location of geographical features, such as coastline, forest, relatively greater altitude, and the location of settlements marked on the map (figure 1). For example, zone 1 was predominantly coastal and exposed, zone 2 was the most urban environment included in the study, and zones 3 and 4 were areas of 2–300 m elevation above the lake. It was these varied conditions that necessitated stratification. The association between helminth infection and *P. falciparum* infection, adjusted for potential confounding factors, were examined after data were stratified by geographical zone to assess variations in the probability of coinfection over the geographical area. Finally, associations were examined after adjusting for zone, in addition to other potential confounding factors.

RESULTS

Enrollment and baseline characteristics have been described elsewhere [37]. In brief, 11,783 women were assessed to enroll a cohort of 2507 pregnant women. The chief reasons for exclusion were living outside the study area (6243), not wishing to undergo an HIV test (1186), not wishing to participate in the study (874), and not returning for enrollment after screening (596). The age range of the women enrolled was 14-47 years (mean age, 23.7 years). More than 6 tribes were represented; of these, the largest proportion of women were Baganda (1231 of 2506 [49%]). The prevalence of asymptomatic *P. falciparum* infection was 11% (268 of 2459), and the geometric mean parasite count in infected individuals was 43 parasites per 200 white blood cells. Of 2498 women, 1693 (68%) were infected with one or more species of helminth. The dominant species were as follows: hookworm (recovered from 1112 of 2498 subjects [45%]), *M. perstans* (531 of 2499 subjects [21%]), *S. mansoni* (458 of 2498 subjects [18%]), *S. stercoralis* (306 of 2485 subjects [12%]), *T. trichiura* (226 of

Table 1. Associations between helminth and *Plasmodium falciparum* infection, according to helminth species.

Helminth type, infection status	*P. falciparum* infection prevalence, proportion (%)	Crude		Adjusted	
		OR	*P*	OR[a]	*P*
Hookworm			.002		.072
Absent	118/1278 (9.2)	1		1	
Present	138/1043 (13.2)	1.50		1.28 (0.98–1.68)	
Mansonella perstans			<.001		<.001
Absent	168/1829 (9.2)	1		1	
Present	88/500 (17.6)	2.11		1.67 (1.25–2.24)	
Strongyloides stercoralis			.53		.24
Absent	228/2031 (11.2)	1		1	
Present	28/280 (10.0)	0.88		0.78 (0.51–1.20)	
Schistosoma mansoni			.36		.19
Absent	214/1892 (11.3)	1		1	
Present	42/429 (9.8)	0.85		0.79 (0.55–1.13)	
Ascaris lumbricoides			.98		.70
Absent	250/2267 (11.0)	1		1	
Present	6/54 (11.1)	1.01		0.85 (0.35–2.03)	
Trichuris trichiura			.69		.68
Absent	231/2110 (11.0)	1		1	
Present	25/211 (11.8)	1.09		0.91 (0.58–1.43)	

NOTE. Data presented here do not include the full enrollment sample of 2507 because women were excluded from a calculation if data were not available for any required variable.

[a] Adjusted for age, tribe, HIV status, and woman's socioeconomic status.

2498 subjects [9%]), and *A. lumbricoides* (58 of 2498 subjects [2%]). Among 1112 subjects with hookworm infection, the intensity of infection was low in 942 (85%), moderate in 127 (11%), and heavy in 43 (4%); among subjects with *M. perstans* infection, the geometric mean parasite count was 57 microfilariae per milliliter.

Initial crude analyses showed a strong positive association between hookworm infection and *P. falciparum* infection and between *M. perstans* infection and *P. falciparum* infection. There were no statistically significant associations between *S. mansoni, T. Trichiura,* or *S. stercoralis* infection and *P. falciparum* infection (table 1). The strength of the association increased with intensity of infection for hookworm (odds ratio [OR] for *P. falciparum* infection, compared to individuals without hookworm infection: 1.43 for light hookworm infection, 2.14 for moderate infection, and 2.36 for heavy infection; $P < .001$, test for trend). No such trend was observed with respect to the intensity of *M. perstans* infection. Hookworm, *M. perstans,* and *P. falciparum* infection were significantly associated with age and socioeconomic status; hookworm and *M. perstans* infection were associated with tribe; and hookworm and *P. falciparum* infection were associated with HIV infection status (data not shown). After adjusting for these potential confounding factors, the association between hookworm and *P. falciparum* infection was reduced. The association between *M. perstans* and *P. falciparum* infection was reduced, but remained strong.

There was also a statistically significant association between hookworm and *M. perstans* infection (OR, 2.70 [95% confidence interval {CI}, 2.20–3.31]; $P < .001$) and an interaction between hookworm and *M. perstans* infection in relation to their associations with *P. falciparum* infection ($P = .047$). The prevalence of *P. falciparum* infection was 7.5% (88 of 1171) among participants with neither hookworm nor *M. perstans* infection, 11.5% (87 of 755) among those with hookworm infection only, 18.8% (35 of 186) among those with *M. perstans* infection only, and 17.2% (58 of 337) among those with both. Thus the hookworm–*P. falciparum* infection association was seen only in the absence of *M. perstans* infection. Adding the interaction term to the model increased the strength of the individual associations with *P. falciparum* infection for hookworm infection and *M. perstans* infection (adjusted odds ratio [aOR] for hookworm–*P. falciparum* coinfection in the absence of *M. perstans* infection: 1.43 [95% CI, 1.03–1.98], $P = .034$; aOR for *M. perstans*–*P. falciparum* coinfection in the absence of hookworm infection: 2.29 [95% CI, 1.46–3.59], $P < .001$; and aOR for both hookworm and *M. perstans* infection with *P. falciparum* infection: 1.80 [95% CI, 1.23–2.65], $P = .003$).

The geographical distribution of women's homes and of zones is shown in figure 1, and the distribution of infections by zone is indicated in table 2. Mapping of the individual infections (not shown) indicated that there was a low prevalence of *P. falciparum* infection in the area to the extreme southwest of the penin-

Table 2. Distribution of helminth infection, *Plasmodium falciparum* infection, and helminth–*P. falciparum* coinfections, according to geographical zone.

		Infection prevalence, %			aOR for coinfection			
Zone	*n*	*P. falciparum*	Hookworm	*Mansonella perstans*	Hookworm and *P. falciparum* only	*M. perstans* and *P. falciparum* only	Hookworm, *M. perstans*, and *P. falciparum*	*P*[a]
1	267	4	58	23	4.70	17.23	6.35	.15
2	287	7	40	17	0.96	2.16	2.43	.49
3	502	14	44	20	1.82	1.55	1.45	.30
4	232	9	33	17	0.77	5.21	0.68	.24
5	366	11	38	19	1.37	4.54	2.37	.046
6	170	14	44	21	1.57	0.60	2.67	.42
7	151	10	40	16	0.60	NC[b]	1.76	.50
8	198	11	38	29	0.30	3.56	2.14	.024
9	172	15	64	30	13.87	2.98	4.16	.002

NOTE. Zones 10–13 were not included in this table because the number of participants in these zones was small (<41). A separate logistic regression was performed for each locality. NC, not calculated; aOR, adjusted odds ratio.

[a] Overall *P* value for heterogeneity, comparing prevalence of *P. falciparum* infection in mothers with hookworm infection only, *M. perstans* infection only, or hookworm and *M. perstans* infection, with the reference group of subjects who were not infected with either of the 2 worms.

[b] aOR could not be calculated because only 7 participants in this zone had *M. perstans* infection without hookworm infection, and none of these had *P. falciparum* infection.

sula (zone 1) and in the urban area of Entebbe town center to the east of the airport runway (zone 2). Two areas with increased density of infection were found to the northwest of the town; one at the northwest tip of the spur that reaches the inlet of the lake (zone 3) and one on the edge of the adjacent swamp (zone 3). Moving inland to the north was a band of more diffuse *P. falciparum* infection. Hookworm infection was spread throughout the study area, with little geographical clustering. *M. perstans* infection was spread across the study area with increased density of infection in the easternmost spur (zone 12). Moving north and west from this area, there were two further areas with increased density of infection.

In addition to the prevalence of *P. falciparum,* hookworm, and *M. perstans* infection, the adjusted odds ratios for coinfection, stratified by zone (figure 1), are shown in table 2. The adjusted odds ratios for hookworm–*P. falciparum* coinfection varied by geographical location: for example, in zone 9 there was a particularly strong association, which was not observed in zones 4, 7, and 8. The association between *M. perstans* and *P. falciparum* infection was more consistent.

After adjusting for zone in addition to potential confounding factors, the odds ratios for both the hookworm–*P. falciparum* infection association and the *M. perstans*–*P. falciparum* infection association increased slightly (aOR for hookworm–*P. falciparum* coinfection in the absence of *M. perstans* infection: 1.53 [95% CI, 1.09–2.14], $P = .014$; aOR for *M. perstans*–*P. falciparum* coinfection in the absence of hookworm infection: 2.33 [95% CI, 1.47–3.69], $P < .001$; and aOR for both hookworm and *M. perstans* infection with *P. falciparum* infection: 1.85 [95% CI, 1.24–2.76], $P = .002$). As in the crude analysis, no associations between other helminth species and *P. falciparum* infection were observed in the adjusted model.

DISCUSSION

This study offered a unique opportunity to examine helminth–*P. falciparum* coinfection in the neglected demographic stratum of pregnant women. The principal finding was a strong association between asymptomatic infection with *P. falciparum* and infection with *M. perstans*. A weaker association was observed between hookworm infection and *P. falciparum* infection, and there was an interaction between infections with the 2 helminths, such that the effect of hookworm infection was only seen in the absence of the stronger association with *M. perstans* infection. To our knowledge, this analysis provides the first report of an association between a filarial helminth infection and *P. falciparum* infection in humans. The results have implications for understanding of the host-parasite relationship, particularly during pregnancy, and for targeting the treatment of coinfections among vulnerable groups.

This study focused on the fact that the geographical distribution of parasitic infections exhibits spatial dependency over small distances [27], and it represents a step forward from studies conducted in a single location that assumed no spatial clustering or did not measure residential location [18, 22, 38]. Geographical zones were defined on the basis of simple geography, altitude, vegetation, and location of settlements, as these have been found to correlate spatially with parasite infection [27, 39]. The zones provide a means to analyze the different environments of, for example, an exposed costal location in zone 1 and the very different urban environment of zone 3 as separate entities, and to adjust for these differences in analysis. However, the stratification had limitations. Although the aim was to provide a detailed stratification by environment, there was a need to strike a balance between achieving homogeneity within the zones and

creating zones so small that the analysis was not sufficiently powered. Given that the probability of infection is known to exhibit spatial dependency over small distances [27], it may have been incorrect to assume homogenous parasite density within study zones of up to 4 km in diameter. The use of zones in the analysis presented here enabled the description of variation between, but not within, areas.

Stratification by zone revealed considerable variation in the probability of coinfection by geographical location, particularly for hookworm–*P. falciparum* infection. This may be related, in part, to the observed variability in the prevalence of hookworm and *P. falciparum* infections. The associations were strongest in zones where the prevalences of both hookworm and *P. falciparum* infection were highest, consistent with a hypothesis that probability of infection with *P. falciparum* increases with the frequency of hookworm transmission.

A considerable number of women seen at the antenatal clinic were excluded from this study, but it is unlikely that the major reasons for exclusion created an important bias. The principal reason for exclusion, residence outside the study area, was appropriate to this analysis. A bias in relation to HIV infection status of those excluded is unlikely to have affected the results, because the principal effects showed no interaction with HIV infection among those analyzed.

Women were included in this study only if they were well on the screening day, with no complaints (e.g., fever) and no gross evidence of severe, helminth-induced disease (such as anemia, bloody diarrhea, or overt liver disease). This analysis, therefore, addresses the associations between helminth infection and asymptomatic *P. falciparum* parasitemia, which may differ from the associations between helminth infection and symptomatic *P. falciparum* infection [40]. Assuming that helminth infection is more often chronic and long-lasting than infection with *P. falciparum,* the observed positive association between helminth infection and asymptomatic *P. falciparum* parasitemia may imply an increased likelihood of *P. falciparum* infection, a reduced likelihood of clearing *P. falciparum,* and/or a reduced likelihood of developing symptoms and seeking medication.

The first possibility, a helminth–*P. falciparum* infection association due to an increased likelihood of infection with *P. falciparum* among women with helminth infections, could arise through behavioral or environmental factors that lead to increased exposure to both types of infection. Both *M. perstans* and *P. falciparum* are transmitted by flying insect vectors, *M. perstans* by *Culicoides* midges [41] and *P. falciparum* by *Anopheles* mosquitoes [26]. It is plausible that the distribution of these 2 vectors may be spatially correlated, as both require water sources for larval breeding [26, 42], although it is not clear whether the required conditions are exactly the same. Similarly, hookworm larvae flourish in damp soil and grass, which may be found close to stagnant water that is a breeding ground for *P. falciparum*. The slight reduction in the helminth–*P. falciparum* infection associations with adjustment for socioeconomic and demographic factors suggests a possible contribution of other behavioral effects; such as differences in the usage of antimalarial drugs during pregnancy, prior to enrollment in the study; however, prior consumption of antimalarial drugs showed no statistically significant association with helminth infection and adjustment for prior consumption of these drugs did not alter the observed effects (data not shown). On the other hand, adjustment for geographical zone strengthened the associations, suggesting that, at the zone level, common environmental factors could not explain the effect. Thus the possibility that helminth infection may lead to a biological increase in susceptibility to infection, or to persistence of asymptomatic infection with *P. falciparum,* remains plausible. This is in accord with previous studies that suggest associations between helminth infection and an increased incidence of *P. falciparum* infection [20] and higher parasite counts and delayed parasite clearance [17], as well as a reduction in disease severity [21–24]. From the data in this cross sectional study, it is not possible to say whether the higher prevalence of *P. falciparum* infection among helminth-infected women resulted in an increased incidence of disease events.

Hookworm and *M. perstans* were the helminths that most commonly infected participants in this study. The helminth infections observed less commonly, those due to *S. mansoni, S. stercoralis, T. trichiura,* and *A. lumbricoides*, showed no associations with *P. falciparum* infection, in conflict with the results of some previous reports [20, 43–45], but in agreement with another study from Uganda that reported no association [17]. For these species, a real association (if present) might not have been detected in this study because few women were infected (particularly with *A. lumbricoides*), because the intensity of the helminth infection was low, or because low-intensity infections were misclassified as negative as a result of examining a single stool sample (multiple samples are required for high sensitivity of detection) [46–48]. Such misclassification may also have contributed to the relatively weak observed effect of hookworm infection. By contrast, preliminary results suggest that the Knott's method used for assessment of *M. perstans* infection was particularly robust, with serial results in the same women showing 96% agreement for infection status and a correlation coefficient for microfilarial counts per milliliter of 0.88 ($P < .001$) (A.M.E., unpublished data).

This study does not explore the potential biological mechanisms for the observed associations between helminth infection and *P. falciparum* infection. However, previously proposed mechanisms include the suggestion that the immunoregulatory effects of helminths, which allow their own long-term survival in the host [9], "spill over" to impair the immune response required to protect against or eliminate malaria parasites. *M. perstans* is a long-lived filarial worm that inhabits serosal body cavities and reproduces through microfilaria that circulate in the blood and are transmitted through biting midges [42]. Despite

residence in and migration through blood and tissues, *M. perstans* infection seldom causes detectable pathology, and this attests to its particularly potent immunomodulating properties. It is thus interesting to speculate that *M. perstans* might produce a particularly strong immunomodulating effect on the response to other pathogens and that this might override the effects of related helminths, such as hookworm, when both are present, perhaps accounting for the observed interaction between the 2 helminth species. This will be more comprehensively described in a future article.

This study specifically examined coinfection in pregnant women. The unique environment that exists in the pregnant body means that one should be cautious in applying these results to the general population. This may be particularly important in relation to associations with *P. falciparum* infection, because parasites are sequestered in the placenta during pregnancy [33] and may be less readily detected in the peripheral blood (sampled in this study). Apparent biological associations might possibly reflect the effects of the helminth(s) on the sequestration of *P. falciparum* parasites in the placenta, rather than effects on the prevalence of infection.

In summary, this analysis has examined helminth–*P. falciparum* coinfection in pregnancy and attempted to address the influence of residential location on associations between these environment-dependent parasites. It provides evidence of an association between hookworm and *P. falciparum* infection and the first report of an association between *M. perstans* and *P. falciparum* infection, effects not explained by the social or geographical factors measured. Given the plausible hypothesis of a biological interaction between helminths and *P. falciparum* and increasing advocacy for deworming, there is a need for prospective studies of the effects of helminths and the treatment of helminth infection on *P. falciparum* and other malaria parasites, studies that incorporate surveys of residential location and vector entomology, as well as recording *P. falciparum* infection rates and illness events.

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