

Asymptomatic malaria and intestinal helminth co-infection among children in a rural community in Southwest Nigeria

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Abstract

Background. Malaria is prevalent in sub-Saharan Africa, where other concomitant parasitic infections, including intestinal helminths, are common. However, little is known about how concurrent infections affect the expression or pathogenesis of each other. This study aimed to document the prevalence rates of malaria and intestinal helminths individually and as co-infection among asymptomatic children in a rural community in southwest Nigeria.

Materials and Methods. Apparently healthy children aged 1-17 years, who were enrolled into a larger study that evaluated the efficacy and safety of two anti-helminthic drugs, were evaluated for intestinal helminths by stool examination using the saline wet mount and Kato-Katz methods. Capillary blood from finger prick samples was used for haematocrit determination and malaria screening by microscopy. Data analysis was conducted using SPSS and significance levels were set at $p < 0.05$.

Results. Eighty-nine of 178 (50%) enrollees were male. One hundred and fifteen of the 178 (64.6%) children had at least one intestinal helminthic infection while 69 (60%) thereof harboured multiple helminthic infections. Malaria parasites were encountered in 35/178 (19.7%) of the enrollees. Parasite density was $\leq 500/\mu\text{l}$ in 51.4% (18/35), 501–1,000/ μl in 9 (25.7%) and 1,000–4,720/ μl in 8 (22.9%) of the children. Malaria-helminth co-infection was detected in 24/115 (20.9%) of the children. The prevalence [60/115 (52.2%) versus 8/63 (12.7%) $p < 0.0001$] and severity of anaemia were significantly higher among children with worms compared to those without worms. For mild anaemia this was 53/115 (46.8%; with worms) versus 7/63 (11.1%; no worms $p < 0.0001$); for moderate anaemia 2/115 (1.74%; with worms) versus 1/63 (1.59%; without worms; $p < 0.271$).

Conclusion. Malaria and helminths co-infection is common among apparently asymptomatic children in the rural community studied. Co-infections increase the problems associated with anaemia and aggravate the burden of disease in Nigerian children.

1 Introduction

Helminths are among the most common chronic infections in the tropics while malaria caused by *Plasmodium falciparum* is a major cause of morbidity and mortality [1-5]. Malaria and intestinal helminth co-infection are thus common in sub-Saharan Africa because of supportive environmental factors. Soil-transmitted helminths (geo-helminths) are widely distributed in rural communities because of inadequate and sometimes non-existent sanitary facilities. Socio-cultural practices such as barefoot walking and eating without washing hands are additional factors that increase susceptibility of the indigenous population to helminthic infections.

Subsistence farming, which is widely practiced in rural communities in Africa, also exposes populations to geo-helminths. The overlapping distribution of helminths and malaria cause problems of poor nutrition and anaemia in the humans [6-9]. The extent and outcome of co-existence of malaria and helminths in a single host has not been fully elucidated and several conflicting findings in the clinical consequences of co-infection that range from protective to aggravating effects have been reported in studies done in different parts of the world [10-16], with few reports on

the co-existence in asymptomatic individuals [9,14,17]. While Benjon *et al.* [9] found no significant difference in the average haemoglobin levels among children with gastrointestinal helminthic infections, and no altered susceptibility to malaria associated with these infections, other studies reported increased susceptibility to malaria or a worsening of malaria symptoms [10,15,19]. In contrast, others reported a reduction in risk of malaria infection in the presence of helminthic infections [12,13] or no difference in susceptibility [11].

Mechanisms of anaemia include lysis and phagocytosis of infected red blood cells while the degree thereof is dependent on the intensity of the malaria infection [4,15-16]. Intestinal parasitic infections, on the other hand, cause anaemia from petechial haemorrhages by activities such as direct blood sucking, which also leads to deprivation of nutrients and loss of appetite in the patient [7,16-19]. Intestinal helminths can thus be the cause of malnutrition, or aggravate existing malnutrition, through damage to the gastrointestinal mucosal epithelium and inflammation, reduced food intake, malabsorption, and increased nitrogen loss in faeces and diarrhoea [8, 18-19]. It appears obvious, therefore, that co-infections compromise the health condition of the patient.

Table 1. Gender and parasite distribution among infected children.

Gender	Ascaris	Hookworm	<i>Trichuris trichiura</i>	<i>Enterobius vermicularis</i>	<i>Strongyloides stercoralis</i>	Malaria
Male	51	23	17	3	0	18
Female	52	31	21	3	4	17
Total	103	54	38	6	4	35

Helminthic and malaria infections, either singly or jointly, can be present in a host without any noticeable symptoms. Asymptomatic carriers as such are the major reservoirs of infection and the source of new cases, re-infection and even auto-infection [18-20]. It is therefore important to evaluate the extent of co-infection among asymptomatic individuals, especially children who are most prone to parasitic infections. The current study was designed to understand such kind of (co)infections among children in a rural Nigerian community.

2 Materials and Methods

2.1 Study site

This study was conducted in Olode-Adetoun village, a rural farming community in southwest Nigeria, as part of a larger study that evaluated the comparative safety, efficacy and tolerability of oxibendazole and mebendazole for the treatment of intestinal helminths in children below the age of 17 years. The study site was chosen because it represents a typical rural community in Nigeria with no access to sanitary facilities, no source of piped water, no electricity, or access by paved roads. Waste is left unattended in the open environment due to absence of waste management or sewage and refuse disposal.

2.2 Study design

The University of Ibadan/University College Hospital Ethical Review Board provided ethical clearance for the study. Community consent was obtained at different stages starting from the Local Government chairman and his management team, the traditional head of the village and community opinion leaders. Individual signed or witnessed verbal informed consent was also obtained from the parent or guardian of prospective enrollees before any study-related procedure was carried out.

Inclusion criteria were: Children aged 1-17 years of age, residence in the community for at least one year before enrolment, no history of anti-helminthic drug intake in the last three months or antimalarial treatments in the last four weeks before the start of the study. Children whose parents or guardians failed to provide informed consent or did not meet these inclusion criteria were excluded. All enrolled children underwent physical examination, anthropometric measurements and inspection of vital signs.

The body-mass-index (BMI) was calculated from their

bodyweight and height measurements (Weight/Height squared) and interpreted according to WHO [21] as <18: underweight to anorexic; 19-27: healthy; 28-39: overweight; ≥ 40 : severe obesity. Thick blood films prepared from finger prick samples were stained with Giemsa and observed under a light microscope at 1000x magnification using standard procedures. Asexual forms of malaria parasites were counted against white blood cells (WBC) and expressed as number of parasites/ μ l of blood assuming a total WBC count of 8000/ μ l. Blood was collected into heparinised capillary tubes for haematocrit estimation. Capillary tubes were filled to mark and spun for 10 min in a Hawksley[®] micro-haematocrit centrifuge at 1000g/m² after which the haematocrit was determined using a Hawksley[®] micro-haematocrit reader. Study participants whose PCV was less than 33% were considered anaemic and further categorised as mild (26 – 32%), moderate (19 – 25%) or severely anaemic ($\leq 18\%$).

Any enrollee with an axillary temperature $\geq 37.5^{\circ}\text{C}$ in the presence of any level of asexual malaria parasitaemia and absence of any other obvious cause of fever was considered to have clinical malaria. Diagnosis of asymptomatic malaria was made if the slide was positive for malaria parasite in the absence of complaints of fever, headache, malaise and body temperature $<37.5^{\circ}\text{C}$. Each study participant was given a wide-mouthed bottle and spatula for stool specimen collection. A fresh stool specimen was collected and screened. Intestinal helminths were identified by examination of saline wet mount while quantification was done using the Kato-Katz technique [22]. Baermanization was carried out for *Strongyloides stercoralis* whereas *Enterobius vermicularis* was diagnosed by use of scotch tape applied to the anus of suspected children overnight. The scotch tape was removed first thing in the morning and processed for identification of the typical ova of *Enterobius vermicularis*. Quantification of intestinal helminths was expressed as the number of eggs per gram of stool, for each helminth, the arithmetic mean of the helminth species specific egg counts from Kato-Katz thick smears was counted and multiplied by a factor of 24 to obtain a standardised measure of infection intensity expressed as eggs per gram of stool (EPG). Infection intensities were classified as light (1- 999), moderate (1,000-9,999), or heavy ($\geq 10,000$), according to thresholds.

2.3 Data analysis

Information from all completed case record forms (CRFs) was analysed using SPSS (SPSS Inc., Chicago, IL, USA,

Table 2. Prevalence of worm infection(s) in the different age groups.

Geo-helminths	Age groups (Years)				Total (178)
	0 – 5 (N=43)	>5-10 (N=81)	>10-15 (N=48)	>15 (N=6)	
No Helminths	17	27	15	4	63
<i>A. lumbricoides</i> only	16	16	10	0	42
<i>A. lumbricoides</i> + Hookworm	4	16	5	0	25
<i>A. lumbricoides</i> + <i>T. trichiura</i> + Hookworm	1	10	10	0	21
<i>A. lumbricoides</i> + <i>T. trichiura</i>	1	6	5	1	13
<i>A. lumbricoides</i> + <i>T. trichiura</i> + Hookworm + <i>E. vermicularis</i>	0	3	0	1	4
Hookworm only	2	0	1	0	3
<i>A. lumbricoides</i> + Hookworm + <i>S. stercoralis</i>	0	1	1	0	2
<i>A. lumbricoides</i> + Hookworm + <i>E. vermicularis</i>	0	1	1	0	2
<i>A. lumbricoides</i> + <i>T. trichiura</i> + <i>S. stercoralis</i>	1	1	0	0	2
<i>T. trichiura</i> only	1	0	0	0	1
Intestinal worm present (%)	26 (60.46)	54 (66.67)	33 (68.75)	2 (33.3)	115 (64.61)

version 15). Frequency tables were generated for relevant variables. Descriptive statistics such as means \pm standard deviations (\pm sd) were used to summarise quantitative variables while qualitative variables were summarised with proportions. The mean values of malaria parasite densities were expressed as geometric means. Chi square (χ^2) tests were used to investigate associations between two qualitative variables while analysis of variance (ANOVA) was used to compare more than two mean values. Significance levels were set at $p < 0.05$.

3 Results

Out of a total of 178 enrolees, 89 (50%) were males. The mean age of all enrolees combined was 8.56 ± 3.63 years (range 2-16 yrs). The prevalence of helminthic and malaria infections among the different age groups ($p=0.304$ and $p=0.97$, respectively) and sexes ($p= 0.377$ and 1.000 , respectively) were not significantly different.

3.1 Malaria screening

The prevalence of malaria parasitemia was 19.7% (35/178) with a geometric mean parasite density (GMPD) of $384/\mu\text{l}$ (range 62 - $4720/\mu\text{l}$). Out of 35 malaria cases, 18 (51.4%) had a malaria parasite density of $<500/\mu\text{l}$, 9 (25.7%) had 501 – $999/\mu\text{L}$ and 8 (22.9%) had between 1000 – 4720 asexual malaria parasites/ μl . Not only were children below five years of age more likely to have malaria parasitemia compared with those >5 years of age [12/43 (27.9%)] versus [23/135 (17.0%)], $p=0.104$ (χ^2), the GMPD among them was significantly higher than for older children [889/ μL ; (80 – $4720/\mu\text{l}$) versus $248/\mu\text{l}$; (62 - $1098/\mu\text{l}$) ($p=0.001$)]. Malaria parasite density was low (parasite count $\leq 2000/\mu\text{l}$) in 32 and moderate (absolute malaria parasite count 2001 – $100,000/\mu\text{l}$) in 3 cases.

3.2 Geo-helminth screening

Almost two thirds (64.6%; 115/178) of the participants had at least one helminthic infection. *Ascaris lumbricoides* was most prevalent (89.6%; 103/115). Other intestinal helminths include hookworm (47.8%; 55/115), *Trichuris trichiura* (35.7%; 41/115), *Enterobius vermicularis* (4.4%; 5/115) and *Strongyloides stercoralis* (3.5%; 4/115). Two (1.1%) of the enrolees had *Giardia lamblia* while one (0.6%) had *Gastrodiscoides hominis*. Highest prevalence of geo-helminths was in children aged 5 -15 yrs (Tables 2 and 3).

Nearly 60% of the helminth-infected cases had multiple intestinal infections. About 33% (38/115) had double infections while 27 (23.5%) had triple infections. Four (3.5%) had quadruple infections. The commonest combination was hookworm and *Ascaris lumbricoides* (Table 2). Worm loads for *Ascaris lumbricoides* were in the range of 744 – 216,000/g and for hookworm were in the range of 48- 24,888/g. The worm loads of *A. lumbricoides* and hookworm were considered heavy in 95.7% (110/115) of enrolees and occurred in both sexes with no statistical difference in worm load carriage ($p= 0.191$). Prevalence of hookworm was significantly higher among girls [33/89 (37.1%)] compared to boys [12/89 (13.5%)] ($p= 0.0001$), but an association between worm load and gender was not seen ($p=1.0$).

3.3 Malaria-helminth co-infection

Twenty-four of the 115 (20.9%) children with helminthic infection had malaria parasitemia. The prevalence of helminthic infection was similar among individuals with or without malaria [24/35 (68.6%)] and [91/143 (63.6%)], respectively ($p=0.695$). There was also no significant difference between the presence of malaria parasites and multiple worm types as there were single, double, triple and quadruple worm infections in 10, 9, 4 and 1 malaria para-

Table 3. Prevalence of individual major parasites among different age groups.

Age range (years)	Total	<i>Ascaris lumbricoides</i>	<i>Trichuris trichiura</i>	Hookworm	<i>Enterobius vermicularis</i>	Malaria
0-5	43	21	6	6	0	12
>5-10	81	48	20	28	4	15
>10-15	48	29	13	17	1	6
>15	6	5	2	3	1	2
Total	178	103	41	54	6	35

site positive cases, respectively, ($p=0.785$). *Ascaris lumbricoides* was present in 62.9% (22/35) of children with malaria parasites against 56.3% (81/143) children without malaria parasites ($p=0.024$). Generally, children with a heavy *Ascaris* load ($\geq 10,000$ eggs/g) tended to have low levels of malaria parasitaemia [20/35 (70%)] versus those who had low *Ascaris* load [2/35 (5.7%)] ($p<0.0001$). Hookworm was found in 15/35 (42.9%) and 39/143 (27.3%) children with and without malaria parasites, respectively ($p=0.231$). The prevalence of co-infection had no sex predilection.

3.4 Nutritional status and parasitic infections

About a third 57/178 (32.4%) of the children were 'underweight', 85 (47.5%) fell within the 'healthy' category, 34 (19.0%) of the children were 'overweight', and 2 (1.1%) were in the 'obese's category. Malaria parasite were significantly more common in the underweight children [17/57 (29.8%)] compared to 18/121 (14.9%) of those not underweight ($p=0.026$).

3.5 Anaemia and presence of malaria and intestinal helminths parasites

The prevalence of anaemia within the study population was 35.4% (63/179). Anaemia was mild in 60/63 (95.2%) and moderate in three children (4.8%). The presence of anaemia had no significant association with age ($p=0.226$). The prevalence of anaemia was, however, significantly higher among children with helminthic infections [(53/115 (46.1%)] compared to those without helminthic infection (s) [7/63 (11.1%)] ($p<0.0001$). Anaemia was also more common among cases that had multiple infections compared to those with single infection and significantly associated with hookworm infection [74.1% versus 40.8%; $p<0.0001$, Odds Ratio= 4.146, CI 95% (2.047-8.394)]. Mild anaemia was present in 52 cases that had high *Ascaris lumbricoides* loads, and 3 cases with moderate *Ascaris* loads. The presence of malaria parasites did not significantly affect the proportion of children who were anaemic (16/35; 45.7% with malaria parasite compared to 91/178 (51.1%) of the study population; $p=0.695$).

4 Discussion

In this study, carried out in a rural community in southwest Nigeria where malaria transmission is intense, we recorded a high prevalence of helminthic infections among schoolchildren with asymptomatic malaria. There was also clustering of helminthic infection among children between 5-15 yrs of age (Tables 1 and 2) and generally infrequent and relatively light intensity among children below 5 yrs of age. These findings are similar to the findings of Kimbi *et al.* [17] and other studies [18-20] that report consequences of malaria infection and clustering of helminthiasis among schoolchildren.

Malaria and soil-transmitted helminths are common problems of people living in rural areas. In the current study, 20.9% (24/115) of the enrollees were asymptomatic for malaria-helminth co-infection. We showed that 68.6% and 17.5% of the asymptomatic malaria cases were with and without intestinal helminths, respectively, which corroborates previous findings that describe overlapping distribution of intestinal helminths and malaria infections [23-26].

The densities of malaria parasitemia were generally low with only 8/35 (22.9%) of parasitaemic children having parasite densities above 1000/ μ l. Out of the 35 children with malaria parasitaemia, 18 (51.4%) had malaria parasite densities of $<500/\mu$ l while 9/35 (25.7%) had 501 – $<1000/\mu$ l. The higher prevalence rates and load of helminths were found in children above 5 yrs. However this age group was found to have lower malaria parasite densities. A similar study with an asymptomatic population in Osogbo, also in southwest Nigeria, reported 4.3% prevalence [14], which is low compared to our findings. Studies from Ghana (16.6%) and Ethiopia (55.7%) were higher in this regard [23-24], which suggests that the pattern of co-infections may vary even within sub-Saharan Africa.

The occurrence of asymptomatic malaria was more common among children with *Ascaris lumbricoides* ($p=0.024$) compared to other helminths. Sixteen of 68 (11.1%) children with ascariasis with an EPG load $<10,000$ were infected with malaria ($p=0.003$ compared to those with higher ascaris egg load). This corroborates the reports by Mwangi *et al.* [23]. Many other researchers reported high hookworm and malaria co-infection [25,27], supposedly due to the wider thermal tolerance of hookworm eggs compared to those of *Ascaris lumbricoides* and *Trichuris trichiura* [7]. In our study we found a higher

association between malarial parasites and *Ascaris lumbricoides*, possibly because it is the most prevalent helminth to infect children. It is noteworthy, that 54/57 (94.7%) of children with ascariasis also had hookworm infections. It has been observed that participants with *Ascaris lumbricoides* and other helminthic infections were almost two to five times more likely to have *P. falciparum* infection compared to individuals without helminths [23,25]. The mechanism behind this association is not clearly understood but could be that Th-2 profile-associated immunoglobulin E production seen in *Ascaris* infections may down-modulate Th-1 antimalarial immune responses, resulting in increased risk of malaria infection [28-29].

Among children with worms 46.8%, (53) and 1.74%, (2) had mild and moderate anaemia respectively. However, in children without worms, only 7 cases of mild and 1 case of moderate anaemia were reported ($p=0.0001$). Anaemia was more prevalent [53/69 (76.8%)] among children with multiple worm infections and higher worm load. Anaemia was also significantly associated with hookworm infection ($p=0.0001$, OR=4.416 CI=95%, 2.047-8.394). This finding is in line with previous reports [18,30] suggesting that hookworm infection contributes more to anaemia than other intestinal helminths [7,24].

Seventeen of 35 (48.6%) enrollees with malaria infection were children whose nutritional status was sub-optimal. In addition to malaria infection, the majority [40/57 (70.2%)] who had malnutrition also had intestinal helminthic infection(s). We conclude that helminthic infections predispose children to nutritional insufficiency and loss of nutrients and trace elements [30]. In conclusion, this study was able to establish that malaria and helminth infections are common in an asymptomatic way among children in rural communities. This finding should be used for improved treatment and control of malaria and other diseases.

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