



Research Article

Co-Infection of Soil Transmitted Helminthes and Malaria Parasites: Relationship with Anaemia in Individual Living In Igbo-Ora, Oyo State. Nigeria

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Abstract

Sub-Saharan Africa is endemic with malaria and soil transmitted helminthes. Helminth co-infection with malaria has detrimental effects on humans. This study aimed to evaluate the prevalence of each infection, co-infection and its effect on anaemia among individuals at Igbo-Ora, Oyo State. A cross-sectional study involving 274 individuals at Igbo-Ora was conducted from March to August 2013. *Plasmodium* and intestinal helminth infections were diagnosed using Giemsa-stained blood films and Kato-Katz technique, respectively and anaemia was determined by measuring the Packed Cell Volume (PCV) using the haematocrit centrifuge and reader. Among the participants, 21.2% were positive for *Plasmodium* parasites only, 28.8% were infected with intestinal helminthes only, while 6.9% were co-infected with *Plasmodium* and intestinal helminthes. Malaria parasite-hookworm had the highest prevalence of 27.0% among other co-infections but this was not statistically significant ($P=0.198$, $OR=1.532$ 95% $CI=0.798-2.943$). The overall prevalence of anemia was 12.8% ranging from individuals with no infection to individuals with co-infection. It was observed among individuals with *Plasmodium* infection that co-infection with *Ascaris* (malaria-*Ascaris*), hookworm (malaria-hookworm) and *Ascaris*-hookworm (malaria-*Ascaris*-hookworm) all had a negative association ($\rho = -0.127, -0.124, -0.123, \text{ and } -0.123$ respectively) with PCV. The negative association of malaria parasites infection and malaria parasite-hookworm co-infection with anaemia were statistically significant ($P=0.036$ and $P=0.025$ respectively). Malaria parasite-*Ascaris*, malaria parasite-hookworm and malaria parasite-*Ascaris*-hookworm all gave rise to low PCV values leading to anaemia in the population of individuals living in Igbo-Ora.

Keywords: Malaria, Helminth, Co-infection, Packed Cell Volume, Anaemia, Igbo-Ora

INTRODUCTION

Humans have been infected with parasites throughout evolutionary history. One of the most intractable public-health problems that poses an enormous public health burden is malaria and more than 75% of the global clinical episodes cause by *Plasmodium* species each year are concentrated in Africa (Snow *et al.*, 2005; Ojurongbe *et al.*, 2011). Malaria continues to plague millions of individuals annually, with an estimated 216 million cases reported each year and an estimated 655,000 deaths in 2010, 86% of which occurred in children under five years of age (WHO, 2011). In Sub-Saharan Africa, malaria and helminth infections are major public health problems in both rural and urban areas (de Silva *et al.*, 2003; Mboera *et al.*, 2011). The overlapping distribution of these parasitic infections in sub-Saharan Africa results in high rates of co-infection (Petney and Andrews, 1998; Dada-Adegbola *et al.*, 2013). An estimated 45 million school-aged children are at risk of co-infection; in Nigeria malaria-helminth co-infections pose a significant health problem among children (Brooker *et al.*, 2006; Ojurongbe *et al.*, 2010). A number of helminthes species across the continent, share the same spatial extents as

Plasmodium species. *A. lumbricoides*, *T. trichiura*, *S. stercoralis* and hookworms are the most ubiquitous soil-transmitted helminthes, which infect more than one third of the continents population at a time (Brooker *et al.*, 2006). The etiology of anaemia is complex and multi-factorial in origin. Parasitic diseases including *P. falciparum* and helminth infections, have long been recognized as major contributors to anemia in endemic countries (Ojurongbe *et al.*, 2010). *P. falciparum* infection generally causes anaemia, particularly among children and pregnant women (Desai *et al.*, 2003; Nyakeriga, 2004; Ekejiuba *et al.*, 2011). The destruction of red blood cells by malaria parasite proliferation and clearance of malaria-infected red blood cells by the immune system as suggested from evidences from human and animal malaria infections, are only contributory factors to the severity of malarial anaemia (Price *et al.*, 2001; Chang *et al.*, 2004). Hookworm infection on the other hand, results in intestinal blood loss and is probably second only to malaria as an infections cause of anemia (Stoltzfus *et al.*, 1997; Ekejiuba *et al.*, 2011). In Sub-Saharan Africa, about 45.1 million school-aged children are at coincidental risk of hookworm and malaria infections which can result in anaemia (Brooker *et al.*, 2006).

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Some studies reported that helminth infected individuals are susceptible to *Plasmodium* infection (Nacher, 2001; Druilhe *et al.*, 2005; Ojuronbe *et al.*, 2011), increased malaria gametocyte carriage, decreased haemoglobin concentration and increased risk for clinical and severe malaria (Spiegel *et al.*, 2003; Sokhna *et al.*, 2004; Roussilhon *et al.*, 2010); while other studies reported the absence of significant association between helminth infection and malaria (Nacher *et al.*, 2002; Shapiro *et al.*, 2005; Degarege *et al.*, 2009). Apart from malaria-helminth co-infection, there had been studies on other co-infection such hepatitis B virus (HBV) and Human immunodeficiency virus (HIV), HIV and tuberculosis (TB) among others (Le Hesran *et al.*, 2004; Shapiro *et al.*, 2005; Kourtis *et al.*, 2012; Gao *et al.*, 2013). Several studies have been carried out on malaria in Igbo-Ora (Nwuba *et al.*, 2002; Omosun *et al.*, 2007; Ngoundou-Langdi *et al.*, 2011) however, little is known about the prevalence and severity of soil transmitted helminthes and malaria parasite co-infection in Igbo Ora. This study was therefore conducted to determine the prevalence and association of soil transmitted helminthes-malaria parasite co-infection and its effect on packed cell volume among individuals living in Igbo-Ora, a semi-urban community in southwest Nigeria.

MATERIALS AND METHODS

Study site:

Igbo Ora is the administrative headquarters of Ibarapa Central Local Government. There are six main communities in the town: Idofin, Sagaun-un, Isale-Oba, Iberekodo, Pako and Igbole. Majority of the residents are of Yoruba descendant and farming is the predominant occupation.

Study design: This was a cross sectional study carried out between April to August, 2013. Participants were recruited from house to house.

The inclusion criteria were: the individual residing in the community for at least 12 months, and the participant was willing and able to give consent, in case of minor, the parent or guardian are willing to give consent on his/her behalf. While the exclusion criteria were: the person attend school or work full-time outside the study area, received anti-malaria and anti-helminthic treatment within the last 3 months.

Ethical approval: The ethical clearance for the study was obtained from the University of Ibadan/University College Hospital Ethical Review Board. Community consent was obtained from the traditional head of the communities and family heads. Individual signed consent was obtained from participants and parents or guardians of minors before any related procedure was carried out.

Parasitological Analysis:

Two thick blood smears through finger pricking were made on a single slide from each participant, and these were stained with Giemsa solution for detection and quantification of malaria parasites. The presence of *P. falciparum* malaria parasites was determined by counting infected erythrocytes amongst 200 white blood cells using 100 high power fields under oil immersion. The parasite density was expressed per μL of blood assuming 8,000 leucocytes per μL of blood.

A clean, dry, leak-proof bottle was given to the participants for collection of freshly passed stool specimen the next day. The stool sample was examined using normal saline wet

preparation for identification of motile parasite and then Kato-Katz technique was used for both identification and quantification. Quantification of intestinal helminthes was expressed as the number of eggs per gram of stool, for each helminth, 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 standardized measure of infection intensity expressed as eggs per gram of stool (EPG).

Determination of anaemia using Packed Cell Volume (PCV):

Heparinised capillary tubes were used to collect blood for haematocrit estimation. Capillary tubes were filled to mark, sealed and spun for 15 min in a Hawksley micro-haematocrit centrifuge at 1500 rpm. The haematocrit was then determined using a Hawksley micro-haematocrit reader. According to WHO (1994), the normal PCV blood range for the different age groups were as follows: 0-15yrs (33-36%), adult men (39%), pregnant and non-pregnant women (33-36%). For this study participants whose PCV was less than 32% were considered anaemic.

Data analysis

The data was analyzed using SPSS version 19 statistical packages software and statistical comparison was done using Chi-square (X^2) test. A stepwise Spearman's correlation was done for the determination of a possible association between malaria-helminth co-infection and anaemia. Descriptive statistics was used to assess the prevalence of each infection and this was represented using charts, and tables. Values were considered statistically significant when p-values < 0.05

RESULTS

Prevalence and intensity of malaria parasite

The demographic characteristics of the participants are represented in Table 1. A total of 274 participants were recruited, the male: female ratio was 1:1.6. About 58 individuals (21.2%) were infected with *Plasmodium* species. Malaria Parasite Density (MPD) calculated in this study had a range of 1-11,400 (mean of 101.39 malaria parasite/ μL blood), 11 (18.9%) of the participants had low parasitaemia (Fig. 1).

Prevalence of malaria parasite in relation to age and sex.

The prevalence in malaria parasite was found to be very high among children aged 6-10 years old followed by age groups 0-5 and 11-15 (Fig. 2). The prevalence of malaria parasite among the various age groups was found to be statistically significance (<0.001) (Fig. 2). About 31 (11.3%) of the population infected with malaria parasite were female but this was not found to be statistically significance (Table 2).

Prevalence and intensity of intestinal-helminthes infection.

A total number of 79 individuals (28.8%) had helminthes infection. The most frequent intestinal helminthes present within the population were hookworm, *Ascaris lumbricoides*, *Strongyloides stercoralis* and *Trichuris trichiura*. In this study, there was no significant difference between individuals the anaemia in individuals infected with STH and those that were not (Table 2).

Table 1:

Demographic characteristics of the 274 Igbo-Ora participants, their malaria-intestinal helminthes co-infection and PCV status

Characteristics	Malaria-helminthes co-infection PCV						P value	
	All (274)		Present (N=19)		Anaemic (%)	Non-Anaemic (%)		
	N	%	Yes	%				
Sex	Male	106	38.7	11	57.9	14 (40)	92 (38.5)	0.076
	Female	168	61.3	8	42.1	21 (60)	147 (61.5)	
Age (years)	0-5	43	15.7	1	5.3	13 (37.1)	30 (12.6)	0.026
	6-10	46	16.8	7	36.8	9 (25.7)	37 (15.5)	
	11-15	33	12.0	4	21.1	1 (2.9)	32 (13.4)	
	16-20	12	4.4	0	0	1 (2.9)	11 (4.6)	
	21-30	35	12.8	4	20.1	2 (5.7)	33 (13.8)	
	31-40	26	9.5	1	5.3	3 (8.6)	23 (9.6)	
	>40	79	28.8	2	10.6	6 (17.1)	73 (30.5)	
Formal education	None	75	27.4	1	5.3	22 (62.9)	89 (37.2)	0.236
	Primary	113	41.2	10	52.6	1 (2.9)	60 (25.1)	
	Secondary	61	22.3	6	31.6	1 (2.9)	23 (9.6)	
	Tertiary	24	8.8	2	10.5	11 (31.4)	66 (27.6)	
Literacy class	1	0.4	0	0	0 (0)	1 (0.4)		
Marital status	Single	140	51.5	16	84.2	24 (68.6)	116 (48.5)	0.014
	Married	116	42.3	2	10.5	11 (31.4)	105 (43.9)	
	Widowed	14	5.1	1	5.3	0 (0)	14 (5.9)	
	Separated	4	1.5	0	0	0 (0)	4 (1.7)	
*Treatment of malaria								
Herb	38	13.9	4	21.1	4 (11.4)	34 (14.2)	0.233	
Chemist	81	29.6	5	26.3	6 (17.1)	33 (13.8)		
Hospital	80	29.2	4	21.1	1 (2.9)	20 (8.4)		
Herb/chemist	39	14.2	4	21.1	9 (25.7)	72 (30.1)		
Herb/hospital	21	7.7	1	5.3	0 (0)	3 (1.3)		
Chemist/hospital	3	1.1	1	5.3	14 (40)	66 (27.6)		

p value in bold are statistically significant (p ≤0.05), *12 participants declined in giving the information

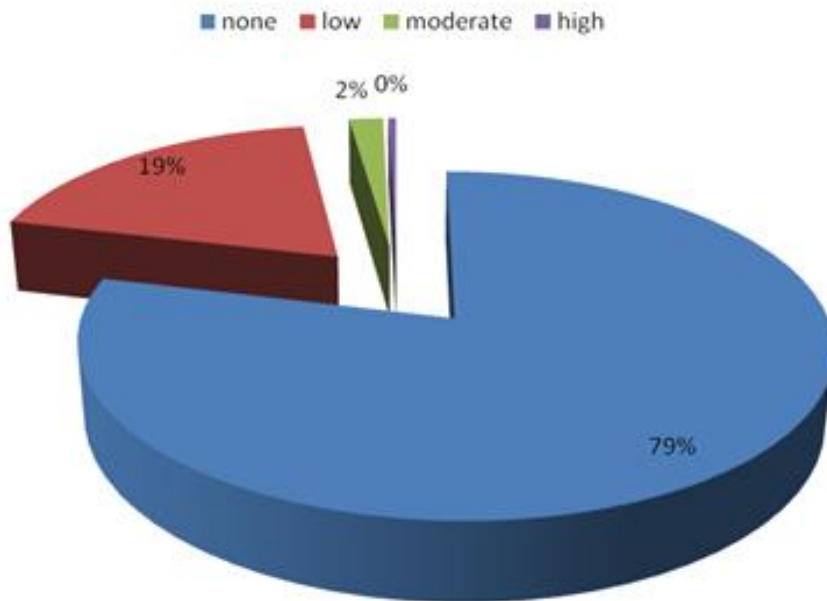


Figure 1:

Prevalence of malaria parasite density in participants in Igboora.

Prevalence was rounded-up to the nearest whole number i.e 78.8%≈79%, 1.8%≈2, 18.9% ≈19% and 0.4% ≈0%.

1-499 number of parasites/μL blood = low parasitaemia, 500-4999 number of parasites per μL blood = moderate parasitaemia, >5000 number of parasites per μL blood = high parasitaemia (WHO, 2000)

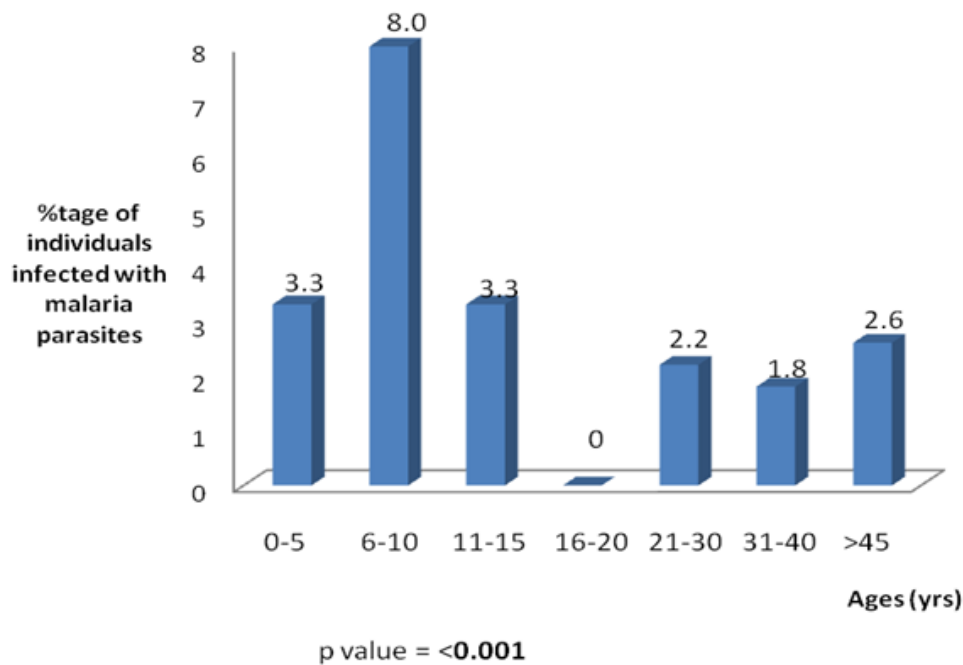


Figure 2:

Prevalence of malaria parasites in relation to ages. Graphical representation of the percentage of individuals infected with malaria parasites among the 274 participant

Table 2:

The prevalence of anaemia among the 79 helminth infected participants.

Variables	Parasite	Packed Cell Volume (PCV)		P values	
		No (%)	Anaemic (%)	Non-anaemia (%)	
Single helminthic infection	<i>Ascaris</i>	47 (17.2%)	6 (2.2%)	41 (15.0%)	0.999
	Hookworm	63 (23.0%)	7 (2.6%)	56 (20.4%)	0.652
	<i>Trichiuris</i>	1 (0.4%)	0 (0%)	1 (0.4%)	0.201
	<i>Strongyloides</i>	7 (2.6%)	0 (0%)	7 (2.6%)	0.305
Double helminthic infection	<i>Ascaris</i> + Hookworm	29 (10.6%)	4 (1.5%)	25 (9.1%)	0.889
	<i>Ascaris</i> + <i>Strongyloides</i>	2 (0.7%)	0 (0%)	2 (0.7%)	0.788
	Hookworm + <i>Strongyloides</i>	4 (1.5%)	0 (0%)	4 (1.5%)	0.763
Triple helminthic infection	<i>Ascaris</i> + Hookworm + <i>Strongyloides</i>	2 (0.7%)	0 (0%)	2 (0.7%)	0.788

Table 3:

Prevalence of malaria and specific intestinal helminthes co-infection in Igbo-Ora

Malaria-helminthes infection	No (%)	OR (95% CI)	P value
P.f-Hkw	17 (6.2)	1.53 (0.798-2.943)	0.198
P.f-A.lum	11 (4.0)	1.17 (0.554-2.472)	0.680
P.f-Strg	2(0.7)	1.51 (0.285-7.975)	0.627
P.f-A.lum&Hkw	8(2.9)	1.06 (0.347-3.228)	0.921
P.f-A.lum&Strg	1(0.4)	4.00 (0.117-136.957)	0.427
P.f-Hkw&Strg	1(0.4)	0.67 (0.025-18.059)	0.809
P.f-A.lum,Hkw&Strg	1(0.4)	0.00	0.309

OR= Odd Ratio; CI= Confidence Intervals; P.f= *Plasmodium falciparum*, A.lum= *Ascaris lumbricoides*, Hkw= Hookworm, Strg= *Strongyloides stercoralis*

Parasite intensity for Hookworm, *A. lumbricoides* and *T. trichiura* infections were determined using direct egg per gram count (epg) according WHO, 2002. In this study, 55 (20.1%) and 1 (0.4%) participants had light and moderate hookworm infection respectively, for *A. lumbricoides* infection, 43 (15.7%) and 5 (1.8%) participants had light and moderate infections respectively while 1 (0.4%) was recorded for *T. trichiura*. In this study, no record of heavy infection was found for the three STH. Mean intensity of infections were 219 eggs/g (epg) with a range of 24–12000 and 55egg/gram (epg) (range: 24-2400) for *A. lumbricoides* and hookworm respectively (WHO, 2002).

The prevalence of malaria parasite-specific intestinal helminthes co-infection

The prevalence of malaria parasite-helminthes co-infection among the participants was 19 (6.9%) and this was found to be higher among males than females (57.9%, 42.1% respectively) but the difference was not significant (P =0.076). Specifically, malaria parasite-hookworm co-infection had the highest prevalence of 17 (6.2%) (Table 3) but this was not statistically

significant.. The overall prevalence of anaemia (Fig. 3) was 12.8% ranging from individuals with no infection to individuals with one/two infections (Table 4). Individuals who were anaemic and were also infected with *A. lumbricoides* and hookworm only, were not statistically significant ($P= 0.675$ and 0.830 respectively) unlike individuals with malaria (0.036) (Table 4). It was observed that the co-infection of

Plasmodium with *Ascaris* (malaria parasite-*Ascaris*), hookworm (malaria parasite-hookworm) and *Ascaris*-hookworm (malaria parasite-*Ascaris*-hookworm) all had a negative association with PCV leading to anaemia (Spearman correlation coefficient = $-0.124, -0.123$ and -0.123 respectively) but only malaria parasite-hookworm was statistically significant ($P = 0.025$) (Table 4).

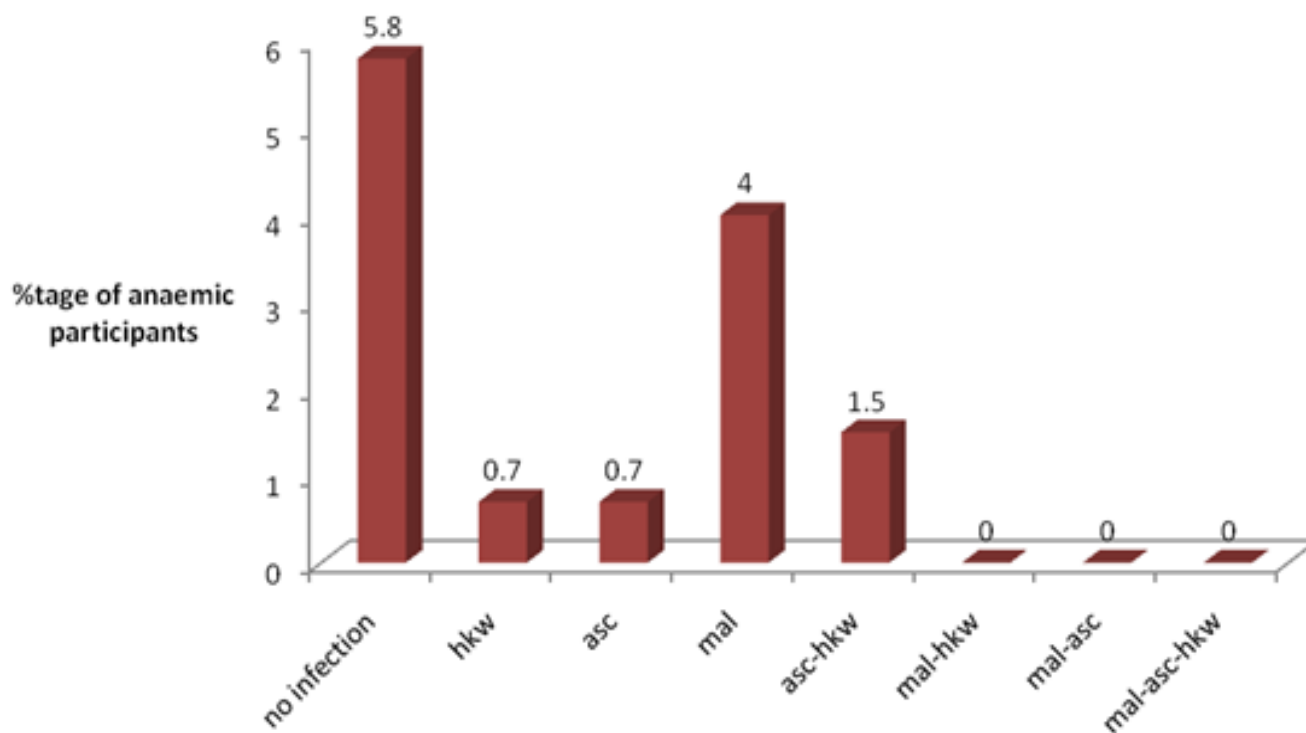


Figure 3:

Prevalence of anaemia in the 274 participants with no infection, single infection, multiple infection and co-infection. Hkw=hookworm, asc=*Ascaris*, mal=malaria parasite, asc-hkw= *Ascaris*-hookworm, mal-hkw=malaria parasite-hookworm, mal-asc=malaria parasite-*Ascaris*, mal-asc-hkw= malaria parasite-*Ascaris*-hookworm

Table 4:

Effect of intensity of infection (single, multiple and co-infection) on Packed Cell Volume of infected participants.

Intensity of infections		Parked Cell Volume		P value	ρ
		Non-anaemic (%)	Anaemic (%)		
<i>A. lumbricoides</i>	Low	37 (13.5)	6 (2.2)	0.675	0.019
	Moderate	5 (1.8)	0 (0)		
Hookworm	Low	49 (17.9)	6 (2.2)	0.830	0.340
	Moderate	1 (0.4)	0 (0)		
Malaria	Low	43 (15.7)	9 (3.3)	0.036	-0.127
	Moderate	4 (1.5)	1 (0.4)		
	High	0 (0)	1 (0.4)		
<i>Ascaris</i> -hookworm	Low	21 (9.9)	4 (1.5)	0.931	0.210
	Moderate	4 (1.5)	0 (0)		
Malaria- <i>Ascaris</i>	Low	7 (2.6)	0 (0)	0.082	-0.124
	Moderate	5 (1.8)	1 (0.4)		
	High	0 (0)	1 (0.4)		
Malaria-hookworm	Low	11 (4.0)	0 (0)	0.025	-0.123
	Moderate	5 (1.8)	1 (0.4)		
	High	0 (0)	1 (0.4)		

P values in bold are statistically significant ($p \leq 0.05$)

PCV <32% was regarded as anaemic while PCV >32% was regarded as non-anaemic

DISCUSSION

The results from this study showed the prevalence of intestinal helminthes parasites and malaria among individuals in Igbo-Ora community. In this study, a prevalence of 58(21.2%) was recorded for malaria infection, out of which children had a prevalence of 14.6%. This is in contrast to Ngoundou-Landji *et al.*, (2010), who recorded a prevalence of 75% in children in the same community. The values observed were lower compared to asymptomatic values found in a longitudinal survey of malaria infection in individuals living in Osogbo (Ogungbamigbe *et al.*, 2007) and other highly malarious endemic region of Papua New Guinea (Bruce *et al.*, 2000).

This study recorded a prevalence of 79(28.8%) for helminth infections, out of which hookworm (23%) was the highest while the prevalence of *A. lumbricoides*, *S. stercoralis* and *T. trichiura* were 17.5%, 2.6% and 0.4% respectively. This is in contrast to earlier studies conducted in Osun State Nigeria by Ojurongbe *et al.*, (2011) who recorded a prevalence of 43.6% helminth infection with *A. lumbricoides* having the highest prevalence.

In this study, the co-infection of malaria parasite-intestinal helminthes was 6.9% and this is in contrast to Dada-Adegbola *et al.*, (2013), who recorded a prevalence of 20.9% in a study conducted in Olode-Adetoun village, a rural community in southwest Nigeria. When this was subjected to statistical test, it was observed that individuals who had helminth infection had the tendency of developing malaria ($p=0.56$) but this was not significant ($P=0.445$). Similarly, Nacher *et al.*, (2002), observed a positive association between geohelminth and malarial infection in Thailand, and this was statistically significant. Several hypotheses have been put forth to explain this observation. It has been suggested that helminth infection creates a cytokine milieu favorable to the production of non-cytophilic antibodies, thus making individuals more susceptible to malaria (Mwangi *et al.*, 2006). It is also thought that the presence of T-regulatory cells is amplified during helminth infection, and if present in sufficient numbers, could induce a non-specific suppression (Yazdanbakhsh *et al.*, 2001), making individuals susceptible to infections such as malaria (Nacher 2001) and HIV (Bentwich *et al.*, 2000).

In this study, it was observed that there was a positive association between *A. lumbricoides* and *P. falciparum* ($\rho = 0.109$) which indicates that those individuals with *A. lumbricoides* infection may easily develop malaria. This is in contrast to earlier studies which suggested that *A. lumbricoides* infection might be protective against malarial disease (Murray *et al.*, 1978) but confirms other several reports, which suggested that Soil Transmitted Helminth (STH) infections may increase the risk of malaria infection (Nacher *et al.*, 2002; Spiegel *et al.*, 2003; Sokhna *et al.*, 2004). The mechanism behind this association is not clearly understood, but could be that Th2 profile associated immunoglobulin E production seen in *Ascaris* infection may down-modulate Th1 antimalarial immune responses, resulting in increased risk of malaria infection (Yatich *et al.*, 2009). Similarly, a positive association was observed among cohort of pregnant women in Ghana by Yatich *et al.*, (2009). In Uganda, geohelminth positive children tend to develop malaria but this was not statistically significant (Shapiro *et al.*, 2005).

Anaemia is one of the most widespread and common health condition afflicting individuals living in the tropics, and in Africa, it contributes to 23% of nutrition-related disability adjusted life years (WHO, 2002). The consequences of anaemia are particularly severe for children and pregnant women (Brabin *et al.*, 2001; Crawley, 2004). In developing countries, although mild anaemia occurs commonly among the general population, moderately severe anaemia is most frequently seen in areas where infections can cause or exacerbate anaemia (van den Broek and Letsky, 2000). In this study, the overall prevalence of anaemia was 12.8% ranging from individuals with no infection to individuals with one/two infection(s) and co-infection. Age was found to be positively associated with malaria-helminthes co-infection in this study with $p < 0.05$ (Table I). The presence of both malaria and helminthes parasites among participants was associated with anaemia ($p = -0.124$ and -0.123 for malaria parasite-*Ascaris* and malaria parasite-hookworm respectively). This observation could be attributed to the deleterious effect of malaria as it contributes to the reduction of hemoglobin concentrations through a number of mechanisms; principally by the destruction and removal of parasitized red cells and the shortening of the life span of non-parasitized red cells, and decreasing the rate of erythrocyte production in the bone marrow (McDevitt *et al.*, 2004); hookworm on the other hand are blood feeders, hence they causes iron deficiency anemia through the process of intestinal blood loss (Hotez *et al.*, 2004). This hereby explain the significant association observed in participant with malaria parasite-hookworm infection and anaemia ($p = 0.025$). *A. lumbricoides* was said to have little impact on iron deficiency (Stephenson *et al.*, 2000), but it indirectly leads to anaemia through reduction/obstruction of nutrients absorption. It was observed in this study, that there was a negative association between the intensity of malaria-helminth co-infection and PCV (packed cell volume), this was statistically significant in malaria-hookworm and ($P = 0.025$). This is in contrast to Ojurongbe *et al.*, (2011), who observed that the presence of both malaria and helminthes parasites was not associated with anaemia. In individuals with precarious iron balance, however, relatively small hookworm loads may result in anemia. It should be noted that anaemia may be confounded by socio-economic, genetic, and nutritional factors and that the effects of co-infection may vary by malaria and helminth transmission intensities. For instance, in this study there were people who harbor single, multiple and co-infection and yet were not anaemic whereas those people without infection were anaemic. Additionally, sickle cell disease (Odunvbun *et al.*, 2008) and other haemoglobinopathies (Taylor *et al.*, 2012) as well as HIV status (Onankpa *et al.*, 2008) may be contributing factors to anaemia. It is therefore imperative to investigate these confounding factors that may be responsible for anaemia.

In conclusion, this study observed co-infection of *P. falciparum* and soil transmitted helminthes among individuals in Igbo-Ora. A strong positive association between worm burden as expressed by helminthes egg intensity and malaria parasite density was observed indicating that an increase in helminthes intensity (i.e helminthes parasite load) is proportional to susceptibility to malaria infection. On the other hand, this study observed a strong negative association between the increase in the intensity of malaria-helminth co-infection and packed cell volume leading to anaemia.

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