

Effect of malaria and geohelminth infection on birth outcomes in Kumasi, Ghana

Abstract.

Aim: In 2005, Ghana Health Service mandated malaria and helminths chemoprophylaxis during antenatal care visits. The aim of this study was to investigate the prevalence of malaria and helminths infection and their relationship with adverse birth outcomes (low birth weight, stillbirth, and preterm) following the implementation of these changes.

Study design: A quantitative cross-sectional study

Method: Study was conducted on 630 women presenting for delivery in two hospitals. Socio-demographic information, medical and obstetric history was collected. Laboratory analyses for the presence of malaria and helminths were performed. Association of malaria and helminths with birth outcomes was assessed using Chi-square and logistic regression.

Results: The prevalence of malaria, helminths and adverse birth outcomes was 9.0%, 5.0% and 22.2%, respectively. Women without malaria prophylaxis were two times more likely to have malaria infection (aOR = 2.10; 95% CI = 1.06-4.17). Women who were not screened for helminths were twice as likely to be infected with helminths (aOR = 2.43; 95% CI = 1.15-5.12). Adjusted odds of having an adverse birth outcome increased four-fold (aOR = 3.9; 95% CI = 1.09-14.20) in women infected with hookworm or *Schistosoma mansoni* and eight-fold for stillbirth (aOR = 7.7; 95% CI = 1.21-36.38).

Conclusion: The prevalence of malaria, helminths and adverse birth outcomes was lower than previously reported 36.3 vs. 9.0%, 25.7 vs. 5.0% and 44.6 vs. 22.2%, respectively. Malaria was not found to be associated with adverse birth outcomes.

Geohelminths Malaria, Pregnancy outcomes, Kumasi

1. INTRODUCTION

Malaria and helminths are endemic in most sub-Saharan African countries. A study in Nigeria demonstrated that over 45% of Plasmodium infected near-term mothers also had intestinal helminths [1]. These infections have been associated with low hemoglobin levels and iron/folate deficiency anemia especially in primigravid women [1]. Fifty percent of pregnant women in developing countries are often at a high risk of experiencing adverse birth outcomes due to iron/folate deficiency [1, 2]. Iron deficiency anemia during pregnancy is associated with lower iron stores in the fetus, thus there is need for iron supplementation during pregnancy [3, 4]. Moderate to severe anemia is associated with an increased risk of low birth weight and preterm delivery [4].

Pregnant women living in malaria endemic areas of Africa are at an increased risk of *Plasmodium falciparum* infection [3, 5]. Malaria in pregnancy is a major cause of maternal and fetal morbidity and mortality [2, 6]. The prevalence of malaria is influenced by a number of factors such as maternal age, parity, use of prophylaxis, nutritional status, host genetics, parasite genetics and transmission rate [7]. Compared to other malaria parasites, *P. falciparum* has been found to be a stronger contributor to pregnancy anemia especially in nulliparous women [4, 6]. Kumasi, Ghana is endemic for malaria, and the predominant malaria parasite is *P. falciparum*. The area is also endemic for both hookworm and schistosomiasis [5]. The combined effects of poor nutrition, inadequate potable water supply, poor sanitation and perennial malaria transmission contribute significantly to pregnancy anemia and consequently adverse birth outcomes [3, 8]. Prevalence of hookworm infection among pregnant women in sub-Saharan Africa is estimated at 32% [9]. Studies in Nepal suggested that 54-58% of moderate to severe anemia in pregnancy was due to hookworm [4]. The role of malaria and hookworm and trichuris infections in pregnancy anemia has been established [8]. The helminth parasites cause blood loss that sometime induce pregnancy anemia [10]. Both synergistic and antagonistic effects due to malaria and helminths co-infections have been

suggested. While one study reported a positive association between *Ascaris lumbricoides* and *P. falciparum* [11], another study reported suppression of malaria infection in patients with *A. lumbricoides* [12]. The synergistic action from the co-infection was linked to the fact that helminth parasites induce elevated T-helper-2 (Th₂) cytokines and down regulate Th₁ type immune response increasing susceptibility to other infections including malaria [13].

A 44.6% prevalence of adverse birth outcomes, and malaria and helminth prevalence of 36.3% and 25.7% respectively has been previously reported among women with uncomplicated pregnancy in Kumasi [6]. Acknowledging the impact of malaria and helminths in pregnancy, Ghana Health Service in 2005 modified its antenatal care (ANC) protocol to include mandatory chemoprophylaxis for malaria and helminths during ANC visits. While WHO recommends four ANC visits for women with uncomplicated pregnancy, Ghana Health Services requires 8-13 ANC visits. During these visits women are expected to receive at least three doses of Sulfadoxin-pyrimethamine (SP). The first dose is given any time after the first trimester and subsequent doses given at least one month apart as directly observed therapy (DOT) [14]. For women deficient in glucose-6-phosphate dehydrogenase (G6PD), a single dose of an artemisinin combination therapy (ACT) or derivative is recommended. Two doses of anthelmintic are also recommended during the 2nd and 3rd trimesters [15].

Although Ghana Health Service modified the ANC protocol in 2005, Yatich et al study was done in 2006. This study is the first to really assess the full implementation of the protocol. Therefore this study was conducted to investigate; i) the prevalence of malaria and helminth infections among pregnant women, and ii) the association of these parasitic infections with adverse birth outcomes.

2. MATERIALS AND METHODS

2.1. The study setting. A quantitative cross-sectional study was conducted to investigate the prevalence of malaria and helminth infections and the relationship of these infections with adverse

birth outcomes among women with uncomplicated pregnancy in Kumasi the capital of the Ashanti Region of Ghana. Kumasi has an estimated daytime population of 1.7 million people (Kumasi Metro Profile, 2011 estimate; Unpublished; Joana Tawia Burgesson). Kumasi has 5 health sub-metros (Asokwa, Bantama, Manhyia North, Manhyia South and Subin). This study was conducted in two health facilities in Kumasi; namely the Komfo Anokye Teaching Hospital (KATH) and the Manhyia District Hospital (a tertiary and secondary hospital, respectively) from July-November 2011. KATH is a referral hospital that provides most ANC, labor and delivery services and serves the entire Ashanti Region and the bordering Brong-Ahafo, Central, Eastern and Western Regions. Manhyia District hospital covers Manhyia North and South and serves 34.6% of the Kumasi population. Kumasi has perennial malaria transmission (mainly *P. falciparum*) with two rainy seasons lasting from April to June and September to October [16]. Kumasi is also endemic for helminths [5].

2.2. Ethical considerations. The study protocol was approved by the Institutional Review Board of the University of Alabama at Birmingham, USA and the Committee on Human Research, Publications and Ethics, School of Medical Sciences, Kwame Nkrumah University of Science and Technology, Kumasi.

2.3. Participant recruitment. Eligible participants were pregnant women, 19 years and older, who resided or moved to Kumasi within 1-2 months following conception. Women who presented for delivery at the two study sites within the study period, met the eligibility criteria and consented to the study were recruited. Women with spontaneous, vaginal, singleton deliveries, without complications were eligible for enrollment in this study. Informed consent was obtained from all the study participants. Data for 630 participants were used for these analyses. The questionnaire was administered to the participants 1-2 hours following delivery in a private area by trained study personnel. No identifying information was recorded and confidentiality was assured. The questionnaires were reviewed for completeness.

2.4. *Study instrument.* The details of the study instrument and data collected has been described elsewhere [17]. Information obtained included: 1) socio-demographics 2) malaria prophylaxis; 3) use of insecticide treated bed nets; 4) duration of pregnancy; and 5) helminths screening and prophylaxis. Data on intermittent preventive therapy with sulfadoxine-pyrimethamine (IPT-SP) and hemoglobin concentration were abstracted from the women's antenatal booklets while data on pregnancy outcome were ascertained from the delivery records.

2.5. *Sample collection and analyses.* During delivery, 5-10 g of stool were collected and preserved in a 30 ml tube containing 15 ml of 10% formalin. The samples were agitated several times, assigned participant's unique identification number (PID) and stored at room temperature. Samples were analyzed at the end of the study in the parasitological laboratory of the outpatient unit at KATH. Determination of helminths was done using the Formalin-Ether concentration method. Samples were processed in conformity to the standard protocol [18, 19]. The preparation was examined microscopically and helminth types were documented.

Peripheral blood (5 ml) was drawn by venipuncture soon after delivery into a vacutainer tube without anti-coagulant to facilitate clotting and labeled with the participant's ID number. The clotted blood samples were spun at 4000 rpm at 4°C and the extracted serum frozen at -20°C until analyzed for malaria antigen. Determination of malaria antigen was done using the Malaria Antigen Celisa kit (Cellabs, Brookvale, Australia). The Celisa kit is a monoclonal antibody assay based on the detection of malaria antigen (HRP2) a highly sensitive marker for *P. falciparum* malaria in blood and serum sample. The assay detects the merozoite antigen that circulates in the blood and a positive result is suggestive of current or very recent infection. The ELISA test results were considered positive when the optical density was >0.2 over the negative control. The assay has been shown to detect *P. falciparum* parasitaemia as low as 0.001% with a sensitivity of approximately 98.8% and specificity of 100% [20].

2.6. *Definition of variables.* Overall pregnancy outcome in this study refers to a combination of the following outcomes; i) low birth weight defined as birth weight < 2,500 g; ii) preterm delivery (<37 weeks of gestation); iii) stillbirth defined as death of a fetus prior to, during or soon after delivery, but before discharge from the delivery ward. After delivery in Kumasi, a woman stays in the maternity for about 1-2 hrs, she is then taken to the “Lying Inn Ward” for observation for another 2–4 hrs before discharge from the hospital. *Malaria infection:* Presence of malaria antigen in the peripheral blood at the time of delivery. *Helminth infection:* Presence of helminth eggs or larvae in stool at the time of delivery. *Co-infection:* Presence of both malaria antigen and any helminths at delivery. *Severe anemia:* hemoglobin level <8 g/dL of blood, *moderate to severe anemia:* hemoglobin levels ≥ 8 and ≤ 11 g/dL of blood.

2.7. *Data analysis.* The data were single-entered in a Microsoft Access 2010 database and imported into SAS for coding and analysis. Cochran-Mantel Haenszel Chi-square or Fisher’s exact tests were used to assess the associations between participants’ characteristics by infection status, and also association of ANC services received, adverse birth outcomes by infection status. Stratum specific estimates to assess effect modification by study sites were obtained. To assess the validity of the self-reported data, Kappa coefficients were calculated to test the agreements between self-reported malaria prophylaxis and data abstracted from maternal antenatal record. Values of 0.4-0.6 indicate moderate, 0.6-0.8 substantial, and 0.8 or higher excellent agreement [21]. Logistic regression models were used to examine the association between malaria and helminth infection with adverse birth outcomes: a) a crude model examined the association of malaria and helminths infection with overall adverse outcome and type of adverse birth outcomes (low birth weight, preterm and stillbirth); b) a final multivariable logistic model examined the association of participant’s infection status and adverse birth outcomes while adjusting for age, parity, HIV status and hemoglobin level. Crude and adjusted odds ratios (ORs) with 95% confidence intervals (CI) and *p*-values were calculated. The change-in-estimate criteria were used to select potential confounders. A variable

was considered a confounder if the change in estimate from the crude and adjusted model was at least 10 % [22]. All tests were two sided and p -values ≤ 0.05 were considered statistically significant. All analyses were done using SAS[®] 9.3 (SAS Institute, Cary, NC, USA).

3. RESULTS

3.1. Participant's characteristics and infection status. Participation rate in the study was 99.7%. Median age of the women was 27 years (range 19-48). Approximately 38% of participants were less than 25 years. Sixty-eight percent of the women had a monthly income of less than GH¢500.00 (US\$ 333.3). Twenty-one percent were unemployed while 69.0% were self-employed. Approximately 58% of the self-employed were traders and 30.6% were hairdressers or seamstresses. Women who were infected with malaria were more likely to be single and unemployed. Forty-three percent of the participants attended ANC more than the required minimum of 8 visits (Ghana standard). The rate of malaria infection was higher in single (15.4%; $P = 0.04$) and unemployed women (13.9%; $P = 0.04$) than among married and employed women. Rate of helminths infection was also higher for women who earned less than GH¢500.00 (6.3%) than those who earned more than GH¢ 500.00 (2.8%) (Table 1).

Table 1: Infection status by participant's characteristics, Kumasi 2011 (Row %)

	N = 630		Malaria N = 57		Helminths N = 32		
Characteristics	N	%	n	%	p-value	n	% p-value
Age group					0.424		
≤ 25	239	37.9	25	10.5		12	5.0 0.687
26 - 35	328	52.1	25	7.6		17	5.2
> 35	63	10.0	7	11.1		3	4.8
Level of education					0.317		
Primary/None	196	31.1	21	10.7		14	7.1 0.264
Junior secondary	271	43.0	27	10.0		14	5.2
Senior secondary	92	14.6	6	6.5		3	3.3
Vocational/University	71	11.3	3	4.2		1	1.4
Marital status					0.043		
Single	104	16.5	16	15.4		3	2.9 0.519
Married	450	71.4	34	7.6		26	5.8
Living as married	76	12.1	7	9.2		3	4.0
Employment^a					0.040		
Unemployed	130	20.7	18	13.9		10	7.7 0.219
Employed	64	10.2	2	3.1		2	3.1
Self-employed	435	69.2	37	8.5		20	4.6
Religion					0.942		
Christianity	460	73.0	43	9.4		22	4.8 0.695
Islam	162	25.7	14	8.6		10	6.2
None	8	1.3	0	0.0		0	0.0
Income (Cedis)					0.395		
< 500	427	67.8	36	8.4		27	6.3 0.130
500 - 2000	176	27.9	17	9.7		5	2.8
> 2000	27	4.3	4	14.8		0	0.0
Parity					0.485		
1	224	35.6	22	9.8		14	6.3 0.227
2 - 5	385	61.1	32	8.3		16	4.2
> 5	21	3.3	3	14.3		2	9.2
ANC visit (times)					0.856		
<4	69	11.0	7	10.1		6	8.7 0.215
4-7	290	46.0	28	9.7		16	5.5
≥ 8 ^b	271	43.0	22	8.1		10	3.4

^a = One missing, ^b = Ghana standard for antenatal care visits, **Bold** = statistically significant

3.2. Infection status and predictors of malaria and helminths infection. Participants' malaria and helminth infection status and ANC services related to these infections are presented in Table 2. The prevalence of helminths and malaria in the study population was 5.0% and 9.0% respectively. Helminths that were identified were *Dicrocoelium dendriticum* (liver fluke), *Strongyloides stercoralis*, *Schistosoma mansoni* (blood fluke) and *Ancylostoma sp.* (hookworm). The rate of infection of malaria was higher (15.3%) in women who did not receive malaria prophylaxis than those who did (8.4%). The latter women were two times more likely to be infected with malaria

(aOR = 2.10; 95% CI = 1.06-4.17) compared with women who received a complete regimen of malaria prophylaxis. The rate of helminths infection was also higher for women who were not screened for helminths (8.6%) than women who were screened (4.0%). For unscreened women, the risk of helminths infection was two times higher compared with women who were screened (aOR = 2.43; 95% CI = 1.15-5.12) after controlling for the study site. Women with low hemoglobin (severe anemia) tended to have higher proportions of malaria and helminth infections than women with normal hemoglobin concentration, but this trend was not statistically significant (Table 2).

Table 2: Predictors of parasitism and adverse birth outcome by infection status in Kumasi, 2011

Predictors	N = 630			Malaria Yes = 57				Helminths = 32				
	N	(%)	n	(%)	OR	aOR	CI	n	(%)	OR	aOR	CI
Malaria prophylaxis					1.96	1.98	(0.92-4.28)				NA	
Yes	571	90.6	48	8.4								
No	59	9.4	9	15.3								
IPT doses ^a											NA	
0	99	15.7	15	15.2	2.11	2.10	(1.06-4.17)					
1	80	12.7	4	5.0	0.62	0.62	(0.21-1.82)					
2	130	20.6	13	10.0	1.32	1.33	(0.66-2.70)					
3	321	51.0	25	7.8	ref							
Bed nets use					0.90	0.90	(0.52-1.57)				NA	
Yes	240	38.1	23	9.6								
No	390	61.9	34	8.7								
Anemia status ^b												
Severe (<8 g/dL)	53	8.4	7	13.2	1.67	1.65	(0.68-4.00)	4	7.6	1.63	1.66	(0.53-5.17)
Moderate(8-11g/dL)	241	38.3	22	9.1	1.11	1.13	(0.63-2.03)	12	5.0	1.05	1.03	(0.48-2.22)
Normal(> 11 g/dL)	336	53.3	28	8.3	ref			16	4.8	ref		
Helminths screening						NA				2.30	2.43	(1.15-5.12)
Yes	479	76.0						19	4.0			
No	151	24.0						13	8.6			
Anthelmintics						NA				0.78	0.76	(0.34-1.70)
Yes	149	23.6						9	6.0			
No	481	76.4						23	4.8			
Adverse outcome					1.40	1.34	(0.75-2.55)			1.63	1.68	(0.77-3.65)
Yes	140	22.2	16	11.4				10	7.1			
No	490	77.8	41	8.4				22	4.5			

OR = Crude odds ratio, aOR = Adjusted for recruiting, ^aFishers Exact test, ^bHemoglobin concentration level, IPT = Number of times prophylactic antimalarial drug (SP) was taken, **Bold** = statistically significant, NA = Not applicable

3.3. *Infection status and adverse birth outcomes.* Twenty-two percent of the women experienced an adverse birth outcome. The rate of adverse birth outcomes was higher in women infected with malaria (11.4%) or helminths (7.1%) compared with uninfected women (8.4% and 4.5%, respectively). Though not statistically significant, women with malaria or helminths were 40% and 60%, respectively, more likely to experience an adverse birth outcome compared with women without these infections (Table 2). However, women infected with helminths associated with blood loss (hookworm or blood fluke) were three and a half times more likely to experience an adverse birth outcome (OR = 3.6; 95% CI = 1.03-12.63), four times more likely to have a low birth weight baby (OR = 4.1; 95% CI = 1.02-16.17), and six times more likely to have a stillbirth (OR = 6.0; 95% CI = 1.49-24.0). After adjusting for confounders (age, parity, HIV, and hemoglobin level), women infected with hookworm or blood fluke were four times more likely to experience an adverse birth outcome (aOR = 3.9; 95% CI = 1.09-14.20) and eight times more likely to have a stillbirth (aOR = 7.7; 95% CI = 1.21-36.38) compared with women who were not infected with these helminths. In both the crude and adjusted models, malaria and malaria-helminth co-infections were not statistically significantly associated with adverse birth outcomes (Table 3).

Table 3: Crude and adjusted odd ratios of malaria and helminths infections and pregnancy outcomes of 630 women in Kumasi, Ghana 2011

Infections status	Overall		Low birth weight		Preterm		Stillbirth	
	OR (95% CI)	aOR (95% CI)	OR (95% CI)	aOR (95% CI)	OR (95% CI)	aOR (95% CI)	OR (95% CI)	aOR (95% CI)
Malaria	1.4 (.78-2.60)	1.3 (.66-2.38)	1.3 (.56-2.99)	1.0 (.41-2.52)	1.6 (.70-3.83)	1.7 (.70-3.88)	1.0 (.36-3.00)	1.0 (.34-2.96)
All Helminths	1.6 (.76-3.54)	1.7 (.75-3.66)	2.2 (.86-5.54)	2.1 (.80-5.14)	1.6 (.55-4.86)	1.6 (.54-4.91)	1.4 (.42-4.94)	1.6 (.44-5.51)
Helminth types								
Blood suckers ^a	3.6 (1.03-12.63)	3.9 (1.09-14.20)	4.1 (1.02-16.17)	4.0 (.96-16.89)	2.9 (.59-13.87)	3.3 (.67-16.22)	6.0 (1.49-24.00)	7.7 (1.21-36.38)
Non-blood suckers	1.1 (.38-2.92)	1.1 (.36-2.92)	1.5 (.43-5.22)	1.4 (.38-5.03)	1.2 (.26-5.05)	1.1 (.23-4.78)	0.5 (.0-2.11)	0.4 (0-2.09)
Malaria+ Helminths	7.1 (.64-78.55)	4.7 (.40-55.73)	4.6 (.41-50.97)	3.5 (.27-44.93)	5.7 (.50-63.38)	4.9 (.40-59.91)	3.6 (0-23.70)	2.0 (0-14.08)

OR = crude odd ratios, aOR = *Adjusted for HIV status, hemoglobin concentration, age and parity (primipara or multipara)*

^a *Helminths associated with blood loss (hookworm and blood fluke), **Bold** = statistically significant*

4. DISCUSSION AND CONCLUSION

Malaria and helminths infections are of serious public health concerns in developing countries especially in countries of sub-Saharan Africa. This study found a lower prevalence of malaria (9.0%), helminths (5.0%) and adverse birth outcomes (22.2%) among women in Kumasi than previously reported [6]. This reduction could be due to the fact that the data of the study by Yatich et al was collected in 2006, while the changes to the ANC protocol were initiated in 2005. The changes would not have been fully implemented in 2006 but in full implementation by 2011 when this study was conducted. The finding partly corroborates another study that found an association between malaria and helminths with adverse birth outcomes [8]. In this study, only helminths that cause blood loss were associated with adverse birth outcomes. The data did not support the association of adverse birth outcomes with malaria. This could be due to the small case numbers or the high uptake of IPT (SP or ACT). The high rate of IPT uptake could be attributed to the fact that the medication is free, and is administered as DOT, and that when a woman initiates ANC, the date of the next visit is indicated in the maternal antenatal booklet. As previously reported, the ANC services received is dependent on the time of ANC initiation and the frequency of ANC attendance [17]. It is intriguing and worth pointing out that malaria infection is lowest in women with one dose of SP compared with women with three doses of SP. The reasons are not obvious and warrant further investigation. It is common practice that pregnant women receive folic acid as nutritional supplement. Concomitant administration of SP and folic acid could be contributing to development of resistance to SP.

Though malaria infection was not directly associated with adverse birth outcomes in this study, a high proportion of women with malaria had severe anemia. Malaria especially *P. falciparum* has often been associated with anemia in developing countries [4] and severe anemia is a predictor for adverse birth outcomes [17]. A review of the impact of malaria related anemia among pregnant women in sub-Saharan Africa suggested that over a quarter of cases of severe

anemia were attributable to malaria infection [23]. The malaria pathogen acts by directly destroying erythrocytes while malaria pigments and pro-inflammatory mediators may also inhibit erythropoiesis [24]. Hypersplenism, sequestration of red blood cells and phagocytosis of parasitized and un-parasitized red blood cells have also been suggested as possible mechanisms by which malaria causes anemia [25]. Though malaria has often been associated with adverse birth outcomes, our data did not support this assertion. More than 84% of the women received at least one dose of SP (mean dose = 2.1) given as DOT to ensure compliance [17]. The timing of the IPT regimen could have played a role in controlling adverse birth outcomes especially during growth and development (2nd trimester of pregnancy). Other factors such as blood aflatoxins B1 levels could predispose pregnant women to pregnancy anemia thereby contributing to adverse birth outcomes. An association between aflatoxins B1 blood levels and anemia and adverse birth outcomes among pregnant women in the same study area has been previously reported [26].

The results from this study suggest that infection with any helminths was marginally associated with low birth weight. However, infection with any of the helminths that cause blood loss (hookworm or blood fluke) was significantly associated with stillbirth and low birth weight. A prior study in the same geographic area did not find any association between helminths infection and stillbirth [6]. The fact that the study did not categorize these helminths according to their association with blood loss as was done in this study could explain the absence of an association as demonstrated by this study. This study corroborates the result of a study in the Amazon region of Peru that found an association between helminths and stillbirth [27]. Schistosomiasis and hookworm cause blood loss [3] and it is recommended that pregnant women receive antihelminthics after the first trimester especially in areas with >20–30% prevalence of hookworm and prevalent anemia [28]. Hookworm releases anti-coagulants and cause mechanical lacerations to the walls of the small intestines leading to blood loss in the stool and depletion of iron store. Intestinal blood loss, mal-absorption and reduced appetite further exacerbate iron deficiency anemia in pregnant

women [3, 25]. While the drugs of choice (albendazole and mebendazole) are effective against hookworm they may not be as effective for schistosomes. A clinical trial on the use of mefloquine with activity against *S. haematobium* as IPTp in Gabon may provide a solution and reduce the reliance on praziquantel. In rodent models, mefloquine has been shown to have considerable activity against *S. mansoni* and *S. japonicum*- the causative agents of intestinal schistosomiasis [29]. Seventy-six percent of the participants were screened for intestinal helminths but only 23.6% reported receiving antihelmintics. This low report rate could be due to the fact that these women were treated but were not informed of the treatment. There is also the possibility of self-medication; albendazole the drug of choice is readily available without prescription. The low sensitivity of the Direct Wet Mount method that is routinely used for parasitological screening could produce false negative results and consequently no treatment administered. According to the revised ANC protocol, these women should have received 2 doses of antihelmintics during the 2nd and 3rd trimesters [15] if they attended ANC regularly. The inclusion of antihelmintics as DOT as is the case with SP in the revised Ghana protocol could save time for the women and also the resources that go into stool examination. A 26% reduction in the prevalence of malaria prevalence through IPTp (DOT) could be replicated in the fight against helminths in pregnancy.

Brooker *et al.* (2008) in their review summarized that deworming and iron supplementation would have a greater impact on hemoglobin level than deworming alone especially in populations whose diets are low in bioavailable iron [4, 23]. In a study in the South West Province of Cameroon, 69% of women who were given pyrimethamine, iron and folate but not mebendazole had maternal anemia at mean gestational age of 24 weeks [2]. Despite the low prevalence of helminths (5.0%), their association with adverse birth outcomes in this study underscores the serious adverse health impact of these parasites. The high prevalence of adverse birth outcomes observed despite the low prevalence of malaria and helminth infections in the study population suggest that there could be other factors such as hemoglobinopathies (sickle cell, thalassemia,

G6PD deficiency) genetics, and environment that are yet to be investigated. Nutritional status during pregnancy, metabolic diseases and HIV status are among many other factors that could adversely impact pregnancy outcomes. HIV prevalence in this study population was < 2% (8/630) and was adjusted for in the multivariable analyses.

This is the first study to investigate the prevalence of both malaria and helminths in this region of Ghana since the full implementation of the changes made in the ANC protocol. This study demonstrates a low prevalence of both malaria and helminth infections and a reduced prevalence of adverse birth outcomes in this cohort of pregnant women in Kumasi. It is tempting to speculate that the changes made to the ANC delivery system are responsible for the lower prevalence of these infections. However, we recommend that more studies be conducted in both urban and rural areas to determine the true prevalence of these infections and their association with adverse birth outcomes in pregnant women. The relatively low number of cases should be taken into consideration in interpreting the results. However, the small cell counts was not a problem since the adequacy of the sample size is determined by the across strata sample size [21] and the study had sufficient power. Since our cross-sectional study design limits our ability to draw causal or temporal associations a longitudinal study to establish causality and temporality need to be conducted. There is always the problem of recall bias in collecting data with the use of questionnaire. However, the substantial agreement ($\kappa = 0.65$) between self-reported use of IPT and the data abstracted from maternal antenatal record indicates that the effect of recall bias could be minimal. This study could be used as a proxy for the evaluation of the effectiveness of the changes made to the ANC protocol because the indicators (malaria and helminth infection status) were objectively assessed. Also, the number of doses of IPT received was obtained from maternal antenatal records and not from participants. Thus, we consider these findings to be representative of women with uncomplicated pregnancies in Kumasi.

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COMPETING INTEREST: Authors declare no conflict of interest

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