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CLINICAL ARTICLE

The effects of malaria and HIV co-infection on hemoglobin levels among pregnant women in Sekondi-Takoradi, Ghana

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Objective: To assess the burden of maternal malaria and HIV among pregnant women in Ghana and to determine the risk of anemia among women with dual infection. *Methods:* A cross-sectional study was conducted at 4 hospitals in the Sekondi-Takoradi metropolis, Ghana. The study group comprised 872 consenting pregnant women attending prenatal care clinics. Venous blood samples were screened for malaria, HIV, and hemoglobin level. Multivariate logistic regression analysis was performed to determine the association between malaria, HIV, and risk of anemia. *Results:* In all, 34.4% of the study cohort had anemia. Multivariate logistic regression analysis indicated that pregnant women with either malaria (odds ratio 1.99; 95% confidence interval, 1.43–2.77; $P=<0.001$) or HIV (odds ratio 1.78; 95% confidence interval, 1.13–2.80; $P=0.014$) had an increased risk of anemia. In adjusted models, pregnant women co-infected with both malaria and HIV displayed twice the risk of anemia. The adjusted odds ratio was 2.67 (95% confidence interval, 1.44–4.97; $P=0.002$). *Conclusion:* Pregnant women infected with both malaria and HIV are twice as likely to be anemic than women with a single infection or no infection. Measures to control malaria, HIV, and anemia during pregnancy are imperative to improve birth outcomes in this region of Ghana.

1. Introduction

Malaria in pregnancy remains a major global health problem with adverse consequences for the pregnant women and the developing fetus. In Sub-Saharan Africa, approximately 30 million pregnant women are affected with malaria annually; up to 10 000 maternal deaths and 200 000 newborn deaths occur as a result of *Plasmodium falciparum* infection each year [1,2]. The distribution of malaria and HIV overlap in endemic regions with important public-health consequences [3]. Evidence shows that such dual infection increases the spread of both diseases in Sub-Saharan Africa [4], and their interaction remains a silent alliance in terms of concerted actions and comprehensive disease control policy [5]. Malaria during pregnancy is associated with a number of complications, including low birth weight, maternal anemia, and maternal and infant mortality [6,7]. Likewise, maternal HIV infection correlates with low birth weight, maternal anemia, and maternal malaria associated with high parasitic load [7,8]. In addition, maternal HIV infection seems to compromise immunity to malaria, particularly among multigravidae [9].

Interventions currently available for the prevention of malaria in pregnancy comprise the use of insecticide-treated bed nets, intermittent preventive treatment (IPTp), and case management according to WHO recommendations [10]. Furthermore, WHO recommends the administration of 2 or more doses of sulfadoxine–pyrimethamine (SP) after the first trimester and additional doses of SP are recommended for pregnant women with HIV who are not taking daily co-trimoxazole (trimethoprim–sulfamethoxazole) [10]. However, WHO also recommends a third option (Option B+), which is designed to provide triple antiretroviral therapy to all HIV-infected pregnant women throughout life starting immediately after diagnosis regardless of the CD4-positive cell count [11].

Anemia in pregnancy is a global public-health problem that affects nearly half of all pregnant women worldwide [12]. Anemia primarily affects women of low socioeconomic status and the risk of anemia increases as pregnancy progresses [13]. The etiology of anemia in pregnancy in multifaceted and may reflect iron deficiency, folate deficiency, malnutrition, vitamin A or vitamin B_{12} deficiency, infectious diseases (hookworm, malaria, and HIV), and hemoglobinopathies [13]. Of note,

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the hallmark of *P. falciparum*-associated malaria is the development of anemia [14].

The aim of the present study was to assess the burden of malaria and HIV co-infection among pregnant women in Sekondi-Takoradi metropolis, Ghana, and to determine the risk of anemia among those women found to be dually infected.

2. Materials and methods

A cross-sectional study was conducted at 4 hospitals in the Sekondi-Takoradi metropolis (Effia-Nkwanta Regional Hospital, Essikado Hospital, Takoradi Hospital, and Jemima Crentil Hospital) from March 1 to October 31, 2010. Details of the study design have been published elsewhere [15]. Briefly, consenting pregnant women attending their usual prenatal care were recruited to participate in the present study; pregnancy status was confirmed by ultrasonography or by clinical signs of on-going pregnancy. Each facility was visited once every week and all recruited women were given adequate clinical care. The use of IPTp-SP was initiated during the second trimester after quickening (16–34 weeks of gestation). Demographic characteristics were recorded, as were past and present obstetric history. Written informed consent was received from the participants and the study protocol was approved by the Research and Ethics Committee of the Ghana Health Service, Accra.

For each participant, a 5-mL sample of venous blood was collected into a bottle containing EDTA before administration of IPTp-SP to test for malaria, HIV, and hemoglobin levels. Laboratory diagnosis of malaria was performed using a rapid response antibody kit specific for the detection of *P. falciparum* antigens (Premier Medical Corporation, Daman, India) and confirmed by Giemsa staining using thick and thin smears examined microscopically. HIV screening was performed at the prevention of mother-to-child transmission clinic for all 4 study centers. Serostatus for HIV was determined by applying the national diagnostic algorithm of 2 rapid antibody tests and western blot confirmation, while indeterminate cases were confirmed at the public health reference laboratory at Effia-Nkwanta Regional Hospital, Sekondi-Takoradi. Hemoglobin level was estimated using an established cyanmethemoglobin method [16] and anemia was defined per the WHO criterion of a hemoglobin level below 11 g/dL [17].

Data were analyzed using SPSS version 17.0 (IBM, Armonk, NY, USA). Baseline characteristics were analyzed using either Pearson χ^2 or exact χ^2 tests; analysis of variance was used for comparison of the mean. Univariate and multivariate logistic regression models were used to identify factors independently associated with the risk of anemia in pregnancy after adjusting for confounding, co-linearity, and interaction. Logistic regression was applied for the analysis of association with hemoglobin levels (<11 g/dL and ≥11 g/dL), which was used as the dependent variable against age groups, gravida, education, IPTp-SP, malaria, HIV, and malaria/HIV co-infection. A final parsimonious multivariable model was selected after regression assumptions, confounding, and interaction. All tests were 2-tailed. The odds ratio (OR) and 95% confidence interval (CI) were used to measure the strength of the association. A *P* value below 0.05 was considered statistically significant.

3. Results

A total of 872 pregnant women were included in the present study. In all, 300 women (34.4%) had hemoglobin levels below 11 g/dL, while 572 women (65.6%) had hemoglobin levels of at least 11 g/dL. Table 1 shows the analysis of baseline demographic characteristics by hemoglobin level. No significant differences were detected in mean age, age group, gravida, education, and occupation between the women with anemia and those without anemia. However, significant differences were identified for malaria status ($P<0.001$), HIV status ($P=0.012$), and co-infection with malaria and HIV ($P=0.001$).

Table 1
Baseline demographic characteristics according to hemoglobin level.[a]

Characteristic	Hemoglobin <11 g/dL (n = 300)	Hemoglobin ≥11 g/dL (n = 572)	*P* value [b]
Age, y	25.92 ± 5.8	26.29 ± 5.7	0.36
Age group, y			
15–19	15.9	10.8	
20–29	56.6	62.2	0.16
30–39	25.8	25.2	
>40	1.7	1.8	
Gravida			
Primigravid	56.9	60.2	
Secundigravid	33.2	31.2	0.64
Multigravid	9.8	8.6	
Education			
None	19.9	19.7	
Primary	15.0	13.9	0.11
Secondary	63.4	61.1	
Tertiary	1.7	5.2	
Occupation			
Farmer or trader	96.8	94.7	
Civil service	0.6	3.0	0.27
Teacher	2.6	2.3	
Malaria status			
Negative	68.0	81.3	<0.001
Positive	32.0	18.7	
HIV status			
Negative	86.3	92.0	0.012
Positive	13.7	8.0	
Malaria and HIV co-infection			
No infection or single infection	91.3	96.7	0.001
Dual infection	8.7	3.3	

[a] Values are given as mean ± standard deviation or percentage.
[b] *P* values for univariate analysis are based on either Pearson χ^2 or exact Pearson χ^2 tests for comparison of proportions and on analysis of variance for the mean of continuous variables.

No differences were found in the hemoglobin levels of women who received IPTp-SP versus those who did not (Table 2). Similarly, gravida was not associated with hemoglobin level in either group (median 11.4 g/dL, range 9.0–13.9 g/dL; $P=0.096$).

Table 3 shows factors that independently predicted the risk of anemia in pregnancy. In the univariate analysis, pregnant women with tertiary education were less likely to have anemia than women with other levels of education ($P=0.03$); however, significance disappeared after controlling for confounding ($P=0.075$). Malaria infection was independently associated with an increased risk of anemia in pregnancy. This inference remained significant after adjusting for age, gravida, IPTp-SP, and education as potential confounders in the multivariate logistic regression analysis. The adjusted OR was 1.99 (95% CI, 1.43–2.77; $P<0.001$). Using the same model, pregnant women infected with HIV were also found to have an elevated risk of anemia; the adjusted OR was 1.78 (95% CI, 1.13–2.80; $P=0.014$).

As women with a single infection (either malaria or HIV) were at increased risk of developing anemia during pregnancy, the 45 women (5.2%) who were co-infected with both malaria and HIV were selected for further analysis. Of these women, 26 (57.8%) had anemia while 19 (42.2%) did not. Furthermore, multivariate regression analysis indicated

Table 2
Effect of intermittent preventive treatment with sulfadoxine–pyrimethamine on hemoglobin level.

Treatment	Hemoglobin level, <11 g/dL/≥11 g/dL[a]	Odds ratio (95% confidence interval)	*P* value
No IPTp-SP	33.3/37.4	0.87 (0.57–1.29)	0.94
IPTp-SP	52.0/48.1	1.20 (0.89–1.65)	0.22

Abbreviation: IPTp-SP, intermittent preventive treatment with sulfadoxine–pyrimethamine.
[a] Values are given as percentage.

Table 3
Multivariate logistic regression analysis of anemia risk among the study group.

Variable	Unadjusted OR (95% CI)	*P* value	Adjusted OR (95% CI)	*P* value
Age, y	0.99 (0.96–1.01)	0.36	0.97 (0.94–1.00)	0.063
Age group, y				
15–19	1.57 (0.50–4.90)	0.44	1.50 (0.25–8.83)	0.66
20–29	0.96 (0.32–2.86)	0.95	0.93 (0.22–3.98)	0.93
30–39	1.05 (0.36–3.27)	0.89	0.99 (0.93–3.33)	0.99
>40	1		1	
Gravida				
Primigravid	0.83 (0.51–1.37)	0.47	0.82 (0.50–1.34)	0.42
Secundigravid	0.94 (0.56–1.58)	0.81	0.93 (0.55–1.56)	0.77
Multigravid	1		1	
Education				
None	1		1	
Primary	1.07 (0.65–1.75)	0.79	1.09 (0.67–1.80)	0.72
Secondary	1.03 (0.11–1.49)	0.88	1.10 (0.74–1.63)	0.63
Tertiary	0.33 (0.12–0.90)	0.03	0.40 (0.14–1.10)	0.075
IPTp-SP				
0 dose	1		1	
1 dose	1.26 (0.90–1.76)	0.17	1.32 (0.94–1.86)	0.11
≥2 doses	1.11 (0.72–1.71)	0.64	1.10 (0.71–1.72)	0.66
Malaria status				
Negative	1		1	
Positive	2.05 (1.48–2.82)	<0.001	1.99 (1.43–2.77)	<0.001
HIV status				
Negative	1		1	
Positive	1.81 (1.16–2.83)	0.009	1.78 (1.13–2.80)	0.014
Malaria and HIV co-infection				
No infection or single infection	1		1	
Dual infection	2.76 (1.50–5.08)	0.001	2.67 (1.44–4.97)	0.002

Abbreviations: CI, confidence interval; IPTp-SP, intermittent preventive treatment with sulfadoxine–pyrimethamine; OR, odds ratio.

that pregnant women with dual infection had a higher risk of developing anemia than women with a single infection or no infection. The adjusted OR was 2.67 (95% CI, 1.44–4.97; $P=0.002$).

4. Discussion

The present study aimed to determine the relationship between anemia and infections, such as malaria and HIV, among a group of pregnant women in Sekondi-Takoradi metropolis, Ghana. The results revealed that pregnant women with either malaria or HIV infection had increased risk of anemia. Furthermore, the findings indicated that women affected by both malaria and HIV were twice as likely to be anemic as those with a single infection or no infection.

Anemia affects many pregnant women worldwide [12]. During pregnancy, women lack sufficient macro- and micro-nutrients required for the second and third trimesters, and in the absence of iron, folate, and vitamin B_{12} supplementation maternal hemoglobin levels decline progressively from the first to the ninth month of gestation [18,19]. In Sub-Saharan Africa, some pregnant women face the complex consequences of suboptimal nutritional intake. They are also faced with other micronutrient deficiencies owing to poor socioeconomic status. These deficiencies are compounded by infectious diseases, predominantly malaria and HIV. Although the present study did not evaluate nutritional status, ensuring good nutrition is the recommended method to prevent anemia in pregnancy; however, infectious diseases can lead to complex physiologic interactions. A previous study found an association between malarial parasitemia and increased risk of anemia [20]. Another study reported malaria as a risk factor of concurrent HIV infection at the population level [21]. In other studies, infection with HIV was associated with anemia, irrespective of pregnancy status [22,23]. It is evident from these previous studies that the incidence of maternal anemia is strongly associated with malaria or HIV infection. The findings of the present study now suggest that pregnant women co-infected with malaria and HIV have twice the risk of developing maternal anemia than women with a single infection.

Anemia is often worsened by the presence of communicable and non-communicable diseases, especially malaria, HIV, tuberculosis, and diabetes mellitus [24]. When anemia occurs in pregnancy, it leads to poor pregnancy outcome, chronic maternal conditions, impaired cognitive development of offspring, and reduced work capacity of the mother [9]. The present study indicates an urgent need for preventive actions against malaria, HIV, and anemia in this region, with the view to implementing infection control measures.

The use of IPTp-SP among pregnant women has been shown to be effective in reducing the prevalence of placental parasitemia, maternal anemia, spontaneous abortion, pre-term delivery, and low birth weight [25]. In the present study, no significant differences were found in the proportion of women who used IPTp-SP with maternal anemia and non-anemia. The discrepancies could be a result of differences in study design. The earlier was a cohort study at a tertiary hospital, while the present study had a cross-sectional prospective design.

The present study has several limitations and may not represent the entire population of the Sekondi-Takoradi metropolis. The present study was not a randomized controlled clinical trial but rather cross-sectional and observational in design. Additionally, the participants may not represent the population of Sekondi-Takoradi receiving care at the respective healthcare institutions and none of the pregnant women were followed until delivery. Furthermore, CD4-postive cell counts were not performed owing to limited resources at the time of the present study, and the study design allowed for only a single encounter with the pregnant women when the venous blood sample was taken. Finally, other potential causes of anemia in pregnancy and weight at birth were not measured. In view of such limitations, the present data should be interpreted with reference to these variables.

In conclusion, the present study indicates that pregnant women infected with both malaria and HIV are twice as likely to be anemic as women with a single infection or no infection. This finding suggests that it is important to focus on malaria, HIV, and anemia control measures in this region of Ghana, especially for all pregnant women.

Conflict of interest

The authors have no conflicts of interest.

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