MALARIA AND ANEMIA IN ANTENATAL WOMEN IN BLANTYRE, MALAWI: A TWELVE-MONTH SURVEY

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Abstract. Malaria and anemia are common in pregnant African women. We screened 4,764 Malawian women at first antenatal visits for malaria and anemia. A total of 42.7% had a malaria infection, which was more common and of higher density in primigravidae (prevalence = 47.3%, geometric mean = 332 parasites/µl) and teenagers (49.8%, 390/µl) than in multigravidae (40.4%, 214/µl) or older women (40.6%, 227/µl). However, 35% of gravida 3+ women were parasitemic. A total of 57.2% of the women was anemic (hemoglobin < 11 g/dl), with moderate anemia (7.0–8.9 g/dl) in 14.9% and severe anemia (< 7 g/dl) in 3.2%. Prevalences of malaria and anemia were highest in the rainy season. Women with moderate/severe anemia had higher parasite prevalences and densities than women with mild/no anemia. Logistic regression showed that age, season, and trimester of presentation were significantly associated with the prevalence of malaria, but gravidity was not. In this urban setting, age and season are more important than gravidity as predictors of malaria at first antenatal visit, and parasitemia is frequent in women of all gravidities.

INTRODUCTION

Plasmodium falciparum malaria infection in pregnant women may have significant adverse consequences for both mother and child.1 Malaria is more frequent in pregnant women than in age-matched controls, and in areas of low endemicity such as Southeast Asia, severe or complicated malaria may also be increased.1 There is evidence that severe malaria may also be a significant problem in pregnant women in urban areas in sub-Saharan Africa.2 Malaria is an important preventable cause of low birth weight, which is in turn a predisposing factor for infant mortality.3 Maternal malaria may predispose to or exacerbate maternal anemia, itself a predisposing factor for low birth weight.4–6 Most studies suggest that malarial infection is more prevalent and intense in primigravid women than in multigravid women in areas endemic for malaria such as sub-Saharan Africa.1,3,8

As part of studies investigating the pathogenesis of malaria in pregnancy,4 we have screened women attending an urban teaching hospital in Malawi at their first antenatal visit for malaria and anemia. We were particularly interested in examining the hypothesis that in an urban population subject to relatively low malaria transmission, age and gravidity are independent determinants of malaria prevalence and density. We examined the relationship between malaria and anemia in this population, but other factors associated with anemia in these women are discussed in more detail elsewhere.9

METHODS

Studies took place between August 1997 and July 1998, at Queen Elizabeth Central Hospital (QECH) in Blantyre, Malawi. This is the principal hospital in the largest city in Malawi, and the referral center for the southern region of the country. Unselected women attending the QECH Antenatal Clinic (ANC) for their first visit were offered screening for malaria and anemia. After verbal consent was obtained, demographic data were recorded. These included age, gravidity, and gestation, as estimated by the patient. Fingerprick blood samples were used to make a thick blood film and to measure hemoglobin concentrations using a HemoCue® hemoglobinometer (HemoCue AB, Angelholm, Sweden).

Hemoglobin concentrations were recorded immediately on the patient’s antenatal card. Blood films were dried, stained with Field’s stain, counted, and screened in the clinic. Strongly positive results and results from films from patients with suspected symptomatic malaria were entered immediately onto the patients’ cards. Other results were entered before the end of the clinic visit, and were available to the midwives either at that visit or the next one. After screening, all patients were treated with sulfadoxine (1,500 mg), pyrimethamine (75 mg), and prescribed daily ferrous sulfate (200 mg) and folic acid (0.25 mg) according to the national policy of Malawi.

All thick blood films were subsequently examined for malaria parasites by counting against 200 leukocytes. Parasitemia was calculated using an assumed white blood cell count of 6,000/µl, and parasitemia was graded as low (+ = 1–999/µl), moderate (++ = 1,000–9,999/µl), high (+++ = 10,000–99,999/µl), or very high (+++++ ≥ 100,000/µl). Films were examined at least twice; if there were significant differences (e.g., 0 to +, + to +++) an additional count was made by another observer, and the average of the two agreeing counts (in parasites per microliter) was recorded.

Seasons were classified as rainy/post rainy (November to April) or dry (May to October). Anemia was defined as a hemoglobin concentration < 11.0 g/dl, moderate anemia as a hemoglobin concentration 7.0–8.9 g/dl, and severe anemia as a hemoglobin concentration < 7.0 g/dl.11 Trimester was assessed as first (< 14 weeks), second (14–26 weeks), or third (> 26 weeks). Young women were teenagers (< 20 years old). Older women were subaged as 20–24 years old, 25–29 years old, or ≥ 30 years old for some analyses. Gravidity was grouped as primigravida, gravida 2, gravida 3 or 4, or gravida 5 or more.

Ethical approval for these studies was granted by the Malawi Health Sciences Research Committee and the Research Committee of the College of Medicine, University of Malawi.

Statistical analysis. Data were not available for all variables for all women; numbers and percentages refer to wom-
en for whom data were available in that field. Data were entered into Epi-Info version 6.04a (Centers for Disease Control and Prevention, Atlanta, Ga). After cleaning and checking, data were analyzed with Epi-Info, Excel® (Microsoft Corporation, Richmond WA), and Stata version 5.0 (Stata Corporation, College Station, Tex). For qualitative data, chi-square analysis was used. For quantitative data, parametric (Student’s t-tests) or nonparametric (Mann-Whitney) tests were used as appropriate, and t or z and P values are reported. Logistic regressions were performed with the presence of malaria parasitemia as a dependent variable, using those variables (age, gravidity, gestation, season) identified as possibly influencing malaria.

RESULTS

Screening for malaria and anemia was performed at 43 of 50 clinics over a 12-month period. During that time, 4,764 of 6,765 women attending the ANC for the first time were screened. Presentation to the screening desk was voluntary, and some women who did present refused consent for the finger prick. Table 1 shows the prevalence and severity of malaria infection and anemia in all women, by gravidity or age groups. Malaria parasitemia was detected in 42.7% of anemic women compared with 15.6% in women who were gravida 3 or greater. Similarly, chi-square analysis was used. For quantitative data, parasite densities did not differ between the presence of anemia and the presence of malaria; infection was still common in later pregnancies, with higher parasite densities in multigravidae (z = 1.65, 95% CI = 1.27–1.20, P < 0.0001) and their mean parasite densities (z = 1.20, 95% CI = 0.86–1.53, P < 0.0001) and when parasitemic they had higher mean parasite densities than multigravidas (z = 1.43, 95% CI = 1.27–1.20, P < 0.0001). Parasitemia was still common in later pregnancies, and although generally of lower density, 32.8% of the parasitemias >10,000/μl were seen in gravida 2 women, and 15.6% in women who were gravida 3 or greater. Similarly, young women were parasitemic more often than women >20 years old (49.8% versus 40.6%, OR = 1.47, 95% CI = 1.28–1.68, P < 0.0001) and their mean parasite densities were higher (z = 7.2, P < 0.0001). Most women attended in the second trimester (as is generally the custom in Malawi), with few attendees in the first trimester. Median gestation at first attendance was 20 weeks. Moderate or high-grade parasitemia was less common in the first or third trimesters than in the second and overall parasite prevalence was slightly lower in third trimester than in the first or second (Table 2). Gestational age at first attendance was lower for primigravidae than multigravidae, and lower for young women than for older women (Table 1).

The prevalence of parasitemia varied by month (Figure 1), with the highest prevalence in January (rainy season) and lowest in July (cool, dry season). Overall, the parasite prevalence was 45.9% in the wet season and 38.6% in the dry season (OR = 1.43, 95% CI = 1.27–1.62, P < 0.0001). Among parasitemic women, parasite densities did not differ significantly with season. Anemia was also more common in the wet season (Figure 1). There was a strong correlation between the presence of anemia and the presence of malaria: 48.3% of anemic women were parasitemic compared with 36.2% of women with normal hemoglobin levels (OR = 1.65, 95% CI = 1.46–1.86, P < 0.0001).

| Associations of age and gravidity (G) with malaria prevalence and density* |
|--------------------------|-----------------------------|-----------------------------|
| Age (years) | Prevalence (%) | Mean (SD) parasite density (×1000/μl) |
| 0–9 | 87 (5.2%) | 47 (12.0) |
| 10–19 | 288 (52.7%) | 111 (35.2%) |
| 20–29 | 1,108 (59.4%) | 22.0 (5.1) |
| 30+ | 2,137 (59.4%) | 22.0 (5.1) |
| Gravidity | Prevalence (%) | Mean (SD) parasite density (×1000/μl) |
| 1 | 336 (55.0%) | 22.0 (5.1) |
| 2 | 1,115 (50.2%) | 22.0 (5.1) |
| 3 | 560 (50.0%) | 22.0 (5.1) |
| 4 | 91 (8.2%) | 22.0 (5.1) |

*Parasitemia was defined as the presence of at least one parasite per 10 μl of blood. Gravidity was calculated as the number of gravid pregnancies. Mean (SD) and geometric mean (IQR) parasite densities were calculated as described previously. The Mann-Whitney U test was used to compare the distribution of parasite densities between different groups. The geometric mean parasite density was calculated as log10(1 + parasite density) and was compared between groups using the t test. The chi-square test was used to compare the distribution of parasitemia between different groups. The logistic regression model was used to compare the distribution of parasitemia between different groups, controlling for age, gravidity, and season. The Mantel-Haenszel chi-square test was used to compare the distribution of parasitemia between different groups, controlling for age and season. The logistic regression model was used to compare the distribution of parasitemia between different groups, controlling for age and season. The Mantel-Haenszel chi-square test was used to compare the distribution of parasitemia between different groups, controlling for age and season.
Mean ± SD hemoglobin levels were lower in women with malaria (10.3 ± 1.8 g/dl) than in aparasitemic women (10.8 ± 1.8 g/dl; t = −4.4, P < 0.0001). There was evidence of a correlation between hemoglobin and parasite count. Parasite grades and anemia classes are cross-tabulated in Table 3. The mean hemoglobin level decreased as parasite grade increased, and moderately or severely anemic women had higher parasite densities (geometric mean density 391/μl) than mildly anemic women (geometric mean density 210/μl) than mildly anemic women (geometric mean density 210/μl). The lowest densities were observed in women without anemia.

Women with malaria were more likely to be moderately or severely anemic, and this relationship was seen in both primigravidae and multigravidae. A total of 25.4% of primigravidae with malaria were moderately or severely anemic, but only 14.7% of parasite-free primigravidae were moderately or severely anemic (OR = 1.97, 95% CI = 1.52–2.56, P < 0.0001). In multigravidae, 20.4% of parasitic women and 14.8% of aparasitic women had moderate or severe anemia (OR = 1.45, 95% CI = 1.20–1.76, P < 0.0001). Similarly, moderate or severe anemia was more common in both younger (24.8% versus 12.4%, OR = 2.31, 95% CI = 1.67–3.22, P < 0.0001) and older (21.4% versus 15.5%, OR = 1.48, 95% CI = 1.24–1.76, P < 0.0001) women with malaria.

Logistic regression was performed to evaluate the relative influence of age, gravidity, gestation, and season of the first clinic visit on the prevalence of malaria parasitemia. We initially examined the whole data set, then separated and examined younger (<20 years old) or older (≥20 years old) women and primigravidae and multigravidae for influences on malaria. When all data were examined, first attendance at a clinic in the wet season and a younger age were associated with the presence of parasitemia, but there was no significant difference in malaria prevalence with gravidity (Table 4).

When data were analyzed according to age group and parity, we found that the trimester of presentation at a clinic had an independent impact on malaria prevalence in teenagers (most marked in the second trimester), but season only weakly influenced malaria prevalence in young women (Table 5). In contrast, season was highly associated with the presence of parasitemia in older women, but the trimester of pregnancy at clinic attendance was not. Findings for primigravidae were similar to those for teenagers. In multigravidae, as in older women, the season of clinic attendance was significantly associated with parasitemia (Table 5), but the trimester of attendance was not.

Parasitemia was significantly more common in teenage primigravidae than in primigravidae 20–24 or 25–29 years old and significantly less common in older multigravidae (≥25 years old) than in teenage multigravidae or those 20–24 years old. When age and gravidity were combined, young primigravidae were infected with malaria more often in the first or second trimester, but showed no seasonal difference; the converse was observed for multigravidae.

Presentation at a clinic in the malaria season, and young age, rather than low gravidity, are the principal risk factors for malaria infection in the pregnant women studied.

**DISCUSSION**

In this study we have investigated the prevalence of malaria and anemia in a large group of pregnant women in an urban African hospital. There are major deficiencies in our understanding of susceptibility to and prevention of malaria and anemia in pregnancy (conditions that affect 40–60% of the women in our study population), but we believe that a first step is to appreciate the magnitude of the problem. We studied first-time attendees at the ANC in Blantyre. Malaria transmission occurs year-round in Blantyre, although there is significant seasonality, with higher rates during the rainy and post-rainy months (November to April) than in the dry season (May to October; Figure 1). For this reason, we performed a 12-month survey to allow for seasonal fluctuations in prevalence or intensity of infection.

More than 90% of women delivering at our hospital attend ANC at least once (Rogerson SJ, unpublished observations).
Over a 12-month period we screened more than 70% of them during their first visit. We were unable to attend 9 of 50 clinics over the 12-month study period, and screened about 90% of the women attending clinics on the days we were present. Demographic data on age, gravidity, and residence of women who were not screened were not available, but we believe that our data from the ANC are reasonably representative of urban pregnant women in Malawi. Women attending the ANC have a high prevalence of malaria and/or anemia; our findings and those of others working in Malawi12 suggest that antenatal measures that can successfully target these problems are of critical importance.

The frequency of antenatal parasitemia was similar to that reported in other studies from Africa,7,8 but there are noteworthy differences in the relationships between several of the variables we assessed. A similar study was performed in Mangochi district around the southern shores of Lake Malawi,9 in this rural community, entomologic inoculation rates are estimated to be about 10 times higher than in Blantyre, with corresponding changes in the patterns of malaria disease. Malaria parasite prevalence was similar overall, but there was a much steeper decrease with age or gravidity in Mangochi, perhaps reflecting the greater number of infective episodes a woman might have there during pregnancy. Stektée and others found the parasite prevalence to be higher in the second trimester than in the third trimester,8 but reported higher prevalences in the post rainy season than we found in Blantyre, where the higher elevation means that cooling conditions do not favor malaria transmission in these months.

Logistic regression analysis indicated that season and age, rather than gravidity, appeared to be the principal influences of malaria prevalence. In separate analyses, after stratifying by gravidity, associations between age and parasite prevalence were stronger than those between gravidity and prevalence after stratifying by age. Why do age-related differences in malaria prevalence occur? This may be related to host or environmental factors. For example, age at first pregnancy may be lower in women with less education, or lower socioeconomic status, who live in conditions conducive to malaria exposure. Our data suggest that under conditions of low-to-moderate transmission, pregnancy-specific immunity is slow to develop, and that age-related immunity may influence malaria prevalence in childbearing years. The difference in prevalence of malaria we found between teenage and older primigravidae is consistent with this. Data from Ndip, Senegal, a village with estimated entomologic inoculation rates of 20 per year, show that clinical malaria attacks are also decreasing in frequency over this age range.13 We are not aware of other studies showing a similar independent effect of age in pregnancy. A prospective study in Thailand found no independent association between age and birth weight, but did not report analysis of frequency of parasitemia according to age.14 In other studies, we have found younger women to have lower birth weight babies, and higher peripheral and placental parasite prevalence, after controlling for gravidity (Rogerson S and others, unpublished data). Teenage pregnant women appear to be at greatest risk of malaria parasitemia in our population, and we believe that urban young women may be a group at particular risk from malaria in pregnancy, as suggested by findings from Maputo, Mozambique.2

Most women in Malawi first attend a clinic for antenatal care in the second trimester of pregnancy.8 There were small
but significant differences in gestation at first attendance at a clinic according to age and gravidity (Table 1), with primigravidae and young women attending earlier. We found an association between the trimester of the first visit and the prevalence of parasitemia, with a lower prevalence of parasitemia and of a moderate-to-high parasitemia in the third trimester than in the second. Logistic regression showed that the trimester of presentation was most important for primigravidae and young women, with highest prevalence of parasitemia in the second trimester, and a higher prevalence in first trimester than in the third (Tables 2 and 5). For multigravidae and women > 20 years old, trimester did not influence parasite prevalence (Table 5). Studies from Kenya and Mangochi found a similar pattern of parasite prevalence; neither study commented on parasite densities.

Women with moderate anemia had the highest prevalence of malaria (53.1%), and higher grade (++ to ++++) parasitemia was most common in women with moderate or severe anemia than in those with mild or no anemia (Table 3). Similar findings were reported from Mangochi, where the overall prevalence of anemia (hematocrit ≤ 34%) was 55.1% and malaria prevalence was highest in mild to moderately anemic women. The reasons why women with moderate anemia should be more likely to have malaria than those with severe anemia are uncertain, but it is possible that moderate anemia may be a result of, rather than a risk for, parasitemia, and that the etiology of severe malaria may differ. Anemia was associated with an iron deficiency in 61% of antenatal women undergoing bone marrow aspiration in Blantyre, and iron or other deficiencies in severely anemic women may be marked enough to inhibit parasite growth.

Among women at first visit to ANC, we found a positive association between malaria and maternal anemia. The prevalence of anemia and malaria both increased during the rainy season. The prevalence of moderate and severe anemia in Blantyre was lower than that of several other series, but similar to that reported elsewhere in Malawi. Staff constraints meant that we were not able to evaluate confounding factors such as socioeconomic status or type of housing, and were not able to measure blood levels of hematocrit, human immunodeficiency virus (HIV) serostatus, or stool hookworm burden. It may be that malaria and/or anemia are influenced by one or more of these agents. In Zanzibar, Tanzania, neither iron status nor education were associated with malaria, whereas anemic and malaria-infected women in Kenya frequently had iron deficiency, and were much more commonly infected with hookworm than women in Blantyre. Previous studies in anemic women from the same clinic found a high prevalence of HIV (48%) and of hematocrit deficiencies (58%), but a low prevalence of hookworm (6%). Our findings are in general accordance with findings from Papua New Guinea and coastal Kenya, although the effect of malaria on anemia in coastal Kenyan women was confined to primigravidae. In Blantyre, anemia was associated with malaria in primigravidae and multigravidae. In our study, the prevalence of malarial infection was associated with a 0.5 g/dl lower hemoglobin concentration that was rather less dramatic than the decrease observed in Kenyan women with malaria.

Our findings have implications for planning interventions to prevent malaria in pregnancy. Although women in their first pregnancies were more likely to be parasitemic and had higher mean parasitemias than women in subsequent pregnancies, as others have found, 40% of all multigravidae and 37% of women in third or later pregnancies (almost 40% of women attending our clinic) were parasitemic. Almost half of the high-grade (> 10,000/μl) parasitemias occurred in multigravidae, and many of these were in secundigravidae. Our findings suggest that in this community, restriction of antimalarial prophylaxis to first pregnancies would deprive a significant proportion of women at risk for malaria of protection. Targeting an intervention to first and second pregnancies would reach 65% of parasitemic women, 78% of those with parasitemias > 1,000/μl, and 84% of women with parasitemias > 10,000/μl, figures that are lower than those reported in Mangochi. It may not be easy to implement such a targeted policy at clinic level. Little is known about the relative significance of low-density versus high-density parasitemia in maternal blood for pregnancy outcomes, although recent information suggests that past infection detected at delivery correlates with low birth weight due to intrauterine growth retardation, whereas active infection at delivery may correlate with prematurity.

In an urban African setting at a moderate elevation (approximately 1,100 meters), we have found malaria infection and anemia to be frequent in pregnant women. Both anemia and malaria are more common in first pregnancies than subsequent ones, but age appears to be a greater determinant of malaria risk than gravidity in our population. Malaria infection is associated with anemia and is most prevalent and intense in women with moderate anemia (hemoglobin = 7–8.9 g/dl). Significant proportions of low-grade and high-grade malarial infection occur in second or subsequent pregnancies, and we would caution against targeting only primigravidae for antimalarial interventions in pregnancy because in our population this strategy would miss half the women with high-grade parasitemia. Women in third or later pregnancies accounted for approximately 35% of the parasitemic women. The population of pregnant women at risk for malaria-related morbidity in urban centers may be larger than that in rural areas.

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