

Failure of a Chloroquine Chemoprophylaxis Program to Adequately Prevent Malaria during Pregnancy in Koupéla District, Burkina Faso

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In West Africa, administration of chloroquine chemoprophylaxis during pregnancy is common, but little is known about its impact on *Plasmodium falciparum* infection during pregnancy. Therefore, cross-sectional studies in antenatal care clinics (ANCs) and delivery units (DUs) were conducted in Koupéla District, Burkina Faso. Chloroquine chemoprophylaxis was reported by 69% of 597 pregnant women at ANCs and by 93% of 853 women in DUs. *P. falciparum* peripheral parasitemia was identified in 29% of women at both ANCs and DUs. Placental parasitemia was identified in 22% of delivering women and was strongly associated with low birth weight (LBW) (risk ratio [RR], 1.7; 95% confidence interval [CI], 1.2–2.4) and prematurity (RR, 2.9; 95% CI, 1.6–5.4). In multivariate analysis, use of chemoprophylaxis was not associated with a reduction in the prevalence of placental parasitemia, LBW, or prematurity. Despite the high reported chloroquine chemoprophylaxis coverage, peripheral and placental malaria rates remain high and are associated with known adverse outcomes during pregnancy, including maternal anemia, prematurity, and LBW. Alternative prevention strategies, such as use of insecticide-treated mosquito nets and intermittent preventive treatment with more-effective antimalarials, are needed.

Malarial infection during pregnancy poses substantial risk to the mother, her fetus, and the neonate. In areas of stable transmission, where women have substantial acquired immunity, *Plasmodium falciparum* infection during pregnancy typically does not cause symptomatic

malaria but may lead to maternal anemia, placental malarial infection, and low birth weight (LBW) [1–3]. In these areas, primigravidae and, to a lesser extent, secundigravidae are at highest risk for malarial infection and LBW [4–7]. Primigravidae have higher-density parasitemias than do multigravidae [5, 8, 9] and are more likely to have placental parasitemia, in part because the level of placenta-specific antimalarial antibodies that prevent binding of the infected RBCs to chondroitin sulfate A increases with each pregnancy [4, 5, 10, 11]. This placental malarial infection contributes to LBW [2, 4, 5], the single greatest risk factor for neonatal mortality and a major contributor to infant mortality [12].

To prevent the adverse consequences of malaria during pregnancy, the Burkina Faso Ministry of Health

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guidelines recommend that pregnant women receive initial treatment with chloroquine and then weekly chloroquine chemoprophylaxis throughout pregnancy [13]; this policy is widely implemented. However, poor compliance with weekly chemoprophylaxis regimens and increasing rates of *P. falciparum* resistance to chloroquine compelled the World Health Organization to abandon its recommendation of chloroquine chemoprophylaxis for pregnant women. Instead, insecticide-treated bednets and intermittent preventive treatment, which involves the administration of treatment doses of an antimalarial during pregnancy, are recommended for women living in areas of stable malaria transmission [14]. We undertook 2 cross-sectional studies in Koupéla District, Burkina Faso, to evaluate use of strategies to prevent malaria during pregnancy and to examine the associations between malaria and adverse pregnancy outcomes in the setting of these prevention activities.

METHODS

Study sites. We selected 6 sites in Koupéla District, ~120 km east of Ouagadougou, the country capital. Koupéla has a short rainy season from June through October, corresponding to the high malaria transmission season. There were 6 antenatal care clinic (ANC) sites (2 in the major towns of Koupéla and Pouytenga and 4 in rural locations) and 2 delivery unit (DU) sites (in Koupéla and Pouytenga towns). The study occurred from June through November 2001.

Study subjects. At ANC sites, we enrolled an average of 6 women per day. Women >15 years of age, at 15–34 weeks of gestation, who were not reportedly allergic to antimalarial medications, and who had not previously been enrolled in the study were enrolled. Women were seen only once at an ANC visit; each study participant is represented only once. At DUs, delivering women >15 years of age who had placentas available for examination were enrolled.

Informed consent was obtained (by signature or thumbprint) after the consent document was read to the woman in the local language. The study was reviewed and approved by Human Subjects review committee at the Centers for Disease Control and Prevention (Atlanta, GA) and Johns Hopkins University (Baltimore, MD) in the United States and by the Burkina Faso Ministry of Health (Ouagadougou).

Clinical procedures. Enrolled women were administered a questionnaire focused on sociodemographic characteristics, history of fever and antimalarial drug use, and the use of antimalarial chemoprophylaxis and bednets. At ANCs, an axillary temperature measurement ($\pm 0.1^\circ\text{C}$) was obtained. Capillary blood (ANCs and DUs) was obtained by a fingerstick for hemoglobin determination (ANCs) and malaria blood film preparation (ANCs and DUs). Placental blood films were prepared

by identifying the maternal side of the placenta, wiping away excess blood, cutting into the surface, and placing pooled blood onto a slide. Umbilical cord blood samples were obtained by wiping away excess blood from a clamped cord, piercing it with a lancet, and placing a drop of expressed blood on a slide. Neonates were weighed (± 10 g) with an electronic digital scale (Tanita). Gestational age was estimated by use of a Ballard examination [15] within 24 h of delivery.

Laboratory procedures. All blood films were stained with Giemsa and examined for parasites. For thick films, parasites and leukocytes were counted in the same fields until 500 leukocytes were counted. Parasite densities were estimated by use of an assumed leukocyte count of 8000 leukocytes/ μL . Thin films were used to determine species when thick films yielded positive results. All blood films were read twice at a reference laboratory. Discordant results were given a third reading, the result of which was considered final. The hemoglobin level was

Table 1. Characteristics of women enrolled in study of the burden of malaria during pregnancy and use of malaria prevention measures, Koupéla District, Burkina Faso.

Characteristic	Women from ANCs ^a (n = 597)	Women from DUs ^b (n = 853)
Age, median years (range)	22 (15–47)	22 (15–52)
Gravidity, median no. (range)	2 (1–11)	2 (1–11)
ANC visits, median no. (range)	1 (1–7)	2 (0–6)
Able to read	14.6	20.5
Attended any school	16.1	22.6
Married	90.8	89.2
Owns moped	40.4	46.3
Owns radio	81.2	78.3
Works for cash	30.1	30.7
Self-reported use of bednets		
Owns bednet	35.5	34.0
Sleeps under bednet all of the time	23.1	21.9
Use of chloroquine chemoprophylaxis ^c		
Complete chemoprophylaxis	50.2	64.1
Incomplete chemoprophylaxis	19.0	28.7
No chemoprophylaxis	30.9	7.3
Gestational age when chemoprophylaxis was started, median months	5	5

NOTE. Data are % of subjects, unless otherwise indicated. ANC, antenatal care clinic; DU, delivery unit.

^a Six sites.

^b Two sites.

^c Complete chemoprophylaxis is defined as self-reported taking of correct number of chloroquine tablets as initial treatment dose, followed by weekly taking of correct number of chloroquine tablets until delivery. For women attending ANCs, analysis of chemoprophylaxis is restricted to 311 women with ≥ 1 previous ANC visit and information about chemoprophylaxis use recorded. For DUs, analysis is limited to 840 women with information about chemoprophylaxis recorded.

Table 2. Rates of parasitemia, reported fever, and anemia among women attending antenatal clinics (ANCs) in Koupéla District, Burkina Faso.

Characteristic	All women (n = 597)	Women with no prior ANC visits (n = 282)	Women with ≥1 prior ANC visit, by chemoprophylaxis use ^a (n = 311)			P ^b
			Complete (n = 156)	Incomplete (n = 59)	None (n = 96)	
Parasitemia						
Overall	29.2	37.2	18.0	28.8	25.0	.18
Primigravidae	42.3	56.3	27.1	36.0	35.7	.43
Secundigravidae	29.8	43.2	20.9	15.4	30.4	.39
Multigravidae	20.8 ^c	26.1 ^c	9.4	28.6	15.9	.31
Fever (temperature, ≥37.5°C)						
Reported during pregnancy	33.0	27.0	40.7	33.9	41.1	.95
Reported within week before enrollment	10.9	8.9	10.5	12.3	16.8	.15
At visit	29.9	31.1	22.4	23.7	41.7	.001
Hemoglobin level, mean g/dL ± SD	9.9 ± 1.6	9.7 ± 1.6	10.1 ± 1.5	9.9 ± 1.5	10.1 ± 1.7	.65
Anemia (hemoglobin level, <11 g/dL)						
Overall	76.2	81.6	68.6	76.3	72.9	.46
Primigravidae	80.2	93.8	70.8	68.0	67.9	.79
Secundigravidae	76.6	93.2	69.8	69.2	60.9	.47
Multigravidae	73.2 ^d	72.0 ^c	65.6	90.5	81.8	.07
Moderate-to-severe anemia (hemoglobin level, <8 g/dL)						
Overall	12.0	13.5	9.6	8.5	12.5	.47
Primigravidae	20.9	25.0	14.6	16.0	21.4	.53
Secundigravidae	10.5	9.1	11.6	7.7	13.0	1.0
Multigravidae	6.9 ^c	8.9 ^e	4.7	0	6.9	.69

NOTE. Data are % of subjects, unless otherwise indicated. Multigravidae, ≥3 pregnancies.

^a Complete chemoprophylaxis is defined as self-reported taking of correct number of chloroquine tablets as initial treatment dose, followed by weekly taking of correct number of chloroquine tablets until delivery. Women attending their first ANC visit are excluded from chemoprophylaxis comparison.

^b Determined by χ^2 test (2 × 2; complete chemoprophylaxis vs. none) or Fisher's exact test for categorical variables and by Kruskal-Wallis test for the continuous variable (i.e., hemoglobin).

^c $P < .0001$, by χ^2 test for trend.

^d $P = .08$, by χ^2 test for trend.

^e $P = .001$, by χ^2 test for trend.

measured (± 0.1 g/dL) with use of a Hemocue machine (Hemocue).

Treatment of anemia and malaria. Anemic women (hemoglobin level, <11 g/dL) at ANCs were treated, in accordance with national policy, with ferrous sulfate (200 mg) and folic acid (0.25 mg) given as a single combined tablet daily for 30 days. All women receive prophylactic iron and folate throughout pregnancy, in accordance with Ministry of Health policy. Women at ANCs and DUs who reported recent fever (within 7 days), had a documented fever (axillary temperature, ≥37.5°C), or had peripheral malaria parasitemia received presumptive antimalarial treatment in accordance with the national policy. Neonates with umbilical cord malaria parasitemia were treated with chloroquine syrup at standard dosing.

Definitions. All blood film results were considered to be positive if any asexual-stage parasites were identified and negative if no parasites were seen in 100 fields. We defined LBW as a birth weight of <2500 g, prematurity as a gestational age of <37 weeks (determined by Ballard examination), anemia as a hemoglobin level of <11 g/dL, and moderate-to-severe anemia as a hemoglobin level of <8 g/dL [16]. We considered a woman to have received complete chemoprophylaxis if she had taken the correct number of chloroquine pills for a curative dose and then the correct number of chloroquine pills weekly until delivery. Any woman who took some chloroquine for chemoprophylaxis but did not meet all the criteria for complete chemoprophylaxis was considered to have received incomplete chemoprophylaxis.

Table 3. Relationship between peripheral malaria parasitemia, fever, and anemia among women attending antenatal clinics, Koupéla District, Burkina Faso.

Characteristic	Percentage of women		Risk ratio (95% CI)	P
	Parasitemic (n = 174)	Aparasitemic (n = 423)		
Reported fever within week before enrollment	14.3	9.9	1.44 (0.90–2.30)	.13
Anemia (hemoglobin level, <11 g/dL)	87.9	71.4	1.23 (1.14–1.34)	<.0001
Moderate-to-severe anemia (hemoglobin level, <8 g/dL)	20.1	8.5	2.36 (1.54–3.64)	<.0001

Statistical analysis. Data were double-entered and validated with EpiInfo, version 6 (Centers for Disease Control and Prevention). Univariate analyses were done with χ^2 or Fisher's exact tests to compare proportions for categorical variables; the χ^2 test for trend was used to compare proportions across ≥ 3 groups. The Kruskal-Wallis test was used to compare continuous variables with nonnormal distributions. To evaluate the relationship of chemoprophylaxis use and placental malaria, LBW, and prematurity, Poisson log-linear models were constructed through backward elimination. Use of chemoprophylaxis was maintained in each of the models, regardless of statistical significance. Test results were considered to be significant when the 2-sided *P* value was <.05. STATA software, release 7.0 (STATA), was used for statistical analyses.

RESULTS

We enrolled 597 women in ANCs and 853 women in DUs. Overall, 2 eligible women in ANCs (0.2%) and 9 eligible women in DUs (0.9%) refused enrollment. There were no notable differences among enrolled or nonenrolled women (those who refused or were not selected) with respect to median age.

Characteristics of enrolled women. Characteristics of enrolled women are summarized in table 1. In general, the characteristics of women at DUs were similar to those at ANCs. However, delivering women were more likely to report having used chemoprophylaxis with chloroquine (92.8% vs. 69.2%; *P* < .0001) and to have completed the regimen (64.1% vs. 50.2%; *P* < .0001) than were women at ANCs. Ownership of a bednet was reported by approximately one-third of women in both DUs and ANCs. The majority of women who owned a bednet reported sleeping under it all or most of the time. Most bednets in this region are not treated with insecticides (unpublished data).

Malaria parasitemia and anemia among women at ANCs. The overall proportion of women with malaria parasitemia was 29.2% (table 2), which varied from 42.3% among primigravidae to 20.8% among multigravidae (*P* < .0001, by χ^2 for trend); this proportion did not vary significantly by reported use of chloroquine chemoprophylaxis. Parasitemic women were younger

(median age, 21 years) than were aparasitemic women (median age, 24 years; *P* < .0001). There were no differences in the rates of parasitemia by gestational age (data not shown). Fevers were reported at any time during pregnancy by 33.0% of women and in the week before enrollment by 10.9% of women; this did not vary significantly by reported chloroquine chemoprophylaxis use. Documented fever on the day of examination was more common among those who had not received chemoprophylaxis than among those who had received complete chemoprophylaxis (41.7% vs. 22.4%; *P* = .001). The mean hemoglobin level was 9.9 g/dL. Rates of anemia (hemoglobin level, <11 g/dL) and moderate-to-severe anemia (hemoglobin level, <8 g/dL) were 76.2% and 12.0%, respectively, and did not differ by reported use of chemoprophylaxis. Moderate-to-severe anemia rates, but not overall anemia rates, significantly decreased with increasing gravidity (*P* < .0001, by χ^2 for trend).

Parasitemic women were more likely to have had a fever in the week before their ANC visit than were aparasitemic women (14.3% vs. 9.9%), although this finding was not statistically significant (table 3). Parasitemic women were also more likely to have either anemia or moderate-to-severe anemia than were aparasitemic women. This relationship was most marked for moderate-to-severe anemia: parasitemic women were 2.36 times more likely than aparasitemic women to have a hemoglobin level of <8 g/dL (20.1% vs. 8.5%; *P* < .0001).

Malaria parasitemia and birth outcomes among delivering women. The overall rate of parasitemia was 29.3% (table 4), with multigravidae at lower risk (21.6%) than secundigravidae (36.0%) or primigravidae (36.3%; *P* < .0001, by χ^2 for trend). There were no significant differences in the rates of peripheral parasitemia between women who reported taking chemoprophylaxis completely and those who reported taking no chemoprophylaxis at any gravidity. Placental parasitemia was observed in 22.0% of all delivering women and was inversely associated with gravidity (*P* < .0001, by χ^2 for trend). Overall, women who reported taking chloroquine chemoprophylaxis completely had lower rates of placental parasitemia than did women who reported not taking it at all (19.9% vs. 30.8%); this association was most pronounced among multigravidae (10.3% vs. 23.8%). Fever was reported at any time during preg-

Table 4. Rates of peripheral and placental parasitemia, reported fever, low birth weight, and prematurity among delivering women in Koupéla District, Burkina Faso.

Characteristic	All women (n = 853)	Use of chemoprophylaxis ^a			P ^b
		Complete (n = 538)	Incomplete (n = 241)	None (n = 61)	
Peripheral parasitemia					
Overall	29.3	27.2	34.9	29.5	.70
Primigravidae	36.3	35.4	38.6	40.9	.61
Secundigravidae	36.0	38.0	32.7	30.8	.77
Multigravidae	21.6 ^c	16.9	33.0	20.0	.78
Placental parasitemia					
Overall	22.0	19.9	26.7	30.8	.07
Primigravidae	34.0	31.9	35.6	42.1	.37
Secundigravidae	24.3	24.6	24.5	27.3	1.0
Multigravidae	13.9 ^c	10.3	20.4	23.8	.07
Umbilical cord parasitemia	1.4	1.3	1.2	3.9	.19
Fever during pregnancy	31.4	31.0	32.1	35.0	.52
Self-reported use of an antimalarial for treatment during pregnancy	24.9	25.4	24.7	19.7	.33
Fever within week before enrollment	9.5	9.3	8.8	17.0	.07
Singleton live-born birth weight, mean g ± SD	2919 ± 450	2918 ± 454	2951 ± 417	2797 ± 538	.25
Low birth weight (live-born singletons weighing <2500 g)					
Overall	14.1	15.1	11.9	17.4	.67
Primigravidae	24.2	25.5	17.4	33.3	.57
Secundigravidae	13.6	11.2	17.8	0	.60
Multigravidae	8.2 ^c	9.5	4.2	11.8	.67
Premature delivery (live-born singletons of <37 weeks' gestation)					
Overall	4.7	2.8	7.8	10.9	.02
Primigravidae	6.5	3.3	10.5	16.7	.04
Secundigravidae	4.6	2.5	11.1	0	1.0
Multigravidae	3.2 ^c	2.2	3.3	11.8	.08

NOTE. Data are % of subjects, unless otherwise indicated. Multigravidae, ≥3 pregnancies.

^a Complete chemoprophylaxis is defined as self-reported taking of correct number of chloroquine tablets as initial treatment dose, followed by weekly taking of correct number of chloroquine tablets until delivery.

^b Determined by χ^2 test (2 × 2 table; complete chemoprophylaxis vs. none) or Fisher's exact test for categorical variables and by Kruskal-Wallis test for the continuous variable (i.e., birth weight).

^c $P < .0001$, by χ^2 test for trend.

nancy by 31.4% of delivering women; 24.9% reported taking an antimalarial for treatment of a fever. Among neonates, 1.4% had malaria parasites identified on umbilical cord blood films.

There were 806 live births, of which 794 were singletons. The mean birth weight among singleton live-born infants was 2919 g. The rate of LBW delivery was 14.1% and was strongly associated with gravidity. There were no significant associations between either the mean birth weight or the rate of LBW and the use of chemoprophylaxis. The risk of LBW was 1.67 times greater among women with placental parasitemia ($P = .005$; table 5), and the mean birth weight of their infants was 128 g lower for these women ($P = .01$).

Overall, preterm delivery occurred in 4.7% of live-born singletons. The rate was highest among primigravidae (6.5%) and lowest among multigravidae (3.2%; $P < .0001$, by χ^2 for trend). The rate of premature delivery was lowest among women who reported taking chemoprophylaxis completely (2.8%) and highest among those who reported taking no chemoprophylaxis (10.9%; $P = .02$). The risk of premature delivery was 2.90 times greater among women with placental parasitemia ($P = .0005$; table 5). Women who reported fever during the week before delivery were 1.67 times more likely to deliver prematurely than were those who did not report fever, although this result did not reach statistical significance (data not shown).

Table 5. Relationship between placental malaria parasitemia and peripheral malaria parasitemia, low birth weight, and premature delivery among delivering women in Koupéla District, Burkina Faso.

Characteristic	Result of placental blood film examination		Risk ratio (95% CI)	P
	Positive (n = 188)	Negative (n = 644)		
Positive result of peripheral blood film	81.4	14.4	10.42 (7.45–14.57)	<.0001
Low birth weight (<2500 g) ^a	20.7	12.3	1.67 (1.17–2.39)	.005
Birth weight, mean g ± SD	2821 ± 534	2949 ± 417	—	.01 ^b
Premature delivery (<37 weeks) ^c	9.6	3.3	2.90 (1.55–5.42)	.0005

NOTE. Data are % of subjects, unless otherwise indicated.

^a Singleton live-born infants only.

^b Determined by Kruskal-Wallis test.

^c Singleton live-born infants with Ballard examination within first 24 h.

We further examined risk factors for placental parasitemia, LBW, and prematurity in multivariate analyses (table 6). Low gravidity, delivery in the medical center of Koupéla District, and a history of treatment with an antimalarial during pregnancy were independent risk factors for placental malarial infection; use of chemoprophylaxis was neither significantly protective nor a risk factor. Short maternal height (<150 cm), low gravidity, placental malaria, and female sex of the neonate were independently associated with increased risk of LBW; use of chemoprophylaxis was neither significantly protective nor a risk factor. Placental malaria was the sole significant risk factor for premature delivery; ownership of a bednet was a protective factor. Women who reported taking chemoprophylaxis completely (but not those who reported taking chemoprophylaxis incompletely) appeared to be at lower risk for premature delivery than were women who reported taking no chemoprophylaxis, but this finding did not quite reach statistical significance.

DISCUSSION

In 2 cross-sectional studies in Koupéla District, Burkina Faso, we found that peripheral and placental malaria remain common despite the widespread use of chloroquine chemoprophylaxis by pregnant women. We also found that peripheral malarial infection was strongly associated with anemia and moderate-to-severe anemia among women at ANCs and that placental malaria was strongly associated with LBW, an absolute reduction in birth weight, and premature delivery. In general, the use of chemoprophylaxis did not appear to be associated with a reduced risk of either placental malaria or its associated adverse outcomes after adjustment for other risk factors. However, women who reported using chloroquine chemoprophylaxis completely appeared to be at lower risk of premature delivery, although this finding just missed statistical signifi-

cance. The study also confirmed the well-documented finding that primigravidae and secundigravidae are at higher risk of peripheral and placental malarial infection and associated adverse outcomes, including anemia, LBW, and prematurity.

The reasons for the inadequate performance of chloroquine chemoprophylaxis in preventing placental parasitemia and adverse outcomes related to malaria during pregnancy in this setting are likely multiple. The most likely reason is the high rate of parasitological failure (>50% by day 14) that has been observed when treating malaria with chloroquine in eastern Burkina Faso (unpublished data). Another possibility is the long-recognized difficulty in complying with a chemoprophylaxis regimen that involves weekly dosing. Although >60% of delivering women in our study reported taking chloroquine completely, we were unable to corroborate this with observation or chemical detection.

Several trials of chloroquine chemoprophylaxis (with or without the addition of proguanil) have demonstrated a protective effect against the adverse consequences of malaria during pregnancy [17–20]. However, some trials have demonstrated a less-convincing impact. One trial from Burkina Faso and another from Cameroon showed statistically significant but small increases in maternal hematocrit at delivery among women taking chloroquine but no difference in the rates of anemia [21]. Another study demonstrated a decrease in the prevalence of placental parasitemia associated with chloroquine use but no impact on LBW [18], whereas an observational study from Malawi found high rates of peripheral and placental parasitemia despite directly observed chloroquine chemoprophylaxis [22]. Given that levels of chloroquine resistance have increased across sub-Saharan Africa since most of these studies were done, it should be expected that the efficacy of chloroquine in preventing malaria during pregnancy would be even poorer today.

In programmatic evaluations, the results have been even less uniformly convincing. Two studies, one from Malawi [23] and

Table 6. Results of multivariate analysis of factors associated with placental parasitemia, prematurity, and low birth weight among delivering women in Koupéla District, Burkina Faso.

Multivariate model, characteristic, factor ^a	Adjusted risk ratio (95% CI)	P
Placental malaria^b		
Gravidity		
Multigravid	1.0 (Reference)	—
Secundigravid	1.8 (1.2–2.7)	.003
Primigravid	2.3 (1.6–3.3)	.001
Delivery in Koupéla DU ^c	1.5 (1.1–2.1)	.007
Treatment with antimalarial	1.4 (1.0–1.9)	.03
Use of chemoprophylaxis ^d		
None	1.0 (Reference)	—
Incomplete	0.9 (0.5–1.5)	.6
Complete	0.8 (0.4–1.3)	.3
Low birth weight (<2500 g)^e		
Maternal height of <150 cm	2.73 (1.10–6.77)	.03
Gravidity		
Multigravid	1.0 (Reference)	—
Primigravid or secundigravid	2.13 (1.35–3.36)	.001
Placental malaria	1.54 (1.01–2.35)	.04
Female sex of neonate	1.48 (1.0–2.21)	.05
Use of chemoprophylaxis		
None	1.0 (Reference)	—
Incomplete	1.08 (0.38–3.14)	.88
Complete	1.57 (0.57–4.30)	.39
Premature delivery (<37 weeks)^f		
Placental malaria	2.74 (1.42–5.31)	.003
Ownership of bednet	0.25 (0.09–0.72)	.01
Use of chemoprophylaxis		
None	1.0 (Reference)	—
Incomplete	0.95 (0.35–2.60)	.92
Complete	0.37 (0.13–1.03)	.06

NOTE. Multigravid, ≥ 3 pregnancies.

^a All models retain chemoprophylaxis regardless of significance. Other variables evaluated for each model, but not retained in any, include age, religion, schooling, ability to read, socioeconomic indicators (type of floor, ownership of a radio, bicycle, or moped), urban versus rural residence, number of antenatal care visits, history of fever, mid-upper-arm circumference, and malaria parasitemia noted on peripheral blood film at delivery.

^b For 809 women.

^c Compared with delivery in market town of Pouytenga.

^d Correct chemoprophylaxis is defined as self-reported taking of correct number of chloroquine tablets as initial treatment dose, followed by weekly taking of correct number of chloroquine tablets until delivery.

^e Analysis restricted to live-born, singleton neonates ($n = 754$).

^f Analysis restricted to singleton neonates with Ballard examination in first 24 h ($n = 771$).

the other from Papua New Guinea [24], described inadequate prevention afforded to pregnant women through chloroquine chemoprophylaxis. A third programmatic evaluation, which was from Zaire (now the Democratic Republic of the Congo), found that delivering women who took chloroquine chemo-

prophylaxis did have lower rates of maternal malaria and LBW [25]. However, the analysis in this study adjusted only for parity and ANC attendance and no other potential confounding factors. Given the difficulty in adhering to a weekly dosing regimen with chloroquine chemoprophylaxis, the poor translation of research studies into practice is not surprising.

This study has 2 important limitations. We were unable to continue this study for an entire calendar year. Given the seasonal variation of malaria transmission in this region, our study may have overestimated the overall prevalence of placental parasitemia. However, the risk of adverse outcomes associated with peripheral and placental malaria would not likely be seasonal. Also, the information we have about chloroquine chemoprophylaxis is self-reported. We do not know for sure whether women who claimed to have taken chloroquine chemoprophylaxis completely did so, although we believe that the questions we asked were sufficiently detailed to make false-positive responses less likely.

Perhaps the most encouraging result of this study is the frequency with which pregnant women attempt to prevent malaria during pregnancy. This is contrary to widespread experience in much of Africa showing that uptake of weekly chloroquine chemoprophylaxis has usually been poor (estimates ranged from 1% to 18% in a 4-country survey [26] and were only as high as 36% in other programmatic evaluations [23]). Reasons that have been given for poor compliance include the logistic difficulties in distributing a drug requiring weekly dosing [27], saving medicine for future use [28], unpleasant side effects such as pruritus [28, 29], and fear of taking bitter-tasting medicines during pregnancy [29–31]. Another factor may be the difficulty in remembering to take a drug with a weekly dosing schedule, although this has not been well studied. The reasons for the unusually high degree of reported compliance with chloroquine chemoprophylaxis among pregnant women in Burkina Faso remain unclear. However, these findings suggest that these women are aware of the dangers of malaria during pregnancy and are likely to be receptive to other, potentially more effective interventions to prevent malaria.

Currently, the World Health Organization no longer recommends the use of chemoprophylaxis for prevention of malaria during pregnancy but rather a package of interventions for pregnant women living in areas where malaria is endemic, including intermittent preventive treatment, insecticide-treated bednets, case management of clinical malaria, and diagnosis and treatment of anemia [14]. Numerous clinical trials have demonstrated the positive impact of intermittent preventive treatment with sulfadoxine-pyrimethamine or other effective antimalarials, such as mefloquine, on placental parasitemia, anemia, and LBW [32–36]. There is also evidence suggesting that intermittent preventive treatment is cost-effective [37], much more so than chloroquine chemoprophylaxis [38]. In

addition, a recent programmatic evaluation from Malawi demonstrated that women who had taken ≥ 2 doses of intermittent preventive treatment with sulfadoxine-pyrimethamine had a lower rate of placental parasitemia, decreased prevalence of LBW, and higher mean hemoglobin concentrations than did women who did not take intermittent preventive treatment [39]. A recently completed bednet trial from Kenya demonstrated a 47% reduction in maternal anemia, a 35% reduction in placental malaria, and a 28% reduction in LBW among gravida 1–4 women who slept under insecticide-treated bednets during pregnancy [40]. Convincing data such as these led African heads of state to set a goal of achieving 60% coverage of pregnant women with intermittent preventive treatment and insecticide-treated bednets by 2005 [41].

In summary, in spite of the high reported chloroquine chemoprophylaxis coverage, peripheral and placental malaria rates remain very high in eastern Burkina Faso during the high-transmission season for malaria and are associated with known adverse outcomes during pregnancy, including maternal anemia, prematurity, and LBW. Given the apparent poor programmatic effectiveness of chloroquine chemoprophylaxis, alternative prevention strategies, such as the use of insecticide-treated bednets and intermittent preventive treatment with more-effective antimalarials, should be implemented.

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