MALARIA PREVENTION DURING PREGNANCY: ASSESSING THE DISEASE BURDEN ONE YEAR AFTER IMPLEMENTING A PROGRAM OF INTERMITTENT PREVENTIVE TREATMENT IN KOUPELA DISTRICT, BURKINA FASO

SODIOMON B. SIRIMA, AMANDOU KONATÉ, ALLISYN C. MORAN, KWAME ASAMOAH, EDITH C. BOUGOUMA, AMIDOU DIARRA, ALPHONSE OUÉDRAOGO, MONICA E. PARISE, AND ROBERT D. NEWMAN*

Centre National de Recherche et de Formation sur le Paludisme, Ministère de la Santé, Ouagadougou, Burkina Faso; Malaria Branch, Division of Parasitic Diseases, Coordinating Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia; Maternal and Neonatal Health Program, JHPIEGO Corporation, Baltimore, Maryland

Abstract. The World Health Organization recommends that pregnant women in malaria-endemic areas receive ≥2 doses of intermittent preventive treatment with sulfadoxine-pyrimethamine (IPTp/SP) in the second and third trimesters of pregnancy to prevent maternal anemia, placental parasitemia, and low birth weight (LBW). In 2001, a program evaluation in Koupéla District, Burkina Faso demonstrated that despite widespread use of chloroquine chemoprophylaxis, the burden of malaria during pregnancy remained high. In 2003, the Burkina Faso Ministry of Health piloted a program of IPTp/SP (three doses) and accelerated distribution of insecticide-treated nets (ITN) to pregnant women in Koupéla District. In 2004, a follow-up program evaluation was conducted. Coverage with ≥1 doses of IPTp/SP was high among women attending antenatal clinics (ANCs) (96.2%) and delivery units (DUs) (93.5%); ITN ownership was moderately high (ANC = 53.9%, DU = 61.6%). In multivariate analysis, ≥1 dose of IPTp/SP was associated with a significant reduction in the prevalence of peripheral parasitemia at ANCs (risk ratio [RR] = 0.49, P = 0.008), ≥2 doses of IPTp/SP were associated with a reduction in the prevalence of placental parasitemia (RR = 0.56, P = 0.02), and three doses of IPTp/SP were associated with a reduced risk of LBW (RR = 0.51, P = 0.04). The proportions of women at ANCs with peripheral parasitemia and anemia were significantly lower in 2004 than in 2001 (RR = 0.53, P = 0.001 and RR = 0.78, P = 0.003, respectively). The proportions of women at DUs with peripheral and placental parasitemia were also significantly lower in 2004 than in 2001 (RR = 0.66, P < 0.0001 and RR = 0.71, P = 0.0002, respectively). These data suggest that a package of IPTp/SP and ITNs is effective in reducing the burden of malaria during pregnancy in Burkina Faso.

INTRODUCTION

Malaria infection during pregnancy poses substantial risk to the mother, her fetus, and the neonate. In areas of stable malaria transmission such as Burkina Faso, where adult women have considerable acquired immunity, Plasmodium falciparum infection during pregnancy typically does not cause symptomatic malaria, but may lead to maternal anemia and placental malaria infection, especially among primigravidae and secundigravidae.1,2 This placental malarial infection contributes to low birth weight (LBW), a major contributor to infant mortality.3 Malaria infection even when asymptomatic is associated with maternal anemia, which may also contribute to LBW. Malaria contributes up to 15% of maternal anemia, 14% of LBW, 30% of preventable LBW, 70% of intrauterine growth retardation, 36% of premature delivery, and 8% of infant mortality.2

To prevent malaria during pregnancy and its adverse outcomes, the World Health Organization (WHO) recommends at least two doses of intermittent preventive treatment with sulfadoxine-pyrimethamine (IPTp/SP) during the second and third trimesters of pregnancy.4 Clinical trials5–9 and program evaluations10–12 in stable transmission areas have shown that this intervention is safe, efficacious, and effective in preventing maternal anemia, placental parasitemia, and LBW.7,12,13 Since chloroquine resistance is increasing in almost all malaria-endemic areas and treatment adherence to weekly chloroquine chemoprophylaxis is low, it is no longer recommended.4

Because of the WHO recommendation of IPTp/SP and increasing chloroquine resistance in Burkina Faso, the Burkina Faso Ministry of Health, in collaboration with JHPIEGO Corporation and the Centers for Disease Control and Prevention, conducted an evaluation in 2001 in Koupéla District to determine coverage of chloroquine chemoprophylaxis and the burden of malaria during pregnancy.14 The assessment showed moderately high rates of malaria during pregnancy despite widespread use of chloroquine chemoprophylaxis and no association between use of chloroquine chemoprophylaxis and reduction in adverse outcomes such as anemia, LBW, and prematurity.14,15

In February 2003, the Burkina Faso Ministry of Health implemented a pilot program of IPTp/SP in Koupéla District as part of a package of focused antenatal care. From June to November 2004, approximately 17 months after IPTp implementation began in Koupéla District, a follow-up assessment was conducted at the same sites used in the 2001 baseline assessment.15 To compare these new results to the baseline assessment, the focus remained on the same outcome measures, including maternal anemia, placental and peripheral parasitemia, and LBW.

MATERIALS AND METHODS

Assessment sites. The assessment was completed at eight sites in Koupéla District from June to November 2004. Six antenatal clinics (ANCs) were included, with two located in the major towns of Koupéla and Poytenga and four located in more rural areas. Two delivery units (DUs) were chosen (Koupéla and Poytenga) because they represent the only two high-level delivery facilities in the district. These sites were the same as those sampled in the 2001 baseline evaluation.15

Assessment subjects. At ANCs, enrollment was limited to women in their third trimester (≥28 weeks gestation) who...
were ≥ 15 years of age, gave informed consent, and were not reportedly allergic to antimalarial medications. Women enrolled in the ANCs were seen only once by our assessment staff immediately after they had completed their routine ANC visit at which time they were given IPTp/SP. Therefore, each woman is represented only once in the analysis. At the DUs, enrollment was limited to women who were ≥ 15 years of age who had placentas available, gave informed consent, and were not reportedly allergic to antimalarial medications.

Informed consent was obtained after reading the consent document to the woman in the local language. The assessment received human subjects approval from the Centers for Disease Control and Prevention (Atlanta, GA), the Western Institutional Review Board (Institutional Review Board of record for JHPIEGO), and the Burkina Faso Ethical Committee for Health Research.

**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 insecticide-treated nets (ITNs). At ANCs, an axillary temperature measurement (± 0.1°C) was taken. Capillary blood was obtained through a finger stick for a hemoglobin (Hb) measurement (ANC) and malaria blood film preparation (ANC and DU). At the DUs, placental blood films were prepared from the maternal side of the placenta. Excess blood was wiped away, a cut was made into the surface, and pooled blood was placed onto a slide. Neonates were weighed (± 10 grams) using an electronic digital scale (Tanita Corporation, Tokyo, Japan).

**Laboratory procedures.** All blood films were stained with Giemsa and examined for parasites. Slides were fixed and stained daily and transported weekly to the laboratories of the Centre National de Recherche et de Formation sur le Paludisme in Ouagadougou. For thick films, parasites and leukocytes were counted in the same fields until 500 leukocytes were counted. Parasite densities were estimated using an assumed leukocyte count of 8,000 leukocytes/μL. Thin films were used to determine species when thick films were positive. All blood films were read twice at a reference laboratory. Discordant results were given a third reading, the result of which was considered final. Hemoglobin was measured (± 0.1 g/dL) using a Hemocue® machine (Hemocue AB, Ängelholm, Sweden).

**Treatment of anemia and malaria.** Women found to be anemic at ANCs (Hb level < 11 g/dL) were treated per national guidelines with ferrous sulfate (200 mg) and folic acid (0.25 mg) given as a single combined tablet daily for 30 days. All febrile women (axillary temperature ≥ 37.5°C) in the assessment and women at ANCs who reported episodes of fever in the week before enrollment had a rapid diagnostic test (RDT) for malaria performed (OptiMAL-IT®, DiaMed AG, Cressier sur Morat, Switzerland). Women with a positive RDT result were given treatment with either quinine or SP based on the specific species when thick films were positive. All blood films were read twice at a reference laboratory. discordant results were given a third reading, the result of which was considered final. Hemoglobin was measured (± 0.1 g/dL) using a Hemocue® machine (Hemocue AB, Ängelholm, Sweden).

**Definitions.** All blood films were considered positive if any asexual stage parasites were identified, and negative if no parasites were seen in 100 fields. We defined anemia as a Hb level < 11 g/dL, moderate-to-severe anemia as a Hb level < 8 g/dL, and LBW as < 2,500 grams.

**Statistical analysis.** Data were double entered and validated using Epi-Info version 6 (Centers for Disease Control, Atlanta, GA). Univariate analyses were performed using chi-square or Fisher’s exact tests to compare proportions for categorical variables. The chi-square test for trend was used to compare proportions across three or more groups. The Kruskall-Wallis test (birth weight) and the Wilcoxon rank sum test (Hb) were used to compare continuous variables with non-normal distributions. Doses of IPTp/SP were collapsed into any dose versus no dose for stratified analysis at ANCs because of limited sample size within strata. To evaluate the relationship of IPTp/SP use and peripheral malaria infection, anemia, placental malaria infection, and LBW, Poisson log-linear models were constructed through backward elimination. Use of IPTp/SP was maintained in each of the models regardless of statistical significance. Tests were considered significant when the two-sided P value was < 0.05. Stata software release 7.0 (Stata Corporation, College Station, TX) and SAS release 9.1 (SAS Institute, Cary, NC) were used for all analyses.

**RESULTS**

We enrolled 826 women at the 6 ANCs and 1,188 women at the 2 DUs. Overall, 20 eligible women (2.4%) refused enrollment at ANCs and 33 (2.8%) at DUs.

### Table 1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>2004 Antenatal clinic (6 sites n = 826)</th>
<th>2004 Delivery unit (2 sites n = 1,188)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age in years (range)</td>
<td>25 (15–51)</td>
<td>24 (15–54)</td>
</tr>
<tr>
<td>Median gravidity (range)</td>
<td>3 (1–13)</td>
<td>2 (1–12)</td>
</tr>
<tr>
<td>Median number ANC visits (range)</td>
<td>2 (1–5)</td>
<td>3 (0–6)</td>
</tr>
<tr>
<td>Urban</td>
<td>46.1</td>
<td>81.4</td>
</tr>
<tr>
<td>Language. Mooré</td>
<td>92.9</td>
<td>95.0</td>
</tr>
<tr>
<td>Religion, Muslim</td>
<td>65.4</td>
<td>64.1</td>
</tr>
<tr>
<td>Able to read French</td>
<td>11.5</td>
<td>20.6</td>
</tr>
<tr>
<td>Attended school (any)</td>
<td>12.7</td>
<td>22.9</td>
</tr>
<tr>
<td>Married</td>
<td>90.9</td>
<td>87.5</td>
</tr>
<tr>
<td>Type of housing/cement floor</td>
<td>63.0</td>
<td>83.9</td>
</tr>
<tr>
<td>Owns moped</td>
<td>47.3</td>
<td>61.5</td>
</tr>
<tr>
<td>Owns radio</td>
<td>89.9</td>
<td>94.6</td>
</tr>
<tr>
<td>Works for cash</td>
<td>45.5</td>
<td>38.9</td>
</tr>
<tr>
<td>Self-reported ownership and use of bed nets</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Owns bed net</td>
<td>53.9</td>
<td>61.6</td>
</tr>
<tr>
<td>Owns insecticide-treated bed net†</td>
<td>58.4</td>
<td>57.3</td>
</tr>
<tr>
<td>Sleeps under bed net all the time†</td>
<td>69.7</td>
<td>59.5</td>
</tr>
<tr>
<td>Use of IPTp with SP</td>
<td>n = 826§</td>
<td>n = 1,174§</td>
</tr>
<tr>
<td>None</td>
<td>3.8</td>
<td>6.5</td>
</tr>
<tr>
<td>Any dose</td>
<td>96.2</td>
<td>93.5</td>
</tr>
<tr>
<td>1</td>
<td>38.6</td>
<td>14.9</td>
</tr>
<tr>
<td>2</td>
<td>36.7</td>
<td>31.7</td>
</tr>
<tr>
<td>3</td>
<td>20.9</td>
<td>46.9</td>
</tr>
<tr>
<td>Gestational age at first dose of IPTp with SP, median weeks, (range)</td>
<td>28 (16–41)</td>
<td>27 (12–42)</td>
</tr>
</tbody>
</table>

* Data are % unless otherwise indicated. ANC = antenatal clinic; IPTp = intermittent preventive treatment during pregnancy.
† Of women who reported owning a net.
‡ Data on the use of IPTp/SP were taken directly from ANC cards/maternal health cards.
§ Data include women who received doses on the date of the interview to determine overall coverage.
Characteristics of enrolled women. Characteristics of enrolled women are summarized in Table 1. The median age of enrolled women at the ANC and DU sites was 25 and 24 years, respectively. Most women spoke Mooré. Self report indicated that 53.9% of the women enrolled at ANCs and 61.6% of the enrolled women at DUs owned a bed net. Of those who owned bed nets, more than half of the nets were treated with insecticide.

The proportion of women who took any dose of IPTp/SP was 93.5% among those enrolled at ANCs and 96.2% of those enrolled at DUs. Two or more doses of IPTp/SP (WHO standard) were taken by 57.6% of women at ANCs and 78.6% at DUs. The pilot program’s recommended three doses of SP were taken by 20.9% of enrolled women at ANCs and 46.9% of enrolled women at DUs. The median gestational age at start of first dose of SP was 28 weeks for those at ANCs and 27 weeks for those at DUs.

Malaria parasitemia and anemia among women at ANCs. The overall proportion of pregnant women who had *P. falciparum* infection was 25.1% (0.36% were infected with *P. malariae* and 0.24% with *P. ovale*), ranging from 29.3% in primigravidas to 20.4% in multigravidas (*P = 0.003*, by chi-square test for trend; Table 2). Among pregnant women with at least one prior ANC visit, the proportion of parasitemic primigravidas was lower among those with ≥ 1 dose of IPTp/SP (16.7%) than among women with no use of IPTp/SP (44.4%; *P = 0.01*). This difference was not observed for secundigravidas or multigravidas.

Among all women, 28.2% reported having had one or multiple episodes of fever during the course of their pregnancies. Among pregnant women with at least one prior ANC visit, the proportion reporting fever was lower among those with ≥ 1 dose of IPTp/SP (29.1%) than among women with no use of IPTp/SP (52.5%; *P = 0.0002*; Table 2).

Among pregnant women with ≥ 1 ANC visit, the mean Hb level was not statistically different between women with ≥ 1 dose of IPTp/SP and women with no use of IPTp/SP (Table 2). The proportion of anemia among all women was 63.7%; 4.8% had moderate-to-severe anemia. There were no differences in the proportion of women with anemia or moderate-to-severe anemia when comparing women who did or did not take IPTp/SP (Table 2).

Multivariate analysis showed a statistically significant association between use of IPTp/SP (≥ 1 dose) and peripheral parasitemia at ANC (risk ratio [RR] = 0.49, *P = 0.008*; Table 3) after adjusting for gravidity, number of ANC visits, fever within week before enrollment, and living in a rural area.

In multivariate analysis, the use of IPTp (≥ 1 dose) was not associated with maternal anemia at ANCs (Table 3). High use of ANC services (≥ 3 ANC visits) was associated with a reduced risk of anemia when compared with those having made no ANC visits (Table 3).

Malaria parasitemia and birth outcomes among delivering women. Overall, 19.4% of delivering women had peripheral *P. falciparum* infection (0.08% were infected with *P. malariae* and no women were infected with *P. ovale*) ranging from 22.9% in primigravidas to 20.0% in secundigravidas and 17.1% in multigravidas (*P = 0.03*, by chi-square test for trend) (Table 4). Overall, the proportion of women with peripheral parasitemia was lower among those with three doses of IPTp/SP (17.4%) than among those with no dose of IPTp/SP (36.8%). This difference was also significant in stratified analysis for primigravid and secundigravid women but not for multigravid women (Table 4).

Overall, 15.9% of delivering women had placental *P. falciparum* infection (no women were infected with either *P. malariae* or *P. ovale*), which varied from 23.4% in primigravidas to 10.9% in multigravidas (*P < 0.0001*, by chi-square test for trend) (Table 4). Overall, the proportion of women with placental parasitemia was lower among those with three

---

**Table 2**

Peripheral parasitemia, reported fever, and anemia among women attending antenatal clinics (ANCs) in Koupéla District, Burkina Faso, 2004

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All women (n = 826)</th>
<th>Women with no prior ANC visits (n = 258)</th>
<th>Women with at least 1 prior ANC visit (n = 568)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Peripheral parasitemia</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>25.1</td>
<td>57.6% ± 8.9</td>
<td>45.7</td>
</tr>
<tr>
<td>Primigravidas</td>
<td>29.3</td>
<td>59.0% ± 8.7</td>
<td>67.8</td>
</tr>
<tr>
<td>Secundigravidas</td>
<td>33.3</td>
<td>65.3% ± 7.8</td>
<td>50.0</td>
</tr>
<tr>
<td>Multigravidas (≥ 3 pregnancies)</td>
<td>20.4%</td>
<td>36.7% ± 7.4</td>
<td>17.8</td>
</tr>
<tr>
<td>Reported fever during pregnancy (%)</td>
<td>28.2</td>
<td>20.9% ± 7.9</td>
<td>29.1</td>
</tr>
<tr>
<td>Reported fever within week before enrollment</td>
<td>6.3</td>
<td>6.6% ± 7.0</td>
<td>5.9</td>
</tr>
<tr>
<td>Fever (≥ 37.5°C) at visit</td>
<td>1.1</td>
<td>1.6% ± 0.9</td>
<td>1.5</td>
</tr>
<tr>
<td>Hemoglobin g/dL, mean ± SD</td>
<td>10.5 ± 1.5</td>
<td>10.0 ± 1.4</td>
<td>10.6 ± 1.4</td>
</tr>
<tr>
<td>Anemia (% Hb &lt; 11 g/dL)</td>
<td>Overall</td>
<td>63.7% ± 7.3</td>
<td>60.3</td>
</tr>
<tr>
<td>Primigravidas</td>
<td>63.2% ± 7.2</td>
<td>62.3% ± 5.5</td>
<td>55.3</td>
</tr>
<tr>
<td>Secundigravidas</td>
<td>63.8% ± 7.3</td>
<td>73.5% ± 8.6</td>
<td>59.7</td>
</tr>
<tr>
<td>Multigravidas (≥ 3 pregnancies)</td>
<td>63.9% ± 8.8%</td>
<td>68.6% ± 9.6</td>
<td>62.6</td>
</tr>
<tr>
<td>Moderate to severe anemia (%Hb &lt; 8 g/dL)</td>
<td>Overall</td>
<td>4.8% ± 0.7</td>
<td>3.5</td>
</tr>
<tr>
<td>Primigravidas</td>
<td>5.9% ± 0.7</td>
<td>12.8% ± 6.0</td>
<td>3.5</td>
</tr>
<tr>
<td>Secundigravidas</td>
<td>4.0% ± 0.7</td>
<td>4.1% ± 0.5</td>
<td>4.4</td>
</tr>
<tr>
<td>Multigravidas (≥ 3 pregnancies)</td>
<td>4.8% ± 0.7</td>
<td>7.7% ± 1.0</td>
<td>3.2</td>
</tr>
</tbody>
</table>

* Data are % unless otherwise indicated. IPTp = intermittent preventive treatment during pregnancy; SP = sulfadoxine-pyrimethamine; Hb = hemoglobin.
† Data on IPTp with SP were taken from maternal health cards, not self-report.
‡ P value from *χ²* for categorical variables, Fisher’s exact test for variables with an expected cell value < 5, Wilcoxon test statistic for continuous variables (hemoglobin); comparison is between women who took any dose of IPTp and those who took no dose.
¶ P = 0.003, by χ² test for trend.
§ P = 0.0007, by χ² test for trend.
# P = 0.004, by χ² test for trend.
Table 3
Multivariate analysis of factors associated with peripheral parasitemia and anemia among women visiting any of the six antenatal clinics in Koupéla District, Burkina Faso, 2004 *

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adjusted risk ratio</th>
<th>95% confidence interval</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Associated with peripheral malaria†‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of IPTp with SP§</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>1</td>
<td>Reference</td>
<td>–</td>
</tr>
<tr>
<td>1, 2, or 3 doses</td>
<td>0.49</td>
<td>0.29–0.83</td>
<td>0.008</td>
</tr>
<tr>
<td>Gravidity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multigravid (≥ 3 pregnancies)</td>
<td>1</td>
<td>Reference</td>
<td>–</td>
</tr>
<tr>
<td>Secundigravid</td>
<td>1.79</td>
<td>1.29–2.48</td>
<td>0.0004</td>
</tr>
<tr>
<td>Primigravid</td>
<td>1.75</td>
<td>1.23–2.48</td>
<td>0.002</td>
</tr>
<tr>
<td>ANC visits</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 or 1</td>
<td>1</td>
<td>Reference</td>
<td>–</td>
</tr>
<tr>
<td>2</td>
<td>0.63</td>
<td>0.37–1.08</td>
<td>0.09</td>
</tr>
<tr>
<td>≥ 3</td>
<td>0.56</td>
<td>0.32–0.99</td>
<td>0.05</td>
</tr>
<tr>
<td>Fever within week before enrollment</td>
<td>1.75</td>
<td>1.12–2.73</td>
<td>0.01</td>
</tr>
<tr>
<td>Rural</td>
<td>1.70</td>
<td>1.27–2.29</td>
<td>0.0004</td>
</tr>
</tbody>
</table>

Associated with anemia†#

| Use of IPTp with SP§    |                     |                         |       |
| None                    | 1                   | Reference               | –     |
| 1, 2, or 3 doses        | 1.19                | 0.83–1.70               | 0.34  |
| Rural                   | 1.27                | 1.06–1.51               | 0.009 |
| ANC visits              |                     |                         |       |
| 0 or 1                  | 1                   | Reference               | –     |
| 2                       | 0.75                | 0.51–1.09               | 0.13  |
| ≥ 3                     | 0.66                | 0.44–0.97               | 0.03  |

* Multigravid ≥ 3 pregnancies. IPTp = intermittent preventive treatment during pregnancy; SP = sulfadoxine-pyrimethamine; ANC = antenatal clinic.
† Model retains IPTp with SP regardless of significance. Other variables evaluated for this model, but not retained, included insecticide-treated net use or ownership, religion (Muslim), malaria treatment, and age. No other variables were significant in bivariate analysis with peripheral parasitemia.
‡ Information for correct number of SP doses was obtained from ANC cards; doses given on the same day as the interview were not counted.
§ Model retains IPTp with SP regardless of significance. Other variables evaluated for this model, but not retained, included ITN use or ownership, age, peripheral parasitemia, owning a stove, livestock and red meat, religion (Muslim), and gravidity.
# n = 826.

Doses of IPTp/SP (13.7%) than among those with no IPTp/SP (30.3%). This difference was also significant in stratified analysis for primigravid and secundigravid women but not for multigravid women (Table 4).

Among all delivering women, 27.9% reported having one or multiple episodes of fever during the course of their pregnancies (Table 4). The proportion of delivering women reporting fever was lower among those with three doses of IPTp/SP (29.6%) than among those with no use of IPTp/SP (38.2%).

The overall proportion of delivering women who reported episodes of fever within the week before enrollment was 2.7% (Table 4). The proportion of women reporting fever in the week before enrollment was lower among those with three doses of IPTp/SP (2.7%) than among those with no use of IPTp/SP (7.9%).

Among all delivering women, 20.8% reported having used antimalarials for treatment during the course of their pregnancies (Table 4). The proportion of delivering women reporting antimalarial use was lower among those with three doses of IPTp/SP (22.3%) than among women with no use of IPTp/SP (31.6%).

The mean ± SD singleton live-born birth weight was 2,981 ± 438 grams (Table 4). Overall, the mean singleton live-born birth weight was 3,062 grams for three SP doses, 2,869 grams for 1 SP dose, and 2,861 grams for no SP doses (P < 0.0001).

The overall proportion of delivering women with an LBW live-born singleton was 12.2%, ranging from 23.9% in primigravidae to 5.9% in multigravidae (P < 0.0001, by chi-square test for trend, Table 4). Overall, the proportion of women with an LBW infant was lower among those with three doses of IPTp/SP (7.8%) than among those with no IPTp/SP (24.2%). This difference was noted for primigravid and multigravid women but not for secundigravid women (Table 4).

In multivariate analysis, women who took two or three doses of IPTp/SP had a lower risk of placental parasitemia when compared with those who took no doses (RR = 0.56 and 0.51, P = 0.006 and P = 0.02) (Table 5). Low gravidity, a history of treatment with an antimalarial during pregnancy, living in a rural area, and having no education were also independent risk factors for placental malaria infection.

In multivariate analysis, women who took three doses of IPTp/SP had a lower risk of delivering LBW infants when compared with those who took no dose (RR = 0.51, P = 0.04; Table 5). Women who had ≥ 3 ANC visits had a lower risk of having an LBW infant compared with those who had no ANC visit (RR = 1.39, P = 0.01). Low gravidity and being female were also independently associated with increased risk of LBW.

Comparison between 2001 (baseline) and 2004 (follow-up). Figure 1 summarizes key outcome variables from the 2001 and 2004 evaluations at ANCs. The proportion of pregnant women with peripheral parasitemia at ANCs was lower in 2004 (15.7%) compared with women in 2001 (29.7%; RR = 0.53, P = 0.001). The proportion of pregnant women with anemia was significantly lower in 2004 (59.3%) compared with those in 2001 (75.8%; RR = 0.78, P = 0.003). The proportion of pregnant women with moderate-to-severe anemia was also significantly lower in 2004 (3.5%) when compared with pregnant women in 2001 (11.0%; RR = 0.32, P = 0.004).

Figure 2 summarizes key outcome variables from the 2001 and 2004 evaluations at DUs. The proportion of pregnant women with peripheral parasitemia at DUs was significantly lower in 2004 (19.4%) compared with women in 2001 (29.4%; RR = 0.66, P < 0.0001). The proportion of pregnant women with placental parasitemia was significantly lower in 2004 (15.9%) compared with those in 2001 (22.6%; RR = 0.71, P = 0.0002). Although the proportion of women delivering LBW babies was lower in 2004 (12.2%) than in 2001 (14.4%), this result did not reach statistical significance.

DISCUSSION

In a rapid assessment of a program to prevent malaria during pregnancy in Koupéla District, Burkina Faso, we found very high coverage with the primary intervention (IPTp/SP) among women attending antenatal and delivery facilities. The proportion of women with peripheral and placental parasitemia and with anemia was significantly lower in the 2004 assessment than in 2001. We also found in multivariate analysis that use of IPTp/SP was associated with reductions in peripheral parasitemia among women attending ANCs, and peripheral and placental parasitemia and LBW among delivering women. In general, this effect was statistically significant for women who received two or three doses of IPTp/SP, but not for women receiving a single dose. Only taking three doses of IPTp/SP was associated with a reduction in LBW.
Peripheral and placental parasitemia, reported fever, and low birth weight among delivering women in Koupéla District, Burkina Faso, 2004*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All women (n = 1,188)</th>
<th>Use of IPTp with SP</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of women with peripheral parasitemia (n = 1,163)</td>
<td>19.4</td>
<td>17.4</td>
</tr>
<tr>
<td>Overall</td>
<td>22.9</td>
<td>19.9</td>
</tr>
<tr>
<td>Primigravidae</td>
<td>23.4</td>
<td>20.4</td>
</tr>
<tr>
<td>Secundigravida</td>
<td>17.3</td>
<td>9.1</td>
</tr>
<tr>
<td>% of women with placental parasitemia (n = 1,173)</td>
<td>15.9</td>
<td>13.7</td>
</tr>
<tr>
<td>Overall</td>
<td>23.4</td>
<td>19.1</td>
</tr>
<tr>
<td>Primigravidae</td>
<td>17.3</td>
<td>9.1</td>
</tr>
<tr>
<td>% of women who reported fever during pregnancy</td>
<td>10.9 (§)</td>
<td>11.6</td>
</tr>
<tr>
<td>% of women who reported taking an antimalarial for treatment during pregnancy</td>
<td>27.9</td>
<td>29.6</td>
</tr>
<tr>
<td>% of women who reported fever within week before enrollment (n = 1,186)</td>
<td>20.8</td>
<td>22.3</td>
</tr>
<tr>
<td>Singleton live-born birth weight, mean (g) ± SD</td>
<td>2,981 ± 438</td>
<td>3,062 ± 414</td>
</tr>
<tr>
<td>% of women who reported fever within week before enrollment (n = 1,133)</td>
<td>2.7</td>
<td>2.7</td>
</tr>
<tr>
<td>% of women who reported taking a reduction in malaria during pregnancy (n = 1,186)</td>
<td>12.2</td>
<td>7.8</td>
</tr>
<tr>
<td>Overall</td>
<td>23.9</td>
<td>13.0</td>
</tr>
<tr>
<td>Primigravidae</td>
<td>9.9</td>
<td>7.7</td>
</tr>
<tr>
<td>Secundigravida</td>
<td>5.9 (¶)</td>
<td>4.6</td>
</tr>
</tbody>
</table>

* Data are % unless otherwise indicated. IPTp = intermittent preventive treatment during pregnancy; SP = sulfadoxine-pyrimethamine.
† P value from χ² for categorical variables or Fisher's exact test for variables with expected cell value < 5. Kruskal-Wallis test for continuous variable (birth weight); χ², Fisher's exact test statistic, and Kruskal-Wallis test statistic across all 4 groups (0, 1, 2, or 3 doses).
‡ P < 0.05, by χ² test for trend.
§ P < 0.0001, by χ² test for trend.
¶ P < 0.0001, by χ² test for trend.

As we found in the baseline assessment in 2001 and has been observed elsewhere,17–19 primigravid women, and to a lesser extent secundigravid women, were at greater risk of peripheral and placental parasitemia and LBW; we did not note this association for anemia in the 2004 assessment. In stratified analysis, the association between IPTp/SP use and a reduction in malaria during pregnancy was generally stronger (and only significant) for primigravid and secundigravid women, although the assessment was not powered to examine these stratified differences.

Our evaluation also showed an increase in the ownership of ITNs by pregnant women in Koupéla District. More than half of women reported owning a bed net in 2004, increased from one-third of the women in 2001. Multivariate analysis of the 2004 data did not show an association between ITN ownership and a reduction in malaria during pregnancy or its adverse consequences, perhaps because of the high coverage with IPTp/SP in this population.

Although we cannot be sure that the reduction in malaria during pregnancy observed from 2001 to 2004 is attributable to IPTp/SP and ITNs, this remains the most likely explanation. The assessment sites chosen and the time frame used were identical between 2001 and 2004. There have been no other known changes to the malaria control strategy or to malaria transmission in the district that would plausibly account for the observed reduction. In fact, the average amount of rainfall for the months of June through October was greater in 2004 than 2001 and the number of cases of uncomplicated and severe malaria was also greater in 2004 than 2001. These differences should have biased our results towards the null hypothesis.

The principal findings of this assessment are concurrent with published efficacy trials5–9 and program effectiveness evaluations.10–12 For example, a clinical trial in Mali found that IPTp/SP was more efficacious in reducing adverse outcomes compared with chloroquine chemoprophylaxis or two doses of IPTp/SP with chloroquine.7 The effectiveness of IPTp/SP has also been demonstrated in previous studies.10–12

In Malawi, a program evaluation showed that IPTp/SP was associated with reductions in anemia, placental parasitemia, and LBW (comparing ≥ 2 doses of SP with no dose).10

The assessment has several important limitations. The evaluation was completed during the peak malaria transmission season from June through November (the same time period as the baseline). Given the seasonal variation in the region, overall proportions of parasitemia may be overestimated. However, the risks associated with peripheral and placental parasitemia are not thought to be seasonally dependent and therefore should not bias results demonstrating associations between the use of IPTp/SP and reductions in peripheral and placental malaria infection and LBW. Although enrollment of women at ANCs was limited to those in their third trimester, a number of women were nonetheless presenting for a first ANC visit, and therefore, were receiving their first dose of IPTp/SP. Some women took IPTp/SP doses at home rather than observed in clinic; it is possible that not all of these doses were actually taken as reported. In addition, pre- and post-intervention assessments such as were done in Koupéla District are prone to the introduction of hidden biases. Although we made every effort to make the assessments comparable (in terms of sites and timing of enrollment), and we have data that suggest 2004 was a year with an even greater malaria burden than 2001, it is possible that the populations differed in unmeasured ways that might have affected the results. Finally, data regarding bed net ownership and usage was gathered from self-report because observational data on bed nets and their use could not be collected in the context of this facility-based assessment.
Table 5
Multivariate analysis of factors associated with placental parasitemia and low birth weight among delivering women in Koupéla District, Burkina Faso, 2004*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adjusted risk ratio</th>
<th>95% confidence interval</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Associated with placental malaria†</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of IPTp with SP‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>1 Reference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 dose</td>
<td>0.77</td>
<td>0.45–1.33</td>
<td>0.36</td>
</tr>
<tr>
<td>2 doses</td>
<td>0.56</td>
<td>0.34–0.93</td>
<td>0.02</td>
</tr>
<tr>
<td>3 doses</td>
<td>0.51</td>
<td>0.32–0.83</td>
<td>0.006</td>
</tr>
<tr>
<td>Gravidity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multigravid (≥ 3 pregnancies)</td>
<td>1 Reference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secundigravid</td>
<td>1.55</td>
<td>1.04–2.33</td>
<td>0.03</td>
</tr>
<tr>
<td>Primigravid</td>
<td>2.04</td>
<td>1.46–2.89 &lt; 0.0001</td>
<td></td>
</tr>
<tr>
<td>Treatment with antimalarial</td>
<td>1.97</td>
<td>1.45–2.69 &lt; 0.0001</td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>1.58</td>
<td>1.14–2.19</td>
<td>0.006</td>
</tr>
<tr>
<td>No school</td>
<td>1.52</td>
<td>1.04–2.22</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>Associated with low birth weight</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(&lt;2,500 grams)§¶</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of IPTp with SP‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>1 Reference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 dose</td>
<td>0.59</td>
<td>0.27–1.28</td>
<td>0.18</td>
</tr>
<tr>
<td>2 doses</td>
<td>0.67</td>
<td>0.36–1.27</td>
<td>0.23</td>
</tr>
<tr>
<td>3 doses</td>
<td>0.51</td>
<td>0.27–0.95</td>
<td>0.04</td>
</tr>
<tr>
<td>Gravidity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multigravid</td>
<td>1 Reference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secundigravid</td>
<td>1.94</td>
<td>1.12–3.36</td>
<td>0.02</td>
</tr>
<tr>
<td>Primigravid</td>
<td>4.59</td>
<td>3.01–7.00 &lt; 0.0001</td>
<td></td>
</tr>
<tr>
<td>ANC visits</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 or 1</td>
<td>1 Reference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>0.54</td>
<td>0.26–1.13</td>
<td>0.10</td>
</tr>
<tr>
<td>≥ 3</td>
<td>0.37</td>
<td>0.17–0.82</td>
<td>0.01</td>
</tr>
<tr>
<td>Female sex of neonate</td>
<td>1.39</td>
<td>0.99–1.96</td>
<td>0.06</td>
</tr>
</tbody>
</table>

* Multigravid ≥ 3 pregnancies IPTp = intermittent preventive treatment during pregnancy; SP = sulfadoxine-pyrimethamine.
† Model retains IPTp/SP regardless of significance. Other variables evaluated for this model, but not retained, include insecticide-treated net (ITN) use or ownership; age; socioeconomic indicators (type of floor, ownership of radio, bicycle, moped, car), history of fever, and peripheral malaria parasitemia at delivery; n = 1,173.
‡ Information for correct number of SP doses was obtained from ANC cards.
§ Analysis restricted to live-born singleton neonates (n = 1,136).
¶ Model retains IPTp with SP regardless of significance. Other variables evaluated for this model, but not retained, include ITN use or ownership; age; history of fever; malaria treatment, placental parasitemia, socioeconomic indicators (type of floor, ownership of radio, bicycle, moped, car), living in a rural area, mid-upper-arm circumference, short height, and delivery site.

The fact that such high coverage rates with IPTp/SP (and with ITNs) were achieved in the 17 months during which this pilot program was ongoing demonstrates that the intervention is appropriate and feasible for Burkina Faso. However, this pilot experience also uncovered some programmatic challenges that will need addressing if the program is to be scaled-up nationally. One is that more than half of all enrolled women at both ANCs and DUs took SP at home, not as directly observed therapy (DOT), as was stated in the guidelines. The reasons given by health care workers for this failure to follow the DOT guidelines included women not bringing their own water or cup to an ANC visit (although those items were supposed to be available in all clinics) and some health care workers believing erroneously that SP should not be given to a woman who had not eaten prior to her ANC visit. These health care workers advised the women to take the drug at home at dinner time. There is no evidence of any side effects of SP if taken on an empty stomach and the WHO guidelines for malaria prevention during pregnancy using IPTp/SP do not include such a limitation. Another limitation was that women were often charged for the SP, despite the initial Ministry of Health declaration that the medicine would be free.

The fact that such high coverage was achieved in the face of charging for the intervention is surprising and encouraging and may have a direct relationship to improved quality of antenatal care services. Finally, women continue to come relatively late for antenatal care. Although WHO recommends four ANC visits, one of which should take place before quickening, women at the health facilities in this assessment did not make a first ANC visit until a median of 28 weeks gestation for ANCs and 24 weeks gestation for DUs. This late delivery of a first dose of IPTp likely results in diminished effectiveness of the intervention. Our finding that an increase in number of ANC visits is independently correlated with a reduction in many of the relevant indicators of malaria during pregnancy only serves to underscore the importance of access to quality ANC services.

Currently, WHO recommends that pregnant women living in malaria-endemic areas receive at least two doses of IPTp/SP during their scheduled ANC visit in the second or third trimesters. These program data continue to lend support to the effectiveness of this intervention. These data also suggest that a package of three doses of IPTp/SP and ITNs is...
effective in reducing malaria during pregnancy and its adverse outcomes in Burkina Faso. It would be worthwhile to investigate the impact of this package elsewhere in sub-Saharan Africa.

Although the follow-up assessment in Koupéla District was not powered to look at two versus three doses of SP, multivariate analysis showed that women who took three doses of SP had a significantly lower risk of delivering an LBW infant compared with those who took no dose of SP. This package of three doses of SP and ITNs appears to reduce adverse outcomes of malaria infection during pregnancy and it is plausible that an intervention aiming at three doses may result in more women getting ≥ 2 doses of SP. Furthermore, it is evident that an overall improvement of ANC services including multiple interventions may inherently lower a woman’s risk of malaria infection during pregnancy.

In summary, this program assessment in Burkina Faso demonstrated high coverage rates with IPTp and ITNs, and showed a reduction in the proportion of women with malaria during pregnancy and its adverse outcomes when comparing 2004 with 2001 (when a program of chloroquine chemoprophylaxis was in place). These results suggest that IPTp/SP and ITNs may be a more effective strategy to prevent malaria during pregnancy in Burkina Faso than chloroquine chemoprophylaxis.

Received December 6, 2005. Accepted for publication March 26, 2006.

Acknowledgments: We thank JHPIEGO, including Jérémie Zoungrana, Cecile Somda, Sidibé Samba, Aimee Dickerson, and Rebecca Dineen, and Dr. Xavier Pitríopa (Director of the Centre National de Recherche et de Formation sur le Paludisme) for program assistance, Amidou Ouédraogo (Centre National de Recherche et de Formation sur le Paludisme) for data management, Dr. Sara Crawford (Centers for Disease Control and Prevention) for assistance with data analysis, and members of the team in Burkina Faso and all women and their newborns who participated in this assessment.

Financial support: This assessment was supported by the United States Agency for International Development through the Malaria Action Coalition, the Centers for Disease Control and Prevention, and JHPIEGO Corporation.

Disclaimer: Use of trade names is for identification only and does not imply endorsement by the Public Health Service or by the U.S. Department of Health and Human Services.

Disclosure: None of the authors had any conflicts of interest.


Reprint requests: Robert D. Newman, Malaria Branch, Centers for Disease Control and Prevention, 4770 Buford Highway NE, Mailstop F-22, Atlanta, GA 30341, Telephone: 4770-488-7755, Fax: 4770-488-4206, E-mail rdnS@cdc.gov.

REFERENCES


