

# Determinants of anemia among pregnant women in Mali

Mohamed Ag Ayoya, Gerburg Maria Spiekermann-Brouwer, Abdel Kader Traoré, Rebecca Joyce Stoltzfus, and Cutberto Garza

## Abstract

**Background.** Anemia in pregnancy remains a major problem in nearly all developing and many industrialized countries. In Mali, the subpopulation prevalence and etiology of anemia during pregnancy are largely unknown.

**Objective.** To examine the prevalence and likely etiologies of anemia in pregnancy in a poor urban population in Bamako, Mali.

**Methods.** Pregnant women ( $n = 190$ ) were selected randomly. Hemoglobin, serum iron, and total iron-binding capacity were measured; blood smears were examined for *Plasmodium falciparum* malaria; and single stool and urine samples were examined for *Schistosoma haematobium* and hookworm. Gynecologic examinations were performed and interviews conducted to qualitatively assess food consumption and other socioeconomic characteristics. Associations among mild, moderate, and severe anemia; iron and parasite status; erythrocyte sedimentation rates; and the presence of abnormal vaginal discharge were evaluated. Differences in hemoglobin and serum iron concentrations, total iron-binding capacity, and anemia were compared according to trimester of pregnancy and between infected and noninfected women. The relative and attributable risks of anemia were calculated, and adjusted odds ratios for anemia and low serum iron were estimated by multivariate logistic regression.

**Results.** Of the 131 women for whom complete data were available, 47% had hemoglobin concentrations below 110 g/L; 13% had serum iron concentrations below

12  $\mu\text{mol/L}$ ; none had transferrin saturation values below 16%; 11%, 23%, and 8% harbored *P. falciparum*, *S. haematobium*, and hookworm, respectively; and 82% had an abnormal vaginal discharge. Food restrictions were reported by 45% of the women. Abnormal vaginal discharge correlated significantly with anemia (Pearson  $\chi^2 = 62.4$ ;  $p < .01$ ). Univariate and multivariate analyses found that infections were strongly associated with and predictive of anemia.

**Conclusions.** Our data suggest that infections and food accessibility contribute to the high rates of anemia during pregnancy in Mali.

**Key words:** anemia, pregnancy, malaria, hookworm, *Schistosoma haematobium*, vaginal discharge, food restrictions, Mali

## Introduction

Anemia in pregnancy remains a major problem in nearly all developing and many industrialized countries. The World Health Organization (WHO) estimates that 35% to 75% (56% on average) of pregnant women in developing countries and 18% of those in industrialized countries are anemic [1]. In 1995, the WHO projected the average prevalence of anemia in pregnant women to be about 52% in Africa [2]; however, its prevalence varies considerably among that continent's countries and in subpopulations within countries. Reports from regional surveys in Mali estimated that the mean prevalence of anemia among pregnant women was between 41% and 59% [3]. These unacceptably elevated rates are of concern because of the high likelihood that anemia during pregnancy places affected women at greater risk of pre- and postpartum morbidities and mortality [4–6] and is also associated with an increased risk of poor infant outcomes that may be long-lasting and only partially reversible unless corrected early [7, 8].

The most common worldwide cause of anemia

---

Mohamed Ag Ayoya, Gerburg Maria Spiekermann-Brouwer and Rebecca Joyce Stoltzfus are affiliated with the Division of Nutritional Sciences, Cornell University, Ithaca, New York, USA. Abdel Kader Traoré is affiliated with the Ministry of Health and the School of Medicine, Bamako, Mali. Cutberto Garza is affiliated with Boston College, Boston, Massachusetts, USA.

Please direct queries to the corresponding author: Cutberto Garza, MD, PhD, Academic Vice President and Dean of Faculties, Bourneuf House, Boston College, Chestnut Hill, MA 02467, USA; e-mail: Bert.Garza@bc.edu.

during pregnancy is purported to be iron deficiency due to chronically inadequate dietary iron; this inadequacy is heightened by the physiologic demands for this essential element imposed by fetal needs and maternal blood volume expansion during pregnancy. In many tropical regions, the absorption of dietary iron and the utilization of endogenous and exogenous iron are also influenced adversely by common states of chronic infection and inflammation due to malaria and multiple helminthic infections [9–11]. The relative impacts of these potential causes vary by sex, age, geography, and various other sociodemographic risk factors that are not well described in most presumably iron-deficient populations [10].

The subpopulation prevalence and etiology of anemia during pregnancy are largely unknown in Mali. Thus, a cross-sectional study was undertaken to examine the prevalence of anemia during pregnancy and the likely etiologic factors associated with it in a presumably high-risk population. The study was designed to assess relationships among anemia, malaria, and other parasitic diseases (e.g., hookworm and schistosomiasis), inform local and regional micronutrient fortification and supplementation policies, promote effective prevention and control strategies in Mali, and identify research needs to strengthen those aims in future efforts undertaken by the government and other actors with interests in enhancing the well-being of pregnant women.

## Methods

The study was conducted in Banconi, one of the poorest and most densely populated suburban areas of the capital city of Bamako, from June to August 2002. *Plasmodium falciparum* malaria and infections with *Schistosoma haematobium* and hookworm were suspected to be highly endemic in this area.

The study protocol was reviewed and approved by the Malian Ministry of Health in Bamako, the board of directors and medical staff of the community health center in Bamako, and the Cornell University committee on human subjects, Ithaca, New York, USA. The women were informed individually of the purpose of the study in Bamanan (the local dialect) and asked to sign a consent form prior to enrollment.

### Subjects and data collection

The study population consisted of women 18 to 45 years old who were attending the community health center. All pregnant women who visited the center during the study period were invited to participate. None of those invited to participate declined. The eligibility criteria for consenting participants included no oral iron or anthelmintic treatment since the beginning

of the pregnancy and no blood transfusion within the 3 months preceding entry into the study. Of the 190 pregnant women enrolled, 131 (69%) provided information on selected demographic characteristics and food habits and gave blood, urine, and stool specimens for the assessment of various hematologic indicators and chronic infections.

Initial participant interviews were used to ascertain various demographic and dietary factors associated with nutritional risk. Venous blood was obtained for a complete blood count (including hemoglobin concentration), for measurement of erythrocyte sedimentation rate, serum iron, and total iron-binding capacity, and to determine the presence of malarial parasitemia. Stool and urine samples were requested to determine whether hookworm or schistosomiasis infection was present. A gynecologic examination also was performed during the initial clinical contact.

All participants were provided with sufficient supplements for a 30-day course of ferrous fumarate and folate tablets containing 64 mg of elemental iron and 400 µg of folate. A 4-week course of chloroquine (three 100-mg tablets per week) was also provided as a preventative against malaria.

The examining physician used a structured questionnaire at the initial interview to record the participant's age, weight, height, parity, stage of pregnancy, diet, marital status, literacy, household possessions, workload, and socioeconomic status. Self-imposed or socially imposed food restrictions were identified and categorized as present or absent, and workloads were classified as unchanged from, less than, or more than those before the current pregnancy.

Weight was measured to the nearest 0.1 kg with a battery-powered electronic scale (Seca, Hamburg, Germany) and height was measured to the nearest 0.1 cm with a locally produced portable instrument whose design is based on a model recommended by UNICEF. Height was measured when the subject was not wearing shoes or head covering.

Venous blood samples (10 mL) were collected from the antecubital fossa by standard antiseptic techniques. Urine and stool samples were collected in the clinic. Women unable to provide a stool sample on the initial visit were asked to bring in a sample on the following day. All samples were processed on the day of collection.

Complete blood counts were obtained from a Diana-5 hematology analyzer calibrated regularly with appropriate controls according to the manufacturer's recommended specifications (Hycel Diagnostics, Massy, France). The erythrocyte sedimentation rate was determined by the Westergren method recommended by the International Committee for Standardization in Hematology [12]. Hemoglobin and serum iron concentrations and total iron-binding capacity were measured. Transferrin saturation was derived from

serum iron and total iron-binding capacity. Hemoglobin also was measured as part of the complete blood count from the Diana-5 hematology analyzer. Serum iron and total iron-binding capacity were determined with a commercial chemical kit (SCrifer-Kit, BioMérieux, Marcy l'Étoile, France). Women found to have hemoglobin concentrations below 110 g/L were advised to take higher doses of iron/folate according to the type of anemia: i.e., two tablets containing 64 mg elemental iron per day for moderate and mild anemia (70–110 g/L), and three tablets per day for severe anemia (hemoglobin < 70 g/L). Anemic patients were also advised to consume iron-rich foods, such as beef, eggs, and green leafy vegetables.

To detect malaria parasitemia, thick and thin blood films were collected, fixed, and stained with Giemsa and then examined. A minimum of 100 microscopic fields were examined in all blood films. In general, 200 leukocytes were counted, and if fewer than 10 parasites were seen, the microscopist continued counting up to 500 leukocytes. Malarial parasite counts were converted to number of parasites per microliter of whole blood by using the conversion factor 8,000 leukocytes per microliter of blood [13].

Schistosomiasis and hookworm infections were diagnosed by the presence of schistosomes or hookworm eggs in urine or stool samples, as appropriate. To assess the presence of other helminthic infections, stool samples were also examined macroscopically for general characteristics. Stools were stained by the Kato-Katz method and examined microscopically [14]. For *S. haematobium*, urine samples were shaken well to ensure adequate dispersal of eggs, and 10 mL was processed by the Nuclepore filtration technique [15]. Schistosome eggs were then detected microscopically after the addition of Lugol iodine solution. Hookworm and schistosomiasis infections were classified as 0 for absent (negative) or + for present (positive).

Abnormal vaginal discharge was defined as a thick, white, gray-white, or yellow-green vaginal discharge with a fetid odor accompanied by itching. Diagnoses were made clinically by an experienced midwife and confirmed by the attending physician. As was done routinely within the health center, metronidazole and nystatin were prescribed to women with this condition.

Those diagnosed with malaria were treated with chloroquine (500 mg per day for 5 days), and those with hookworm eggs received a single dose (400 mg) of albendazole if they were in the second or third trimester of pregnancy. For safety reasons, those infected with schistosomiasis were not treated with praziquantel. They were, however, informed about their status and advised to report back to the center for treatment after delivery.

## Statistical analysis

The data were analyzed by SPSS for Windows version 11.5 (SPSS, Chicago, IL, USA). The frequencies of general demographic and socioeconomic characteristics were computed, and the prevalence of protein–energy malnutrition (body-mass index < 18.5 kg/m<sup>2</sup>) was estimated. Mild anemia was defined as a hemoglobin level less than 110 g/L, moderate anemia as a hemoglobin level less than 90 g/L, and severe anemia as a hemoglobin level less than 70 g/L [16]. Low serum iron was defined as an iron level less than 12 μmol/L (normal, 12–30 μmol/L) and high total iron-binding capacity as greater than 64 μmol/L (normal, 32–64 μmol/L). Associations among mild, moderate, and severe anemia, iron and parasite status, erythrocyte sedimentation rate values, and the presence of abnormal vaginal discharge were evaluated. Student's *t*-test and the  $\chi^2$  test were used, as appropriate, to compare differences in hemoglobin concentrations, serum iron, and total iron-binding capacity, anemia and serum iron according to trimester of pregnancy between infected and noninfected women.

The relative risks of anemia were calculated for women infected with malaria, schistosomiasis, and hookworm and for those with abnormal vaginal discharge. Population-attributable risks [17] were also calculated to estimate the proportion of anemia that could be prevented by the elimination of each of the assessed risk factors. The adjusted odds ratios for anemia and low serum iron were estimated from multivariate logistic regression models that included gestational stage, helminthic infection, abnormal vaginal discharge, food constraints, and various sociodemographic variables. Unless otherwise stated, all values are presented as means  $\pm$  SD. A *p* value less than .05 was used to determine statistical significance.

## Results

Complete clinical and biochemical data were obtained from 131 of the 190 women who were enrolled. No significant differences in baseline characteristics were noted between the 59 women who were excluded because of incomplete information and the remainder of the sample. **Table 1** summarizes the characteristics of those included in all subsequent analyses. The women included in these analyses ranged in age from 18 to 45 years; 51% were between 20 and 29 years of age. Almost two-thirds (64%) visited the health center for the first time during the second trimester of the index pregnancy (13 to 24 weeks). The remainder first visited the center during the first or the third trimester (20% and 16%, respectively). Very few were literate (16%), and only 55% came from families that owned the houses in which they lived. Approximately 20% of the women

TABLE 1. Characteristics of the study sample (N = 131)

Characteristic	% of sample
Age (yr)	
< 20	29
20–29	51
≥ 30	20
Married	98
Parity	
0	23
1–2	21
3–4	26
≥ 5	30
Gestational age (wk)	
≤ 12	20
13–24	64
≥ 25	16
Height < 145.0 cm	0
BMI (kg/m <sup>2</sup> )	
< 18.5	12
> 25	18
Subject to food restrictions	45
Serum iron (μmol/L)	
Low (< 12)	13
Normal (12–30)	84
High (> 30)	3
TIBC (μmol/L) <sup>a</sup>	
Low (< 32)	11
Normal (32–64)	89
Parasitic infection	
<i>Plasmodium falciparum</i>	11
<i>Schistosoma haematobium</i>	23
Hookworm	8
> 1 infection	4
<i>P. falciparum</i> + <i>S. haematobium</i>	3
<i>P. falciparum</i> + hookworm	0
<i>S. haematobium</i> + hookworm	0.8
Abnormal vaginal discharge	82
High ESR (> 16mm/h)	90

BMI, body-mass index; TIBC, total iron-binding capacity; ESR, erythrocyte sedimentation rate

a. To convert TIBC values from micromoles per liter to micrograms per deciliter, divide by 0.179.

consumed coffee or tea, and none smoked. Food accessibility was constrained in 45% of the women because of cultural or self-imposed food restrictions arising from beliefs that some foods cause malaria (e.g., eggs and milk) or may lead to difficult deliveries because they help produce large infants (e.g., salt, bananas, meat, and eggs). These foods are commonly either avoided completely or rarely consumed during pregnancy. Low body-mass index (< 18.5 kg/m<sup>2</sup>) was

observed in 27% of the enrolled women in their first trimester of pregnancy.

Low serum iron (< 12 μmol/L) was observed in 13% of the analyzed sample. No increases in total iron-binding capacity (> 64 μmol/L) and no abnormally low transferrin saturation values (< 16%) were observed. However, 11% of the women had abnormally low total iron-binding capacity (< 32 μmol/L) (**table 1**).

Hemoglobin values and other hematologic indicators are summarized in **table 2** according to trimester. The prevalence of anemia in this group was high. The hemoglobin level was less than 110 g/L in 47% of the women and less than 70 g/L (severe anemia) in 2%. Anemia was associated with the stage of pregnancy (Pearson  $\chi^2 = 6.35$ ,  $p = .04$ ); the highest proportions of women with anemia (51%) and with severe anemia (6%) were found in women examined during the second trimester. This result was not unexpected, since maternal–fetal iron transfer increases and maternal red-cell mass and vascular volume expand during this period of pregnancy. Among these women, 13% (11/82) had low serum iron, a percentage not different from that observed in the total sample (**table 2**).

The frequency distribution of hemoglobin concentrations is shown in **figure 1**. The prevalence of anemia did not differ significantly between nulliparous women (41%) and the remainder of the sample (47%;  $p = .78$ ), but a significantly higher prevalence of severe anemia was observed among nulliparous women (7%) than among multiparous women (1%;  $p = .04$ ). The distribution of parity was comparable among all groups. No significant associations were noted between hemoglobin concentrations and maternal height ( $p = .08$ ), weight ( $p = .20$ ), or age ( $p = .43$ ).

Malaria parasitemia, *S. haematobium*, and hookworm infections were detected in 11%, 23%, and 8% of the women, respectively. All detected cases of malaria were caused by *P. falciparum*. Three percent of the women had both *P. falciparum* and *S. haematobium*, and 0.8% had both *S. haematobium* and hookworm. *P. falciparum* and hookworm were not found to occur jointly (**table 1**). The prevalence and severity of anemia were greatest in women with hookworm and *S. haematobium*, but the frequency of low serum iron was higher in women with hookworm or malaria than in those who had *S. haematobium* or abnormal vaginal discharge or who had food constraints (**table 3**).

Abnormal vaginal discharge was observed in 82% of the women. A significant correlation was noted between abnormal vaginal discharge and anemia (Pearson  $\chi^2 = 62.4$ ;  $p < .01$ ). Abnormal vaginal discharge appeared to be more significantly associated with anemia (hemoglobin < 110 g/L) than with low serum iron (< 12 μmol/L) (**table 3**).

The relative and population-attributable risks for anemia (hemoglobin < 110 g/L) are summarized in **table 4**.

TABLE 2. Indicators of anemia and low serum iron in pregnant women according to trimester of pregnancy

Trimester	N	Hemoglobin			Serum iron		TIBC		Transferrin saturation
		< 110 g/L (%)	< 70 g/L (%)	Mean $\pm$ SD (g/L)	< 12 $\mu$ mol/L (%)	Mean $\pm$ SD ( $\mu$ mol/L)	> 64 $\mu$ mol/L (%)	Mean $\pm$ SD ( $\mu$ mol/L)	Mean $\pm$ SD (%)
1	26	31	0	115 $\pm$ 11	19	19 $\pm$ 7	0	38 $\pm$ 5	49.72 $\pm$ 21.51
2	84	51 <sup>a</sup>	6 <sup>a</sup>	107 $\pm$ 16 <sup>b</sup>	13 <sup>c</sup>	17 $\pm$ 6	0	38 $\pm$ 5	44.18 $\pm$ 14.45
3	21	33	0	112 $\pm$ 14	5	19 $\pm$ 5	0	40 $\pm$ 5	46.76 $\pm$ 10.45
Total	131	47	2	110 $\pm$ 15	13	18 $\pm$ 6	0	39 $\pm$ 5	45.70 $\pm$ 15.62

TIBC, total iron-binding capacity

a. Significantly different from 1st and 3rd trimesters ( $p < .05$ ,  $\chi^2$  test).

b. Significantly different from 1st trimester but not from 3rd trimester ( $p < .05$ ,  $t$ - test).

c. Not significantly different from either 1st and 3rd trimester alone or both combined ( $p > .05$ ,  $\chi^2$  test).

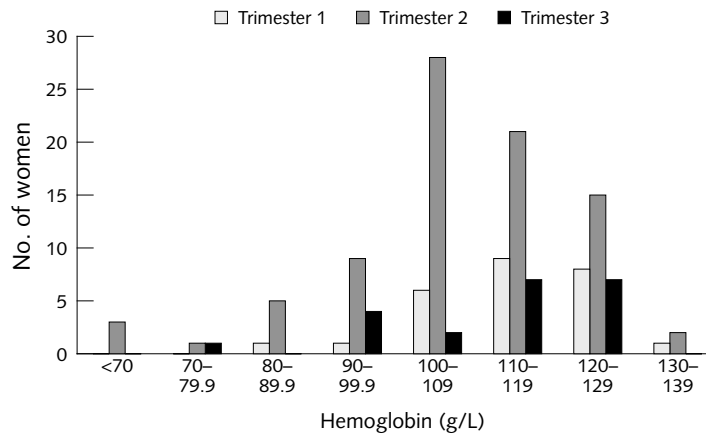


FIG. 1. Distribution of hemoglobin concentrations among pregnant women according to trimester.

TABLE 3. Indicators of anemia and low serum iron according to risk factor

Risk factor	Hemoglobin			Serum iron		TIBC	
	< 110 g/L (%)	< 70 g/L (%)	Mean $\pm$ SD (g/L)	< 12 $\mu$ mol/L (%)	Mean $\pm$ SD ( $\mu$ mol/L)	> 64 $\mu$ mol/L (%)	Mean $\pm$ SD ( $\mu$ mol/L)
<i>Plasmodium falciparum</i> malaria							
Positive (N = 14)	64*	0.7	100 $\pm$ 24***	36	15 $\pm$ 7***	0	37 $\pm$ 6
Negative (N = 117)	44	2	111 $\pm$ 13	11	18 $\pm$ 6	0	39 $\pm$ 7
<i>Schistosoma haematobium</i> infection							
Positive (N = 30)	67**	10***	101 $\pm$ 17***	27	15 $\pm$ 4***	0	37 $\pm$ 4
Negative (N = 101)	41	0	113 $\pm$ 13	9	19 $\pm$ 6	0	39 $\pm$ 7
Hookworm infection							
Positive (N = 10)	100***	10**	92 $\pm$ 13***	40	14 $\pm$ 4**	0	39 $\pm$ 15
Negative (N = 121)	40	2	111 $\pm$ 14	11	18 $\pm$ 6	0	39 $\pm$ 5
Abnormal vaginal discharge							
Yes (N = 107)	52***	4	101 $\pm$ 15***	13	18 $\pm$ 6	0	39 $\pm$ 5
No (N = 24)	21	0	112 $\pm$ 11	13	16 $\pm$ 5	0	39 $\pm$ 5
Food restrictions							
Yes (N = 59)	66***	3	103 $\pm$ 14**	20	17 $\pm$ 5	0	39 $\pm$ 6
No (N = 72)	31	1	115 $\pm$ 14	7	18 $\pm$ 6	0	38 $\pm$ 5

TIBC, total iron-binding capacity

\* $p < .160$ , \*\* $p < .05$ , \*\*\* $p < .01$  ( $\chi^2$  test). All comparisons are between infected and noninfected women for parasites, and between women with and without food restrictions.

TABLE 4. Relative risk and population-attributable risk of anemia (hemoglobin &lt; 110 g/L)

Risk factors	RR (95% CI)	PAR—%
<i>Plasmodium falciparum</i> malaria parasitemia	1.45 (1.14–2.06)	32
<i>Schistosoma haematobium</i> infection	1.64 (1.16–2.32)	13
Hookworm infection	2.37 (1.92–2.92)	10
Abnormal vaginal discharge	2.51 (1.13–5.59)	55
Food restrictions	1.50 (1.02–2.20)	22

RR, relative risk; CI, confidence interval; PAR, population-attributable risk

In multivariate analyses, *S. haematobium* appeared to be the only parasitic infection that was significantly associated with anemia ( $p = .005$ ). However all parasitic infections—i.e., malaria ( $p = .004$ ), *S. haematobium* ( $p = .009$ ), and hookworm ( $p = .002$ )—were significantly associated with low serum iron. Hookworm infection was the strongest predictor of low serum iron (table 5).

## Discussion

In this study, biologic and other determinants of anemia were examined among pregnant women in Mali. The results indicate that infections and food constraints are probably important causes of anemia in this population.

The prevalence of anemia among these pregnant women was high (47%). This figure is consistent with the results obtained by Bouvier et al. [3] in Mali and similar to prevalences reported in other areas in Africa [2, 18–20]. However, it is lower than the 73% prevalence estimate of the most recent Demographic and Health Survey (DHS) in Mali [21]. The present study was conducted in a neighborhood of the capital city, whereas the DHS was national and also covered rural areas in which the prevalence of anemia among pregnant women is extremely high because the accessibility

of food, potable water, good sanitation, and medical care is low. It is important to note that these values are based on cutoff points recommended by the WHO. This is relevant because of growing concerns about possible differences in hemoglobin regulation among disparate ethnic groups [22, 23].

Most of the women in this group had mild to moderate anemia; that is, their hemoglobin levels were slightly lower than the threshold of 110 g/L (fig. 1). Nevertheless, even this level of anemia may adversely affect physical performance [24, 25] and increase intrauterine growth retardation and the risk of preterm delivery [26, 27]. Only 8% of the women studied had hemoglobin levels under 90 g/L (a cutoff proposed to identify groups with substantial risk of morbidity and mortality [28]), and only 2% had severe anemia (hemoglobin < 70 g/L). The urban setting of these women and the easy accessibility of health clinics may explain these low rates.

Anemia among pregnant women in developing countries is generally presumed to be due primarily to iron deficiency, even though its pathogenesis is known to be multifactorial. In the present study, we focused on the importance of infections and food constraints that may result in the restriction of vitamin- and mineral-rich foods and thereby also inadequate micronutrient intakes. Serum iron and total iron-binding capacity also were assessed. These were the only measurements related to iron status that were technically possible in Bamako at the time of the study. These measurements are insufficient to assess iron status, especially in areas with a high prevalence of infections and chronic inflammation. Both measurements show large diurnal variation, and they decrease in the presence of inflammatory processes. Other measurements of iron status, such as serum ferritin and transferrin receptors, are often more sensitive indicators of iron-deficient erythropoiesis. Unfortunately, none of those measurements was feasible. Thus, it is not possible to rule out that iron is the principal limiting factor accounting for the high rates of anemia. However, infections were most strongly predictive of anemia (tables 4 and 5).

TABLE 5. Adjusted odds ratios for anemia and low serum iron according to risk factors<sup>a</sup>

Risk factor	N	AOR (95% CI)	
		Anemia (Hb < 110 g/L)	Low SI (< 12 $\mu$ mol/L)
<i>Plasmodium falciparum</i>	14	2.8 (0.85–9.23)*	8.2 (2–34)**
<i>Schistosoma haematobium</i>	30	3.6 (1.5–8.7)**	5.2 (1.5–17.8)***
Hookworm	10	—	13.0 (2.6–63.4)**
SI < 12 $\mu$ mol/L	17	1.0 (0.97–1.12)*	—
Abnormal vaginal discharge	107	17.8 (6–52)**	—

AOR, adjusted odds ratio; CI, confidence interval; Hb, hemoglobin; SI, serum iron

\* $p = .09$ , \*\* $p = .05$ , \*\*\* $p < .01$

a. Adjusted odds ratios and 95% confidence intervals are calculated from multivariate backward stepwise (Wald) logistic regression models. Sociodemographic (age, parity) and gestational age variables were not retained because they were not statistically significant ( $p > .05$ ).

Given that total iron-binding capacity may be within normal limits in individuals with concurrent chronic infections and iron deficiency, the facts that only 13% of the women had low serum iron and none had low transferrin saturation or increased total iron-binding capacity also suggest that inadequate dietary iron is not the only cause of the anemia. Infections and other nutrient deficiencies are likely to contribute to the high rates of anemia observed in this population. We do not know of any indicator of chronic inflammation that may help resolve this question. Nevertheless, the findings that 55%, 32%, 13%, and 10% of the anemia cases were attributable to abnormal vaginal discharge, malaria, *S. haematobium*, and hookworm, respectively, stress the likely role infections play.

These data also suggest that treatment with iron alone is unlikely to be an effective strategy against anemia. These results agree with those of earlier studies in two other West African countries, Côte d'Ivoire [29] and northern Ghana [19]. They also agree with other evidence that malaria contributes significantly to the high prevalence of anemia in Africa and elsewhere [3, 30–34].

Urinary schistosomiasis and hookworm infections were also reported to be strongly associated with anemia in pregnant women [10, 34–37] and in other African populations [9, 38–41]. Similarly, we have shown that *S. haematobium* and hookworm contributed to an important proportion of the anemia in this population, suggesting that Malian pregnant women and those living in similar areas should be screened and treated for those infections during prenatal care visits. This is possible because anthelmintic therapy is efficacious, inexpensive, and safe to administer to pregnant women [42–44].

The most interesting finding is that abnormal vaginal discharge, a sign of vaginal infection, was found on gynecologic examination in 82% of the women. This condition correlated significantly with anemia (Pearson  $\chi^2 = 62.4$ ;  $p < .01$ ). On the basis of computed attributable risks, this condition contributed to 55% of all cases of anemia. To the best of our knowledge, this is the first study in Africa that has linked anemia to abnormal vaginal discharge. The association between this condition and anemia has also been reported once in Mexican pregnant women by Lopez-Martinez et al. [45]. Such vaginal infections are unlikely to be reported routinely by women, and they are likely to be chronic. Their chronicity probably impairs erythropoiesis, shortens red-cell survival, and interferes with the mobilization of reticuloendothelial iron stores [46]. Thus, the impact on hemoglobin is likely to be high. The high prevalence of abnormal vaginal discharge in our population, and possibly in populations in similar developing countries, also raises the need to examine this relationship further. In particular, there is a need to investigate and under-

stand the contribution of the most common causes of vaginal infection—bacterial vaginosis, trichomoniasis, and candidiasis—to this association. Furthermore, the high prevalence of simultaneous infections probably contributes to the high rate of anemia. These combinations may exacerbate underlying dietary deficiencies or complicate their assessment.

Other single or combined micronutrient deficiencies, such as vitamin A, vitamin B<sub>12</sub>, and folate deficiency, may also partially explain the high rate of anemia in these women. This possibility is supported by the commonality of food restrictions experienced by pregnant women in all regions of Mali [47]. These have been described as important underlying causes of undernutrition and anemia in Africa and elsewhere [48–51]. Many vitamin- and mineral-rich foods (e.g., eggs, meat, milk, and mangoes) often are not consumed or their consumption is limited because of the belief that they result in big babies, and thus difficult deliveries, or in malaria. Financial constraints also commonly limit access to animal proteins and other more expensive foods. Unequal household distribution of animal protein that favors men over women and children further exacerbates this problem. All of these factors limit women's access to nutrient-rich foods and thus are probably important factors that account for the high rates of anemia in this population. Unfortunately, local technical limitations precluded the assessment of those deficiencies, and therefore further work in this area is warranted.

Hemoglobinopathies have also been reported to be prevalent and associated with anemia in pregnant African women [19, 52, 53]. These also may help explain the high rates of maternal anemia, but data on such disorders are not available in Mali. Therefore, the prevalence and type of hemoglobinopathies and their relationship to anemia in this group also need to be explored.

These findings underscore the difficulties of determining the etiology of anemia in populations with poor diets, high rates of infection and inflammation, and limited resources and technical facilities. They also highlight the need for multiple methodologic approaches in addressing this question. Clearly, it is important to expand the capabilities to assess serum ferritin, zinc protoporphyrin, serum transferrin receptors, reticulocyte counts and hemoglobin content, C-reactive protein,  $\alpha_1$ -acid glycoprotein, erythrocyte folate concentration, serum retinol and vitamin B<sub>12</sub>, hepcidin, and other potentially important indicators related to anemia. Assessments of the prevalence and severity of hemoglobin disorders also are important in many countries in Africa and Asia. Enhancement of these capabilities, coupled with therapeutic interventions that address the potential causes of anemia, is required.

## Conclusions

Anemia is frequent among women in Mali, and its causes are probably multiple and complex. Our data suggest that vaginal infections and parasitic diseases are important factors that contribute to the high rates of anemia among pregnant women in that setting. Therefore, a stronger focus on their prevention, diagnosis, and treatment is needed, and especially on the assessment of the causal link between abnormal vaginal discharge and anemia. Widespread unnecessary self- or culturally imposed food restrictions also limit the food intake of pregnant women, thereby adding to the problem. Hence, minimizing or eliminating such harmful practices is also desirable.

## References

- World Health Organization. The prevalence of anemia in women. A tabulation of available information, 2nd ed. Geneva: WHO, 1992.
- World Health Organization. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. WHO Technical Report Series No. 854. Geneva: WHO, 1995.
- Bouvier P, Doumbo O, Dreslow N, Robert CF, Mauris A, Picquet M, Kouriba B, Dembele HK, Delley V, Rougemont A. Seasonality, malaria, and impact of prophylaxis in a West African village. I. Effect on anemia in pregnancy. *Am J Trop Med Hyg* 1997;56:378–83.
- World Health Organization. Nutritional anemias. *World Health Organ Tech Rep Ser* 1968;405.
- Centers for Disease Control and Prevention (CDC). Recommendations to prevent and control iron deficiency in the United States. *MMWR Morb Mortal Wkly Rep* 1998; 47:1–29.
- Stoltzfus RJ. Iron deficiency: global prevalence and consequences. *Food Nutr Bull* 2003;24(Suppl):S99–103.
- Allen LH. Pregnancy and iron deficiency: unresolved issues. *Nutr Rev* 1997;55:91–101.
- Lozoff B, Jimenez E, Wolf AW. Long-term developmental outcome of infants with iron deficiency. *N Engl J Med* 1991;325:687–94.
- Stoltzfus RJ, Chwaya HM, Tielsch JM, Schulze KJ, Albonico M, Savioli L. Epidemiology of iron deficiency anemia in Zanzibari schoolchildren: the importance of hookworms. *Am J Clin Nutr* 1997;65:153–9.
- Dreyfuss ML, Stoltzfus RJ, Shrestha JB, Pradhan EK, LeClerq SC, Khatri SK, Shrestha SR, Katz J, Albonico M, West KP Jr. Hookworms, malaria and vitamin A deficiency contribute to anemia and iron deficiency among pregnant women in the plains of Nepal. *J Nutr* 2000;130:2527–36.
- van den Broek NR, Letsky EA. Etiology of anemia in pregnancy in south Malawi. *Am J Clin Nutr* 2000;72 (1 Suppl):247S–56S.
- International Council for Standardization in Haematology (Expert Panel on Blood Rheology). ICSH recommendations for measurement of erythrocyte sedimentation rate. *J Clin Pathol* 1993;46:198–203.
- World Health Organization. Basic laboratory methods in medical parasitology. Geneva: WHO, 1991.
- World Health Organization. Bench aids in the diagnosis of intestinal parasites. Geneva: WHO, 1994.
- Peters PA, Mahmoud AA, Warren KS, Ouma JH, Siongok TK. Field studies of a rapid, accurate means of quantifying *Schistosoma haematobium* eggs in urine samples. *Bull World Health Organ* 1976;54:159–62.
- World Health Organization, UNICEF, UNU. Iron deficiency: indicators for assessment and strategies for prevention. Geneva: WHO, 1998.
- Rothman KJ. *Epidemiology: an introduction*. New York: Oxford University Press, 2002.
- Isah HS, Fleming AF, Ujah IA, Ekwempu CC. Anaemia and iron status of pregnant and non-pregnant women in the guinea savanna of Nigeria. *Ann Trop Med Parasitol* 1985;79:485–93.
- Mockenhaupt FP, Rong B, Gunther M, Beck S, Till H, Kohne E, Thompson WN, Bienzle U. Anaemia in pregnant Ghanaian women: importance of malaria, iron deficiency, and haemoglobinopathies. *Trans R Soc Trop Med Hyg* 2000;94:477–83.
- Kalenga MK, Nyembo MK, Nshimba M, Foidart JM. Anemia associated with malaria and intestinal helminthiasis in Lubumbashi [in French]. *Sante Publique* 2003;15:413–21.
- DHS: Cellule de Planification et de Statistique du Ministère de la Santé (CPS/MS), Direction Nationale de la Statistique et de l'Informatique (DNSI) et ORC Macro. 2002. Enquête Démographique et de Santé du Mali 2001. Calverton, MD, USA: CPS/MS, DNSI and ORC Macro, 2002.
- Meyers LD, Habicht JP, Johnson CL, Brownie C. Prevalences of anemia and iron deficiency anemia in black and white women in the United States estimated by two methods. *Am J Public Health* 1983;73:1042–9.
- Garn SM, Smith NJ, Clark DC. Lifelong differences in hemoglobin levels between blacks and whites. *J Natl Med Assoc* 1975;67:91–6.

## Acknowledgments

We thank the women who participated in this study. We also thank Dr. Akory Ag Iknane, director of the Banconi community health center, Dr. Mahamane Maïga, chief medical officer, Ms. Hawa Sissoko, midwife, and their assistants for allowing us to work in their center and also for their help in conducting this study. Financial support was provided by the Division of Nutritional Sciences at Cornell University and the Ithaca First Presbyterian Church. Mohamed Ag Ayoya was supported by a Nestlé Foundation research grant while writing this paper.

24. Haas JD, Fairchild MV. Summary and conclusions of the International Conference on Iron Deficiency and Behavioral Development. *Am J Clin Nutr* 1988;50:703–5.
25. Haas JD, Brownlie T. Iron deficiency and reduced work capacity: a critical review of the research to determine a causal relationship. *J Nutr* 2001;131:676S–90S.
26. Scholl TO, Hediger ML, Fischer RL, Shearer JW. Anemia vs iron deficiency: increased risk of preterm delivery in a prospective study. *Am J Clin Nutr* 1992;55:985–8.
27. Rasmussen KM. Is there a causal relationship between iron deficiency or iron-deficiency anemia and weight at birth, length of gestation and perinatal mortality? *J Nutr* 2001;131:590S–603S.
28. Stoltzfus RJ. Rethinking anaemia surveillance. *Lancet* 1997;349:1764–6.
29. Asobayire FS, Adou P, Davidsson L, Cook JD, Hurrell RF. Prevalence of iron deficiency with and without concurrent anemia in population groups with high prevalences of malaria and other infections: a study in Côte d'Ivoire. *Am J Clin Nutr* 2001;74:776–82.
30. Brabin BJ, Ginny M, Sapau J, Galme K, Paino J. Consequences of maternal anaemia on outcome of pregnancy in a malaria endemic area in Papua New Guinea. *Ann Trop Med Parasitol* 1990;84:11–24.
31. Fleming AF. The aetiology of severe anaemia in pregnancy in Ndola, Zambia. *Ann Trop Med Parasitol* 1989;83:37–49.
32. Mateelli A, Donato F, Shein A, Muchi JA, Leopardi O, Astori L, Carosi G. Malaria and anemia in pregnant women in urban Zanzibar, Tanzania. *Ann Trop Med Parasitol* 1994;88:475–83.
33. McGregor IA. Epidemiology, malaria and pregnancy. *Am J Trop Med Hyg* 1984;33:517–25.
34. Shulman CE, Graham WJ, Jilo H, Lowe BS, New L, Obiero J, Snow RW, Marsh K. Malaria is an important cause of anaemia in primigravidae: evidence from a district hospital in coastal Kenya. *Trans R Soc Trop Med Hyg* 1996;90:535–9.
35. Greenham R. Anaemia and *Schistosoma haematobium* infection in the North-Eastern Province of Kenya. *Trans R Soc Trop Med Hyg* 1978;72:72–5.
36. Olsen A, Magnussen P, Ouma JH, Andreassen J, Friis H. The contribution of hookworm and other parasitic infections to haemoglobin and iron status among children and adults in western Kenya. *Trans R Soc Trop Med Hyg* 1998;92:643–9.
37. Bondevik GT, Eskeland B, Ulvik RJ, Ulstein M, Lie RT, Schneede J, Kyale G. Anemia in pregnancy: possible causes and risk factors in Nepali women. *Eur J Clin Nutr* 2000;54:3–8.
38. Stephenson LS, Latham MC, Kurz KM, Kinoti SN, Oduori ML, Crompton DW. Relationships of *Schistosoma haematobium*, hookworm and malarial infections and metrifonate treatment to haemoglobin level in Kenyan school children. *Am J Trop Med Hyg* 1985;34:519–28.
39. Wilkins HA, Goll PH, Moore PJ. *Schistosoma haematobium* infection and haemoglobin concentrations in a Gambian community. *Ann Trop Med Parasitol* 1985;79:159–61.
40. Urbani C, Toure A, Hamed AO, Albonico M, Kane I, Cheikna D, Hamed N, Montresor A, Savioli L. Intestinal parasitic infections and schistosomiasis in the valley of the Senegal river in the Islamic Republic of Mauritania [in French]. *Med Trop (Mars)* 1997;57:157–60.
41. Massawe SN, Ronquist G, Nystrom L, Lindmark G. Iron status and iron deficiency anemia in adolescents in a Tanzanian suburban area. *Gynecol Obstet Invest* 2002;54:137–44.
42. Allen HE, Crompton DW, de Silva N, LoVerde PT, Olds GR. New policies for using anthelmintics in high risk groups. *Trends Parasitol* 2002;18:381–2.
43. Stephenson LS, Latham MC. Hookworm. *Curr Treat Options Infect Dis* 2003;5:291–9.
44. Olds RG. Administration of praziquantel to pregnant and lactating women. *Acta Trop* 2003;86:185–95.
45. Lopez-Martinez R, Ruiz-Sanchez D, Vertiz-Chavez E. Vaginal candidosis: opportunistic factors and clinical correlation in 600 patients. *Mycopathologia* 1984;85:167–70.
46. Means RT Jr. Advances in the anemia of chronic disease. *Int J Hematol* 1999;70:7–12.
47. Ag Ayoya M, Theophin C, Moore EC. Nutrition in Mali: a qualitative study of knowledge, perceptions and practices. Report on preliminary and second analyses of data collected in June 1998 for the Groupe ad hoc Santé, Ministry of Health, Republic of Mali. Washington, DC: Chemonics International, 2001.
48. Houdegebe A. Health problems facing rural women. *Child Trop* 1985;159:57–61.
49. Igbedioh SO. Undernutrition in Nigeria: dimension, causes and remedies for alleviation in a changing socio-economic environment. *Nutr Health* 1993;9:1–14.
50. Goodburn L. Bangladesh women report postpartum health problems. *Safe Mother*. 1994 Feb;(13):3.
51. Marchant T, Armstrong Schellenberg JR, Edgar T, Ronsmans C, Nathan R, Abdulla S, Mukasa O, Urassa H, Lengeler C. Anaemia during pregnancy in southern Tanzania. *Ann Trop Med Parasitol* 2002;96:477–87.
52. Menendez C, Todd J, Alonso PL, Francis N, Lulat S, Ceesay S, M'Boge B, Greenwood BM. The effects of iron supplementation during pregnancy, given by traditional birth attendants, on the prevalence of anaemia and malaria. *Trans R Soc Trop Med Hyg* 1994;88:590–3.
53. Brabin BJ, Prinsen-Geerligs PD, Verhoeff FH, Fletcher KA, Chimsuku LH, Ngwira BM, Leich OJ, Broadhead RL. Haematological profiles of the people of rural southern Malawi: an overview. *Ann Trop Med Parasitol* 2004;98:71–83.