

# Fetal and maternal complications of malaria at N'Djamena South District Hospital (Chad)

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## Abstract

**Background:** Malaria infection in pregnancy is a major risk factor for maternal and child health and, substantially, increases the risk of miscarriage, stillbirth, and low birth weight. **Objective:** Identify fetal and maternal complications of malaria and curb the spread of this preventable infectious disease. **Materials and Methods:** This was a prospective and analytic survey of 8 months. The study sample consisted of two groups: (1) the study group composed with pregnant women admitted for symptomatic or asymptomatic malaria and (2) the control group in which of three malaria negative pregnant women were recorded after every malaria positive case. Data were analyzed using SPSS 17.0.  $P < 0.05$  was used. **Results:** We recorded 200 patients admitted for malaria among 1220 patients, giving incidence of 16.4%. The majority of pregnant women (48%) ( $P = 0.0001$ ) had not attended antenatal consultation. Half of patients ( $P = 0.0035$ ) did not receive malaria preventive treatment during pregnancy. Eighty-six patients (43%) declared using insecticide-treated bed nets. The majority (186/200, i.e. 93%) had positive malaria rapid test. The microscopic examination showed *Plasmodium falciparum* malaria in 84%. The majority of patients (89%) received quinine. Sixty-one patients (30.5%) presented anemia. One mother died giving a death rate of 0.5%. Main fetal complications were of low birth weight (12.5%,  $P = 0.016$ ) and intrauterine growth restriction (9%  $P = 0.026$ ). **Conclusion:** Malaria remains a frequent infectious disease during pregnancy. Sensitizations for antenatal consultations are useful to improve malaria management.

**Key words:** Malaria, pregnancy, complications

## INTRODUCTION

Sub Saharian Africa has the largest burden of malarial disease, with over 90% of the world's malaria-related deaths occurring in this region.<sup>[1]</sup> Malaria in pregnancy is an obstetric, social, and medical problem worldwide, particularly in tropical and subtropical countries.<sup>[2,3]</sup> Pregnant women are more susceptible than the general

population to malaria: They are more likely to become infected, suffer a recurrence, develop severe complications, and die from the disease.<sup>[1]</sup> Malaria in pregnancy is different to the disease in the nonpregnant state. The severity of malaria in pregnancy is thought to be due to general impaired immunity plus a diminution of acquired immunity to malaria in endemic areas.<sup>[4]</sup>

Regardless of symptoms, the presence of plasmodial parasites in a pregnant woman's body will have a negative impact on her own health and that of her fetus.<sup>[5]</sup> Malaria

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in pregnancy also contributes to significant perinatal morbidity and mortality. Malaria infection in pregnancy is a major risk factor for maternal and child health and, substantially, increases the risk of miscarriage, stillbirth, and low birth weight.<sup>[6-8]</sup>

According to earlier studies, Chad is an endemic area for malaria.<sup>[9]</sup> Few prior studies focused on fetal and maternal complications of malaria in this country.

Our objective was to identify fetomaternal complications of malaria and to curb the spread of this preventable infectious disease.

## MATERIALS AND METHODS

This was a prospective and analytic survey of 8 months (from January 15, 2014, to September 15, 2014) about fetal and maternal complications of malaria at N'Djamena South District Hospital. N'Djamena South District Hospital is the second level hospital in N'Djamena city which helps take care of referred patients coming from surrounding health centers.

The study sample consisted of two groups: (1) The study group composed of pregnant women admitted for symptomatic or asymptomatic malaria and (2) the control group in which of three malaria negative pregnant women were recorded after every malaria positive case.

Symptomatic malarial cases were defined as the presence of asexual forms of *Plasmodium* species on a blood smear, associated with fever (axillary temperature, above 37.5°C) or history of fever with one or more of the following: Headache, weakness, myalgia, chills, dizziness, abdominal pain, diarrhea, nausea, and vomiting. Malarial cases were asymptomatic when none of the symptoms listed above was reported.

We got the agreement of the Director of N'Djamena South District Hospital and the Ethical Committee. Data were analyzed using the software Statistical package for social sciences (SPSS) 17.0. French version. Chi-square test ( $P < 0.05$ ) was used to compare variables.

## RESULTS

We recorded 200 patients admitted for malaria among 1220 patients, giving incidence of 16.4%.

### Surveillance of pregnancy and the parity

Ninety-six pregnant women (48%,  $P = 0.0001$ ) had not attended antenatal consultation. Forty-five patients (45/200

i.e., 22.5%) did more than four antenatal consultations as recommended by World Health Organization (WHO) ( $P = 0.001$ ).

Primiparous represented 52.5% ( $n = 105$ ,  $P = 0.002$ ) followed by multiparous with 20% ( $n = 60/200$ ) [Table 1].

### Term of pregnancy

Forty-five patients (22.5%) were diagnosed as malaria-positive case at the first term, 63 patients (31.5%) at the second term, and the remaining 92 (46%) at the third trimester or during labor.

### Intermittent preventive treatment

Half (1/2) of patients did not receive malaria preventive treatment during pregnancy and, in the control group, 132 patients did not take preventive treatment ( $P = 0.035$ ). Thirty-six patients (18%) had correctly taken intermittent preventive treatment (ITP) [Table 2].

This preventive treatment composed of sulfadoxine-pyrimethamine must be given after the 16<sup>th</sup> gestation week.

Eighty-six patients (43%) declared using insecticide-treated bed nets.

### Diagnose and confirmation exams

Clinical diagnosis is based on the patients' signs and symptoms and, on physical findings, at examination. The earliest symptoms of malaria are very nonspecific and variable and include fever, headache, weakness, myalgia,

**Table 1: Surveillance of pregnancy and the parity**

	Malaria (+) (%)	No malaria (-) (%)	P
Antenatal visit			
0	$n=96$ (48)	$n=158$ (26.3)	0.0001
1-3	$n=59$ (29.5)	$n=361$ (60.2)	
≥4	$n=45$ (22.5)	$n=81$ (13.5)	
Total	$n=200$ (100)	$n=600$ (100)	
Parity			
Primiparous	$n=105$ (52.5)	$n=154$ (25.6)	0.002
Pauciparas	$n=35$ (17.5)	$n=64$ (10.7)	
Multipara	$n=60$ (30)	$n=382$ (63.7)	
Total	$n=200$ (100)	$n=600$ (100)	

**Table 2: Intermittent preventive treatment**

Intermittent preventive treatment	Malaria (+) (%)	No malaria (-) (%)	P
0	$n=100$ (50)	$n=132$ (22)	0.035
1	$n=64$ (32)	$n=307$ (51.2)	
2	$n=34$ (17)	$n=155$ (25.8)	
3	$n=2$ (1)	$n=6$ (1)	
Total	$n=200$ (100)	$n=600$ (100)	

chills, dizziness, abdominal pain, diarrhea, nausea, vomiting, anorexia, and pruritus. We recorded 60% ( $n = 120/200$ ), 50% ( $n = 100/200$ ), 35% ( $n = 70/200$ ), 20.5% ( $n = 41/200$ ), 16.5% ( $n = 33/200$ ), and 11.5% ( $n = 25/200$ ) of fever, headache, myalgia, abdominal pain, diarrhea, and vomiting, respectively.

In laboratory, malaria is diagnosed using different techniques. In this survey, the rapid diagnostic tests (RDTs) were used first and the conventional microscopic diagnosis by staining thin and thick peripheral blood smears later. The majority (186/200, i.e., 93%) had positive malaria rapid test. The microscopic examination of stained blood films using Giemsa showed *Plasmodium falciparum* malaria diagnosis in 84% (168/200).

### Curative treatment

Quinine and artesunate were used for curative treatment. The majority of patients ( $n = 178/200$ , i.e., 89%) received quinine. All patients admitted during this survey were considered as severe malaria [Table 3].

### The maternal complications

Anemia represented 30.5% ( $n = 61/200$ ); therefore, 3.5% ( $n = 7/200$ ) were in a coma.

Anemia is defined as hemoglobin (hematocrit of  $<30\%$ ) received  $<11$  g/dl. Iron and folic acid treatments were given to all women who developed anemia. Women with severe anemia (hematocrit of  $<20\%$ ) received a blood transfusion ( $n = 6/200$  i.e., 3%). Women were encouraged to deliver at a hospital.

The outcome of malaria infection was fatal for one patient giving a death rate of 0.5%. This death was due to neurologic complications of malaria.

### Fetal complications

Table 4 shows that low birth weight represented 12.5% ( $n = 25/200$ ,  $P = 0.016$ ) followed by intrauterine growth restriction with 9% ( $n = 18/200$ ,  $P = 0.026$ ). Low birth weight was defined as a birth weight of  $<2500$ .

One hundred thirty-five fetuses (67.5%) were normal (no complication).

## DISCUSSION

The number of malaria cases worldwide seems to be increasing due to increasing transmission risk in areas where malaria control has declined, the increasing prevalence of drug-resistant strains of parasites, and in a relatively few cases, massive increases in international travel and migration.<sup>[10]</sup> The prevalence of malaria in this study was

**Table 3: Curative treatment**

Nature	Effectives	Percentage
Quinine	178	89
Artesunate	22	11
Total	200	100

**Table 4: Fetal complications**

Fetal complications	Malaria (+) (%)	No malaria (-) (%)	P
No complication	$n=135$ (67.5)	$n=457$ (76.2)	0.016
Low birth weight	$n=25$ (12.5)	$n=45$ (7.5)	
Premature delivery	$n=11$ (5.5)	$n=35$ (1.8)	
Spontaneous abortion	$n=7$ (3.5)	$n=16$ (1.2)	0.029
Intrauterine death	$n=4$ (2)	$n=13$ (21.7)	
Intrauterine growth restriction	$n=18$ (9)	$n=34$ (5.6)	0.026
Total	$n=200$ (100)	$n=600$ (100)	

16.4%, higher than 14.55% reported among pregnant women attending antenatal consultation at N'Djamena mother and child hospital.<sup>[11]</sup> Such high prevalence could be associated with the high number of patients visiting the study hospital and its proximity to the rural communities whose record of antenatal visits is poor area within the rain forest belt where transmission is perennial.

At least four antenatal consultations are recommended by WHO.<sup>[12]</sup> Antenatal consultations are the moment to institute prevention of malarial disease. Our findings showed that 48% of pregnant women had not attended antenatal consultation and 26.3% in control group ( $P = 0.0001$ ).

The effect of infection on the pregnant is dependent on prepregnancy immunity. This acquired anti-malarial immunity depends on intensity of transmission and the number of previous pregnancies among others. In areas endemic for malaria, it is estimated that at least 25% of pregnant women are infected with malaria, the ill health effects are particularly apparent in the primigravida and secundigravida.<sup>[13]</sup> Previous studies have shown that prevalence of infection is highest in secundigravida while others have reported a higher prevalence in primigravida and the density of parasitemia is reported to be highest in the first trimester and primigravida could be at maximum risk in highly endemic areas. In this survey, primiparous represented 52.5% ( $P = 0.002$ ) that confirms the highest infection risk and morbidity in primigravidas and primipara reported.<sup>[13]</sup>

The focus of malaria prevention during pregnancy has been the use of antimalarial chemoprophylaxis and the use of insecticide-treated nets (ITNs). Our findings showed that half of pregnant women (50%) did not receive ITP and

43% used insecticide-treated bed nets. Pregnant women on antimalarial chemoprophylaxis are at a reduced risk of the harmful effects of malaria<sup>[14]</sup> while ITNs reduce human contact with mosquitoes leading to a significant reduction in the incidence of malaria, severe morbidity and mortality due to malaria, as well as helping reduce the adverse effects of malaria during pregnancy in an area of intense malaria transmission.<sup>[15-17]</sup> IPT with antimalarial medications refers to the administration of 2 or more doses of chemoprophylaxis after 16 weeks of gestation in an attempt to reduce subclinical malarial load.<sup>[12,18]</sup> In a review comparing malarial chemoprophylaxis with prophylaxis during pregnancy, Kalanga<sup>[14]</sup> found a significant reduction in maternal anemia, parasitemia, and perinatal death, and a higher mean birth weight in the groups given IPT.<sup>[14]</sup> Sulfadoxine-pyrimethamine has been found safe in pregnancy when used intermittently as part of IPT.<sup>[19]</sup> Data from clinical trials and program evaluations in stable transmission areas indicate that IPT is safe, efficacious, and effective in preventing maternal anemia, placental parasitemia, and low birth weight.

In laboratory, malaria is diagnosed using different techniques: Conventional microscopic diagnosis by staining thin and thick peripheral blood smears, RDTs, serological test, and molecular diagnostic methods, such as polymerase chain reaction.<sup>[20-24]</sup> Some advantages and shortcomings of these methods have also been described, related to sensitivity, specificity, accuracy, precision, time consumed, cost-effectiveness, labor intensiveness, the need for skilled microscopists, and the problem of inexperienced technicians.<sup>[25]</sup> Since the WHO recognized the urgent need for new, simple, quick, accurate, and cost-effective diagnostic tests for determining the presence of malaria parasites, to overcome the deficiencies of light microscopy, numerous new malaria-diagnostic techniques have been developed.<sup>[26]</sup> This, in turn, has led to an increase in the use of RDTs for malaria, which are fast and easy to perform, and do not require electricity or specific equipment.<sup>[26]</sup> Overall, RDTs appear as highly valuable, rapid malaria-diagnostic tool for healthcare workers; however, it must currently be used in conjunction with other methods to confirm the results, characterize infection, and monitor treatment.<sup>[27]</sup> Our attitude joins this strategy above with 93% positive malaria rapid test and identification of *P. falciparum* malaria diagnosis in 84% (168/200). Microscopic detection and identification of *Plasmodium* species in Giemsa-stained thick blood films (for screening the presenting malaria parasite) and thin blood films (for species' confirmation) remain the gold standard for laboratory diagnosis.<sup>[28]</sup> Malaria is diagnosed microscopically by staining thick and thin blood films on a glass slide to visualize malaria parasites.<sup>[25]</sup>

The *Plasmodium* species seen in this study confirm a previous report that *P. falciparum* is the most prevalent species in tropical Africa accounting for about 80–98% of malaria cases.<sup>[29,30]</sup>

Treatment of uncomplicated malaria in pregnancy is a balance between potential fetal adverse effects from drug toxicity and improved clinical status with clearance of the parasite. In 2006, earlier studies recommended a combination of quinine and clindamycin for treatment of uncomplicated malaria in pregnancy.<sup>[12,18]</sup> For severe malaria in pregnancy, WHO currently recommends treatment with either intravenous (IV) quinine or artesunate or IV artesunate in the second and third trimesters.<sup>[12]</sup> Treatment with artemisinin combination therapies (ACTs) in the first trimester is not recommended because of concerns raised by animal experiments which suggested that artemisinin and its derivatives might be teratogenic and cause fetal resorption if given to experimental animals during a narrow time window in early gestation. Studies have confirmed embryotoxic effects of artemisinin and its derivatives in animals, including primates, with risk being confined to a defined period of gestation.<sup>[31]</sup> According to current WHO guidelines, ACT can be given in the second and third trimester of pregnancy. Quinine can be used in all trimester of pregnancy. It does not cause abortion in therapeutic dose.<sup>[12]</sup> All patients admitted during this survey were considered as severe malaria, and our attitude aimed to reduce complications.

Malaria in pregnancy can cause sudden and dramatic complications. Therefore, it is very much essential to look for any complications by regular monitoring of the patients. Malaria poses substantial risk to the mother, her fetus, and the neonate; the infection contributes to as much as 15% of maternal anemia, 14% of low birth weight infants, 30% of preventable low birth weight, 70% of intrauterine growth retardation, 36% of premature deliveries, and 8% of infant mortality.<sup>[32]</sup>

In areas of stable transmission where adult women have considerable acquired immunity, *P. falciparum* infection during pregnancy typically does not cause symptomatic malaria but may lead to maternal anemia and placental malaria, especially among women having their first and second children.<sup>[32]</sup> This placental malaria contributes to low birth weight, the single greatest risk factor for neonatal death, and a major contributor to infant deaths. In areas of unstable transmission, women do not acquire substantial antimalarial immunity; infection with *P. falciparum* can cause severe clinical illness and has also been linked to poor birth outcomes, including stillbirth and premature delivery.<sup>[32]</sup>

Our findings confirm this with a high rate of maternal anemia and low birth weight infants in 30.5% and



12.5%, respectively. The cause of anemia particularly in pregnant lady is because of hemolysis of parasitized blood and increased demand of blood during pregnancy. Anemia increases perinatal mortality and morbidity and increased risk of postpartum hemorrhage.<sup>[33]</sup> Malaria and anemia are likely to act together to reduce birth weight. Their independent effects are difficult to distinguish. A study conducted in area of Papua New Guinea, which attempted to quantitate the separate effects of anemia- and malaria-attributable low birth weight, concluded that in malarious areas, malaria was a more important risk factor for low birth weight than that of anemia.<sup>[34]</sup>

## CONCLUSION

Malaria remains a frequent infectious disease during pregnancy. Therefore, it is very much essential to look for any complications by regular monitoring of the patients. The focus of malaria prevention during pregnancy is the use of antimalarial chemoprophylaxis and the use of ITNs. Sensitizations for antenatal consultations are useful to improve malaria management.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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