

Prevalence of Clinical Malaria and Relationship with Preventive Measures Among Pregnant Women Living in Libreville Gabon

Ntsame Owono MM¹, Tshibola Mbuyi ML², Tchanchou TDD^{3†}, Mawili-Mboumba DP², M'bondoukwe NP², Mayi-Tsonga S³ and Bouyou-Akotet MK^{2*}

¹Department of Medicine, Faculty of Medicine, Université des Sciences de la Santé, Libreville-Gabon.

²Department of Parasitology-Mycology, Faculty of Medicine, Université des Sciences de la Santé, Libreville-Gabon.

³Department of Obstetrics, Faculty of Medicine, Université des Sciences de la Santé, Libreville-Gabon.

†Deceased.

*Correspondence:

Bouyou Akotet MK. Department of Parasitology-Mycology, Faculty of Medicine, Université des Sciences de la Santé, Libreville-Gabon.

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ABSTRACT

Background: Pregnant women in malaria endemic areas are at high risk of *P.falciparum* infection and its complications. This study investigated for the first time in Libreville, the prevalence and factors associated with clinical malaria, among febrile pregnant women.

Methods: We conducted a cross-sectional study from May to November 2019 at the obstetric ward of the Hôpital d'Instruction des Armées Omar Bongo Ondimba (HIABO) of Libreville. Voluntary pregnant women who consulted for fever were approached. After obtaining their informed consent, the socio-demographic, obstetrical and clinical data, the history of fever treated with an antimalarial drug, the use of IPTp-SP and/or bednet were recorded. Peripheral blood was collected for *P.falciparum* detection by thick and thin blood smears. The associations between the studied variables and malaria were analyzed using a logistic regression analysis.

Results: During the study period, a total of 179 pregnant women were included. Their median age was 29 [25-33] years and 56.4% (n=101) were under IPTp-SP. The prevalence of *P.falciparum* malaria was 31.8%. The bivariate analysis identified the following factors associated with *P.falciparum* clinical malaria: age <20 years (p=0.06), high education level (p<0.01), not working (p<0.01), being single (p<0.01), and fever history (p<0.01). The multivariate analysis confirmed that age below 20 years (p=0.01), higher education level (p<0.01), not working (p<0.01), absence of IPTp-SP use (p<0.01), fever history (p<0.01) remained independent risk factor for clinical malaria in pregnant women.

Conclusion: The frequency of clinical malaria is high in this population of febrile pregnant women. It is associated with an infrequent use of preventive measures.

Keywords

Clinical malaria, Pregnant women, Gabon.

Introduction

Malaria in pregnancy (MiP), especially when caused by *P.falciparum*, poses substantial risk to the mother and foetus. In

areas with stable malaria transmission, MiP is predominantly asymptomatic and constitutes a major cause of maternal anaemia and low birth weight (LBW), the latter increasing the risk of infant death. Indeed, in highly endemic areas, infected pregnant women have acquired a partial immunity that reduces the risk of clinical disease and severe malaria [1,2]. In areas of low transmission,

women acquire little immunity, they are thus often symptomatic and more likely to develop severe malaria [3,4]. In a study carried out in Benin, a highly endemic country, 90% of the malaria episodes were mild forms, fever, headache and shivering were strongly associated with *Plasmodium falciparum* parasitaemia [5].

Intermittent preventive treatment with Sulfadoxine-Pyrimethamine (IPTp-SP) and insecticide treated nets (ITN) high coverages are associated with a lower burden of MiP. The deployment of this preventives measures is effective by Gabon since 2005. Six years after, the country underwent an epidemiological transition marked by a decrease in the prevalence of the *P.falciparum* infection in pregnant women attending antenatal care visits (ANC). The same trend was also observed among febrile children. However, since 2012, a rebound of clinical cases was noted, mainly in older children and adults [4,6,7]. Actually, the prevalence of clinical malaria is estimated at 35,6% in children ([8]; Data from Malaria National Program 2021). Data on clinical malaria among pregnant women are scarce although children, adults and pregnant women would share the same level of exposure to mosquito bites. Indeed, the level of ITN coverage is less than 30% in the country [9,10].

The aim of this study was to estimate the frequency of clinical *Plasmodium (P.) falciparum* infection, as well as associated factors in febrile pregnant women who visited a public hospital of Libreville, Gabon.

Patients and Methods

Study Area

From May to the November 2019, a cross-sectional study was performed at the obstetrical unit of l'Hôpital d'Instruction des Armées Omar Bongo Ondimba (HIABO) in Libreville, the capital city of Gabon. The region is characterized by a perennial hyperendemic malaria transmission with slight seasonal fluctuations, with a great rainy season from October to May that is interrupted by a small dry season between January and February; and a large dry season from June to September. The rate of entomological inoculation in Libreville is 20 to more than 80 infective bites per man per year [11]. IPTp-SP and ITN use have been adopted as national policies for the prevention of malaria in pregnancy since 2005. The prevalence of asymptomatic maternal microscopic malaria was 6% in 2011 and 4% in 2014. In Libreville, *P.falciparum* is the only species identified in pregnant women [4].

Data Collection

All pregnant women presenting at the obstetric ward during the study period were offered to participate in the study. They were included after they signed an informed consent. For each participant, data were obtained through a structured pretested questionnaire that included the following information: sociodemographic (age, residence, and marital status), gynecologic/obstetric history (parity, gestational age (GA), pregnancy information, and date of first visit), socio-economic (educational level, occupation, monthly income data), IPTp-SP intake and ITN use. The clinical symptoms and the complications were recorded using patient clinical files. The axillary temperature was taken using a digital

thermometer and fever was defined as a temperature ≥ 37.5 °C. Maternal peripheral venous blood was collected into tubes for malaria parasite determination.

Malaria Diagnosis

Malaria Rapid Diagnostic Test (RDT)

The malaria Pf/Pan RDTs SD BIOLINE, (SD Standard Diagnostics Inc., South Korea, Seoul) was performed for the rapid diagnosis of malaria according to the manufacturer's instructions. This test allows the detection of *P. falciparum* and non-falciparum species. The results were immediately communicated to the physicians for appropriate management.

Thick Blood Films

Thick smears were performed on study sites, and the procedures for the detection of malaria parasites were performed according to the Lambaréné method [12]. Carefully, 10 μ L of blood were laid on a 10 by 18mm area of a microscope slide, then dried, and stained. The parasitemia was expressed as the number of parasites per microliter of blood (p/ μ L), and parasite species were identified in the matched thin blood smears. Smears were read by two experienced technicians using a light microscope ($\times 100$ oil immersion lenses). Smears were considered negative if no parasite was seen after the examination of at least 100 oil immersion fields. In case of discordant results (presence or lack of asexual/sexual blood stages, mismatch species, or parasite density), the slides were reviewed by a third technician who resolved any discrepancy. For parasite density determination, the mean of the two closest parasitaemia was taken. Each woman with a positive RDT or thick smear received an antimalarial drug according to the national policy.

Study Procedures

The CDC rapid assessment of Malaria during pregnancy was used. It consists of a 10-week survey, including two weeks of information for the teams and the setting up of the study in the selected health facility. Febrile pregnant women from the outpatient and the inpatient wards of the obstetric department of HIAOBO were approached. They were recruited if they agreed to participate and they do not have a previous antimalarial treatment. After obtaining their signed consent, each woman was interviewed by a team member, then a blood sample was taken. Malaria RDT was performed directly on site and the results were given to the physician for a rapid management. Thick and thin blood smears were read at the department of Parasitology-Myecology and the results were communicated to the physicians.

Statistical Analysis

All data collected were analyzed using Statview 5.0 (SAS Institute Inc. USA). The qualitative variables are presented in frequencies and analyzed using the Chi-square or exact Fisher. Quantitative variables are presented as mean \pm standard deviation or median with interquartile (25th and 75th percentile) and analyzed using nonparametric tests (Mann Whitney and Kruskal Wallis). The multivariate analysis was performed by logistic regression to analyze the association between *P.falciparum* clinical malaria and

socio-demographic, obstetrical variables, preventives measures and history of fever. Statistical significance was set up at a p value less than 0.05.

Results

Characteristics of the Study Population

A total of 179 women were enrolled. Their median ages was 29 [25-33] years old. The baseline characteristics of the 179 pregnant women are summarized in Table 1. Briefly, 79.3% (n=142/179) had higher level of school attendance, 74.9% (n=134/179) were multigravidae, 87.2% (n= 156/179) were seen at the second trimester (Table 1). Several pregnant women used preventive measures: 26.5% used bed net and 40.2% (n = 72) had at least two IPTp-SP doses.

Table 1: Baseline characteristics of the study population.

Characteristic	Category	n	(%)
Age group (in years) (N=179)	<20	18	10.1
	≥20	161	89.9
Area of residence (N=179)	Urban	27	15.1
	Semi-urban/rural	152	84.9
Marital status (N=151)	Married	13	8.6
	Single	138	91.4
School attendance (N=174)	No or primary	32	18.4
	Secondary	90	51.7
	Higher	52	29.9
Workers (N=179)	Monthly income	118	65.9
Number of ANC visits (N=179)	< 3	85	47.5
	≥ 3	94	52.5
Age of pregnancy (N=179)	First trimester	32	17.9
	Second trimester	71	39.7
	Third trimester	76	42.4
IPT-SP (N=179)	0 SP dose	78	43.6
	1-2 SP doses	65	36.3
	≥ 3 SP doses	36	20.1
Malaria prevention (N=179)	None	65	38.5
	Bed net only	13	7.2
	IPT-SP only	70	36.9
	Bed net/IPT-SP	31	17.4
History of fever treated with an antimalarial drug (N=179)		37	20.7

Clinical malaria prevalence and signs

The frequency of positive blood smears was 31.8% (n = 57/179). *Plasmodium (P.) falciparum* was the only species identified. The median parasite density varied between 3000 à 100000p/μL. The median parasitaemia was 11000 [9375-13000] p /μL, with no significant difference according to the number of pregnancies. The median parasitaemia was comparable between women who did not receive IPTp-SP (10000[8000-12625] p/μL) and those who were under IPTp-SP (12000[10000-14500] p/μL) (p=0.82). Fever (68.4% vs 20.5%), fatigue (17.5% vs 8.2%), vomiting (10.5% vs 2.5%) were more frequent in women with clinical malaria (p=0.03). Uterine contractions (8.8%), and vaginal bleeding (3.5%) were only present in pregnant women (Figure 1).

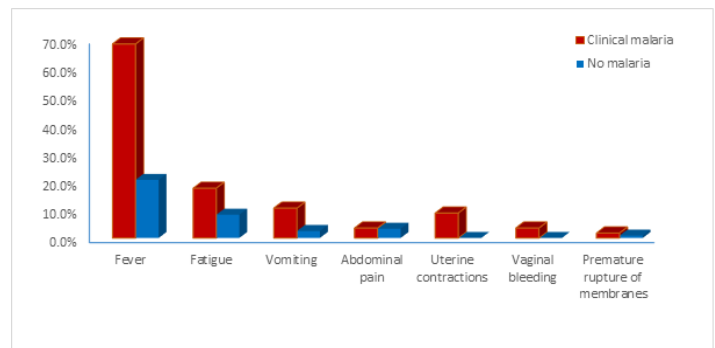


Figure 1: Distribution of clinical signs according to the presence of clinical malaria.

Relationship between the study variables and clinical malaria

The absence of use of preventive measures, particularly IPTp-SP (OR=2.3[1.3-4.5] p<0.01), was associated with a higher frequency of clinical malaria (Table 2).

A recent history of fever (OR= 39[1.8-8.2] (p<0.01)) was also a risk factor for clinical malaria, almost two-third of women with a history of fever had a plasmodial infection (Table 2). A trend towards a higher prevalence of clinical malaria was noted in younger pregnant women, in single ones and in absence of bed net use (Table 2)

Table 2: Relationship between sociodemographic data, malaria prevention and clinical malaria

Variables	n	%	p	
Age group (years)	< 20	9	50.0	0.08
	≥ 20	48	29.8	
Marital status	Married	2	15.4	0.08
	Single	57	39.9	
Any Preventive measure	Yes	24	21.1	< 0.01
	No	33	50.8	
IPTp-SP	No	33	42.3	< 0.01
	Yes	24	23.8	
Bed net use	Yes	9	20.5	0.06
	No	48	35.6	
Fever history during last 7 days	Yes	21	61.8	<0.01
	No	36	25.4	

Discussion

The prevalence of malaria parasitemia was 31.8% among the pregnant women seen at HIAABO. It is comparable to that reported in children and febrile adults in Gabon. According to data from Libreville and Melen, a semi-rural area located in the south of the country, malaria prevalence was between 30 to 39% among febrile children in a sentinelle site for malaria surveillance [8,13]. This is the first study on clinical malaria in pregnancy performed in Libreville. The last report on MIP in Gabon, highlighted a low prevalence of asymptomatic malaria among delivering women [14]. However, the prevalence of clinical MIP found here, is comparable to a hospital report from Ghana (39.7%), but lower than reports of other authors from sub-Saharan Africa [15-17]. Maternal age was associated with clinical malaria, young pregnant

woman (< 20 years) are also at the greatest risk of malaria infection. Similar findings have been previously reported by other authors in Gabon, Sudan and Cameroun [18-20]. Adolescent girls and women under the age of 20 are at highest risk of plasmodial infection during pregnancy, probably because they are more often primigravidae, and lack of information on correct pregnancy care. The effects of malaria in pregnancy have been shown to be lower in multigravidae than in primigravidae as a result of acquisition of specific immunity to placental malaria [21-23].

Our findings suggest that primigravidae share the same risk of clinical malaria with multigravidae as already reported in Gabon several years ago. Thus, efforts to reduce the burden of malaria in pregnancy should target all pregnant women. More than 70% of the study population was under TPI-SP. IPTp-SP reduces the exposure of pregnant women to parasites, putting them at the same level of susceptibility regardless of parity. It is admitted that when IPTp-SP coverage increases, the influence of parity on susceptibility to peripheral or placental maternal malaria infection or asymptomatic malaria disappears [24].

Being married was associated with a low frequency of clinical malaria. Similarly, in Yaoundé, Mbu et al showed that single women were four fold at risk of developing malaria during pregnancy [25]. Unmarried women are often younger and primigravidae. Being married has health benefits, including economic well-being that promotes access to health care [23, 26]. A husband can play an important role in encouraging his wife in attending antenatal care visits, with as a correlates, an effective use of preventive measures [27-29].

The coverage rate of IPTp-SP was 56%, similar to that reported by WHO. In addition, 70% of women had at least two doses and 25% had three. In 2011, only 10% of women seen late in pregnancy received three doses [30]. However, the use of bed net and especially ITN remains low, 28% and 10% respectively. A recent survey highlighted the decrease of ITN use among adolescents and adults [31]. The lack of awareness of the lack of information during ANC visit, as well as the lack of campaigns or ITN distribution campaign could also explain this low coverage. In stable transmission areas such as in Gabon, adult women have acquired a pre-immunity thereby they rarely develop severe malaria: they are often pauci-symptomatic or asymptomatic. The scarcity of studies on clinical MIP would underestimate the frequency of malaria associated symptoms in pregnant women from stable areas [32,33]. Fatigue, fever and vomiting predominated. Fatigue and vomiting would be increased with malaria, as these signs can also be related to the pregnancy. History of fever was also found as a risk factor for clinical malaria among pregnant women in other endemic areas [34-36]. Elsewhere, headache, asthenia, hepatic manifestations and others are described. All these symptoms are non-specific. This emphasizes the need of a biological diagnosis of malaria for a rapid management to avoid consequences such as vaginal bleeding, uterine contraction which were observed only in *P. falciparum* infected women and which are risk factors for preterm delivery.

Conclusion

The prevalence of clinical *P. falciparum* malaria in pregnant febrile women is high in Libreville. The low coverage of IPTp-SP and ITN would explain this high burden. Actions should be taken to improve the access and the use of these preventive measures.

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