

DOI: <http://dx.doi.org/10.18203/2320-1770.ijrcog20170588>

Original Research Article

Assessment of labor and delivery in pregnant women on sulfadoxine-pyrimethamine regimen in Yaoundé gynaeco-obstetric and paediatric hospital: a comparative study of 313 cases

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Received: 08 January 2017

Accepted: 08 February 2017

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ABSTRACT

Background: Malaria is still a major public health problem in sub-Saharan Africa. The aim was to determine the prevalence of malaria infection at the onset of labor and the resulting complications.

Methods: We carried out a five-month cross-sectional study at the Yaoundé Gyneco-Obstetric and Pediatric Hospital. We used results from the rapid diagnostic test (RDT) to compare two groups of pregnant women admitted into the labor room. Women who tested positive were assigned to the exposed group versus negative to the non-exposed group. Independent factors associated with malaria infection were investigated by the logistic regression method.

Results: Up to 79.6% (249/313) of women had received the sulfadoxin-pyrimethamine regimen with 32.9% (82/249) receiving at least 3 doses. Malaria infection was detected in 32.2% (101/313) of women. Only 14.9% (15/101) of the exposed group had received 3 doses of SP versus 31.6% (67/212) of the non-exposed group. After univariate analysis, malaria infection at the onset of labor was associated to premature rupture of membranes (OR=1.39; CI=1.01-1.94), fever during labor (OR=73.37; CI=64.80-681.95), non-reassuring fetal status (OR=2.08; CI=1.36-3.20), low birth weight (OR=1.65; CI=1.23-4.13), prematurity (OR=2.79; CI=2.12-367), a poor Apgar score at the 1st minute and postpartum fever (OR=3.19; CI=2.56-4.00). Linear logistic regression indicated that the occurrence of fever during labor (aOR=63.09), and low Apgar score at the first minute (aOR=6.27) remained significant and malaria infection was significantly associated to the single marital status (aOR=2.56) and a history of malaria during the current pregnancy (aOR=2.56).

Conclusions: Systematic RDTs is thus recommended at the last antenatal consultation to avoid identified complications.

Keywords: Cameroon, Complications, Labor, Malaria, Pregnancy

INTRODUCTION

Malaria is still a major public health problem in sub-Saharan Africa. In 2015, the region was most affected, with up to 88% of malaria cases and 90% of malaria deaths in the world.¹ Each year about 25 million women

are at risk of *Plasmodium falciparum* (PF) infestation. Malaria is endemic in Central and West Africa, with prevalence rates in pregnancy varying from 13.18 to 60.6% depending on the region and the season.²⁻⁷ This constitutes a significant public health issue.

In Africa, malaria is known to cause maternal, fetal and perinatal mortality and morbidity.^{1,8} WHO recommends the use of insecticide treated bed nets, Intermittent preventive treatment of malaria with sulfadoxine-pyrimethamine (IPTsp) and the adequate treatment of cases as effective means of fighting against malaria in pregnancy.

The diagnosis of malaria in pregnancy may not be very easy due to the sequestration of infected red cells by the placenta, varied clinical presentation and the low density of parasite in peripheral blood. Diagnosis of malaria based on symptoms alone appears to be highly inaccurate.⁹ The relative drop in adaptive immunity due to pregnancy may result in milder clinical manifestations and stop disease occurrence. The infection results from red blood cell parasitic invasion, shedding of these parasites into the general circulation, and the body's inflammatory response.¹⁰ The absence of clinical signs does not imply absence of disease since literature describes asymptomatic disease.^{4,6,11,12}

The clinical presentation of PF infection varies greatly from one pregnant woman to another, with some patients having fever and chills, to others being totally asymptomatic.¹³ Fever remains the most dreaded symptom of malaria in pregnancy and as such, most fevers in pregnancy are considered related to malaria until proven otherwise. This opinion has been shared by many authors who found that most fevers in pregnancy are due to malaria.^{14,15} This has led to the indiscriminate prescription of antimalaria drugs in areas where biological confirmation is not readily available.⁸

Some authors found a low prevalence of malaria infection in patients clinically suspected of malaria, and a relatively high prevalence in those not suspected for the same.^{4,16} Asymptomatic parasitemia frequently described in endemic zones negatively impacts the efficacy of diagnosis and treatment. Thus, the detection of circulating antigens of the plasmodium parasite might transform an otherwise normal pregnancy into a pathological one. The proper diagnosis of plasmodium infection in pregnancy is essential to preventing an adverse outcome.

Biological diagnosis is based on finding intra-erythrocytic forms in peripheral blood. Optical microscopy which allows this detection is the gold standard for malaria diagnosis.¹⁷ However microscopic analysis could be dented by fluctuations as well as a low circulating parasite load especially due to placental sequestration. The Rapid diagnostic Test for malaria (RDTm) is more efficient than microscopy and it is more affordable, easy to use and more suitable for use in low resource countries.^{5,9} Kyabayinze et al in Rwanda demonstrated a threefold prevalence of malaria in the febrile pregnant woman via RDTm compared to optical microscopy.¹⁸

RDTm is an immunochromatographic method which detects plasmodium specific proteins in blood as well as specific anti-plasmodium antibodies. Many studies have proven the accuracy of RDTm in the detection of malaria infection, prompting the management thereof with biological evidence.^{9,19-21}

The presence of clinical signs is not an indicator of the severity of the disease and placental malaria, which is the most common form of malaria in pregnant women, is asymptomatic.²² Placental malaria could be responsible for adverse outcomes during labor and delivery for both the mother and her fetus.¹⁸

Sulfadoxine-pyrimethamine (SP) has proven efficiency in the prevention of placental malaria in pregnant women.^{23,24} Fokam et al in Buea, Cameroon, found a low prevalence of malaria in pregnant women who were receiving the IPTsp and were sleeping under the long-lasting insecticide treated bed nets (LLITN).² They also found that 12.73% of patients who had malaria were on malaria prophylaxis.

In Cameroon, authors have sought factors associated with failure of IPTsp during pregnancy but the prevalence of malaria in pregnant women on IPTsp at the onset of labor is unknown.²⁵ National guidelines do not recommend screening for malaria in the absence of symptoms during pregnancy or at the onset of labor. We could not find a study describing the prevalence of malaria at the onset of labor in women on SP regimen in our environment. The goal of our study was to assess the effects of malaria infection on the prognosis of labor and delivery in women on SP regimen at the maternity of the Yaoundé Gynaeco-Obstetric and Paediatric Hospital (YGOPH).

METHODS

We carried out a cross sectional analytical study at the Maternity of the YGOPH between February 23rd and July 23rd 2015, a duration of 5 months. This hospital is one of the four University Teaching Hospitals in Yaounde which offer routine ANC, and labor and delivery services to all women regardless of whether or not they had received any prior ANC. Present study population was made up of pregnant women who gave informed consent, and were admitted into labor and delivery unit for vaginal delivery. We compared 101 women who had a positive rapid diagnostic test for malaria (RDTm) (the exposed group) with 212 who had a negative result (non-exposed group).

After approval of the research protocol by the ethics committee of YGOPH, we recruited women in the active phase of labor, with cervical dilatation at 4cm and above. On admission, the women were consulted either by an obstetrician/gynecologist or a resident in obstetrics and gynecology. Their medical records were examined in order to obtain information about the pregnancy follow-up. A pre-tested questionnaire was administered by the principal investigator and the women were followed up

from the time of their inclusion into the study to their discharge from the hospital. We diagnosed malaria upon admission into the labor ward using the care start malaria HRP2[®] test, an immuno-chromatographic test that detects the histidine rich proteinII (HRP2). The sensitivity of this test varies from 71 to 100% according to literature.^{18,20,26} Labor was managed by midwives and residents, using a partograph, as recommended by the World Health Organization.

The variables evaluated for inclusion were: maternal age, parity, gestational age (based on last menstrual period and/or 1st trimester obstetrical ultrasound), malaria prophylaxis during pregnancy, history of malaria during the pregnancy (after a RDTm, microscopy exam or presumptive treatment), characteristics of labor (uterine contractions, use of oxytocin, premature rupture of membranes, duration of the active phase of labor, the pattern of labor, the mode of delivery), clinical manifestations of malaria, characteristics of the new-born (birth weight, the 5th minute Apgar score, admission to neonatology) and postpartum complications (fever, haemorrhage, hypertension). Cases which presented with signs of urinary tract infections or typhoid fever were excluded from the study, by conducting, respectively, a urine culture and the Widal and Felix serology test. We also excluded cases of prolonged premature rupture of membranes (>24 hours).

To determine the minimum sample size for each group, it was assumed that the presence of circulating *Plasmodium falciparum* antigens in blood is responsible for a twofold

rise in the rate of preterm delivery, about 12.6% estimated by the World Health Organization.²⁷ The calculated minimum sample size using an adapted formula was 100 subjects for each group with a chosen precision and power of 5% and 80%, respectively.²⁸ We therefore retained a ratio of one case to two controls.

Data were analyzed using the computer software Epi info 3.5.4. Qualitative data were expressed in absolute numbers and frequencies. The characteristics of the exposed and non-exposed subjects were compared. Pearson's Chi square and Fisher's exact test were used to compare proportions. The difference was statistically significant for P-values <0.05. The odds ratio (OR) was calculated to measure the association between malaria infection and the variables studied. The variables associated with plasmodium infection following univariate analysis with P-value<0.1 were introduced into a logistic regression table in order to identify the independent factors associated with malaria infection.

RESULTS

Three hundred and thirteen pregnant women who fulfilled the inclusion criteria were included in the study. Among them, 101 (32.2%) tested positive for *Plasmodium falciparum* infection (exposed group) while 212 (67.8%) had a negative result (non-exposed group). Also, 79.6% (249/313) had received IPTsp with 32.9% (82/249) receiving at least 3doses of SP. Of those who had received IPTsp 14.9% (15/101) were in the exposed group and 31.6% (67/212) in the non-exposed group.

Table 1: Variables at inclusion into the study for the exposed (N=101) and the non-exposed (N=212) groups.

Variables	Positive *RDTm n (%)	Negative*RDTm n (%)	P-value
(15-20) years age group	16 (15.8)	8 (3.6)	<0.001
Single (marital status)	49 (49.5)	72 (34)	0.009
Less than secondary level	16 (15.8)	25 (11.8)	0.206
No profession	67 (66.3)	97 (59.1)	<0.001
Nulliparous	60 (59.4)	123 (58.0)	0.457
Multiparous	41(40.6)	76 (35.8)	0.301
No iron intake	18 (17.8)	11 (5.2)	<0.001
No use of mosquito bed nets	35 (34.7)	50 (23.6)	0.028
IPT-SPtaken	62 (61.4)	187 (88.2)	<0.000
≥3 doses of SP	15 (14.9)	67 (31.6)	0.060
Number of antenatal visits<4	44 (43.6)	62 (29.2)	0.009
Malaria during pregnancy	54 (53.5)	50 (23.6)	<0.001
Urinarytractinfection during pregnancy	4 (4.0)	3(1.4)	0.150
Genital tract infection	4 (4.0)	10 (4.7)	0.508
Gestational age <37 weeks	33 (32.7)	28 (13.2)	<0.001

*RDTm= Rapid Diagnostic Test of malaria.

Table 1 shows the characteristics of women included into the study. The (15-20) age group, single (marital status),

lack of financial resources, <4 antenatal visits, the non-use of mosquito bed nets, the absence of iron prophylaxis

and a previous history of malaria crisis during the current pregnancy were associated with malaria infection at the

onset of labor. Other variables showed no significant association.

Table 2: Comparison of different variables observed during labor and in the postpartum between the exposed (N=101) and the non-exposed (N=212) groups.

Variables	Positive *RDTm n (%)	Negative *RDTm n (%)	OR (95% **CI)	P-value
Fever during labor	61 (60.4)	7 (3.3)	73.37 (64.80-81.95)	<0.001
Headache during labor	8 (7.9)	3 (14)	2.36 (1.58-3.52)	0.006
Vomiting during labor	13 (12.9)	1 (0.1)	3.15 (2.75-3.85)	<0.001
Diarrhea during labor	7 (6.9)	0 (0)	3.25 (2.75-3.85)	<0.001
Normal uterine contractions	66 (65.2)	129 (56.2)	1.14 (0.81-1.60)	0.260
Normal labor pattern	86 (85.1)	178 (84.0)	1.06 (0.67-1.68)	0.464
Active phase of labor >6h	6 (5.9)	9 (4.2)	1.25 (0.66-2.38)	0.345
Meconium stained amniotic fluid	13 (12.5)	34 (22.2)	0.83 (0.51-1.37)	0.289
Non-use of Oxytocic drugs	55 (54.5)	106 (50.0)	1.12 (0.82-1.56)	0.268
Vaginal delivery	87 (86.1)	181 (85.4)	1.04 (0.66-1.67)	0.503
Caesarean delivery	14 (13.9)	28 (13.2)	1.03 (0.65-1.65)	0.501
PROM	35 (34.7)	51 (24.9)	1.39 (1.01-1.94)	0.034
non-reassuring fetal status	9 (64.3)	5 (39.3)	2.08 (1.36-3.20)	0.012
Post partum fever Oui	14 (13.9)	1 (0.5)	3.19 (2.56-4.00)	<0.001
Post partum hypertension	2 (2.0)	2 (0.9)	1.56 (0.58-4.21)	0.388
Post partum hemorrhage	15 (14.9)	35 (16.5)	0.91 (0.60-1.45)	0.422
1 st minute Apgar score <7	34 (33.7)	27 (12.7)	2.09 (1.55-2.84)	<0.001
Birth weight <2500	25 (24.8)	27 (12.7)	1.65 (1.23-4.13)	0.006
Neonatal death	2 (2.0)	11 (5.2)	0.46 (0.13-1.69)	0.151
Prematurity	19 (18.8)	5 (2.4)	2.79 (2.12-367)	<0.001
Neonatal Infection	7 (6.9)	5 (2.4)	1.86 (1.13-3.10)	0.052
Respiratory Distress	2 (2.0)	2 (0.9)	1.56 (0.58-4.21)	0.388
Neonatal Asphyxia	4 (4.0)	9 (4.2)	0.95 (0.41-2.18)	0.585

*RDTm= Rapid diagnostic test of malaria; **CI= Confidence interval; OR: Odds ratio; PROM: Premature rupture of membranes.

Table 3: Significant variables after multivariate analysis.

Variables	p-value	Adjusted *OR	95% **CI
Single marital status	0.02	2.56	1.12-5.86
Malaria during the current pregnancy	0.00	7.73	3.27-18.26
Fever during labor	0.00	63.09	20.31-196.00
Apgar score <7 at the first minute	0.00	6.27	1.62-24.26

*OR: Odds ratio; **CI= Confidence interval.

The outcome variables analyzed (Table 2) were: the presence of fever, headache, vomiting and diarrhea during labor, gestational age less than 37 weeks, premature rupture of membranes, non-reassuring fetal status, postpartum fever, first minute Apgar scores less than 7, babies weighing less than 2500g and prematurity. These were shown to be associated with malaria infection at the beginning of labor.

After multivariate adjustment (Table 3), single marital status, a previous history of malaria crisis during the current pregnancy, fever during labor and Apgar score

less than 7 at the first minute of life were independent factors associated with the diagnosis of malaria during labor.

DISCUSSION

Many studies in the literature have evaluated the prevalence of malaria at the beginning of pregnancy, notably at antenatal consultations.^{6,7,11,12} The prevalence rates found are quite variable, given the endemic nature of the disease and the preventive measures put in place to fight the infection. The highest prevalence rates were

found in Nigeria with figures as high as 60%.⁷ In 2016 Fokam et al in Buea, Cameroon, found a low but significant prevalence of 13.4%.² Matangila et al in the Democratic Republic of the Congo had a prevalence of 27.4% in Kinshasa.⁵ Cameroon and the Democratic Republic of the Congo are in a zone of high endemicity and stable transmission of *Plasmodium falciparum*. Preventive measures for malaria in pregnancy are applied in order to reduce both its prevalence and deleterious effects on the fetus and mother.

In present study, the prevalence was studied at the end of pregnancy, at delivery, and in principle, after implementing preventive measures. Present findings revealed that at the onset of labor 32.4% of pregnant women have malaria infection. This very high rate could be due to the fact that a good proportion of the women did not use the LLITNs (34.7%) and IPT with SP (61.4%). Mathanga et al, similar to Fokam et al, found that LLITNs had a protective role against malaria in pregnancy, and the use of both LLITNs and IPT with SP significantly reduced disease prevalence in pregnancy.^{2,29} The time lapse between two doses of IPTsp is important in the protection of the pregnant woman. Long periods between the last dose and the onset of labor could explain the high disease prevalence at delivery. Essiben et al found that 72.2% of women who had malaria despite taking IPT with SP, had a delay of more than 60 days between doses.²⁵

The symptoms of malaria in pregnancy in areas of stable transmission are common but non-specific.³⁰ We also found that among women who received IPT with SP, a past history of malaria in the index pregnancy was associated with malaria infection at the start of labor.

In fact, the appearance of resistant strains of PF to SP in present setting could also be a cause. In Ghana, Yeboah et al found a malaria prevalence of 11.2% in women who received IPT with SP and have thus questioned the efficacy of the treatment.³¹

Single marital status was associated with malaria infection in these patients. Singles are usually young and more prone to malaria infection compared with older women since they are still in the process of acquiring immunity against malaria.³² Single mothers constituted the majority of our population of study (59.4%). Moreover, these single mothers were primigravidae. Placental malaria is more frequent in primigravidae.³³ Immunity is shown to decrease significantly in pregnancy, especially in first pregnancies. Multi-gravid women have acquired sufficient immunity against malaria in their previous pregnancies.^{34,35}

Fever in pregnancy should imply the diagnosis of malaria in women who received prophylaxis. A positive malaria test at the beginning of labor was associated with fever during labor. Fever during pregnancy in present setting is very often due to malaria even though it is not the only

etiology of fever in pregnancy. Implicit stress during labor can trigger a malaria episode which will manifest as fever. This could explain 60.4% of cases presenting as fever during labor. Lucy et al in Cameroon and Orok et al in Nigeria reported the prevalence of malaria in cases of fever in pregnancy to be 80 and 90%, respectively, while typhoid fever occupied the second position.^{14,15} In subtropical regions, typhoid fever is often the second cause of fever in pregnancy. The prevalence rate depends on the type of diagnostic test used. Lucy et al used stool examination and found a prevalence of 7.9% whereas Orock et al used the Widal and Felix test and obtained a prevalence of 46.8% and only 0.8% following hemoculture.^{14,15} The same authors have described cases of co-infection.

The impact of malaria is not limited to fever during labor. Maternal fever will increase fetal temperature, leading to fetal tachycardia which is very dangerous for the fetus. Malaria during pregnancy also affects the placenta. Placental malaria is a frequent form of asymptomatic malaria in pregnant women.^{33,36} The sequestration of infested erythrocytes in the intervillous spaces is responsible for bleeds, placental ischemia and ultimately compromising materno-fetal exchange with intra-partum fetal hypoxemia.³⁷ This can be responsible for fetal distress and neonatal asphyxia as demonstrated in present study. However there exist limitations to our study. We were unable to study placental lesions in present study population in order to directly explain the fetal complications observed in those neonates born of RDT-positive parturients. Also, the screening for congenital malaria in neonates born to at-risk women was not undertaken.

CONCLUSION

The presence of malaria infection at the onset of labor is associated with single marital status, a history of malaria during the current pregnancy, fever during labor and neonatal asphyxia. Therefore, to prevent subsequent morbidities, malaria infection should be systematically checked at last ANC such that treatment can be administered especially when risk factors have been identified.

ACKNOWLEDGMENTS

The authors wish to acknowledge the authorities of the Yaoundé Gynaeco-obstetric and Paediatric Hospital (YGOPH) who allowed us to carry out the study at their institution. This study received no grants from any funding agency be it public, commercial, or non-profit organization.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Approval of the research protocol by the ethics committee of YGOPH

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Cite this article as: Foumane P, Essiben F, Dohbit JS, Tongna CY, Meka EJNU, Ojong S, Mboudou ET. Assessment of labor and delivery in pregnant women on sulfadoxine-pyrimethamine regimen in Yaoundé gynaeco-obstetric and paediatric hospital: a comparative study of 313 cases. *Int J Reprod Contracept Obstet Gynecol* 2017;6:1076-82.