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Original Research Article

Prevalence and risk factors for placental malaria parasitemia in a tertiary hospital in north-central Nigeria

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ABSTRACT

Background: Malaria in pregnancy is a major public health problem in sub-Saharan Africa. Placental malaria is recognized as a complication of malaria in pregnancy in endemic areas with adverse effects on pregnancy. Aim was to determine the prevalence and risk of placental malaria parasitaemia at delivery in Federal University Teaching Hospital, Lafia.
Methods: This was a cross-sectional study where 200 pregnant women in labour were enrolled consecutively by convenient sampling after obtaining informed consents. Maternal, cord and placental blood samples were taken for thick and thin blood film for malaria parasites after delivery. Data analysed using IBM SPSS version 23. Chi square test and regression analysis used for degree of association and independent risk factors for placental malaria determination. A p-value of less than 0.05 was considered statistically significant.
Results: The prevalences of maternal peripheral blood parasitaemia was 18.5% (37/200), placenta parasitaemia was 17,5% (35/200) and cord blood malaria parasitaemia was 13.0% (27/200). The risk factors for placental malaria parasitaemia were non-use of intermittent preventive treatment (OR=0.408, p=0.000), non-use of insecticide treated nets (OR=0.043, p=0.000) and low level of education (OR= 0.012, p=0.000).
Conclusions: The significant contributors to placental malaria parasitaemia are low level of education, non-use of intermittent preventive treatment and non-use of insecticide treated bed nets. Girl child education, use of insecticide treated nets which should be made available and free, and use of IPT as directly observed therapy should be adhered to.

Keywords: Malaria, Nigeria, Placenta parasitemia, Placental malaria, Prevalence, Risk factors

INTRODUCTION

Malaria is an acute febrile illness caused by Plasmodium parasites which are spread to humans through the bites of infected female Anopheles mosquitoes.[1] There are five species that cause malaria in humans and two of these species, *P. falciparum* and *P. vivax* pose the greatest threat.[1]

The global burden of malaria infection is primarily in low and middle-income countries. The World Health Organization (WHO) reported in 2018 that there were 228 million cases; 93% of cases occurred in Africa, followed by southeast Asia (3.4%) and the eastern Mediterranean region (2.1%).[2] Sub-Saharan Africa and India carried 85% of all cases.[2] While cases in 2018 were lower than 2010 (251 million cases), the incidence rate has been relatively stable since 2014 at 57 cases per 1000 population at risk, demonstrating a slowing of the rate of change in addressing malaria infection.[2] Additionally, as the overall number of endemic regions decreases, studies are finding that malarial immunity in previously endemic regions are dropping, leading to more adverse pregnancy outcomes in women who become infected.[3] In Africa, pregnant women and under five children represent the most vulnerable group to malaria infection.[1,2]

The burden of adverse obstetrics and neonatal outcomes occurs as a result of placental malaria, when the parasite-infected red blood cells sequester in the intervillous spaces of the placenta.[3] In endemic regions, placental malaria may be present in up to 63% of pregnant women, irrespective of malaria infection symptomatology.[4]

Placental malaria parasitemia occurs because the parasitized erythrocytes have the ability to adhere to chondroitin sulphate A on the syncytiotrophoblast of the placenta.[5] It is characterized by the accumulation of these infected RBCs in the intervillous space and subsequent infiltration of maternal monocytes/macrophages.[6] Prominent inflammatory infiltration by monocytes/macrophages causing massive chronic intervillositis is related to severe placental malaria.[7]

Placental malaria can only be diagnosed post-partum by assessing the placenta, treatment is primarily preventive. There are two main approaches to prevention in areas with active transmission: intermittent preventive treatment in pregnancy (IPTp) and intermittent screening and treatment in pregnancy (ISTp). These two approaches are active areas of research given the ongoing changes in malaria endemicity and Plasmodium drug resistance. In endemic regions, the WHO recommends IPTp with sulfadoxine-pyrimethamine (SP).[2] However, in sub-Saharan Africa, where the bulk of malarial infections occur, *P. falciparum* has developed sequential mutations in the dihydrofolatereductase (DHFR) and dihydropteroate synthase (DHPS) genes, which confer resistance to pyrimethamine and sulfadoxine, respectively. To combat the developing resistance, the WHO made recommendations for three or more doses of SP during pregnancy starting in the second trimester.[2]

P. falciparum-derived VAR2CSA receptor is the main molecule facilitating the binding of infected red blood cells (RBCs) to chondroitin sulphate A (CSA) in the intervillous space. Formation of antibodies against VAR2CSA inhibits binding of infected RBCs to CSA, thereby preventing complications related to placental malaria.[3]

Maternal ABO blood group, antenatal clinic attendance with the use of intermittent preventive treatment with sulphadoxine-pyrimethamine, primiparity, retroviral status, maternal age, nutritional status, level of anti-parasite immunity, parasite genetics, and transmission rate are among several factors associated with placental malarial parasitemia.[3]

A number of local studies have reported a significant association between maternal age and placenta malaria.[8,9] Studies have shown that young women of child bearing age may be more susceptible than older women to malaria because they are still in the process of acquiring natural immunity.[3] In Cameroun, age was a major factor for placental malaria, similarly in Zaire, mothers with placenta malaria where younger (mean age 24 years old) than mothers with non malarious placentae (mean age 29 years old).[1] It was suggested that development of pregnancy associated immunity i.e. production of anti-bodies that inhibit the adherence of placenta parasites to chondroitin sulphate A may be very important in women younger than 25 years who have lower level of acquired immunity (through less frequency of exposure to the bites of *P. falciparum*-infected mosquitoes) than older women who may have obtained adequate immunity following repeated exposure and thus are less dependent on anti-cytoadherent anti-bodies.[3] However it is important to state that in malaria areas, pregnancy associated and age dependent immunity to placenta malaria may be influenced by host or environmental factors.[10]

Therefore, this study was conducted to determine prevalence and risk factors associated with the occurrence of placental malaria in parturients at Federal University Teaching Hospital (FUTH), Lafia (formally Dalhatu Araf Specialist Hospital, Lafia.).

METHODS

Study area

The study was conducted at the department of obstetrics and gynecology, FUTH, Lafia, Nasarawa state, North-Central Nigeria. The hospital is the only tertiary health institution located in the state capital, receiving patients from other parts of the state and parts of neighbouring states like Plateau, Benue, Taraba and Kaduna.

Study population

The study population comprised all consenting pregnant women who presented to labour ward for delivery and were eligible for the study.

Study design

This was a cross-sectional study.

Sampling technique

Women who presented in the labour suit of the hospital, who were eligible and consented were enrolled consecutively.

Inclusion/exclusion criteria

All pregnant women who presented to the delivery suite (for delivery) except: pregnant women with vaginal bleeding, pregnant women on treatment for malaria, pregnant women who were treated for malaria within the past two weeks and parturients who did not consent.

Sample size determination

The sample size for this study was calculated using Fisher's formula below:

$N = [Z^2P(1-P)] / d^2$

where, N = minimum sample size;

Z = proportion of normal distribution corresponding to the required (5%) significance level (which is1.96);

P = prevalence of placental malaria parasitemia (which is 13.7% or 0.137 from a previous study.[8]

d = degree of accuracy/ precision expected (0.05)

Thus, $N = (1.962)^2 \times 0.137 (1-0.137)/ (0.05)^2 = 182$. The sample size was therefore 182. Giving allowance for a 10% attrition rate, the minimum sample size for the study was 200 participants.

Data collection

The procedure was explained to the subjects and a written consent was obtained from each one of them. Data was collected from each subject using a well-designed questionnaire administered by the researcher with the aid of research assistants and the information was entered into the pro forma. The questionnaires contained information that included maternal age, marital status, educational status, occupation, gravidity, antenatal care, malaria preventive measures. Others were birth weight of babies, maternal blood and placental blood microscopy for malaria parasite detection as well as parasite density.

Two millilitres (ml) of blood collected from the ante cubital vein using disposable syringe, was placed in a specimen bottle containing ethylene diamine tetra-acetic acid (EDTA) and sent to the laboratory for malaria parasites.

Placental blood collection

The aspiration method of placental blood collection was employed. This was done immediately after delivery of the placenta. The placenta (with its maternal surface facing up) was placed on a smooth surface. The maternal placental surface was pierced (to a depth of about 0.5cm) with a sterile disposable syringe on a 14-gauge hypodermic needle. Two millilitres of placental blood was aspirated and put into an EDTA bottle. The specimen was labelled to correspond with the code on the questionnaire (for easy identification) and was sent to the laboratory for processing (smearing, staining and microscopic examination).

The portion of the cord attached to the placental was cleaned and 2 ml of cord blood was collected from this portion into heparinised (EDTA) bottle for blood film for malaria parasites.

Laboratory procedure

Preparation and staining of the thick blood smear: two drops of placental blood sample was placed on a slide using a small rubber pipette. Using the edge of a second slide, the drops of blood was joined and spread to make an even thick smear and was allowed to air-dry. The slide was immersed in the staining trough, containing 10% of freshly prepared Giemsa solution at pH 7.2 and contact maintained for 10 minutes. The slide was then removed and allowed to dry. Preparation and staining of the thin blood smear: one drop of placental blood was placed on a clean slide using a rubber pipette. The edge of a second slide was held steadily at an angle of 45º to the first was used to spread the drop of blood to create the thin blood film. The thin film was fixed using methanol (methyl alcohol) by maintaining contact with methanol for 10 seconds. The slide was then immersed in the staining trough containing 10% of freshly prepared Giemsa solution at pH 7.2 and contact maintained for 10 minutes. The slide was then removed and allowed to dry. The stained placental blood smears were examined under × 100 oil immersion lens of a light microscope. The same procedure was repeated for the maternal and cord blood samples from each patient. Malaria diagnosis was made based on identification of asexual stages of *Plasmodium* species on the thick blood smear while the thin blood smear was used for species identification. Parasite density was determined by counting the number of parasites per high power field in the thick blood smear and the slide was reported as negative if no parasite was identified per 100 high power fields.

Data analysis

Socio-demographic characteristics of the mothers and information from the structured questionnaire were entered and statistical analysis was done using statistical software (IBM SPSS for windows® version 23.0, SPSS Inc.; Chicago, USA). Quantitative data such as age, birth weight and gestational age were presented using mean and standard deviation while qualitative data were presented in percentages. Chi-square test was used for degree of association between placental malaria infestations and risk factors, a p value of <0.05 was considered statistically significant. Logistic regression analysis was used to determine independent risk factors for placental malaria.

RESULTS

During the study period of 10 weeks, between 13th of July to 20th September 2023, there were 450 deliveries, 200 pregnant women who met the inclusion criteria for the study and consented were recruited.

The ages of the 200 women ranged from 17-41 years with mean age of (Mean±SD) 28.0±6.1 years. Majority 82 (41.0%) had secondary education, 77 (38.5%) had tertiary education, few women 21 (10.5%) had primary education while 20 (10.0%) of the women had no formal education. The study further revealed that greater percentage of the women 97.5% were married and only 2.5% were single. Most 103 (51.5%) of the subjects were unemployed while 93 (46.5%) were employed.

Table 1: Sociodemographic characteristics of subjects.

Characteristics	Frequency	Percent
Mean age	28.0±6.1 years	
Age (years)		
17-22	42	21.0
23-28	68	34.0
29-34	50	25.0
35-41	40	20.0
Total	200	100
Mothers level of education		
None	20	10.0
Primary	21	10.5
Secondary	82	41.0
Tertiary	77	38.5
Total	200	100
Marital status		
Married	195	97.5
Single	5	2.5
Total	200	100
Employment status		
Unemployed	103	51.5
Employed	93	46.5
Total	200	100
Place of residence		
Rural	49	24.5
Urban	151	75.5
Total	200	100
Parity		
0	42	21.0
1	51	25.5
2	37	18.5
3+	70	35.0
Total	200	100
Mean parity	2.34	
IPT dosage		
None	54	27.0
1 dose	30	15.0
2 doses	22	11.0
3+ doses	94	47.0
Total	200	100

Majority of the women 151 (75.5%) resided in the city while 49 (24.5%) lived in rural areas. Most of the women 70 (35.0%) were para 3 and above, 51 (25.5%) were para 2 while 42 (21.0%) were para 0. The assessment of IPT usage and doses showed that, of the total number of mothers in this study 54 (27.0%) did not take intermittent preventive treatment for malaria (IPT), 94 (47.0%) had 3 doses and above, 22 (11.0%) had 2 doses while 30 (15.0%) had one dose (Table 1).

Placental blood malaria parasitemia, maternal peripheral blood malaria parasitemia and cord blood malaria parasitemia were 35 (17.5%), 37 (18.5%) and 27 (13.5%) respectively. *Plasmodium falciparum* was the only malaria specie detected in all the blood films (Table 2).

Table 2: Prevalence of malaria infection at delivery.

Characteristics	Frequency (n=200)	Percent
Placental blood malaria parasitemia	35	17.5
Maternal peripheral blood malaria parasitemia	37	18.5
Cord blood malaria parasitemia	27	13.5

The risk factors that were significantly associated with placental malaria parasitemia were none or low educational level, low parity, non-use of insecticide treated nets and non-use of intermittent preventive treatment for malaria with a p value <0.005. The placental malarial infection was highest among women aged 17-23 years 10 (23.8%). However, age was statistically not significant with a p value >0.05 (Table 3).

Table 3: Risk factors for placental malaria.

Characteristics	Placental malaria		χ^2	P value
	Yes (%)	No (%)		
Mothers age (years)				
17-22	10 (23.8)	32 (76.2)	3.73	0.292
23-28	14 (20.6)	54 (79.4)		
29-34	5 (10.0)	45 (90.0)		
35-41	6 (15.0)	34 (85.0)		
Educational level				
None	2 (10.0)	18 (90.0)	10.95	0.002
Primary	7 (33.3)	14 (66.7)		
Secondary	19 (23.2)	63 (76.8)		
Tertiary	7 (9.1)	70 (90.9)		
Use of ITN				
Yes	4 (4.2)	92 (95.8)	22.7	0.000
No	31 (29.8)	73 (70.2)		
IPT dosage				
None	9 (16.7)	45 (83.3)	3.73	0.000
1 dose	12 (40.0)	18 (60.0)		
2 doses	6 (27.3)	16 (72.7)		
3 doses and more	8 (8.5)	86 (91.5)		
Parity				
0	10 (23.8)	32 (76.2)	24.5	0.011
1	12 (23.5)	39 (76.5)		
2	7 (18.9)	30 (81.1)		
3 and above	6 (8.6)	64 (91.4)		

Table 4: Logistic regression analysis of risk factors associated with placental malaria.

Factors	Odd ratio	95% Confident interval	P value
Educational status	0.012	0.010-0.213	0.000
Use of ITN	0.102	0.035-0.303	0.000
IPT dosage	0.408	0.263-0.632	0.000
Parity	1.024	0.913-1.149	0.692

After adjusting for confounding factors, only educational status, ITN use and IPT use remain statistically significant with OR 0.012, 0.102 and 0.408 respectively, and a p value <0.05. Parity was however not an independent risk factor for placental malaria with OR=1.024 and p value >0.05 (Table 4).

DISCUSSION

The prevalence of placental malaria parasitemia, maternal peripheral bood parasitemia, and cord blood parasitemia in this study was 17.5%, 18.5% and 13.5%, respectively using microscopy. The placental malaria prevalence in this study is similar to prevalence of 18.2% reported in Uyo, but much lower than the prevalence of 69.6% in South-Eastern Nigeria, 65.2% in South-South Nigeria and 44.6% reported in Uganda.[11-14] However it is higher than the values of 13.7%, and 14.0% reported by Oweisi and Mokoulu respectively.[8,15] The average placental parasitemia prevalence rate quoted by a multicentre study in Nigeria was 21.5% with a range between 19.0 and 80.0%.[15]

The variations in the prevalence in this study and previous studies could be due to the sociodemographic characteristics of the study population (parity, HIV status), community acquired immunity, seasonal variation, methods of sample collection, diagnostic tool used in the

detection of parasites (Histology, PCR,) and use of ITN and intermittent preventive treatment during pregnancy.

The slightly higher prevalence of maternal peripheral parasitemia of 18.5% compared with placental parasitemia of 17.5% is in keeping with findings in Ile-Ife where peripheral parasitemia was 57.7% and placental parasitemia was 48% and also findings from Abuja and Abeokuta.[1,16,17] However this is in contrast with findings in Cote dIvoire.[18]

The utilization of IPT in this study was 77% which is lower than the recommended 80.0% by WHO.[19] This low IPT utilization was also reported by other studies in Sub-Saharan Africa.[1,20] Use of intermittent preventive treatment for malaria prophylaxis in the study was significantly associated with reduced risk of placenta malaria (χ^2 =3.73, p value 0.000). The more the number of dosages in pregnancy, the better the protection offered. This is consistent with other studies.[8,14,15,21] Because pregnant women in malaria endemic areas are among the most vulnerable to the infection, the World Health Organization has recommended that all pregnant women should sleep inside insecticide treated bed nets.[22]

According to the Nigerian Demographic and Health Survey of 2013 only 18.0% of pregnant women slept inside long-lasting insecticide treated bed nets the night before the survey.[23] Although the result from this study showed 48.0% of consistent use which is below the recommendation for consistent use among all (100%) pregnant women in malaria endemic regions. However non-use of insecticide treated net in this study is an independent risk factor for placental malaria (χ^2=22.7, OR-0.043, p value 0.000). This is in keeping with findings in Ile-Ife.[1]

In this study parity was significantly associated with placental malaria, low parity has increased risk of placental malaria with (p value =0.011), however, it is not an independent risk factor (p value 0.692, OR 1.024). This finding is in contrast with other findings and consistent with several studies.[8,9,14,15,24-26] This is because multiparous women in malaria endemic regions are believed to form blocking antibodies that bind to placenta chondroitin A sulphate, during their subsequent pregnancies and prevent placental sequestration of *Plasmodium falciparum*.[3] Maternal age is also not significantly associated with placenta malaria (χ^2-3.73. OR-1.771, p value 0.292) and this is consistent with findings in Yemen.[26]

As observed in this study, educational level is strongly associated with incidence of placental malaria (p value 0.002). Parturients who had non or primary level of education are at higher risk of having placental malaria as compared with parturients with secondary and higher level of education. High educational standards usually affect health awareness and therefore has a positive impact on health.[27] The reverse may be the case in those with lower standards of education as they may not appreciate the burden of malaria in pregnancy and the importance of adherence to stipulated malaria preventive measures because of their limited understanding and knowledge.

CONCLUSION

Placental malaria parasitemia constitutes a major challenge in pregnancy as it is significantly associated with adverse pregnancy outcome. Intermittent preventive treatment with sulphadoxine pyrimethamine (IPT) and use of insecticide treated net were found to significantly reduce placental parasitemia, while maternal characteristics such as low parity and low educational status increase the risk. There is therefore the need to intensify the existing control measures aimed at reducing malaria in pregnancy in Nigeria.

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