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Prevalence of Placental Malaria and Effects on Birth Weight of Neonate of Mothers Who Had Antenatal Care in Maiduguri Metropolitan City, Nigeria

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Authors' contributions

This work was carried out in collaboration between all authors. Author BUA conceived, designed and performed the statistics of the study. Authors BUA, CR, HBM, FJB, ANC and AY assessed and interpreted the data. Authors BUA, EBE, BKA, YE and ZJF wrote the draft of the report, however, all authors were also involved in the critical revision of the paper.

Original Research Article

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ABSTRACT

Background: Low birth weight (LBW) is an important risk factor for infant morbidity and mortality especially in malarial endemic countries. The study focused on the prevalence of placental malaria and neonatal LBW, as well as the relationship between placental malaria and neonatal LBW outcome in Maiduguri metropolitan city, Nigeria.
Methods: A total of 110 mother-neonatal pairs were studied. Neonatal birth weights were measured using the bassinet weighing scale and placental tissues for the diagnosis of placental malaria were collected from mothers of these neonates. Student t test and

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Chi-square trend ($\chi 2$) with Yate's correction were used to investigate quantitative and categorical variables, whereas, Univariate analytical model was used to estimate the relationship between placental malaria, maternal age, parity and neonatal LBW.
Results: Forty-nine mothers (44.5%) had placental malaria and the association of maternal age group (27-31and32-36) years with placental malaria was significant (p=0.029). Of the 14(100%) neonates with LBW, 10(71.4%) had their mothers diagnosed with placental malaria. The relationship between placental malaria and LBW was however not significant (p=0.207). Also, the relationship between maternal age, parity and neonatal LBW outcome was not significant.
Conclusions: Placental malaria constituted 44.5% and the disease was associated with maternal age bracket (27-31and32-36) years in this work. Although the relationship between placental malaria and neonatal LBW was not significant, most neonates with LBW in present study had their mothers diagnosed with placental malaria.

Keywords: Placental malaria; low birth weight; neonates; antenatal care; Maiduguri; Nigeria.

1. INTRODUCTION

Over 30 million women become pregnant yearly in malarious regions of Africa, and most of these women reside in areas of stable malaria transmission [1]. Guyatt et al. [2], in 2004, in Nairobi observed that vast majority of women with placental malaria during pregnancy are asymptomatic. Probable reason for this could be the fact that most of these women now register for antenatal care (ANC), and are placed on sulfadoxine and pyrimethamine as routine intermittent preventive therapy for malaria (IPT) [3,4]. Placental malaria increases the risk of women delivering low birth weight (LBW) neonates and this is an important risk factor for infant morbidity and mortality [2,3]. Placentas that are infected with malaria parasites tend to recruit antibodies, cytokines and macrophages indicating immune response to these parasites [5]. The LBW akin to placental malaria may be related to impaired nutrient transport to the foetus. High densities of malaria parasites in the placenta coupled with immune response may result in consumption of nutrient that would have been delivered to the foetus, leading to LBW [2].

Ismail et al. [5], in 2000, found that malaria infected placentas have thickening of placental membranes. This may again interfere with nutrient and oxygen transport across the placenta to the foetus. Multiparous mothers were initially thought to have low risk of placental malaria relative to primigravidae and secundigravidae [6]. Multiparous mothers now are known to be at risk of placental malaria like the primigravidae and secundigravidae [6,7]. This could be due to loss of previously acquired immunity in these mothers making them particularly susceptible to placental malaria. In Kenya, Ter Kuile et al. [7], in 2003, had further argued that multiparous mothers could have high risk of placental malaria, particularly if they are living in stable malaria areas. Many authors in Nigeria and other sub-saharan countries of the world on placental malaria looked at its prevalence [3,4,8-12]. Few of them examined the relationship between placental malaria and other febrile illnesses [12], another few of them described the prevalence and impact of placental malaria during pregnancy with an attempt to quantify this burden on neonatal birth weights (BW) [3,4,9-11].

Although histology remains the gold standard for diagnosing placental malaria, inconsistencies regarding placental malaria as a cause of LBW have been reported. Whereas some investigators have published that placental malaria could lead to LBW others

differ [3,4,9-11]. This issue could still be a debatable one and more studies that will throw more light in this regard may be needed. Therefore, learning about the relationship between placental malaria and neonatal LBW outcome cannot be overemphasized. This study, therefore aimed at: 1) Estimate the prevalence of placental malaria and neonatal LBW. 2) To determine the relationship between placental malaria and neonatal LBW outcome in Maiduguri metropolitan city, Nigeria. The study may further bridge the gap in knowledge of the subject in our environment because to our knowledge, no such study has been done in Borno state after extensive search of the literature.

2. MATERIALS AND METHODS

2.1 Study Site

The study was carried out at the Department of Paediatrics and Obstetrics unit of the University of Maiduguri Teaching Hospital (UMTH), Nigeria. The UMTH is a tertiary centre located in North-eastern Nigeria and a centre of excellence in infectious diseases and immunology. It also serves as a referral site for the six North-eastern States and neighboring countries of Chad, Cameroon and Niger Republics [13].

2.2 Study Design

The study was a hospital-based cross-sectional descriptive study of subjects recruited from the obstetric unit and labour ward of the UMTH.

2.3 Study Population

Mother-neonatal pairs who met the following inclusion criteria were recruited: mothers who did ANC and delivered at the labour ward of UMTH, neonates of these mothers and informed consent given by any of the parent. Chronically ill mothers or those with multiple pregnancies were excluded from the study because these conditions could lead to LBW deliveries.

2.4 Sample Size and Collection of Specimens

The minimum sample size was determined using statistical formula ($N=Z^2pq/d^2$) that has a power of 50% [14]. N=minimum sample size, p=proportion of population with placental malaria infection. In this study, the value for p=5% (2), q=1.0-p, Z=standard normal deviate at 95% usually set at 1.96 confidence level, d=level of precision=0.05. Computing 5% prevalence for placental malaria at a confidence interval of 95% at an alpha level of 0.05, gives a sample size of 73. However, 50% of the calculated sample 37 was added to maximize power. Therefore, the minimum sample size for this study was 110 mother-neonatal pairs.

Mother-neonatal pairs were enrolled in this study using the systematic random sampling method where the first of every three mother-neonatal pairs were picked at the labour ward. Where the first mother-neonatal pair did not fulfil the inclusion criteria the immediate next mother-neonatal pair that qualified was selected. On enrolment of the mother-neonatal pairs, study proforma were used to collect information from the mothers and from her ANC record. The information included mothers' bio-data, pregnancy and ANC history. Neonatal BW in Kilogram (kg) was measured using the bassinet weighing scale, which has a sensitivity of

50gms set at zero mark. Neonates weighing <2.5(kg) were considered LBW and those ≥2.5 (kg) were considered to have acceptable BW in this study, similar to a publication elsewhere [2].

Placental biopsies were obtained from maternal side of the placenta with the assistance of a histopathologist and stored in 10% formaldehyde. Paraffin embedded sections of the placental tissues were stained with Giemsa solution and examined by light microscopy under polarised light. Placental malaria infection was defined by the presence of parasites and malaria pigment [3,10,15].

2.5 Data Analysis

Data obtained from the study were entered into a computer for statistical analysis using SPSS statistical software version 16, Illinois, Chicago USA and a computer program for epidemiologist PEPI version 3.01. Quantitative values were expressed as mean ± standard deviation (SD). Student t test and Chi-square trend (χ^2) with Yate's correction were used to investigate the effects of quantitative and qualitative variables respectively. Univariate linear analysis was used to estimate the relationship between placental malaria, maternal age, parity and neonatal LBW. A p value <0.05 was considered significant. Tables were used appropriately for illustrations.

3. RESULTS

One hundred and ten mother-neonatal pairs were enrolled in this study; of which 58 (52.7%) neonates were males and 52 (47.3%) were females. The male to female ratio is 1.12:1. Most of the neonates were male and had acceptable birth weights Table 1.

Table 1. Birth weight and sex of the neonates

BW (kg)	Male	Female	Total
LBW	8	6	14
ABW	50	46	96
Total	58	52	110

BW= Birth weight, LBW= Low birth weight, ABW= Acceptable birth weight

Table 2 reveals placental malarial distribution and parity of the mothers that participated in the study. Forty-nine mothers (44.5%) were found to be positive for placental malaria and majority 92 (83.6%) were multiparous.

All mothers during the course of ANC received intermittent prophylactic therapy for malaria (sulphadoxine and pyrimethamine). Overall mean maternal age was 23.70±5.18 (95%CI, 22.72–24.68) years. Table 3 below shows placental malaria distribution according to maternal age. Even though the overall association between placental malaria and maternal age was not significant (p=0.066), the trend for maternal age groups (27-31 and 32-36) years was however significant (p=0.029), at odds ratio (OR) of 0.11 (95%CI:0.01–0.85).

Table 4 shows association between BW, parity and placental malaria. Of the 14 (100%) neonates with LBW, 10(71.4%) had mothers with placental malaria. Univariate linear analysis of the effect of placental malaria, maternal age and parity on neonatal LBW outcome was not significant Table 5. While the overall mean BW of the neonates was 3.04±0.58(95%CI, 2.93–3.15)kg that for LBW neonates was 2.04±0.36(95%CI,1.84–2.25)kg. Amongst the neonates with LBW, the mean weight for those whose mothers had placental

malaria was 2.02±0.42(95%CI,1.72–2.32)kg, whereas, the mean weight for those whose mothers were negative for placental malaria was 2.10±0.09(95%CI,1.95–2.25)kg. Comparing these mean weights was not significant (p=0.719)

Table 2. Placental malaria distribution and parity of the 110 mothers

Variables	Frequencies	Percentage
Placental malaria		
Positive	49	44.5
Negative	61	55.5
Parity		
Primiparity	18	16.4
Multiparity	92	83.6

Table 3. Association between maternal age and placental malaria

Group MA (yrs)	PMAL+VEN (%)	PMAL-VEN (%)	χ^2 *trend / Yates correction*	p value
17-21	28 (25.6)	26 (23.6)	-	-
22-26	9 (8.2)	16 (14.5)	1.147	0.284
27-31	4 (3.6)	15 (13.6	0.552	0.458
32-36	7 (6.4)	3 (2.7)	4.750	0.029*
37-41	1(0.9)	1 (0.9)	-	1.000

*PMAL+VE = Placental malaria Positive, PMAL-VE=Placental malaria Negative, MA = Maternal age * =p value<0.05 (significant)*

Table 4. Association between birth weight, parity and placental malaria

Characteristics	Placental malaria	
	Positive N (%)	Negative N (%)
BW (kg)		
Acceptable BW	39 (35.5)	57(51.8)
Low BW	10 (9.1)	4(3.6)
Parity		
Primiparity	5(27.8%)	13(72.2%)
Multiparity	44(47.8%)	48 (52.2%)

BW = Birth weight

Table 5. Relationship between placental malaria, maternal age, parity and neonatal low birth weight

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Corrected Model	2.189[a]	4	0.547	1.670	0.162	0.060
Intercept	57.181	1	57.181	174.486	0.000	0.624
MA	0.608	1	0.608	1.855	0.176	0.017
PMAL	0.528	1	0.528	1.610	0.207	0.015
Parity	0.407	1	0.407	1.241	0.268	0.012
PMAL* Parity	0.081	1	0.081	0.247	0.620	0.002
Error	34.409	105	0.328			
Total	1051.048	110				
Corrected Total	36.598	109				

a. R Squared=.060 (Adjusted R Squared=.024); MA=Maternal age, PMAL=Placental malaria

4. DISCUSSION

The prevalence of placental malaria in this study was 44.5%. A slightly lower value of 11.2% and 31% was published by Rachas et al. [12] in 2012 among Beninese Population, and Mohammed et al. [10] in Medani Maternity Hospital in central Sudan in 2013. Higher prevalence of 69.6% and 70.5% was, however, observed in two separate studies conducted in a population of South-eastern Nigerian by Ezebialu et al. [9] in 2012 and Okolie et al. [11] in 2014. The higher prevalence that was reported in South-eastern Nigeria was linked to un-booked maternal status, non use of both IPT and insecticide treated nets (ITN) among other causes like low socio-economic class (SEC) and rural residence. Significant number of pregnant women did not book their pregnancy and were not so privileged to use IPT for malaria in the latter studies. Part of the services offered during ANC includes IPT and pregnant women are also encouraged to sleep under ITN. Pregnant women of low SEC and those from the rural areas may not afford ANC because of lack of funds; as such, they may not benefit from these important services. This could have contributed to the higher prevalence of placental malaria observed in the latter works relative to the values seen in our study and that of other researchers [11-12].

Out of the fourteen neonates with LBW in this study, ten (71.4%) had mothers with placental malaria. Despite this number, no significant relationship was observed between placental malaria and LBW. All mothers in present study had ANC and were given routine ANC drugs that included antimalarials (sulphadoxine and pyrimethamine). Administration of IPT for malaria during ANC could have reduced the transmission of malaria parasite to the placenta. A recent study by Deepak et al. [16] in India showed that physiologically safe and effective anti-malaria drugs can successfully block the transmission of malaria parasite in the blood and possibly at tissue levels. Such anti-malarial drugs activity would minimize placental malarial infection, thereby allowing neonates to have adequate BW.

Malaria is unique in the sense that it is amenable to intervention once pregnant women start IPT [2]. The effective clearance of malaria parasite from the placenta would allow adequate function of the placenta like nutrient transfer in mother-neonatal pair in addition to endocrine and metabolic activities that are needed for normal foetal growth during pregnancy. Although the prevalence of LBW might increase with increasing number of pregnant women diagnosed with placental malaria, the only clear and marked difference observed was when malaria risk of greater and less than 25% were being compared [2]. With this in mind, our finding could hold true because our study population is consistent with that found in holoendemic area for malaria where transmission of the diseases is perennial [1,11]. Recently some colleagues have argued that the linear relationship between placental malaria and LBW outcome may be inconsistent [10]. This is because more LBW neonates were observed only in mothers with non malarial infections, or mothers with mixed infections (non malarial and placental malaria) but not in mothers with placental malaria alone.

Pregnant women who had placental malaria are likely going to give birth to neonates with LBW [3,5-7,11]. This might not be unconnected to *Plasmodium falciparum* parasite being more common during pregnancy [9-11]. The ability of malaria parasite to adhere to chondroitin sulfate A of the placenta makes pregnant women more vulnerable to placental malaria than non-pregnant women [10,17]. As a result, intrauterine growth retardation sets in leading to LBW. Other workers, however, argued that LBW due to placental malaria in malarial endemic regions should be interpreted with caution partly due to lack of enough evidence [2]. Even a marked relationship may not be causal but may simply reflect the association of placental malaria, LBW with other underlying factors such as poverty, which

determines both malaria risk and LBW [2]. However, recent data from an ITN trial in Kenya has provided important evidence that reduction in malaria transmission can also reduce LBW [7]. It therefore means that greater reductions of malaria transmission and LBW are to be expected in the future because of the dynamic approach in malaria control through mass killing of mosquitoes [7].

Association of maternal age groups (27-31 and 32-36) years and placental malaria was significant in current work. This observation differs from the findings of Scott et al. [3] in 2005. Lack of significant antimalarial immunity from exposure to human immunodeficiency virus (HIV) could explain the increased susceptibility to placental malaria with increasing maternal age [2,3,18]. In the past, early maternal age gave higher prevalence of placental malaria [9,11]. Non recruitment of malarial specific immune responses described by a concept called immune tolerance may be the explanation for placental malaria occurring in the very young mothers [12]. Erhabor et al. [8] in 2012 in Niger delta Nigeria had established an inverse relationship between malaria and immune responses like CD 4 lymphocytes. Other colleagues in Kenya had shown that malarial immune responses tend to increase with advancing maternal age and parity [3]. But with the advent of HIV, this may no longer be correct probably due to the immunosuppressive effects of the virus.

Even though placental malaria was reported to be more common in women with low parity [3,9,11], parity was not significantly associated with placental malaria or LBW in this study. The relationship between low parity and high tendency of placental malaria infection is still not lucid. It is possible that multiparous women could have placental malaria memory T cell that makes them less prone to placental malaria when compared to low parity women. Furthermore, maternal age and parity could complement each other as markers of wear and tear of body structures, which could also compromise the functions of the placenta leading to LBW deliveries [19]. The fact that parity was not associated with LBW despite that most mothers who participated in this study were multiparous could be explained by their age. Younger aged mothers in this work had a mean maternal age of 23.70 years, and multiparity in this group of mothers may not produce enough stress for maternal weathering that is needed to yield LBW neonates.

5. CONCLUSION

The prevalence of placental malaria was 44.5% in current study and the disease was associated with maternal age bracket (27-31 and 32-36) years. Though the relationship between placental malaria and neonatal LBW was not significant; majority of neonates with LBW in present study had mothers diagnosed with placental malaria.

6. RECOMMENDATION

Because of the high prevalence of placental malaria in our study cohorts, there is the need to educate pregnant women especially those within the ages of (27 and 36) years on the need to adhere to malarial chemotherapy either as part of ANC or as treatment for malaria. Research of this nature in the future should include mother-neonatal pairs from multiple health centers in order to have a representative cross-section of the study population. Furthermore, future study design should accommodate older mothers and primiparous mothers to avoid skewing of data.

7. LIMITATION

Our study population was not representative of the general population, since it contained only pregnant women who gave birth at the UMTH. It is likely that the present study was skewed towards multiparous younger age mothers. This may be a setback in data interpretation and in the overall analogy.

8. FUNDING SOURCE

Funding of this work was provided by the Authors.

CONSENT

Informed consent was obtained from one or both parent for this study. Parents had unlimited liberty to deny consent without any consequences while confidentiality was maintained.

ETHICAL APPROVAL

The study protocol was examined and authorised by the Medical Research and Ethics Committee of the UMTH in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki on biomedical research on human subjects.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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