CORRELATION BETWEEN PLACENTAL MALARIA PARASITAEMIA AT DELIVERY AND INFANT BIRTH WEIGHT IN A NIGERIAN TERTIARY HEALTH CENTRE

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ABSTRACT

Background: Untreated malaria during pregnancy is detrimental to the health and survival of the mother, foetus and neonate due to its great potential to cause maternal anaemia, foetal death and intrauterine growth restriction leading to low birth weight. The foetal complications are due to impaired placental function that results from placental malaria parasitaemia as well as impaired foetal oxygenation from maternal anaemia. This study was conducted to determine the influence of placental malaria parasitaemia on infant birth weight.

Methodology: This was a prospective cross-sectional analytical study of 205 parturients recruited consecutively as they presented for delivery at the Federal Medical Centre, Yenagoa. An interviewer-administered questionnaire was used to collect data. After delivery, the neonates were weighed and placental blood was collected for microscopy to detect malaria parasites. Data was analysed using SPSS version 22.

Results: The prevalence of placental malaria parasitaemia was 13.7% and Plasmodium falciparum was the only parasite species detected. Placental malaria parasitaemia was associated with a reduction of the mean infant birth weight by 335 grams (P = 0.01).

Conclusion: Malaria during pregnancy is still an important public health problem among our obstetric population, with a high prevalence of placental malaria parasitaemia and a significant negative effect on the birth weight of neonates. To enable the developing foetus achieve its full genetic growth potential, pregnant women should be encouraged to register early for antenatal care and utilize all the recommended malaria preventive measures.

Key words: Placenta, malaria infestation, birth weight

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INTRODUCTION

While malaria during pregnancy is a global public health problem, the burden is highest in sub-Saharan Africa where it is estimated that, every year, 25-30 million pregnant women are at risk of acquiring the infection, and one in every four pregnant women have evidence of placental infection at the time of delivery.[1,2] It is also estimated to account for 26 per cent of severe anaemia in pregnancy and 35 per cent of preventable low birth weight neonates in sub-Saharan Africa. [1]

These adverse outcomes have been described as consequences of sequestration of parasitized erythrocytes in the placenta. Because of this placental sequestration, peripheral blood film microscopy usually underestimates the prevalence of malaria in pregnancy; as the parasites are pooled from the peripheral blood to the placenta, peripheral blood film microscopy may not reveal parasitaemia despite a high burden of malaria parasites in the placenta.[3,4] This may results in misdiagnosis and delay in instituting treatment with potentiation of the adverse effects of malaria in pregnancy.

Placental malaria parasitaemia occurs because the parasitized erythrocytes have the ability to adhere to chondroitin sulphate A on the syncytiotrophoblast of the placenta.[5,6] Malaria-induced low birth weight is a leading cause of infant morbidity

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and mortality and it is estimated to account for between 62,000 and 363,000 infant deaths annually in Africa, translating to 3 to 17 infant deaths per 1000 livebirths. [1] It increases the risk of death within the first month of life by up to nine times.[7]

Recent data from the United Nations Children Fund[8] estimates that 13% of all babies born in sub-Saharan Africa are low-birth weight; and malaria during pregnancy is thought to be an important contributor, accounting for up to 900,000 LBW neonates every year.[9,10] Statistical analysis by Guyatt and Snow, of a collection of studies from sub-Saharan Africa revealed that one-fifth of the LBW babies born to mothers in malaria endemic areas are due to placental malaria infection while the mother was pregnant.[7] Various studies have also shown that babies born to mothers with placental malaria infection are two to four times likely to be low birth weight than those born to mothers without placental malaria infection.[11]

Low birth weight is an important risk factor for neonatal and infant mortality.[12] Studies from sub-Saharan Africa showed that neonatal and infant mortality are nine times and three times respectively, higher for LBW babies than for babies with normal birth weights.[7]Guyatt and Snow, in their review of literature on the risks for the low birth weight baby, [7] noted that the risk of both neonatal and infant mortality increase steadily as the birth weight decreases to below the LBW threshold (i.e. < 2500g). LBW is a well-documented risk factor for poor neurosensory, cognitive and behavioural development as well as for limited school performance and academic achievement. It also places the individual at risk of chronic medical conditions like hypertension and diabetes mellitus in adult life.[13,14]

Malaria parasitized placentae have been observed to carry antibodies, cytokines and macrophages, which are indicative of an active immune response.[15,16] This immune response may be responsible for the stimulation of early labour resulting in premature delivery and invariably preterm, low birth weight neonates.[17]

The restriction of foetal growth in utero due to placental malaria parasitization (resulting in low birth weight) appears to relate to the interference with nutrient transport across the placenta to the foetus in a number of ways; a high density of parasites, longstanding placental infection and the associated immune response may result in the consumption of glucose and oxygen that would have gone to the foetus. Also, the thickening of the cytotrophoblast basement membrane, commonly found in histological studies of infected placentae may directly interfere with nutrient transport to the fetus.[15] Malaria-associated maternal anaemia has also been implicated as an independent contributor to foetal intrauterine growth restriction, most likely through the reduction in oxygen transport to the fetus. [7,18]

Meta-analyses of intervention trials has demonstrated 43% reduction in low birth weight and 27% reduction in perinatal mortality with successful implementation of malaria prevention strategies in pregnancy.[19] These strategies include use of insecticide treated nets, intermittent preventive treatment of malaria in pregnancy with sulphadoxine-pyrimethamine and prompt appropriate case management of malaria in pregnancy.[20] The adoption, application and widespread coverage of these preventive measures are especially deficient in the highly endemic areas of sub-Saharan Africa.

While it is well-recognized that placental malaria parasitization can result in the delivery of low birth weight neonates, different studies have presented contrasting results: some showing statistically significant relationship between placental malaria parasitaemia and low infant birth weight, [21,22] others demonstrating no significant relationship.[23,24]

The above may imply that the effect of placental malaria on infant birth weight rather than being consistent, is variable, and may depend on, among other factors, the population studied.

Due to the important association of placental malaria and low infant birth weight, records of low birth weight deliveries has been incorporated as a key tool for monitoring and evaluating the effectiveness of malaria control programmes among pregnant women in Africa, since birth weight and parity are routinely recorded in many delivery centres across Africa.[1, 25] This serves as a useful indicator at the health facility level, allowing Health workers and programme managers to observe the effects of maternal and neonatal health interventions and to take corrective actions where necessary.[25] This study was conducted to determine the influence of placental malaria parasitaemia on infant birth weight.

METHODOLOGY

Study location: The study was conducted at the Federal Medical Centre, Yenagoa, the capital city of Bayelsa State in the South-South region of Nigeria.

Study design: This was a prospective cross-sectional analytical study.

Study Population: This consisted of both booked and unbooked parturients

Inclusion Criteria: All pregnant women presenting to the delivery suite (for delivery), who gave consent to participate in the study.

Exclusion Criteria

1) Pregnant women with chronic medical disorders including diabetes mellitus, hypertension, chronic renal disease, sickle cell anaemia (haemoglobin genotype SS) as well as those seropositive for Human immunodeficiency virus.
2) Parturients with antepartum haemorrhage (abruptio placentae or placenta previa) and hypertensive disorders in pregnancy.
3) Pregnant women who take alcohol and/or tobacco products.
4) Pregnant women with multiple gestation.
5) Parturients with intrauterine foetal death or congenital foetal malformations.
6) Parturients who did not give consent.

Sample size calculation: The sample size for this study was calculated using the formula for cross-sectional studies below;

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

Where, N = Sample size; Z = Proportion of normal distribution corresponding to the required (5%) significance level (which is 1.96); P = Prevalence of placental malaria parasitaemia (which is 14% or 0.14 from a previous study[27]) and d = Degree of accuracy/ precision expected (0.05)

Thus, $N = 1.962 \times 0.14 (1-0.14) / 0.052 = 185.5$

The sample size was thus calculated to be 186. Giving allowance for a 10% attrition rate, the minimum sample size for the study was 205 participants. The data for this study was collected over a period of five months (August 1, 2016 to December 31, 2016).

Sampling methodology: Every consecutive parturient who satisfied the eligibility criteria and gave consent was recruited until the sample size was obtained.

Study Protocol: With the study protocol in mind, standard laboratory methods as described by Cheesbrough[28] was used.

Data collection: After obtaining a signed informed consent from the eligible participant, a semi-structured interviewer-administered questionnaire was filled. The questionnaire contained information that includes maternal age, marital status, educational status, occupation, gravidity,

antenatal care, malaria preventive measures, infant birth weight and placental blood microscopy for malaria parasite detection as well as parasite density.

Weighing of neonates: Immediately after delivery and necessary neonatal resuscitation, neonates were cleaned and weighed with an electronic baby weighing scale to the nearest 0.1gram. All low birth weight neonates had their gestational ages assessed within twenty four hours using the Dubowitz Method[29] (see appendix III) by a neonatologist that covered the postnatal ward.

Placental blood collection: The aspiration method of placental blood collection[30] 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 washed with 200 millilitres of normal saline, and 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 sent to the laboratory for processing (smearing, staining and microscopic examination).

Laboratory procedure: Preparation and staining of the thick blood smear: Two drops of placental blood sample were placed on a slide using a small rubber pipette. Using the edge of a second slide, the drops of blood were joined and spread to make an even, thick smear and 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 held steadily at an angle of 45^{o} 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 was maintained for 10 minutes. The slide was then removed and allowed to dry.

Microscopic examination of slides for malaria parasite and determination of parasite density

The stained placental blood smears were examined under × 100 oil immersion lens of a light microscope. Malaria diagnosis was 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 reported as follows: + (1–10 parasites per 100 high power fields), ++ (11 – 100 parasites per 100 high power fields), +++ (1–10 parasites per high power field), and ++++ (>10 parasites per high power field). The slide was reported as negative if no parasite was identified per 100 high power fields.

Data Analysis

Data regarding maternal age, marital status, educational status, occupation, parity/gravidity, antenatal care, malaria preventive measures, infant birth weight and placental blood microscopy for malaria parasite detection as well as parasite density was entered and statistical analysis done using statistical software (SPSS for windows® version 22.0, SPSS Inc.; Chicago, USA).

Univariate analysis for categorical variables was performed using chi-square test.

RESULTS

Table 1: Maternal socio-demographic characteristics

	Frequency	Percentage
Age group		
10-14	1	0.5
15-19	6	2.9
20-24	32	15.6
25-29	54	26.3
30-34	58	28.3
35-39	50	24.4
40-44	3	1.5
45-49	1	0.5
Total	205	100.0
Educational status		
No formal education	2	1.0
Primary	18	8.8
Secondary	75	36.6
Tertiary	110	53.6
Total	205	100.0
Marital status		
Single	13	6.3
Married	192	93.7
Total	205	100.0
Employment status		
Unemployed	58	28.3
Employed	147	71.7
Total	205	100.0
Religion		
Christianity	196	95.6
Islam	9	4.4
Total	205	100.0
Tribe		
Ijaw	117	57.1
Yoruba	10	4.9
Ibo	65	31.7
Hausa	2	1.0
Others	11	5.3
Total	205	100.0
Maternal height		
Less than 150cm	18	8.8
151-160cm	185	90.2
Greater than 160cm	2	1.0
Total	205	100.0

Maternal socio-demographic characteristics (Table 1)

Two hundred and five parturients participated in the study. Their ages ranged from 14 to 45 years with a mean age of 29.9 years. The modal age group was 30-34 years followed by the 25-29 years age group. The majority of the parturients had tertiary level of education (53.6%), were married (93.7%) and employed (71.7%). Christians constituted 95.6% and the remaining 4.4% were Muslims. More than half (57.1%) were of the Ijaw ethnic group; the rest were Ibo (31.7%), Yoruba (4.9%), Hausa (1%) and other Nigerian tribes (5.3%). The maternal heights ranged from 1.45m-1.66m with an average height of 1.58±0.05m.

Prevalence and pattern of placental malaria parasitaemia

Two hundred and five placental blood films were analysed. Malaria parasite was detected in 28(13.7%) placental blood films and all had mild (+) parasitaemia. Plasmodium falciparum was the only malaria species detected in all the placental blood films.

Gestational age at delivery, Infant birth weight, APGAR scores and placental weight

The average gestational age at delivery was 38.5±1.9weeks (Range = 31-42weeks); of these, 190(92.7%) parturients delivered at term, 13(6.3%) delivered before term and 2(1.0%) delivered post-term.

The mean infant birth weight was 3213.5 +/-507.4grams (Range = 1490-4700grams). 186(90.7%) were normal birth weight, 9(4.4%) were macrosomic and 10(4.9%) were low birth weight. Of the low birth weight babies, 2(20%) were term while 8(80%) were preterm low birth weight babies.

The APGAR score at the first minute was normal (≥7) in 88.3% and low (<7) in 11.7% of neonates. At the fifth minute, only 2% of neonates had low APGAR scores necessitating admission into the special care baby unit. The average placental weight was 585.6+/-120.8grams (Range = 270-1095grams).

Correlation of placental malaria parasitaemia with infant birth weight

Mothers with placental malaria had babies with birth weights ranging from 1490g to 3500g with an average of 2924±504g while those without placental malaria had babies

with birth weights ranging from 1640g to 4700g with a mean of 3259±494g. There was thus a reduction in mean birth weight by 335grams of babies born to mothers with placental malaria. This difference in mean birth weight was statistically significant (p=0.01).

Influence of placental malaria parasitaemia on APGAR scores, placental weight and gestational age at delivery.

The presence of malaria parasites in the placental blood had no significant association with the APGAR score at the 1st minute (p=0.33) and at the 5th minute (p=0.09). There was also no significant difference (p= 0.58) in the mean placenta weight of those in whom malaria were found (0.57kg) as compared to those without malaria (0.59kg). All the mothers with placental malaria parasitaemia delivered at term.

DISCUSSION

The socio-demographic profile of the participants showed patronage from the more educated and affluent women. It is likely that because of the higher hospital charges in tertiary hospitals, a good number of the less educated and poorer women patronize the primary and secondary health care centres with lower hospital charges. The predominant tribe and religion in the area of study were Ijaw and Christianity respectively; this was reflected in the preponderance of Ijaw and Christian women in the study. The older maternal age predominance may have also accounted for the preponderance of parturients that were multiparous.

The prevalence of placental malaria parasitaemia of 13.7% found in this study is similar to the prevalence of 14% reported by Mokuolu et al in a study from four geopolitical zones in Nigeria[27] and that (13.0%) reported by Falade et al in south western Nigeria[31] but much lower than the 65.2% prevalence reported by Nyengidiki et al[23] in Port Harcourt within the same geographical zone with Bayelsa where this study was conducted. The lower prevalence in this study may be due to the high level of education among the parturients which may have contributed to their health awareness with a positive impact on their health and the effective malaria preventive measures utilized by the parturients including IPTpSP (88.3%) and ITN (50.2%); other factors may include a high level of community acquired immunity and the quality of antenatal care.[23]

The finding that Plasmodium falciparum was the only parasite species detected in all the placental blood films in this study confirms previous reports that placental malaria is an exclusive feature of plasmodium falciparum infection in pregnancy[32] and that Plasmodium falciparum is the most prevalent species in Nigeria accounting for about 98% of malaria cases in the country.[33]

While placental malaria parasitaemia was not significantly associated with low infant birth weight in this study, it was associated with a statistically significant reduction in the mean birth weight. This finding may be due to subtle placental dysfunction from mild placental parasitaemia. A similar finding of a statistically significant reduction in the mean infant birth weight among parturients with placental malaria parasitaemia was reported by Falade in Ibadan.[31] The severity of the placental parasitization may thus correlate directly with the degree of reduction in infant birth weight.

Malaria in pregnancy is still a public health problem. The level of utilization of the preventive measures is still far from what is desired. The observed impact of this condition on the pregnant woman and her baby adds justification for advocacy from all stakeholders to promote the utilization of malaria preventive measures during pregnancy in order to achieve a reduction in the burden of the disease.

CONCLUSION

Malaria during pregnancy is still an important public health problem among our obstetric population, with a high prevalence of placental malaria parasitaemia and a significant negative effect on the birth weight of neonates. To enable the developing foetus achieve its full genetic growth potential, pregnant women should be encouraged to register early for antenatal care and utilize all the recommended malaria preventive measures.

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