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Placental Malaria and Its Relationship with Neonatal Birth Weight among Primigravidae: An Analytical Cross-sectional Study

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Abstract

Background and objectives: Malaria can be fatal during pregnancy, posing a serious risk to both mothers and fetuses, especially in sub-Saharan Africa. Primigravidae are particularly susceptible to placental malaria in areas with high rates of transmission due to insufficient immunity. This study aimed to determine the prevalence of placental malaria infection, risk

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Author contributions

Contributed to study concept and design (KRO), acquisition of data (KRO, OPA, PHO, AY, and NPU), data analysis (OPA, PHO, AY, NPU, KON), drafting of the manuscript (KOR, CC, IOA, CGO, GUE, ACE, EOU, and JCA), critical revision of the manuscript (KRO, CC, IOA, CGO, GUE, ACE, EOU, JCA, OPA, PHO, AY, NPU, and KON), and supervision (CC, IOA),

Conflict of interest

The authors have no conflict of interests related to this publication.

Ethics statement

Ethical approval for this study was obtained from the ATBUTH Ethics Review Committee on August 18, 2020, with the approval number ATBUTH/ADM/42/VOL.1. The study was conducted according to the ethical principles for human scientific research as stated in the Helsinki Declaration. A written informed consent was obtained from each participant prior to recruitment into the study.

factors, types of Plasmodium causing malaria during pregnancy, and its relationship with neonatal birth weight among primigravidae.

Methods: This was an analytical cross-sectional study involving 357 primigravidae who delivered at Abubakar Tafawa Balewa University Teaching Hospital, Bauchi, Nigeria. Placental blocks were taken from the pericentric area of the maternal surface of the placenta, and the birth weights of the neonates were recorded. The samples were fixed in 10% neutral-buffered formalin, and histopathological analysis was performed. The primary outcome measure was to determine the relationship between placental malaria and neonatal birth weight. Demographics and outcomes were analyzed using standard statistical tests. Multivariable regression models accounting for potential confounders were created for the primary and secondary outcomes with adjusted odds ratios as the measures of effect.

Results: The prevalence of placental malaria was 38.4%. Among the participants with positive placenta malaria parasitemia, 49.6%, 36.5%, and 13.9% had chronic, acute, and past placental malaria infections, respectively. Only *Plasmodium falciparum* was found in the placenta. According to the bivariate analysis, unbooked status ($p = 0.001$), non-use of intermittent preventive therapy for malaria ($p < 0.001$), and village dwelling ($p = 0.020$) were significantly associated with placental malaria. However, on multivariable logistic regression, only non-uptake of intermittent preventive therapy for malaria was independently associated with placental malaria (adjusted odds ratio, 2.2, 95% confidence interval: 1.20, 4.1, $p = 0.011$). There was a significant difference in the mean birth weight between those with placental malaria and those without placental malaria (2.8 ± 0.5 kg vs. 3.2 ± 0.4 kg, $p = 0.001$). Additionally, placental malaria was significantly associated with low birth weight among the primigravidae ($p < 0.001$).

Conclusions: In Nigeria, there is a strong correlation between low birth weight and placental malaria in Primidravidae. Placental malaria was found to be independently correlated with non-uptake of intermittent preventive therapy for malaria.

Keywords

Birth weight; Neonates; Intermitent preventive therapy; Placental malaria; Placental histology; Primigravidae

Introduction

Malaria is a preventable, deadly disease and one of the most significant parasitic infections in humans.[1] It is predominant in sub-Saharan Africa, but its endemicity spreads through tropical and sub-tropical regions of the world, accounting for more than 200 million clinical cases and more than 400 thousand deaths each year.[2] In 2017, an estimated 219 million cases of malaria occurred worldwide, resulting in 435,000 deaths.[3] African regions account for 92% of the malaria burden. Fifteen countries in sub-Saharan Africa and India carry approximately 80% of the global malaria burden, with Nigeria accounting for 25%.[3] Nearly 80% of global malaria deaths occur in Africa, with Nigeria accounting for 19%.[3] Under-fives are the most vulnerable group, accounting for 61% of malaria deaths worldwide.[3] The malaria burden is pronounced in poor, underserved, and marginalized populations in remote rural and urban areas.[4] Pregnant women are vulnerable to malaria and its attendant complications as a result of changes that occur during pregnancy.

Malaria is a vector-borne disease transmitted to humans by the bite of infected female Anopheles mosquitoes.[4] Human malaria is caused by five main species of malaria parasites: *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium ovale*, *Plasmodium malariae*, and *Plasmodium knowlesi*.[4,5] *Plasmodium vivax* is the most widely distributed Plasmodium species worldwide and is common in Asia, North Africa, and Central and South America.[4] *Plasmodium falciparum* is the most ubiquitous species in Africa, especially in sub-Saharan Africa.[4] *Plasmodium falciparum* is the most virulent and pathogenic of the plasmodia and is responsible for almost all deaths caused by malaria.[4,6,7]

Approximately 25% of parturients are infected in malaria-stable regions, with the highest risk of infection and morbidity in primigravidae, adolescent parturients, and those with co-existing human immunodeficiency virus (HIV).[8] It is widely known that primigravidae are more vulnerable to *Plasmodium falciparum* malaria than multigravidae in endemic areas.[9] Malaria during pregnancy is associated with maternal anemia, miscarriages, intrauterine fetal death, low birth weight, and preterm delivery.[10] Low birth weight from malaria is a leading cause of infant morbidity and mortality, resulting in the deaths of between 62,000 and 363,000 infants yearly in Africa.[11] In utero exposure of infants to malaria parasite antigens predisposes them to early clinical malaria episodes and more severe clinical malaria than unexposed infants within their first 2 years of life.[12] Therefore, infants delivered by mothers who experienced placental malaria parasitemia during pregnancy are more likely to develop clinical malaria in the early stages of life than those with no in-utero exposure. Low birth weight has been linked to long-term sequelae in children. Studies have shown that there is poor neurosensory, cognitive, and behavioral development as well as limited school performance and academic achievements in children who are products of low birth weight.[12]

In malaria-stable regions, which Nigeria falls into, adults usually develop acquired immunity following a series of malaria infections in childhood.[13–15] However, in women, this acquired immunity is subdued during pregnancy as a result of pregnancy-induced immune suppression.[16] This suppressed immunity and the presence of a new organ in the form of the placenta during pregnancy put these women at high risk of malaria and its complications.

Placental malaria is a well-known complication of malaria during pregnancy with adverse effects on the fetus, and primigravidae are the most susceptible.[13,16] Placental malaria is said to occur when there is sequestration of plasmodium-infected red blood cells in the intervillous spaces of the placenta.[13,17] The placenta has a predilection for the adherence of malaria-parasitized red blood cells as a result of the availability of chondroitin sulfate-A, a surface protein that provides attachment for malaria-parasitizing erythrocytes, in the syncytiotrophoblast.[6,18] Therefore, the detection of malaria parasites in placental tissue has been shown to result in adverse birth outcomes.[6,18] The overwhelming infiltration of infected red blood cells in the intervillous spaces and the resulting inflammatory changes within the placenta appear to cause unwanted effects on the fetus.[17]

The prevalence of placental malaria is high, and the density of the parasite in the peripheral circulation is not a true correlate of placental parasitization.[13,18,19] The prevalence varies in different populations, depending on population characteristics and the method of diagnosis used; Fehintola *et al.*[16] reported a prevalence of 48% using placental blood, while Ezebialu

et al.[19] reported a prevalence of 60% using histopathology of the infected placenta. These studies were carried out on both primigravidae and multigravidae. These studies revealed that the prevalence of this disease is very high in our environment and has far-reaching effects on our vulnerable population.

Pregnancy-related malaria poses a major risk to both the mother and the fetus, especially in primigravidae, as the disease can be lethal. In northern Nigeria, early marriage often results in teen-age pregnancy, which increases the risk of placental malaria for the women involved. The purpose of this study was to ascertain the impact of placental malaria on primigravidae neonates and its relationship to newborn weight at the Abubakar Tafawa Balewa University Teaching Hospital in Bauchi, Nigeria.

Materials and methods

Study design

The study is a hospital-based cross-sectional study.

Study setting

The study was conducted at Abubakar Tafawa Balewa University Teaching Hospital (ATBUTH), Bauchi, North East Nigeria, from September 2020 to March 2021. Ethical approval for this study was obtained from the ATBUTH Ethics Review Committee on August 18, 2020, with the approval number ATBUTH/ADM/42/VOL.1. A written informed consent was obtained from each participant prior to recruitment into the study.

Study population

This group consisted of primigravidae that were delivered in the labor ward of the Department of Obstetrics and Gynaecology unit of the hospital.

Inclusion criteria

This included primigravidae with singleton pregnancies that presented for delivery at a gestational age of ≥28 weeks of gestation and delivered a liveborn neonate.

Exclusion criteria

Those excluded from the study were pregnant women who declined consent after adequate counseling, women with multiple gestations, gestational age less than 28 weeks, and women with chronic medical conditions (hypertensive disorders of pregnancy, sickle cell disease, HIV, and diabetic mellitus).

Sampling strategy

A convenience sampling method was utilized in the study.

Sample size estimation

The minimum sample size (N) for the study was calculated using Fisher's formula.[20] $N = Z^2pq/d^2$, where Z = the desired level of statistical significance, typically 1.96 for an α of

0.05 or 5%, or a 95% confidence interval, p = prevalence, q = (1 - p), and d^2 = precision value (0.05). Using a prevalence of 33%, which was derived from a study conducted in a tertiary health facility in Abakaliki, southeastern Nigeria,[21] and a sample size adjusted to compensate for an attrition rate of 5%, the minimum sample size (N) was calculated to be 357.

Data collection and participant recruitment

Following ethical clearance and Nigerian Postgraduate College approval for this study, two nurses in the antenatal ward and labor ward and two resident doctors were trained on the research and how to translate the information on the consent form and questionnaire into Hausa (the major language spoken in Bauchi State, Nigeria) for those who did not understand English. The nurses were taught how to complete the questionnaire during the recruitment process. The participants were recruited from the antenatal ward and labor ward. Informed written consent was obtained, and a questionnaire was administered. A well-structured, numbered questionnaire was used to elicit information from the pregnant women in the language they understood with the help of trained assistants. Following the delivery of the neonates and the placentae, the babies and placentae were weighed with a mechanical weighing scale in kilograms and grams and recorded in the corresponding questionnaires.

Study procedure

After delivery of both the baby and the placenta, the maternal surface of the placenta was washed with normal saline. Three full-thickness placental blocks measuring 2×2×1 cm were taken from the pericentric area of the maternal surface of the placenta. The biopsy tissue was fixed in 20 ml of freshly prepared 10% neutral buffered formalin in a sample container. The specimens were coded to correspond to the numbers in the questionnaires for easy identification and sent to the histology laboratory for processing and analysis.

In the histopathology laboratory, the fixed placental biopsies were processed and embedded in paraffin wax using standard techniques. Sections of 5 μm thickness were prepared and stained with hematoxylin and eosin and then examined by light microscopy. The slides were read, and the pattern of placental malaria parasitization was graded according to Bulmer's description, as described by Ezebialu *et al.*[19] The grading was as follows.[19,22]

- Grade 0: no evidence of malaria parasites or pigments;
- Grade 1: (active/acute infection): parasites in maternal red blood cells in intervillous spaces but no pigment in fibrin or cells within the fibrin;
- Grade 2: (active-on-past infection/chronic): parasites and pigments in maternal red blood cells and pigments in fibrin or cells within fibrin;
- Grade 3: (past infection): parasites not present but pigments confined to fibrin or cells within it.

Outcome measures

The primary outcome measure was to determine the relationship between placental malaria and neonatal birth weight among primigravidae, while the secondary outcome measures were the prevalence of placental malaria, the types of Plasmodium species present in the placentae, the risk factors associated with placental malaria, neonatal birth weight, and the association between placental malaria and low birth weight.

Data analysis

The data are presented in tables and percentages. Demographics, pregnancy, and labor outcomes were analyzed using t tests for continuous data and the chi-square test or Fisher's exact test for categorical data. ANOVA was used to analyze categorical variables in more than one group. A nonparametric k-sample test on the equality of medians was used to compare variables with integer values. Univariable and multivariable logistic and linear regression models were used to control for prognostic covariates and confounders. The multivariable analyses included clinically significant factors, those with a *p*-value of 0.2 or less in the univariable comparison, those considered to be statistically significant, and those that were clinically associated. The statistical analysis was performed using SPSS version 22. Chi-square tests and logistic regression were used to determine the associations between risk factors, placental malaria, and low birth weight. The covariates in the model included age, booking status, gestational age, and type of residence. An alpha value of 0.05 was used as a measure of statistical significance.

Results

A total of 357 primigravidae were recruited and analyzed in this study. Figure 1 are histological slides showing acute, past, and chronic placental malaria. The flow chart of the study is show in Figure 2. Among the 357 participants, 137 (38.4%) had placenta malaria parasitemia. This is shown in Figure 3.

Socio-demographic characteristics of the participants

The socio-demographic characteristics of the participants are shown in Table 1. The age range of the participants was 18–37 years, with a mean age of 22.2 ± 4.3 years. Adolescents (15–19 years old) constituted 26.3% of the participants. A higher percentage of the women (67.2%) were from the Hausa-Fulani ethnic group and Muslims, accounting for 68.9% and 75.1%, respectively. A greater percentage of the participants had a secondary level of education: 128 (35.4%), while 56 (15.7%) had no formal education. While 74.8% of the participants slept under insecticide-treated mosquito nets, 74.2% of the women received at least one dose of intermittent preventive therapy (IPT) during pregnancy. A quarter of the participants (25.8%) did not receive IPT during their pregnancy.

Bivariate analysis of risk factors for placental malaria

There was a significant association between placenta malaria and unbooked status (x^2 = 17.6, $p = 0.001$), village dweller status ($x^2 = 5.2$, $p = 0.02$), and non-uptake of IPT (χ^2 = 21.6, $p < 0.001$), as shown in Table 2.

Distribution of birthweight and histopathology findings in primigravidae patients with placenta malaria

With regard to birth weight, the mean birth weight of the neonates of all the participants was 3.1 ± 0.5 kg. While 89.9% had a normal birth weight (2.5–3.9 kg), 8.7% had a low birth weight (<2.5 kg). Among the 137 participants with positive placenta malaria parasitemia, 49.6% had chronic placental malaria infection, while 36.5% and 13.9% had acute and past placental malaria infection, respectively (Table 3). Plasmodium falciparum was the only species of Plasmodium recorded in the placentae of the participants.

Associations between low birth weight and different placental malaria types/grades

The associations between low birth weight (LBW) and different placental placental malaria types/grades are shown in Table 4. There was a statistically significant difference between the mean neonatal birth weight in the placenta malaria group and that in the group without placental malaria (2.8 ± 0.5 kg vs. 3.2 ± 0.4 kg; $p < 0.001$). According to our results, the majority of babies (87.1%) with low birth weights had placental malaria, whereas 12.9% of LBW babies without established placental malaria. These findings further imply that 19.7% of women with placental malaria had LBW babies, while 80.3% of women with placental malaria had no LBW babies. There was a significant association between placental malaria and LBW ($p < 0.001$). The mean neonatal birth weights delivered by mothers with acute, chronic, and past placental malaria were 2.8 ± 0.5 kg, 2.7 ± 0.5 kg, and 3.0 ± 0.4 kg, respectively. Although the mean neonatal birth weight was lower in those with chronic placental malaria than in those with active and past placental malaria infections, the difference was not statistically significant ($p > 0.091$).

Regression of factors associated with placental malaria and birthweight

Table 5 shows the factors significantly associated with placental malaria. While booking status and location of residence of the participants had no significant effect on the occurrence of placental malaria, non-use of IPT was independently associated with placental malaria parasitemia (adjusted odds ratio, −2.2, 95% CI-1.2–4.1, $p = 0.011$). However, multivariable logistic regression analysis revealed that there was no association between the age of the primigravidae and LBW in those with placental malaria ($p > 0.05$).

Discussion

The principal findings of our study reveal that placental malaria is endemic in sub-Saharan Africa among primigravidae. In addition, there is a significant association between placental malaria and LBW among primidravidae. Unbooked status, non-use of IPT for malaria, and village dwelling were significantly associated with placental malaria. This study involved histological analysis of the placentae of 357 primiparous women with placental malaria and its association with the birth weights of their neonates in Nigeria.

The mean age of the participants in this study was 22.2 years. The largest age group of the studied population was 20–24 years old, which constituted 44.8% of the participants, followed by the adolescent age group, which made up 26.3% of the participants. In similar studies by Iyare *et al.*,[21] Bako *et al.*,[23] and Oweisi *et al.*,[24] the mean ages of the

participants were 26 years, 27.2 years, and 29.9 years, respectively. This study involved younger parturients compared to other studies. This is because early marriage is common in our environment, and the study involved only primigravidae. Previous studies have shown that malaria and its adverse effects on pregnancy are more common in younger parturients.[19,21] The majority of the participants were of the Hausa-Fulani ethnic (68.9%) group and Muslims (75.1%) by religion. This can explain the younger mean age of the participants, with the youngest being 18 years old, because Hausa Fulani Muslims usually give out their female children for marriage early. The highest educational attainment of most participants (35.4%) was secondary school education, and 15.7% had no normal education. This contrasts with the study by Oweisi *et al.*,[24] where 53.6% had a tertiary level of education.

Among the 357 participants, 137 showed histological evidence of placental malaria in their placentae, for a prevalence of 38.4%. This comprised 36.5% with active placenta malaria infection, 49.6% with chronic placental malaria infection, and 13.9% with past placental malaria infection. The prevalence is similar to the findings from previous studies. Iyare *et al.*[21] reported a prevalence of 33% in Abakiliki, and Bako *et al.*[23] reported a prevalence of 33.9% in Maiduguri both in Nigeria. However, the prevalence was higher than the 10.5%, 13.7%, and 10.5% reported by Falade *et al.*[15] and Oweisi *et al.*[24] in Ibadan and Bayelsa, Nigeria, respectively. The lower prevalence recorded in these studies was likely due to the high utilization of IPT for malaria, the higher educational status of the participants, the use of placental blood microscopy, and the fact that the studies were heterogeneous, as both involved primigravidae and multigravidae, unlike the index study, which involved only primigravidae. It has been noted that histological examination of the placenta is superior to placental blood thin film microscopy in the identification of placental malaria.[19,25,26] Primigravidae carry a higher prevalence of placental malaria because they lack malaria-specific immunity, which usually develops in subsequent pregnancies.[11,13,14,17] Higher prevalences of 48% and 69.6% were noted by Fehintola *et al.*[16] and Ezebialu *et al.*[19] in Ile-Ife and Nnewi in Nigeria, respectively. Ezebialu *et al.*[19] used placental histology, while Fehintola *et al.*[16] utilized microscopy of placental blood. In the study in Ile-Ife, Nigeria, there was poor uptake of IPT for malaria (41.7%), in contrast to 74.2% in ATBUTH Bauchi, and HIV-positive parturients were not excluded from the study.[16] Ezebialu *et al.*[19] did not exclude HIV-positive participants, and the study was carried out during a period of heavy rainfall. The higher prevalence noted by Ezebialu in Nnewi may represent environmental differences in the study populations, as previous studies in Nnewi and Bauchi noted a higher prevalence of malaria in Nnewi than in Bauchi, both in Nigeria.[27,28]

Plasmodium falciparum was the only species found in the placentae of the primigravidae. This finding is consistent with the findings of studies by Ezebialu *et al.*[16] and Fehintola *et al.*,[19] who used placental tissue histology and microscopy of placental blood, respectively. Using microscopy of placental blood, Oweisi *et al.*[24] in Bayelsa, Nigeria, also noted that *Plasmodium falciparum* was the only Plasmodium species discovered in the placentae of the studied population. This buttresses the fact that only *Plasmodium falciparum* possesses a special membrane protein called Plasmodium falciparum membrane protein-1, which aids in the attachment of parasitized red blood cells to chondroitin sulfate A in the syncytiotrophoblast of the placenta.[13,14,18,29,30] Antibodies to this protein build up with

successive pregnancies, thereby blocking the deposition of plasmodium-paralyzed red blood cells in the placenta and hence decreasing the prevalence of placental malaria in multiparous women.

The mean birth weight of the neonates in the study was 3.1 ± 0.5 kg. There was a statistically significant reduction in the mean birth weight of those with placental malaria compared to those without placental malaria infection (2.8 ± 0.5 kg vs. 3.2 ± 0.4 kg, $p < 0.001$). This finding is consistent with a finding from a study by Oweisi *et al.*[24] Cottrell *et al.*,[31] in a study in the Benin Republic, reported that Plasmodium falciparum infection during pregnancy is associated with a low mean birth weight among the new-born of primigravidae. The study demonstrated no significant difference in the mean neonatal birth weight among those with active, chronic, or past placental malaria. However, those with chronic placenta malaria had the lowest mean neonatal birth weight. The sequestration of Plasmodium falciparum-infected red blood cells in the intervillous spaces of the placenta leads to the recruitment of the maternal immune response, leading to intervillositis. This local inflammation has been shown to impair nutrient transfer to the fetus, which likely affects neonatal birth weight.[23,32–34] Fehintola *et al.*[16] also noted that there was a significant association between placental malaria and LBW and that the neonates of mothers with placental malaria had shorter full length, a smaller head circumference, and a lower mean hematocrit. However, Fehintola *et al.*[16] and Bako *et al.*[23] reported a higher LBW rate. This is likely because a larger population of the participants in their studies were HIV positive, and there was poor usage of IPT, which are major risk factors for the high prevalence of placental malaria and LBW.[16,23] This finding is contrary to the findings of Iyare *et al.*[21] and Oweisi *et al.*[24] Iyare *et al.*[21] noted that the mean birth weights of neonates of the primigravidae with placental malaria were higher than those without placental malaria and that there was no significant relationship between placental malaria and LBW. This is likely because the study used a small sample size and placental blood microscopy. Oweisi *et al.*[24] reported no significant relationship between placental malaria and LBW. This may be due to the smaller sample size, and in addition, primigravidae constituted a smaller percentage of the study participants, in contrast to the index study, which was made up of only primigravidae.

Plasmodium falciparum in pregnancy remains a major cause of preventable LBW, constituting approximately 19% of LBW in sub-Saharan Africa, and is a leading cause of neonatal morbidity and death, especially in primigravidae.[11,33,35] According to logistic regression, non-utilization of IPT with sulphadoxine and pyramethamine for malaria was independently associated with a high prevalence of placental malaria in primigravidae. This finding is consistent with findings from previous studies.[15,16,19,23] Intermittent preventive treatment for malaria in pregnant women has been shown to decrease maternal anemia, placental malaria, LBW, and perinatal death in areas with stable malaria transmission.[15,19,36,37] In view of these enormous benefits of IPT, the World Health Organization currently recommends that intermittent preventive treatment for malaria should be given to all pregnant women at each antenatal visit, starting in the second trimester, and each dose should be given at least one month apart, with at least 3 doses in each pregnancy, and should be continued until delivery.[3]

In terms of the strengths, our study involved a large sample size of only primigravidae, as there is an increased risk of placental malaria and its complications. In addition, this study employed histopathological analysis of placental tissue, which was able to detect and categorize placental malaria into acute, chronic, and past placental malaria infections. This approach is superior to microscopy of placental blood, which can only detect asexual forms of Plasmodium, thus leaving out chronic and past placenta malaria infections, which have been shown to have adverse effects on pregnant women and their fetuses. This study has several limitations. It is a single hospital-based cross-sectional study, so the findings from it may not be applicable to the general population. In addition, we could not assess preterm birth, perinatal or neonatal mortality. We were unable to continue monitoring the babies after delivery due to the nature of our study, which prevented us from finding out the newborns' short- and long-term consequences from placental malaria. Only the prevalence of placental malaria in the primigravidae was found in the index research. It may be challenging to infer a cause-and-effect link because we were unable to ascertain the subjects' pre-pregnancy malaria parasitemia levels. Furthermore, the index work was completed in a tertiary teaching hospital, and selection bias may result from the fact that the majority of pregnant women who attended primary and secondary care centers may not have been counted. The study slides were viewed strictly by a single consultant histopathologist, which may introduce bias and may lead to an over- or under-diagnosis of placental malaria in the studied population.

Future directions

This study has added updated evidence on the impact of placental malaria. Hence, adequate attention should be given to measures geared toward the prevention of placental malaria in pregnant women, especially primigravidae. Education of women of reproductive age groups on the importance of the utilization of IPT for malaria and the implementation of directly observed therapy may help to reduce the neonatal morbidities and mortality associated with placental malaria parasitemia.

Conclusions

The prevalence of placental malaria among primigravidae is high in northern Nigeria. Placental malaria is strongly associated with LBW, and the non-use of IPT is found to be significantly associated with placental malaria.

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Data sharing statement

The research data used for this study are available upon request from the authors.

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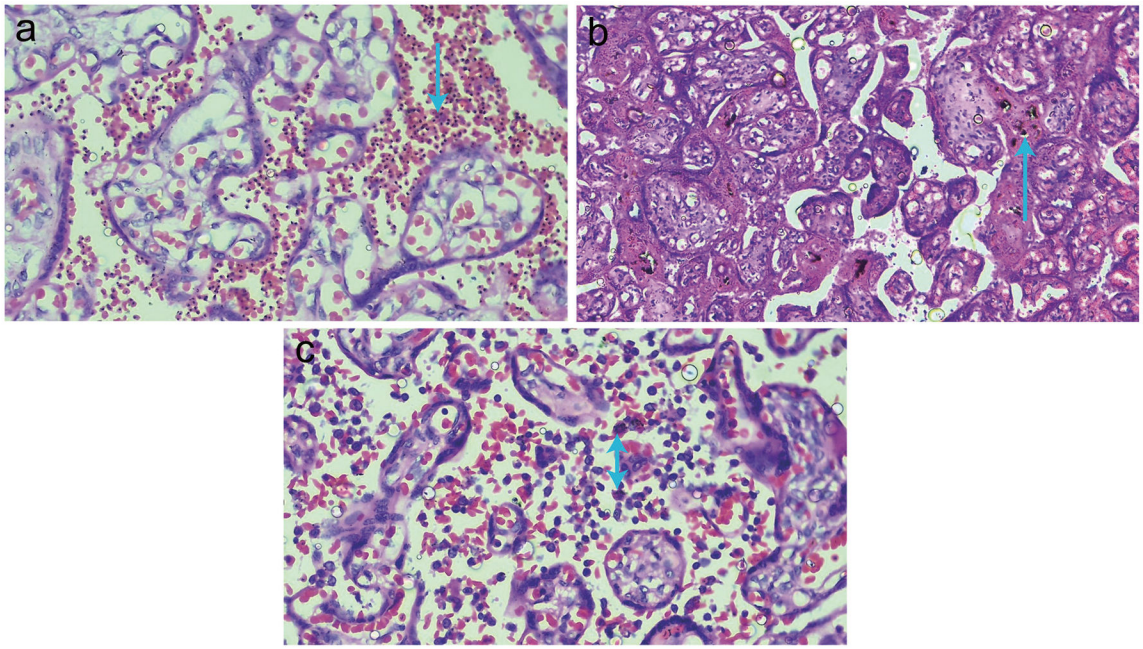

Fig. 1. Histological slides showing different types of placental malaria.

(a) Acute PMI, arrow showing parasitized red blood cells within intervillous space in acute placental malaria ×10 magnification; (b) The Past PMI arrow shows hemozoin pigment deposits in past placenta malaria ×10 magnification. (c) Chronic PMI, arrow showing parasitized red blood cell and and up-down arrow showing haemozoin pigment deposits in chronic placental malaria ×20 magnification. PMI, Posterior Myocardial Infarction.

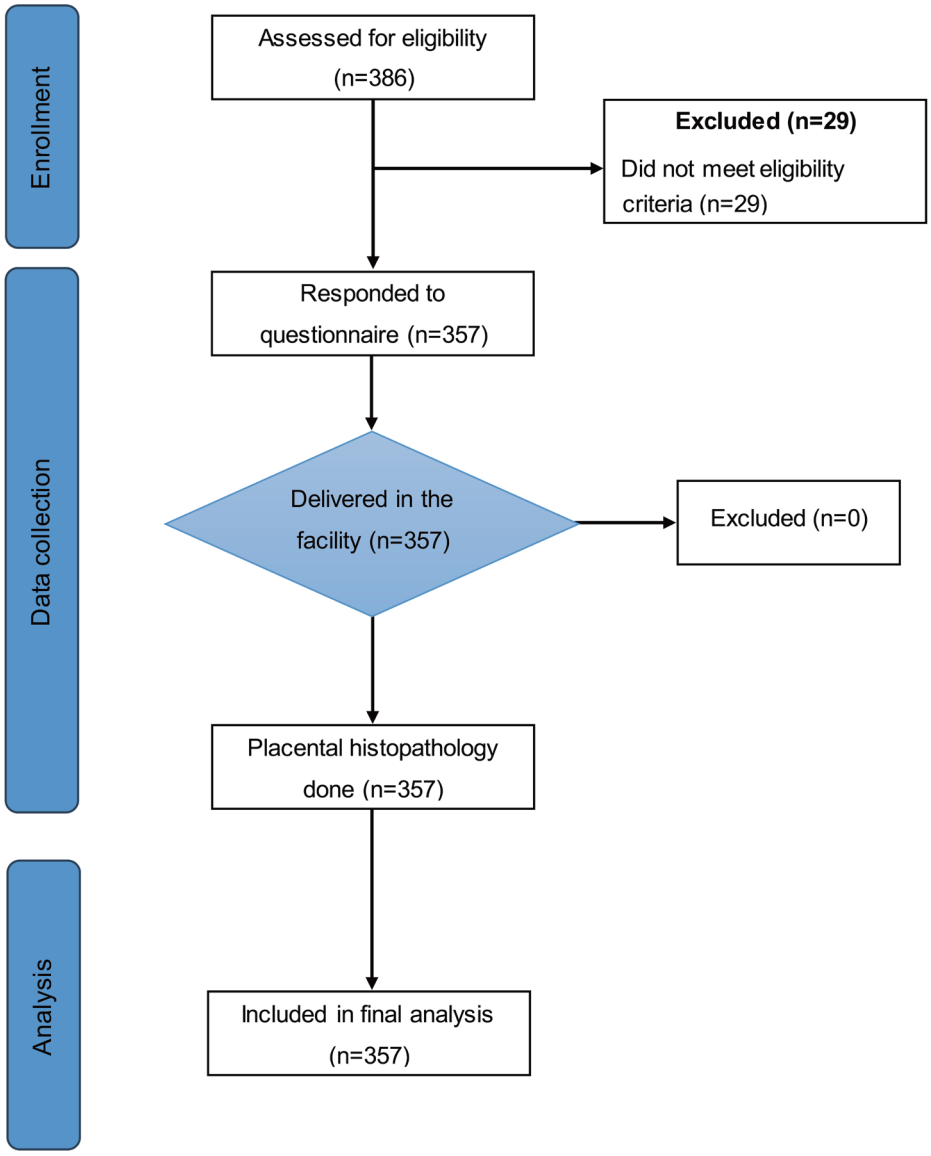

Fig. 2.
Flow chart of participants recruited into the study.

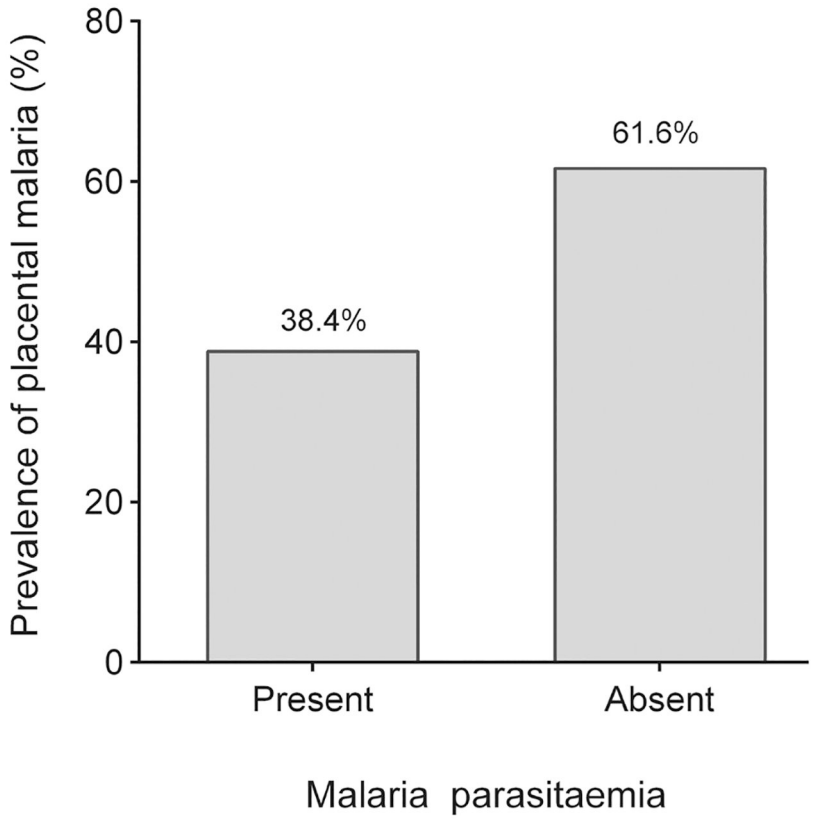

Fig. 3.
Showing the prevalence of placental malaria in the study.

Table 1.

Socio-demographic characteristics of the participants

Variable		Frequency n = 357	Percentage (%)
Age group (years)	18–19	94	26.3
	20–24	160	44.8
	25–29	78	21.8
	30–34	16	4.5
	35–39	9	2.5
	Mean ± SD	22.2 ± 4.3	
Ethnicity	Hausa/Fulani	246	68.9
	Igbo	14	3.9
	Yoruba	12	3.4
	Jarawa	23	6.4
	Others *	62	17.4
Marital status	Single	8	2.2
	Married	349	97.8
Booking status	Booked	240	67.2
	Unbooked	117	32.8
Gestational age	Preterm	15	4.2
	Term	340	95.2
	Post-term	2	0.6
Religion	Christianity	89	24.9
	Islam	268	75.1
Education	None formal	56	15.7
	Primary	67	18.8
	Secondary	128	35.8
	Tertiary	106	29.7
Occupation	Housewife	285	79.8
	Trading	21	5.9
	Civil servant	25	7
	Farming	7	2

Variable		Frequency n = 357	Percentage (%)
	Others**	19	5.3
Residence	City dweller	259	72.5
	Nearby village	98	27.5
Mosquito Net on window and door	Yes	260	72.8
	No	97	27.2
Sleep under mosquito net	Yes	267	74.8
	No	90	25.2
Spraying of insecticide	Always	38	10.6
	Occasionally	233	65.3
	Never	86	24.1
Bush and stagnant water	Yes	219	61.3
	No	138	38.7
Malaria IPT in pregnancy	Yes	265	74.2
	No	92	25.8

*Sayawa, Angas, Kanuri, Tiv, Idoma.

**student, Seamstress. SD, standard deviation.

Table 2.

Variate analysis of risk factors for placental malaria

Variable	Placental Malaria		X^2	*p* value
	Present n = 137, Freq (%)	Absent n = 220, Freq (%)		
Age group (years)			3.333	0.504
18–19	39 (41.5)	55 (58.5)		
20–24	60 (37.5)	100 (62.5)		
25–29	31 (39.7)	47 (60.3)		
30–34	6 (37.5)	10 (62.5)		
35–39	1 (11.1)	8 (88.9)		
Booking status			17.614	0.001 *
Booked	74 (30.8)	166 (69.2)		
Unbooked	63 (53.8)	54 (46.2)		
Residence			5.246	0.022 *
City dweller	90 (34.7)	169 (65.3)		
Nearby village	47 (48.0)	51 (52.0)		
Mosquito Net on window and door			2.748	0.097
Yes	93 (35.8)	167 (64.2)		
No	44 (45.4)	53 (54.6)		
Sleep under mosquito net			0.134	0.714
Yes	101 (37.8)	166 (62.2)		
No	36 (40.0)	54 (24.5)		
Spraying of Insecticide			0.757	0.685
Always	13 (34.2)	25 (65.8)		
Occasionally	88 (37.8)	145 (62.2)		
Never	36 (41.9)	50 (58.1)		
Bush and stagnant water			1.695	0.193
Yes	58 (42.6)	78 (57.4)		
No	79 (35.7)	142 (64.3)		
Malaria IPT in pregnancy			21.640	<0.001 *
Yes	83 (31.3)	182 (68.7)		

Variable	Placental Malaria		X^2	*p* value
	Present n = 137, Freq (%)	Absent n = 220, Freq (%)		
No	54 (58.7)	38 (41.3)		
Dose of malaria IPT			0.284	0.868
1	16 (33.3)	32 (66.7)		
2	40 (32.0)	85 (68)		
≥3	27 (29.3)	65 (70.7)		

*Statistical significance. IPT, intermittent preventive therapy.

Table 3.

Distribution of birthweight and histopathology findings in primigravidae patients with placenta malaria

		Frequency	Percent
Birth weight	Low (<2.5 kg)	31	8.7
	Normal (2.5–3.9 kg)	321	89.9
	Macrosomia (≥4 kg)	5	1.4
	Total	357	100
	Mean ± SD	3.1 ± 0.5	
Variable	Active placental malaria infection	50	36.5
	Chronic placental malaria infection	68	49.6
	Past placental malaria infection	19	13.9
	Total	137	100

SD, standard deviation.

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Table 4.

Association between LBW and different placental malaria types/grades

Variable	Placental malaria		t test	*p* value
	Present	**Absent n=220**		
	Mean ± SD	**Mean ± SD**		
Birth weight (kg)	2.8 ± 0.5	3.2 ± 0.4	9.506	<0.001 *
	Placental malaria			
	Present	Absent		
Low Birth weight	Freq (%)	Freq (%)	X^2	*p* value
Yes	27 (87.1)	4 (12.9)	34.076	<0.001 *
No	110 (34.3)	216 (65.7)		
Total	137 (38.4)	220 (61.6)		
	Placental malaria (Histopathology)			
	Active	Chronic	Past	
	mean ± SD	mean ± SD	mean ± SD	f test (*p* value)
Birth weight (kg)	2.8 ± 0.5	2.7 ± 0.5	3.0 ± 0.4	2.435 (0.091)

* Statistical significance. LBW, low birth weight; SD, standard deviation.

Table 5.

Regression of factors associated with placental malaria and birthweight

	Unadjusted			Adjusted		
Logistic regression of factors that significantly associated with placental malaria						
Variable	Odds ratio	95% CI	*p* value	Odds ratio	95% CI	*p* value
Residence						
City	1			1		
Nearby village	1.7	1.1–2.8	0.023*	1.1	0.6–1.8	0.8
IPT in Pregnancy						
Yes	1			1		
No	3.1	1.9–5.1	<0.001*	2.2	1.2–4.1	0.011*
Booking Status						
Booked	1			1		
Unbooked	2.6	1.7–4.1	<0.001*	1.7	1.0–3.0	0.073
Logistic regression of birth weight and placental malaria controlling for age						
Variable				Odds ratio	95% CI	*p* value
Low Birth weight						
Yes				13.5	4.543–40.061	<0.001*
No				1		
Age group (years)						
18–19				3.8	0.453–32.042	0.219
20–24				4.4	0.514–34.606	0.18
25–29				4.7	0.560–39.716	0.154
30–34				3.5	0.337–37.021	0.293
35–39				1		

*Statistical significance. CI, confidence interval.

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