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IMPACT OF PLACENTAL MALARIA ON MATERNAL AND FOETAL CORD RESPONSES AND ITS ROLE DURING PREGNANCY AMONG WOMEN ATTENDING GENERAL HOSPITAL HADEJIA, JIGAWA STATE

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ABSTRACT

Placental malaria remains a significant public health problem in malaria-endemic regions, posing serious risks to pregnant women and their newborns. This study investigated the prevalence, associated risk factors, and immunological impact of PM among pregnant women attending Hadejia General Hospital in Jigawa State, Nigeria. A hospital-based cross-sectional study was conducted among 356 participants. Maternal and Foetal cord samples were collected and examined for malaria parasitaemia using microscopy. Cytokine levels (IL-4, IL-6, IL-10, IL-17A, and IFN-γ) were measured using ELISA. Data were analyzed using SPSS version 20.0. The prevalence of placental malaria was 30.1%. Placental Malaria was significantly associated with younger maternal age (15-35 years), low educational attainment, primigravidity, rural residence, non-use of insecticide-treated nets (ITNs), and fewer than four antenatal care (ANC) visits. Use of ITNs and adequate ANC attendance were identified as protective factors. Cytokine analysis revealed that IL-4 and IL-10 levels in both maternal and fetal cord blood among malaria-positive women, indicating a predominant anti-inflammatory immune response. In contrast, IL-6 and IFN-γ levels were significantly reduced, suggesting suppression of pro-inflammatory responses, while IL-17A showed no significant difference. Correlation analysis demonstrated that IL-4 and IL-10 were positively associated with placental malaria and low birth weight, whereas IL-6 was inversely associated with malaria infection and linked to improved birth outcomes. These findings highlight the need to strengthen malaria prevention strategies during pregnancy through improved ANC coverage, increased ITN use, and targeted health education. The observed immune response patterns also suggest the potential role of cytokines as biomarkers for placental malaria monitoring.

Keywords: Placental malaria, Malaria in pregnancy, Cytokine immune response, Antenatal care, Low birth weight

INTRODUCTION

Malaria, caused by *Plasmodium* parasites transmitted by *Anopheles* mosquitoes, remains a major public health challenge globally and in sub-Saharan Africa, where most cases and deaths occur (Opi *et al.*, 2021). Pregnant women are especially vulnerable to malaria. Nigeria is one of the countries with the highest malaria burden with significant to maternal and neonatal morbidity and mortality (Omer *et al.*, 2021). Beyond its health impact, the disease imposes heavy economic costs through loss of productivity and healthcare expenses (Cardona Arias and Carmona Fonseca, 2022). Among its complications, placental malaria (PM) stands out as a silent but severe form, occurring when *P. falciparum*–infected erythrocytes accumulate in the placenta. This leads to inflammation, vascular obstruction, and adverse pregnancy outcomes such as maternal anemia, preterm delivery, low birth weight, stillbirth, and neonatal death (Melamed *et al.*, 2021). Despite global progress in malaria control, PM remains a persistent problem in northern Nigeria, including Jigawa State, due to factors such as maternal immunity, parasite characteristics, and vector dynamics.

In Jigawa, PM continues to threaten maternal and child health, often undetected because it lacks typical malaria symptoms. The consequences extend beyond health to social and economic wellbeing, reinforcing poverty in endemic areas. However, there is limited evidence on how PM affects maternal and foetal immune responses in this region. This study therefore seeks to examine the prevalence and risk factors of placental malaria among pregnant women at Hadejia General Hospital, Jigawa State, and to determine how cytokine responses (IL-4, IL-6, IL-10, IL-17A, IFN-γ) relate to infection and pregnancy outcomes. The findings aim to strengthen understanding of PM's impact and guide improved prevention and management strategies for healthier mothers and newborns in malaria-endemic communities.

MATERIALS AND METHODS

Study Area

The study was conducted at Hadejia General Hospital, located in Hadejia, Jigawa State, northwestern Nigeria. Jigawa lies between latitudes 11.00°N–13.00°N and longitudes 8.00°E–10.15°E. It shares borders with Kano and Katsina States to the west, Bauchi State to the east, and Yobe State to the northeast, and has a 70 km international boundary with the Zinder Region of Niger Republic. The State has a semi-arid climate, with average temperatures ranging between 25°C and 35°C. The rainy season extends from June to October, with peak rainfall in July and August.

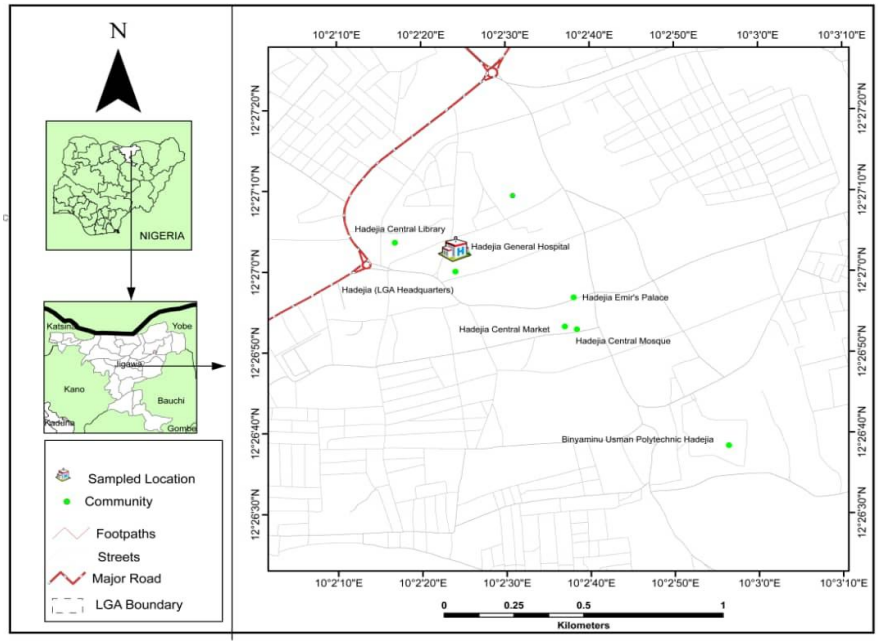

Figure 1: Map of Hadejia Showing Hadejia General Hospital

Study Design

A hospital-based cross-sectional descriptive study was conducted at Hadejia General Hospital over a three-month period. Pregnant women delivering at the facility were enrolled after obtaining informed consent. Participation was voluntary, and women of all ages, educational levels, and socio-economic backgrounds were included. Eligible participants provided three biological samples: maternal peripheral blood, placental blood, and umbilical cord blood.

Sample Size Determination

The sample size was calculated using Araoye's (2004) formula for population studies:

$$N = \frac{Z^2 P(1-P)}{d^2} \quad (1)$$

where Z = 1.96 (95% confidence level), P = 41.6% (prevalence from Fana *et al.*, 2015), and d = 0.05(precision). The estimated sample size was 359 participants, which was used for the study.

Data Collection

A structured questionnaire was used to collect information on demographic characteristics and risk factors. Birth weight was measured within one hour of delivery using an electronic scale with a precision of ±10 g. The scale was calibrated weekly to maintain accuracy.

Collection of Samples

Maternal peripheral blood, placental tissue, and umbilical cord blood samples were collected immediately after delivery using heparinized vacutainer tubes as described by Omer *et al.*, (2021). This approach preserved sample integrity and prevented clotting, ensuring suitability for laboratory analysis.

Parasitological Examination

Thin blood smears were prepared on clean, grease-free glass slides, air-dried, and stained with 10% Giemsa at pH 7.2 for 10 minutes. Stained smears were examined microscopically under ×100 oil immersion to detect *Plasmodium falciparum* parasites (Omer *et al.*, 2021).

Cytokine Measurement

Cytokine levels (IL-4, IL-6, IL-10, IL-17A, and IFN-γ) were quantified using Human ELISA MAX™ Deluxe kits (BioLegend, USA) following the manufacturer's protocol. The assay sensitivity for each cytokine was 2 pg/mL, allowing detection of minor concentration changes.

Statistical Analysis

Data were analyzed using SPSS version 20.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics (frequencies, percentages) were used to determine the prevalence of placental malaria. Bivariate analysis was performed to identify risk factors, and odds ratios (OR) with 95% confidence intervals (CI) were calculated. Cytokine levels were expressed as median (IQR) and spearman's correlation was used to assess relationships between cytokine concentrations, placental malaria, and neonatal birth weight. Statistical significance was set at $p < 0.05$.

RESULTS AND DISCUSSION

Prevalence of Placental Malaria

Out of 356 pregnant women examined at Hadejia General Hospital, 107 tested positives for placental malaria, giving an overall prevalence of 30.1%. The highest prevalence occurred among women aged 26–35 years (37.4%), followed by 15–25 years (34.7%), while the lowest was observed among those aged 36–45 years (20.0%). A chi-square test showed a significant association between age and placental malaria prevalence ($p = 0.0049$), indicating that younger women were more likely to be infected (Table 1).

Table 1: Prevalence of Placental Malaria Among Pregnant Women in Hadejia General Hospital

Age	No. of Examined	Positive (n)	Prevalence (%)	P-Value
15-25	98	34	34.7%	
26-35	123	46	37.4%	
36-45	135	27	20.0%	
Total	356	107	30.1%	0.0049

Risk Factors Associated with Placental Malaria

Table 2 presents the key factors associated with placental malaria. Women aged 15–25 years (OR = 2.12, p = 0.0126) and 26–35 years (OR = 2.39, p = 0.0022) had significantly higher odds of infection compared to those aged 36–45 years. Low educational attainment was associated with twice the odds of infection (OR = 2.05, p = 0.0031). Primigravida women were at greater risk (OR = 2.00, p = 0.0075). Protective factors included use of insecticide-treated nets (ITNs) (OR = 0.41, p = 0.0002) and ≥4 antenatal care (ANC) visits (OR = 0.46, p = 0.0010). Women living in urban areas were also less likely to be infected compared to those in rural communities (OR = 0.55, p = 0.0110).

Table 2: Risk Factors Associated with Placental Malaria Among Pregnant Women

Risk Factor	Variable	OR (Odd Ratio)	95% CI	P-Value
Age Group	15–25 years	2.12	1.18 – 3.84	0.0126*
	26–35 years	2.39	1.37 – 4.17	0.0022*
	36–45 years*	1.00	1.00 – 1.00	1.0000
Education Level	Low (None/Pri)	2.05	1.30 – 3.20	0.0031*
	High (Sec./Tert.) *	1.00	1.00 – 1.00	1.0000
Gravidity	Primigravida	2.00	1.20 – 3.34	0.0075*
	Multigravida*	1.00	1.00 – 1.00	1.0000
Use of ITNs	Yes	0.41	0.26 – 0.66	0.0002*
	No*	1.00	1.00 – 1.00	1.0000
Antenatal Care (ANC) Attendance	≥4 visits	0.46	0.29 – 0.73	0.0010*
	<4 visits*	1.00	1.00 – 1.00	1.0000
Residence	Urban	0.55	0.35 – 0.87	0.0110*
	Rural*	1.00	1.00 – 1.00	1.0000

*Significance between groups comparison

Cytokine Levels in Maternal and Fetal Cord Blood

Five cytokines (IL-4, IL-6, IL-10, IL-17A, and IFN-γ) were analyzed in both maternal and fetal cord blood samples. Elevated IL-4 and IL-10 levels were observed among malaria-positive participants, whereas IL-6 and IFN-γ levels were significantly reduced (Table 3). IL-17A showed no significant difference between infected and non-infected groups.

In maternal blood, IL-4 levels were significantly higher in malaria-positive mothers (6.8 pg/mL) compared with malaria-negative mothers (3.6 pg/mL; p < 0.001), while IL-6 levels were significantly lower in malaria-positive women (28.5 pg/mL) than in negatives (54.3 pg/mL; p < 0.001). Similarly, the anti-inflammatory cytokine IL-10 was markedly increased in malaria-positive mothers (94.0 pg/mL) compared with malaria-negative mothers (49.5 pg/mL; p < 0.001). In contrast, IL-17A showed no statistically significant difference between the two groups (p = 0.071). Maternal IFN-γ concentrations were significantly reduced in malaria-positive women (44.8 pg/mL) relative to malaria-negative women (76.1 pg/mL; p < 0.001). A similar pattern was observed in fetal cord blood, where IL-4 and IL-10 levels were elevated, while IL-6 levels were reduced in malaria-positive samples.

Table 3: Cytokine Concentrations in Maternal and Fetal Cord Blood by Malaria Status

Cytokine	Sample Type	Total (Median, IQR)	Malaria Positive (n = 107)	Malaria Negative (n = 249)	P-Value
IL-4	Maternal	4.8 (3.2–6.7)	6.8 (4.4–9.1)	3.6 (2.3–5.0)	<0.001*
	Fetal Cord	2.3 (1.4–3.2)	2.9 (2.1–4.1)	1.8 (1.0–2.6)	<0.001*
IL-6	Maternal	42.5 (30.3–65.0)	28.5 (20.0–39.2)	54.3 (41.1–73.5)	<0.001*
	Fetal Cord	10.2 (6.5–16.7)	7.8 (4.1–12.3)	11.4 (6.7–18.6)	0.004*
IL-10	Maternal	71.0 (42.3–95.6)	94.0 (62.1–118.4)	49.5 (31.0–70.4)	<0.001*
	Fetal Cord	15.5 (9.0–29.1)	21.5 (13.1–44.6)	13.2 (6.2–21.0)	0.018*
IL-17A	Maternal	3.1 (1.9–5.6)	2.5 (1.4–4.2)	3.5 (2.0–6.5)	0.071
	Fetal Cord	3.3 (2.2–6.5)	2.7 (1.6–5.0)	3.6 (2.4–6.9)	0.063
IFN-γ	Maternal	63.5 (45.0–91.0)	44.8 (30.3–66.5)	76.1 (58.3–102.5)	<0.001*
	Fetal Cord	29.6 (18.1–55.2)	24.1 (13.5–48.3)	32.7 (21.1–58.6)	0.141

*Significance between groups comparison

Correlation Between Cytokine Levels and Placental Malaria

Correlation analysis showed that IL-4 (r = 0.41, p = 0.001) and IL-10 (r = 0.45, p = 0.0005) were positively correlated with placental malaria, indicating higher cytokine levels in infected women. Conversely, IL-6 (r = −0.36, p = 0.004) and IFN-γ (r = −0.39, p = 0.002) were negatively correlated, suggesting lower concentrations in infected participants. IL-17A showed a weak and non-significant negative correlation (r = −0.12, p = 0.091) (Table 4).

Table 4: Correlation Between Cytokine Levels and Placental Malaria Status

Cytokine	Correlation Coefficient (r)	P-Value	Interpretation
IL-4	0.41	0.001*	Moderate positive correlation (significant)
IL-6	-0.36	0.004*	Moderate negative correlation (significant)
IL-10	0.45	0.0005*	Moderate positive correlation (significant)
IL-17A	-0.12	0.091	Weak negative correlation (not significant)
IFN-γ	-0.39	0.002*	Moderate negative correlation (significant)

*Significance between groups comparison

Discussion

The prevalence of placental malaria among pregnant women in Hadejia General Hospital was 30.1%, aligning with reports from sub-Saharan Africa where rates range from 19% to over 40%, depending on transmission intensity and preventive coverage (Schmiegelow *et al.,* 2010; Ajibola *et al.,* 2017). The relatively high prevalence observed in this study may reflect differences in regional transmission, intervention uptake, and socio-demographic characteristics.

Younger women (15–35 years) were more than twice as likely to be infected compared to older women, with the highest prevalence recorded among those aged 26–35 years (37.4%). This agrees with findings from other studies that associate young maternal age with increased malaria risk, primarily due to lower acquired immunity, especially in primigravida women (Rogerson *et al.,* 2020; Tadesse et al., 2020). Similarly, low educational attainment was associated with a two-fold increase in infection risk, consistent with evidence showing that less educated women have limited access and adherence to preventive measures such as insecticide-treated nets (ITNs) and antenatal care (ANC) services (Li *et al.,* 2024).

Urban residence significantly reduced the odds of infection, likely due to improved healthcare access and reduced exposure to malaria vectors compared to rural settings (Li et al., 2024). Primigravida women were twice as likely to be infected, supporting the established notion that lack of pregnancy-specific immunity to P. falciparum antigens increases susceptibility (Tadesse *et al.,* 2020).

The study confirmed the protective role of ITN use and ≥4 ANC visits, which reduced infection risk by 59% and 54%, respectively. These findings are consistent with WHO recommendations and prior research emphasizing these interventions as essential for preventing malaria during pregnancy (Rogerson et al., 2020; Li et al., 2024). Despite their effectiveness, placental malaria remains a persistent threat among young, less-educated, and primigravida women, underscoring the need to strengthen community outreach and address socio-economic barriers (Schmiegelow *et al.,* 2010).

Although intermittent preventive therapy with sulfadoxine–pyrimethamine (IPTp-SP) remains central to malaria prevention in pregnancy, emerging drug resistance calls for integrated control strategies and further research (Uwimana *et al.,* 2023).

Cytokine analysis revealed elevated IL-10 and IL-4 levels among malaria-positive women, consistent with previous reports highlighting increased anti-inflammatory and Th2-skewed responses in placental malaria (Ataide *et al.,* 2015; Sarr *et al.,* 2017; Silveira *et al.,* 2022). IL-10, a regulatory cytokine, suppresses pro-inflammatory activity to protect placental tissue but may also promote parasite persistence. Conversely, IL-6 and IFN-γ levels were significantly reduced, reflecting impaired cellular immune activation. This aligns with studies linking low IFN-γ to higher parasite density and adverse pregnancy outcomes (Megnekou*et al.,* 2015; Simantov *et al.,* 2021).

Correlation analysis confirmed IL-10 and IL-4 as positively associated with infection, while IL-6 and IFN-γ showed negative correlations, reinforcing immune suppression and regulatory dominance that facilitate placental parasite sequestration (Ataide et al., 2015; Simantov et al., 2021). IL-17A did not show a significant association, suggesting a minimal or context-specific role in malaria-related inflammation (Barateiro *et al.,* 2014).

Overall, these immune patterns suggest that placental malaria triggers immune tolerance that compromises parasite clearance and contributes to poor pregnancy outcomes such as low birth weight and preterm delivery. These findings align with growing evidence that cytokine imbalances affect placental function and fetal development (Silveira *et al.,* 2022; Mayor *et al.,* 2015).

CONCLUSION

This study confirmed that placental malaria remains a significant concern among pregnant women in Hadejia, with a prevalence of 30.1%. It is strongly associated with factors such as young age, low education, primigravidity, poor ANC attendance, non-use of ITNs, and rural residence. The findings also revealed that placental malaria alters maternal and fetal immune responses. Higher levels of IL-4 and IL-10, and lower levels of IL-6 and IFN-γ, were observed among infected women, indicating a shift toward an anti-inflammatory immune profile. These changes were linked to low birth weight in newborns. Overall, the study highlights the importance of early ANC visits, ITN use, and targeted health education as key strategies to reduce placental malaria and its impact on pregnancy outcomes.

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