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Predictors of placental malaria in HIV-positive and HIV- negative pregnant women in Enugu, South-Eastern Nigeria

Abstract

Background: Placental malaria has long been recognized as a complication of malaria in pregnancy with serious adverse outcome. Recognition of possible predictors is an effort in the right direction.

Aim of the study: The study determined and compared the Predictors of placental malaria in HIV-positive and HIV- negative pregnant women attending antenatal clinics in Poly General Hospital, South-Eastern Nigeria.

Material and method: A cross-sectional descriptive study, carried out on 200 HIV positive and 200 HIV negative pregnant women attending antenatal clinics in Poly General Hospital, Enugu, selected using simple random sampling technique between May to December 2023. Placenta blood samples were collected and thick blood films were examined for malaria parasite using Giemsa expert microscopy. A structured self-administered questionnaire was used for data collection and the data analysed using SPSS version 23.

Results: The prevalence of malaria in HIV positive and negative pregnant women were 83.5% (167/200) and 75.5%(151/200) respectively ($P < 0.001$). The HIV positive and HIV negative participants were between 16-45 years of age with majority in the age range of 31-35 years. Mean gestational age of HIV positive and HIV negative participants were 24.3±1.1 and 24.4±1.3 weeks respectively. Placental malaria was significantly associated with rural residence, hemoglobin genotype AA, not receiving intermittent preventive treatment in pregnancy (IPTp), and not sleeping under insecticide-treated bed nets (ITN) (($P<0.001$)).

Conclusion: The study showed that Placental malaria was significantly associated with rural residence, hemoglobin genotype AA, not receiving intermittent preventive treatment in pregnancy (IPTp), and not sleeping under insecticide-treated bed nets (ITN). Recognition of these significant predictors will enhance review and implementation of strategies for the prevention of malaria in pregnancy.

Keywords: malaria in pregnancy, predictors, HIV positive, HIV negative

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Introduction

Malaria in HIV pregnant clients is a major public health challenge in tropical and subtropical regions of the world.[1] About 70% of the world's HIV-infected population lives in sub-Saharan Africa, where 350 million people are at risk of malaria infection.[2] Malaria and Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS) are two most devastating global health problems of our time. Both disproportionately affect poor people in developing countries and have been called "Diseases of Poverty".

It causes significant morbidity and mortality in affected women. Malaria and HIV cause more than 4 million deaths yearly.[3,4] Sub-Saharan Africa is also the region most affected by the HIV pandemic and the disease is still responsible for a significant morbidity and mortality especially in under 5 children.[5–7]

Coinfection with malaria and HIV is thought to have a synergistic effect, with studies reporting that repeated infection with malaria leads to a more rapid decline in CD4+ T cells overtime, meanwhile malaria coinfection with HIV results in more episodes of symptomatic malaria,[8] and more episodes of severe or complicated malaria including death in both children and adults.[9]

Malaria is a blood-borne disease caused by *Plasmodium* species, with *Plasmodium falciparum* (*P. falciparum*) being the deadliest species.[10] Pregnant women, especially Primigravidas are at high risk of severe malaria due to *Plasmodium falciparum* erythrocyte membrane protein-1 (PfEMP1), a major variant surface antigen displayed on the surface of. *falciparum*-infected erythrocytes (IEs) that serves as an adhesion.[11] As a result, infected erythrocytes (IEs) accumulate within the placenta, triggering an inflammation in the placental intervillous spaces; the infected and inflamed placenta is commonly regarded as placental malaria (PM).

There are five species of Plasmodium which cause disease in humans namely; Plasmodium ovale, *Plasmodium* vivax, *Plasmodium* malariae, *Plasmodium* knowlesi and *Plasmodium* falciparum, with the latter being the most virulent accounting for the majority of cases and deaths attributed to malaria. As in most parts of Sub-Saharan Africa, *Plasmodium* falciparum is the predominant Plasmodium specie in Cameroon, accounting for almost 100 % of all malaria-related cases.[12]

Risk factors of malaria during pregnancy will include not owning and inappropriate use of Long lasting insecticide treated nets and drug shortages at health institutions.[13,14] Malaria in pregnancy causes several effects on the mother and fetus, including parasite sequestration in

the placental vascular space.[15] Abortion and stillbirth,[16] preterm birth, low birth-weight, mother-to-child transmission (MTCT) of parasites and maternal anaemia.[17] Anaemia due to malaria causes up to 10,000 maternal deaths each year.[18] In areas of stable malaria transmission in sub-Saharan Africa, it is recommended that all pregnant women should receive intermittent preventive treatment with sulfadoxine-pyrimethamine (SP) at each scheduled antenatal-care visit (at least one month apart), until delivery.[19,20] Several studies have shown that HIV during pregnancy amplifies the effects of malaria,[21] which is why administering Cotrimozaxole alongside antiretroviral therapy (ART) to pregnant women is essential during every antenatal-care visit.[21] Therefore, this study was designed to showcase the overlapping effect of malaria and HIV infections among pregnant women to enable the formulation of program(s) for optimal control and improving the clinical management of women during antenatal-care visits.

Methodology

Study design and study population

The patients for the study were selected from women attending antenatal and PMTCT clinics for HIV-negative (Group A) and HIV-positive (Group B) pregnant women respectively, between May to December 2023. Every consecutive delivery that fulfils the inclusion criteria was enrolled. A sample size of 394 was calculated using the prevalence rate documented in a different study. Provision was made for 5% attrition, bringing the sample size to 400. Group A participants were Pregnant women who were HIV positive and willing to participate in the study. Group B participants were Pregnant women who were HIV negative and Willing to participate in the study. Patients who failed to give consent, who have obvious malaria fever, patients with sickle cell disease and patients who have delivered before the study, were excluded.

Laboratory procedures

After delivery of both the baby and the placenta, the maternal surface of the placenta was washed with normal saline and then incised with a scalpel and placental blood collected with a syringe into EDTA bottle within 1 h of delivery. The specimens were coded to correspond with the codes on the questionnaires for easy identification. These samples were then sent to the hematology laboratory for processing. Within four hours of collection, thin and thick films were prepared and air dried and stained using 10% freshly prepared Giemsa stain and pH of 7.2 maintained. The blood smears were fixed with 100% methanol prior to staining. The films were viewed under a light microscope at 100 magnifications.[22]

The diagnosis of placental malaria parasitaemia was based on the identification of asexual stages of plasmodium on the tick films while the thin films were for identification of the species of the plasmodium. Plasmodium parasite density was determined by counting the number of asexual parasites against 200 white blood cells on the thick blood film and converted to parasites per µL using an assumed total white blood cell count of 800 per µL or parasite density ≥ one parasite per µL.[22] A blood film was declared negative if no parasite was seen after viewing five hundred white blood cells by two different blinded microscopists.

Data analysis

Data was recorded in case record forms specially designed for the study and cross-checked. Data entry and analysis was done using version 23 software (SPSS 23) of Statistical Packages for Social Sciences of Chicago in the United States of America that has been programmed to check for errors. Data of HIV-positive pregnant women and HIV-negative pregnant women was compared using Chi-Square Test, relative risk and percentages. Significance level was placed at a P-value of less than 0.05.

The study results were presented using simple percentages and tables as appropriate.

Results

Socio-demographic characteristics of the research participants

Table 1 shows the socio-demographic characteristics of the research participants. Their age group ranged between 16 -45years with majority within the age bracket of 31-35(40.5% and 41.5%) in both HIV positive and negative respectively. Also most of the HIV positive and negative participants were married, 95% and 98% respectively. While 1.5% of the HIV positive were single, less number (0.5%) of the HIV negative were single. Similarly, 1.5% of the positive participants were divorced while 0.5% of the negative were divorced (Tables 2–4).

Table 1 The socio-demographic characteristics of the research participants

Variables	Categories	HIV Positive group		HIV Negative group	
		N	%	N	%
Age(years)	16-20	6	3	4	2
	21-25	28	14	24	12
	26-30	53	26.5	57	28.5
	31-35	81	40.5	83	41.5
	36-40	21	10.5	24	12
	41-45	11	5.5	8	4
Marital status	Single	3	1.5	1	0.5
	Married	190	95	196	98
	Widowed	4	2	2	1
	Divorced	3	1.5	1 0.5	
Level of education	Primary	20	10	18	9
	Secondary	99	49.5	104	52
	Tertiary	66	33	60	30
	Postgraduate	15	7.5	18	9
Occupation	Traders	87	43.5	84	42
	Civil servants	58	29	61	30.5
	Teachers	19	9.5	18	9
	Health workers	14	7	16	8
	Others	22	11	21	10.5
Gravidity	Primigravida	46	23	40	20
	Multigravida	154	77	160	80

Table 2 Malaria Parasitaemia among HIV Positive and HIV Negative participants

Malaria Parasite (MP)	HIV Positive		HIV Negative		p-value
	N	%	N	%	
No MP	33	16.5	49	24.5	
Mild MP (1-999)	73	36.5	68	34	
Moderate MP (1000-9999)	91	45.5	82	41	
High MP	3	1.5	1	0.5	

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Table 3 Predisposing factors for placental malaria in HIV positive pregnant women

Variables	Number	Malaria Parasitaemia in placenta blood, n %		p-value
		Positive	Negative	
Gravidity	200			
Primigravida	46	24	22	0.23
Multigravida	154	73	81	
Residence	200			
Rural	58	43	12	0.001
Urban	152	48	104	
Received IPTP	200			
Yes	182	54	128	0.001
No	18	14	4	
Used ITN	200			
Yes	170	66	104	0.001
No	30	24	6	
HB genotype	200			
AA	142	134	8	0.001
AS	58	11	47	

Table 4 Predisposing factors for placental malaria in HIV negative pregnant women

Variables	Number	Malaria parasitaemia in placenta blood, n %		p-value
		Positive	Negative	
Gravidity	200			
Primigravida	51	25	26	0.3
Multigravida	149	71	78	
Residence	200			
Rural	41	38	3	0.001
Urban	159	53	106	
Received IPTP	200			
Yes	180	83	97	0.3
No	20	12	8	
Used ITN	200			
Yes	173	13	160	0.001
No	27	22	5	
HB genotype	200			
AA	140	130	10	0.001
AS	60	8	52	

As it concerns level of education, majority of the HIV positive and negative participants had secondary level of education, 49.5% and 52% respectively. While 10% of the positive women had primary education, it was 9% in HIV negative women. About 33% of the positive women had tertiary education, while it was 30% in negative women. Least level of education, 7.3% was found amongst the HIV positive who had tertiary level of education. Even though level of education was higher in HIV patients, trading is the major occupation of both HIV positive (43.5%) and negative participants (42%). Amongst the HIV positive participants, 29% were civil servants, 9.5% were Teachers, 7% health workers, while 11% were involved in other works. Amongst the HIV negatives, 30.5% were Civil servants, 9% Teachers, 8% Health workers, while 10.5% carry out other works. Most of the women were multigravida when compared with those that were Primigravida in both HIV positive and negative women. Amongst the HIV positive, 23% were Primigravida, while 77% were multigravida. Amongst the HIV negative, 20% were Primigravida while 80% were multigravida.

Malaria parasitaemia amongst HIV positive and negative women

About 167 HIV positive women had cases of malaria unlike in HIV negative women where only 151 women had cases of malaria. This makes the prevalence of malaria in HIV positive and negative women to be 83.5% and 75.5% respectively. Amongst the HIV positives, 33 (16.5%) had no case of malaria, mild malaria cases were recorded in 73 (36.5%) women, moderate cases in 91(45.5%) women and high cases of malaria in 3 (1.5%) participants. Amongst the HIV negative women, 49 (24.5%) had no case of malaria, mild malaria cases were recorded in 68(34%) women, moderate cases in 82(41%) women and high case of malaria in 1(0.5%). The above finding shows that the prevalence of malaria was higher in the HIV positive than the

HIV negative women, just like all cases of malaria parasitaemia was equally higher in HIV positive participants.

Predisposing factors for placental malaria in HIV positive pregnant women

Concerning the predisposing factors for placental malaria in HIV Positive pregnant women, it was discovered that 46 participants were Primigravida while 154 were multigravida. Out of the 46primips, 24 had placental malaria while 22 did not. Out of the 154 multips, less number 73 had placental malaria while 81 participants did not (P =0.32). Out of the 200 participants, 58 resided in the rural environment with majority, 43 of them having malaria parasitaemia as against only 12 persons that were not affected. The rest of 152 person resided in the urban area with only few 48 persons being affected as against 104 persons that were not affected ($p < 0.001$). About 182 had access to IPT_p out of which only 54 had placental malaria while the majority did not. The remaining 18 participants did not receive IPT_p and majority 14 of them had placental malaria while only 4 did not ($p < 0.001$). Out of 200 participants, about 170 respondents made use of ITN, out of which few 66 had placental malaria while greater number 104 did not. The remaining 30 did not use ITN for which 24 had placental malaria while 6 did not ($p < 0.001$).

Hamoglobin genotype AA was found in 142 participants out of which 134 was noted to have placental malaria while 8 did not. The remaining 58 participants had haemoglobin genotype of AS and 11 of them had placental malaria while 47 were negative ($p < 0.001$).

Predisposing factors for placental malaria in HIV negative pregnant women

Concerning the predisposing factors for placental malaria in HIV negative pregnant women, it was discovered that 51 participants were Primigravida while 149 were multigravida. Out of the 51 primips, 25 had placental malaria while 26 did not. Out of the 149 multips, less number 71 had placental malaria while 78 participants did not (P =0.32). Out of the 200 participants, 41 resided in the rural environment with majority, 38 of them having malaria parasitaemia as against only 3 persons that were not affected. The rest of 159 person resided in the urban area with only few 53 persons being affected as against 106 persons that were not affected ($p < 0.001$). About 180 had access to IPT_p out of which only 83 had placental malaria while the majority,97 did not. The remaining 20 participants did not receive IPT_p and majority 12 of them had placental malaria while only 8 did not ($p < 0.001$). Out of 200 participants, about 173 respondents made use of ITN, out of which few 13 had placental malaria while greater number 160 did not. The remaining 27 did not use ITN for which 22 had placental malaria while 5 did not ($p < 0.001$).

Hamoglobin genotype AA was found in 140 participants out of which 130 was noted to have placental malaria while 10 did not. The remaining 60 participants had haemoglobin genotype of AS and 8 of them had placental malaria while 52 were negative ($p < 0.001$).

Discussion

The prevalence of placental malaria in HIV positive and negative pregnant women as observed in this study were 82% and 75.5% respectively. This finding was statistically significant and also aligns with a similar malaria prevalence of 81% and 75% in HIV positive and negatives pregnant women respectively from previous research work done in Enugu[23] just like similar malaria prevalence of 86.5% found in another study conducted in Cameron[24] and Menendez in Tanzania that reported a prevalence of 75.5%.[25] This figure is higher than that observed by Bako et al. that reported a prevalence of 33.9% in Maiduguri, northeastern Nigeria,[26] and 32% reported by Adam et al in Sudan.[27] It is also higher than that reported in other studies that have used placental blood in Nigeria.[28,29] however, the differences may be partly that this study was done at the peak of rainy season (May - December) as well as environmental factors in the study populations. Enugu State is situated in the rainforest area of Nigeria where malaria vectors are more likely to breed/ thrive when compared with northeastern Nigeria. Higher malaria prevalence of 96.92% was also observed in another study.[30]

In this study, rural residence, hemoglobin genotype AA, non-use of IPTp and non-use of ITN were identified to be the significant determinants of placental malaria in both HIV positive and HIV negative pregnant women. Similar findings have been documented in previous works.[31] Monthly intermittent prophylactic treatment of malaria is recommended currently in obstetrics to enable clearance of asymptomatic parasitaemia in pregnant women residing in malaria endemic areas. This practice drastically reduces the prevalence and severity of malaria in pregnancy, including placental malaria based on the available evidence. In Maiduguri, the non-use of IPTp was a significant risk factor for placental malaria.[26] as observed in this study. The finding of a significant association between rural residence and placental malaria may be due to the concentration of many programs designed to reduce the menace of malaria in the cities. Cot et al found that malaria was more common among pregnant women who lived in peripheral districts of Burkina Faso than in those who lived in the central districts.[32]

Conclusion

The study showed that Placental malaria was significantly associated with rural residence, hemoglobin genotype AA, not receiving intermittent preventive treatment in pregnancy (IPTp), and not sleeping under insecticide-treated bed nets (ITN). Recognition of these significant predictors will enhance review and implementation of strategies for the prevention of malaria in pregnancy.

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Ethical approval

Approval for the study was obtained from the management of Poly General Hospital Enugu and written consent obtained from the research participants.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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