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Original Article

Comparison of malaria occurrence among HIV-negative and HIV-infected pregnant women attending a rural antenatal clinic in central Nigeria

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ABSTRACT

Background: Malaria and HIV are infectious diseases plaguing people living in sub-Saharan where poverty is rampant. **Aim:** This study investigated malarial infection and predisposing risk factors in HIV-negative and HIV-infected pregnant women attending a rural antenatal clinic in Nigeria. **Methods:** Pregnant women were screened for HIV using the Alere Determine HIV-1/2 rapid immunoassay test strip and positive samples were confirmed using the Trinity Unigold HIV-1/2 kit. Thick blood smears were prepared and stained with Giemsa for malaria microscopy. **Results:** HIV-infected pregnant women (37.5%, 30/80) were significantly predisposed ($\chi 2$ =10.41; *P=0.001*) and at higher malaria risk (AOR=3.40, *P=0.002*) than the HIV-negatives (15.0%, 12/80). In relation to the socio-demographic factors of the pregnant women, age-related malaria varied between 9.7% - 21.1% in the HIV-negatives and 33.3%-50.0% in the HIV-infected. With regards to educational level, malarial infection varied between 6.3% - 18.6% in the HIV-negatives and 30.3%-50.0% in the HIV-infected pregnant women, while for occupation, malarial infection varied between 10.0%-23.1% in the HIV-negatives and 30.0% - 42.0% in the HIV-infected. For marital status, malarial infection varied between 7.1%-20.0% in the HIV-negatives and 23.1%–46.5% in the HIV-infected. In HIV-negative, primigravidas were at higher risk of becoming infected with malaria, while in HIV-infected, women at their second trimester were at higher risk of having malaria. **Conclusion:** HIV-infected pregnant women were more predisposed to malaria than their HIV-negative counterparts. Parity (primigravida) and gestational age (2nd trimester) are risk factors predisposing pregnant women respectively to malaria.

Keywords: Malaria, HIV, pregnancy, women, rural, Nigeria

INTRODUCTION

Malaria and HIV are the two most important infectious diseases plaguing people living in sub-Saharan where poverty is rampant. Both diseases have caused more than 3 million deaths in 2007 and are still affecting millions every year.[1]

However, during the 6th Multilateral Initiative on Malaria (MIM) Pan-African and the World AIDS conferences held in South-Africa and the USA respectively in 2013, it was reported that there was a dramatic decline in death of both malaria and HIV infected people in Africa mostly to the large-scale vector control coverage programme and the administration of Highly Active Antiretroviral Therapy respectively. Likewise new infections from both diseases are declining from many affected countries.

In sub-Saharan Africa, pregnant women are well known to be the most vulnerable to both malaria and HIV infections. Recent estimates show that about 440,000 pregnant women had malarial infection attributable to HIV and their pregnancies have specific risks of complications from these diseases.[2] In Nigeria, despite the concerted efforts undertaken by the Federal Government to half and reverse the trend of infections by 2015 so that it could meet up with the Millennium Development Goals, not much has been achieved and both diseases remain stable. It is estimated that 3,300,000 individuals live with HIV/AIDS and over 100 million malaria cases are being reported every year in Nigeria.[3,4] From these 215,000 and 300,000 individuals die respectively every year from these infections.

Malaria causes anaemia which increases the risk for HIV infection. Also, people living with HIV/AIDS are more susceptible to malaria and other severe illnesses. Malaria contributes to a temporary increase in viral load among HIV-infected people which may worsen the clinical disease and increase mother-to child transmission.[5] In pregnant women, HIV infection increases the risk of high-density *Plasmodium falciparum* infection, higher risk of maternal anaemia and low birth weight.[6]

Malaria has been reported to be endemic in Benue State with prevalence varying between 14.5% - 76.9% among children, pregnant women and adults.[7-11] However, the state has been in the lead for HIV/AIDS in the country since 1999 except in 2003 when it became second. For this cause, unavailability of data in many parts (mostly rural areas) of the country has made control of these two infections a major public health dilemma among the pregnant women. Therefore, to bring baseline and valuable data that will help in the planning of control programmes of these two infections in rural areas of the state and the country at large, we determined and compared the occurrence of malarial infection and the predisposing risk factors in HIV-infected and HIV-negative pregnant women attending antenatal clinic of the General Hospital Vandeikya, Vandekiya Local Government Area (LGA), Benue State, central Nigeria.

METHODOLOGY

Study area

Vandeikya Local Government Area (LGA), located in the south eastern part of Benue state is at latitude $7^{o}50'$ - 7^{o} 15'N, longitude 9°00'-9°60'E and at 183 m above sea level. It is bounded to the South by Obudu and Bekwara LGAs of Cross River State, to the North by Ushongo LGA, to the West by Konshisha LGA and to the East by Kwande LGA. The LGA is divided into twelve administrative wards and dominated by the Tiv indigenous community. The mean annual rainfall is between 1,200-2000 mm and the mean annual temperature is about 32.5°C. The wet season is usually between April and October, while the dry season is between November and March.

Study design and sample size

This is an observational cross-sectional study conducted between June and October 2013 in the General hospital Vandeikya which receives patients from all villages around Vandeikya LGA. Prior, to the commencement of the study ethical approval was given by the Ministry of Health, Benue state and permission to carry out the study was granted by the hospital's management. Each pregnant woman signed and filled an informed consent form and pretested questionnaire that included information on socio-demographic factors and pregnancy parameters. We assured them of utmost confidentiality and all dispositions were taken into consideration to avoid duplication of screening for their subsequent visits during the period under study. The Statemate 2.00 software was used for sample size estimation and it gave a minimum of 144 subjects at 80% power and 5% significance level by taking proportion from a previous study.

Exclusion and inclusion criteria

The study cohort included pregnant women that came for their antenatal clinic in the hospital. On average 30 to 50 pregnant women attended the weekly antenatal service from whom we recruited 8 to10 pregnant women weekly with a variability of 32 to 40 monthly. During the five months of the study we randomly examined 183 pregnant women among whom we enrolled 80 HIV infected and 80 HIV negatives. Prior to the study, ethical clearance was obtained from the institutional Ethics committee, and informed consent was obtained from each patient.

HIV screening and CD4$^+$ counts

About 4 ml of blood sample was collected into a vacutainer tube from each pregnant woman. Each tube was appropriately labelled and immediately sent for HIV screening and malaria parasitaemia respectively. Pregnant women were screened for HIV using the Alere Determine HIV-1/2 rapid immunoassay test strip. Positive samples were confirmed using the Trinity Unigold HIV-1/2 kit (TRINITY BIOTECH PLC, Ireland). The PARTEC Cyflow counter version 2.4 (Flow cytometre) was used to count CD4+ lymphocytes subsets of the HIV-infected pregnant women.

Malaria microscopy

With the aid of a micropipette, a drop of blood was placed on a clean grease-free slide and spread with the edge of another slide to make a thick blood film for determination of *Plasmodium* species. The films were fixed with 3% Giemsa stain (pH 7.0) for 30 minutes.[12] The stained slides were examined by two competent microscopists using oil immersion under x100 objective lens of a light microscope. All slides reported *Plasmodium falciparum* parasites.

Statistical analysis

Collected data were entered into Excel 2007 worksheet and imported into SPSS version 19.0 for Windows. Descriptive statistics using cross-tabulation of the categorical variables were employed to generate tables. Chi-square (χ^2) test was used to compare malaria occurrence between socio-demographic variables, while the logistic regression was used to find association between risk factors that could influence malarial occurrence in HIV infected and negative pregnant women. The adjusted odd ratios with 95% confidence interval were used to measure the strength of associations. All tests were 2-tailed and p-values less than 0.05 were considered statistically significant.

RESULTS

Table 1 shows that malarial infection significantly occurred in the HIV-infected pregnant women (37.5%, 30/80)(χ^2 =10.41, *P=0.001*) and they were at higher risk of having malaria (*AOR=3.40, P=0.002*) than their HIV-negative counterparts (15.0%, 12/80). In relation to the socio-demographic factors, age-related malaria varied between 9.7% - 21.1% in the HIV-negatives (χ^2 = 1.42; *P=0.*84) and between 33.3% - 50.0% in the HIV-infected (χ^2 = 0.94; *P=0.97*). With regards to educational level, malarial infection varied between 6.3% - 18.6% in the HIV-negatives (χ^2= 1.40; *P=0.49*) and 30.3% - 50.0% in the HIV-infected pregnant women (χ^2 **=** 1.30; *P=0.73*), while for occupation, malarial infection varied between 10.0% - 23.1% in the HIV-negatives (χ^2= 1.13; *P=0.77*) and 30.0% - 42.0% in the HIV-infected (χ^2= 1.51; *P=0.46*). With regards to marital status, malarial infection varied between 7.1% - 20.0% in the HIV-negatives (χ^2= 0.92; *P=0.63*) and 23.1% – 46.5% in the HIV- infected (χ^2= 3.80; *P=0.15*).

Table 2 shows the risk factors influencing malarial occurrence in HIV- negative and HIV-infected pregnant women attending antenatal clinic of General Hospital Vandeikya, Benue state, central Nigeria. In HIV-negative pregnant women, primigravidae (28.0%, 7/25) were at higher risk of becoming infected with malaria (AOR = 0.49[0.25 – 0.98]; *P=0.04*), while in HIV-infected, women at their second trimester (44.2%, 19/43) were at higher risk of having malaria (AOR = 0.16[0.06 – 0.40]; *P=0.00*).

DISCUSSION

Nigeria is a country highly endemic for malaria where related morbidity and mortality is high among pregnant women. This present study revealed that HIV-infected pregnant women were more infected (37.50%) and 3.4 times at increased risk of becoming infected with malaria than the HIV- negatives. This can be explained by the combined effect of

pregnancy and change in immune status of the body that has been impaired by HIV to respond against *P. falciparum* antigens as only *falciparum* malaria was reported among the women. In sub-Saharan Africa, both pregnancy and HIV have been reported to reduce women immunity and thereby exposing them to several infections. Previous studies observed similar trends with HIV-infected pregnant women to be more predisposed to malaria than their HIV-negative counterparts.[13-18] Evidence from recent studies reported reduction of antibodies to variant antigens that develop on the surface of placental and chondroitin surface A (CSA) binding infected erythrocytes in HIV-1 infected pregnant women.[19,20] The low malaria occurrence observed in the HIV-negative pregnant women is impressive and encouraging as the study was conducted during the high risk-months of malaria transmission; this is likely due to the scaling up of malaria control through the administration of Intermittent Preventive Treatment (IPT) and distribution of Insecticide Treated Nets (ITNs) during the last decade to all pregnant women attending antenatal clinics in Nigeria. However, all the pregnant women at 2nd and 3rd trimesters reported to have taken at least one dose of Sulfadoxine - Pyrimethamine (SP) regimen during their antenatal visits. Conversely, recent studies reported high occurrence of malaria in HIV negative pregnant women attending antenatal clinics in neighbouring areas.[7,8,11]

Socio-demographic factors did not affect occurrence of malaria in both the HIV-negative and HIV-infected pregnant women, this simply shows that any HIV-negative or infected pregnant woman regardless of her socio-demographic status can be exposed to malaria if she does not take into consideration preventive measures. In the present study, HIV-negative primigravidae were at higher risk of malarial infection contrasting the HIV-infected primi- and multigravidae whose malaria occurrence did not depend on gravidity. This agrees with other cross-sectional studies that reported HIV–negative primigravidae being more exposed to malarial infection than the multigravidae and gravidity not influencing malarial infection in HIV-infected pregnant women.[7,8,21] Recently, evidences from immunological studies showed antibodies to defined parasite expressing *VAR2CSA* dominant transcript much higher among multigravidae than primigravidae and these antibodies were strongly associated with placental malaria among primigravidae.[22-24] Risk of developing malaria was observed to be lower in HIV-negative pregnant women at late gestational age (3rd trimester) than in the HIV-infected, Fried *et al*.[25] hypothesized that phenomenon by the development of malaria specific immunity at that pregnancy period in the former group and presence of low level of antibodies against variant surface antigens (VSA) on infected erythrocytes binding chondroitin surface A (CSA) thought to be protecting against placental malaria in the latter group.[13,19]

It is important to state that the short duration (5 months) was a great limitation to the study because we could not assess malaria and HIV effects on the new born babies. However, this study presents the first comparative study of malaria in HIV-negative and HIV-infected pregnant women attending an antenatal clinic of a rural hospital in Benue state, central Nigeria. HIV-infected pregnant women were more predisposed to malaria than their HIV-negative counterparts. Parity (primigravida) and gestational age (2nd trimester) were reported as risk factors predisposing HIV-negative and HIV-infected respectively to malaria. It is therefore recommended that pregnant women attending antenatal clinics in rural areas should be screened properly for malaria and HIV so that an integrated control of both infections be planned appropriately. Also, HIV-infected pregnant women should be promptly treated for malaria and followed up properly for HIV monitoring and treatment during and after their pregnancy. In addition, HIV-negative primigravidae and HIV-infected pregnant women at their 2nd trimester must be seriously taken into consideration for malaria treatment during antenatal clinics. Lastly, pregnant women should be educated by health officials on the use and benefit of Insecticide Treated Nets. This is to avoid the deleterious effect of malaria in rural pregnant women that are already faced with poverty and hardship.

Table 1: Malarial infection in relation to socio-demographic factors of HIV-negative and HIV-infected pregnant women attending antenatal clinic of General Hospital Vandeikya, Benue state, Nigeria

Malaria in pregnant women								
	HIV – negative				HIV - infected			
Variables	Exam	Pos (%)	χ^2	*p*	Exam	Pos (%)	χ^2	*p*
Occurrence	80	12(15.0)			80	30(37.5)		
Age			1.42	*0.82*			0.74	*0.97*
[16-20]	11	2(18.2)			6	2(33.3)		
[21-25]	19	4(21.1)			23	8(34.8)		
[26-30]	31	3(14.3)			35	13(37.1)		
[31-35]	14	2(14.3)			12	5(41.7)		
[36-40]	5	1(20.0)			4	2(50.0)		
Education			1.40	*0.49*			1.30	*0.73*
Non-educated	0	0(0.0)			5	2(40.0)		
Primary	16	1(6.3)			40	17(42.5)		
Secondary	43	8(18.6)			33	10(30.3)		
Tertiary	21	3(14.3)			2	1(50.0)		
Occupation			1.13	*0.77*			1.51	*0.46*
Housewife	13	3(23.1)			0	0(0.0)		
Trading	29	4(13.8)			30	9(30.0)		
Farming	20	2(10.0)			50	21(42.0)		
Civil service	18	3(16.7)			0	0(0.0)		
Marital Status			0.92	*0.63*			3.80	*0.15*
Single	14	1(7.1)			26	6(23.1)		
Married	56	9(16.1)			11	4(36.4)		
Divorced	10	2(20.0)			43	20(46.5)		

Keys: Exam = Examined; Pos = Positive

Table 2: Risk factors influencing malarial occurrence in HIV-negative and HIV-infected pregnant women attending antenatal clinic of a rural hospital in Benue state, Nigeria

Malaria in pregnant women								
	HIV – negative				HIV - infected			
Variables	Exam	Pos (%)	AOR	*p*	Exam	Pos (%)	AOR	*p*
Parity			0.49	0.04			2.12	0.06
Primigravida	25	7(28.0)			8	3(37.5)		
Multigravida	55	5(9.0)			72	27(37.5)		
Gestation			0.47	0.10			0.16	0.00
1st Trimester	22	4(18.2)			12	5(41.6)		
2nd Trimester	34	8(23.5)			43	19(44.2)		
3rd Trimester	24	0(0.0)			25	6(24.0)		

Key: Exam = examined; Pos = positive; AOR = Adjusted Odd Ratio

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