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Prevalence and risk factors of malaria and human immunodeficiency virus co-infection among pregnant women at Sokoto, Nigeria

Authors: Chisom. E. Okechukwu[1]; Idris. N. Abdullahi[2,*]; D. Aliyu[3]; M. Kabiru[1]; H. Aderisayo Adekola[4]; Emeka. I. Ikeh[4]; Thompson H.I. Spencer[1]; Ngwoke. C. Chinedu[1]

Affiliations: *[1]Department of Medical Microbiology, Faculty of Medical Laboratory Sciences, Usmanu Danfodiyo University, Sokoto; [2]Department of Medical Laboratory Science, Faculty of Allied Health Sciences, Ahmadu Bello University, Zaria, Nigeria; [3]Department of Medical Laboratory Science, University of Calabar, Calabar, Nigeria; [4]Department of Microbiology, Olabisi Onabanjo University, Ogun, Nigeria; [5]Department of Medical Microbiology, Faculty of Medical Sciences, University of Jos, Jos, Nigeria*

ABSTRACT

BACKGROUND: Malaria in pregnant women is a significant cause of obstetric morbidity especially when there is co-infection with human immunodeficiency virus (HIV). This cross-sectional study aimed to determine the prevalence of malaria parasitaemia and associated risk factors among HIV infected pregnant women in Sokoto State, North-Western Nigeria.
METHODS: 103 HIV infected pregnant women attending antenatal clinics of Sokoto state secondary hospitals were enrolled for this study. The socio-demographic variables and risk factors of malaria were assessed from all participants using int questionnaires. Malaria parasitaemia was detected using World Health Organization malaria microscopy protocol while CD4+ T cell count was performed using FASC count analyser.
RESULTS: 58 out of 103 (56.3%) pregnant women were infected with malaria parasites. All were P. falciparum. There was no significant association between malaria parasitaemia and all sociodemographic variables and risk factors of participants ($p > 0.05$). The mean (± standard deviation) CD4+ T-cell counts for pregnant women with malaria-HIV co-infection and HIV mono-infection were 127±45 cells/mm3 and 322±62 cells/mm3, respectively. The CD4+ T-cell counts of subjects with HIV/malaria co-infection were significantly ($p < 0.001$) lower than those with HIV mono-infection.
CONCLUSION: The prevalence of malaria recorded in this study is high, but with negative findings with regards to all sociodemographic variables of participants and risk factors of malaria.

Keywords: Malaria; Coinfection; Lymphopenia; Risk;HIV; Pregnancy

INTRODUCTION

Malaria is a well-known tropical parasitic disease responsible for high morbidity and mortality in sub-Saharan Africa. The Plasmodium species, the etiological agents of malaria are transmitted by the blood meal of female anopheles mosquito at dawn to dusk. So far, six Plasmodium species have been identified to cause human diseases, and these include P. falciparum, P. vivax, P. ovale, P knowlesi, P simium and P. malariae [1]. Plasmodium falciparum is the most virulent species responsible for severe form of disease in humans [2]. Severe malaria is a multi-system disorder, which may arise from several pathological processes which include abrupt hemolysis of infected red blood cells and dyserythropoesis. In addition, interaction of malaria infection with other infectious agents and nutritional deficiencies encourage severe malaria [2]. Malaria, human immunodeficiency virus infection (HIV) and tuberculosis are the three most important communicable diseases of developing countries [3,4].

***Corresponding author**: Mr. Idris Nasir Abdullahi, Department of Medical Laboratory Science, Faculty of Allied Health Sciences, Ahamdu Bello University, Zaria, Nigeria, Email: inabdullahi@abu.edu.ng; **Potential Conflicts of Interest (CoI):** All authors: no potential conflicts of interest disclosed; **Funding:** All authors: no funding was disclosed; **Academic Integrity.** All authors confirm that they have made substantial academic contributions to this manuscript as defined by the ICMJE; **Ethics of human subject participation:** The study was approved by the local Institutional Review Board. Informed consent was sought and gained where applicable; **Originality:** All authors: this manuscript is original has not been published elsewhere;
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Malaria and HIV co-infection is a topical clinical issue in sub-Saharan Africa especially in pregnant women and this can lead to poor obstetric outcomes if not properly managed [5, 6]. Malaria cases tend to increase each year in low- and middle-income countries due to poor healthcare delivery systems, emergence of antimalarial and insecticide resistance, and climate change [7].

Both malaria and HIV infection accounted for over 2 million deaths each year [7]. Malaria and HIV co-infections overlap, primarily in sub-Saharan Africa, Southeast Asia and South America [7]. In sub-Saharan Africa alone, an estimated 25 million people harbour HIV and more than 350 million episodes of malaria (in both HIV seronegative and seropositive persons) occur yearly [8]. HIV increases the risk of malaria infection and the development of clinical malaria [8]. Conversely, malaria infection increases HIV replication rates [8].

Nigeria is the most populous country in Africa with a population of over 180 million, and has the highest number of cases of malaria and HIV infection with a prevalence of 1.4% [9, 10]. HIV/AIDS can increase the adverse effects of malaria in pregnancy, which include anaemia, placental malaria and low birth weight [9, 11]. Individuals considered semi-immune to malaria in endemic regions of tropical countries can also develop clinical malaria, especially if they are HIV co-infected [11]. It has been shown that pregnant women experience reduced immunity to malaria, making them more prone to episodes of severe malaria and subsequent anaemia [12]. Another study reported higher susceptibility of malaria in pregnant women who had never or less episodes of malara prior to preganacy [13].

The immunopathogenesis of malaria is associated with a pro-inflammatory state, providing an ideal condition for the spread and replication of HIV in CD4+ T cells thus enhancing their destruction and reduction in count [14-16].
Due to the clinical and public health significance of HIV/malaria coinfection, this study study sought to investigate the prevalence of malaria parasitemia and associated risk factors among HIV infected pregnant women in Sokoto, North-Western Nigeria

METHODS

Study design and Site: This cross-sectional study was conducted in 103 HIV infected pregnant women attending ante-natal clinics of three secondary hospitals in Sokoto State: Specialist Hospital, Maryam Abacha Hospital, and Women and Children Welfare Clinic in Sokoto State.

The Sokoto township is in the dry Sahel zone surrounded by sandy terrain and isolated hills. Rainfall starts in June and ends in September, sometimes extending into October. The average annual rainfall is 55 cm with peak rainfall occuring in August. The highest temperatures (up to 45°C) occur during the hot season in March and April. Harmattan, a dry, cold, and dusty weather phenomenon is experienced between November and February. Malaria transmission is meso-endemic from September to December and hyperendemic from January to August [17, 18]. This study was conducted between the 20th of April and the 20th of September 2017, which coincides with the wet season, which is presumptively to have high malaria transmission rate [17].

Participants were between the ages of 18 and 50 years. They were all screened for required inclusion criteria, and their HIV status was confirmed using Uni-Gold Recombigen® HIV-1/2 (Trinity Biotech, Ireland) and Determine™ (Alere, New Zealand) proprietary reagents.

Informed consent and ethical approval: The study was explained to the potential participants, and participants who wishes to enroll provided written informed consent. An interviewer-based questionnaire was administered by trained nurses and research assistants to obtain sociodemographic and risk factors variables from study participants. These questions included information on obstetric history, use of insecticide-treated bed nets
(ITNs), and malaria chemoprophylaxis. We also reviewed hospital cards and folders of participants to access information such as gravidity and gestational age of the subjects. This study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Ethical Research Committee of Sokoto State Ministry of Health, Nigeria. Data generated from particpnats were anonymously analyzed throughout the study.

Eligibility Criteria: This study included patients who were HIV positive and pregnant. Women with febrile illness who had history of viral hepatitis and pulmuonary tuberculosis were excluded.

Sample size calculation: The sample size for this study was calculated using the 10.6% prevalence of malaria parasiteamia in pregnant women from a previous cross-sectional study in Sokoto, Nigeria, by Buhari et al [18]. Thus, the minimum sample size required for this study was 100 using a 5% error margin and 95% confidence interval. However, a total of 103 volunteers were enrolled for this study.

Laboratory analytical methods: Two milliliters of peripheral blood were collected through venipuncture from all recruited HIV pregnant women and immediately taken (within 1 hour) to the laboratory at the Specialist Hospital for detection of malaria parasites. Samples were anslysed in batches. Using a clean grease-free microscope slide, a small drop of blood was placed to the center of the slide and the blood was spread to create the thick smear. After drying, the slides were stained for 10–15 min with 10% Giemsa solution. When the thick film was dry, a drop of immersion oil was placed to an area of the film which appears mauve colored (usually around the edges). The slides were examined for malaria parasites and malaria pigment. At least 100 high power (x100 objective) microscope fields were examined for parasites. A slide was considered negative when 100 high-power fields were examined under oil immersion objective, as described by Adefioye et al [19]. Quality control slides (positive and negative) were used by trained microscopists during malaria investigation.

Determination of CD4+ cell count: Based on the manufacturer's instructions, the CD4+ cell counts in the whole blood were analyzed using a FASC count analyser BD™ (ThermoFisher, Paisley, UK). This device used the principle of light scattering property (based

on dissimilarity in cell size or granularity) and the fluorescence of cells following staining with monoclonal antibodies to markers on the cell surface bound to fluorescent dyes. Cell populations of interest were then gated after identification. Absolute CD4+ cell counts were subsequently analyzed using a single-platform technique.

Statistical analysis: Data were analyzed using SPSS software version 24 (IBM Corporation, Armonk, NY, USA) and were presented as percentages. Two tailed Chi-square and unpaired T test were used to assess the association and difference between categorical and continuous variables. Univariate logistic regression was used to determine the odds ratio and relative risk of malaria parasitemia. P values ≤0.05 at a confidence interval of 95% were considered statistically significant.

RESULTS

Malaria prevalence was 56.3%. All were P. falciparum. Almost 50% of the participants in the study were in the age-group of 25-30 (Table 1). The highest prevalence of 71.4 % was found among those in the age group of 37-42. The age groups of 18-24, 25-30, 31-36, 43-48 had prevalences of 45%, 54.9%, 52.9% and 0.0%, respectively (Table 2).

Table 1: Socio-demographic variables of study participants

	Variables	Frequency	%
Age (years)	18-24	20	19.4
	25-30	51	48.5
	31-36	17	16.5
	37-42	14	14.5
	43-48	1	1.1
Household size	1-3	80	77.7
	4-6	18	17.5
	Above 6	5	4.5
Level of education	Primary	12	11.7
	Secondary	58	56.3
	Tertiary	4	3.9
	Religious	29	28.2
Occupation	Farmers	0	0
	Traders	21	21.4
	Civil servants	1	1.0
	Housewife	80	77.7
Number of previous pregnancies	None	8	7.8
	1	34	33.0
	2	34	33.0
	3	10	9.7
	4 and above	17	16.5
Gestational period	1st Trimester	26	25.2
	2nd Trimester	16	15.5
	3rd Trimester	61	59.2

The prevalence of malaria parastaemia was highest among particpants with household size of 4-6 persons (61.1%), followed by those with household size of 1 – 3 persons (56.3%) and least in those with household size of > 6 persons (40%). Over 50% of the participants had only secondary education. The prevalence of malaria was higher among those with only religious education, 68.1%, while in those with primary education, secondary and tertiary the prevalnces were 58.3%, 55.2% and 25.0% respectively.

Table 1: Prevalence of Malaria/ HIV Co-infection by Sociodemographic Variables of Participants

	Variables	No. examined	No. infected	% Infected	P-value
Age group (years)	18-24	20	9	45	0.335
	25-30	51	28	54.9	
	31-36	17	9	52.9	
	37-42	14	10	71.4	
	43-48	1	0	0.0	
Household Size	1-3	80	45	56.3	0.701
	4-6	18	11	61.1	
	Above 6	5	2	40	
Level of education	Primary	12	7	58.3	0.565
	Secondary	58	32	55.2	
	Tertiary	4	1	25.0	
	Religious	29	18	68.1	
Occupation	Traders/Business	22	15	68.2	0.285
	Civil servant	1	1	100.0	
	Housewife	80	42	52.5	
Number of previous pregnancies	None	8	6	75.0	0.228
	1	34	14	41.2	
	2	34	20	58.8	
	3	10	7	70.0	
	4 and above	17	11	64.7	
Gestational age	1st Trimester	26	19	73.1	0.121
	2nd Trimester	16	9	56.3	
	3rd Trimester	67	30	69.3	

Table 3: Risk factor of Malaria parasitemia in HIV infected pregnant women

	Variables	No. examined	No. infected (%)	aOR	RR
Knowledge and use of ART	Yes	1	0 (0.0)	0.234	0.256
	No	102	58 (56.9)		
Insecticide treated net	Yes	31	16 (51.6)	0.76	0.83
	No	72	42 (58.3)		
Use of Sulfadoxine/pyrimethamine (Prophylaxis)	Yes	8	3 (37.5)	0.44	0.47
	No	95	55 (57.9)		
Store water on open containers	Yes	70	37 (52.9)	0.64	0.87
	No	33	21 (63.6)		
Resident in proximity to gutters, refuse dumpsites (≤50 meters)	Yes	73	43 (58.9)	1.43	1.11
	No	30	15 (50.0)		

Analyzed by logistics regression analysis (univariate)

Over 75% of participants were housewives, and this group had a prevalence of 52.5% (Table 2). The prevalence amongst primigravidae was high at 75%, while for secundigravidae the prevalence was 41.2% and the prevalence for multigravidae was 64.5%. More than half of the participants were in their third trimesters. Prevalence of malaria seemed to be higher in the first trimester at 73.1% while second and third trimesters malaria prevlance was 56.3% and 49.2%, respectively. Only one participant knew which antiretroviral agents she was prescribed and was adherent. 56.9% of subjects had no knowledge of which antiretroviral agents they were prescribed. There was a significant association between malaria and history of fever (P = 0.042). Prevalence of malaria in those with a history of fever was 64.1% and in those without a history of fever was 43.5%. There was a prevalence of 51.6% in those who used ITNs while those who do not use ITNs had a malaria prevalence of 58.3%.

Prevalence of malaria amongst non-usage of sulfadoxine/pyrimethamine is higher (57.9%) than those who used sulfadoxine/pyrimethamine (Table 3). However, after univariate analysis, subjects who reside in proximity to gutters and refuse dumpsites had higher Odd ratio for malaria parasitaemia than those who do not [OR: 1.43 (95%: 0.61-3.37)] (Table 3).

The mean (standard deviation) CD4+ T-cell counts for pregnant women with malaria-HIV co-infection and HIV mono-infection were 127±45 cells/mm3 and 322±62 cells/mm3, respectively. The CD4+ T-cell counts of subjects with HIV/malaria co-infection were significantly (p-value = 0.000) lower than those with HIV mono-infection (Table 4).

Table 4: Comparison of CD4+ T-lymphocyte count of subjects with and without malaria

Group	$CD4^+$ T-cell counts (cells/mm^3)		T-test	P value
	Range	Mean± SD		
Participants with HIV/malaria co-infection (n =58)	59 – 439	127±45		
HIV infected participants without malaria (n =45)	82 – 654	322±62	8.49	<0.001*

**Significance determined by student t-test*

DISCUSSION

The present study has yielded some important findings in regard of malaria and HIV coinfections among pregnant women in North-western Nigeria. The increased risk for severe malaria in pregnant women and HIV-infected persons already has been reported in some areas in Nigeria [19, 20].
This present study shows 56.3% prevalence of Malaria in HIV infected pregnant woman, which is slightly higher than a similar study conducted by Adeoti et al [21] where they reported prevalence of 30.2%. The prevalence was also higher when compared to the malaria prevalence of 52.2% among apparently healthy pregnant women attending Antenatal clinics in Sokoto, Nigeria [22]. The increase in prevalence from the present study may be because of HIV/AIDS in our subjects. It has been shown that HIV increases the risk of contracting malaria in an endemic setting [22].

Findings from this study showed that no signifant association between all the sociodemographic variables, risk factors and prevalence of malaria parasitemia. Hence, this is a negative result. This study shows that the mean CD4+ T cell count of pregnant women with malaria/ HIV coinfection was significantly lower than those who had HIV without malaria. This aligns with the previous findings of Nasir et al [23]. The relatively low CD4+ T cell count in the HIV/malaria coinfected subjects could be due to lack of prescribed antiretroviral therapy or lack of adherence to antiretroviral therapy, prolonging the clinical course of malaria and thus reducing the cellular immunity of HIV infected pregnant women [23].

LIMITATIONS

Although the study offers some important findings, it also has limitations: The study was cross sectional, therefore the possibility of sampling error cannot be overruled. Also, the study used ITNs and prophylaxis as the sole indicator of control measures, but the usage of other measures such as indoor residual spraying (IRS), larvicides and mosquito repellent coils was not assessed. In addition, the non-comparison of malaria parasitaemia rate between HIV infected and HIV negative women is another limitation.

CONCLUSIONS

The prevalence of malaria recorded in this study is high, but with negative findings with regards to all sociodemographic variables of participants and risk factors of malaria.

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