

Prevalence of Malaria Parasitaemia in Adult HIV-infected Patients in Jos, North-central Nigeria

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ABSTRACT

BACKGROUND: Human immunodeficiency virus (HIV) and malaria co-infection has become an important public health problem in sub-Saharan Africa. Data on HIV and malaria interaction in Nigerian adults is scanty. We determined the prevalence of malaria parasitaemia in HIV-infected adults and further investigated the role of immune status in the HIV/malaria association.

METHODS: This was a cross-sectional study involving 100 newly-diagnosed HIV-infected adults and 100 age and sex-matched HIV negative controls. Malaria parasitaemia was diagnosed by blood film microscopy using Giemsa staining technique and was defined as the presence of malaria parasites irrespective of species or parasite density. HIV infection was confirmed by western blot assay and CD4 T-lymphocyte count of the HIV-infected patients was quantified by flow cytometry.

RESULTS: The prevalence of malaria parasitaemia was higher in HIV-infected adults (24%) than in the controls (9%) ($\chi^2=8.17$, $p=0.04$). Participants residing in rural areas had higher prevalence of malaria parasitaemia than urban dwellers both for HIV-infected patients (34.1% Vs. 16.1%, $\chi^2=4.3$, $p=0.04$) and controls (18.4% Vs. 6.5%, $\chi^2=3.4$, $p=0.04$). HIV-infected male patients tended to have malaria parasitaemia more than their female counterparts (33.3% Vs. 17.2%, $\chi^2=3.4$, $p=0.06$). Among HIV-infected patients, the prevalence of malaria parasitaemia progressively increased at lower CD4 cell counts, 10.3% for CD4 cell count of = 500, 17.5% for 200-499 and 45.2% for < 200 cells/ μ L ($\chi^2=11.5$, $p=0.003$).

CONCLUSION: HIV is likely to fuel malaria infection in tropical countries where both diseases are endemic. Malaria control practices should be further intensified in HIV-infected populations.

KEY WORDS: HIV/AIDS, Malaria parasitaemia, Nigeria, Adults.

malaria deaths reported annually worldwide, more than 80% occur in sub-Saharan Africa². Nigeria accounts for a quarter of all malaria cases in Africa and currently has the second largest number of people living with HIV globally^{2,3}. Due to shared geographic distribution, co-infection by HIV and malaria has increasingly become an issue of great public health concern in sub-Saharan Africa. This is expected in view of the significant morbidity, mortality and economic consequences already associated with each of these infections.

Although studies carried out in the early years of HIV epidemic in sub-Saharan Africa were inconclusive on the interaction between HIV and malaria infections in adults⁴, evidence of increased rates of malaria parasitaemia in HIV-infected pregnant women and children were clearly documented at that time⁵⁻⁷. Since then, higher prevalence of malaria parasitaemia in HIV-infected adults than in HIV negative groups has been increasingly reported in more recent studies^{8,9}. So far, only few studies in Nigeria¹⁰⁻¹³ have investigated the co-infection of HIV and malaria despite the large burden of both infections in the country. To the best of our knowledge, apart from one of these studies¹³, the available reports have involved a mixed population of children and adults either among the HIV-infected subjects or in the control group¹⁰⁻¹². The only attempt to relate malaria parasitaemia with immune status of HIV-infected patients has come from Southern Nigeria. We therefore conducted this study to describe the prevalence of malaria parasitaemia in a purely adult HIV-infected group in North-central Nigeria.

MATERIALS AND METHODS

Study design/Setting

This was a cross-sectional study conducted at the Jos University Teaching Hospital (JUTH), Jos, Plateau State, North-central Nigeria between August and December, 2009.

A minimum sample size of 75 subjects in each group was calculated using the formula for comparing proportions in two groups¹⁴:

$$N = \frac{Z_{\alpha} \sqrt{2P_1(1-P_1)} + Z(1-\beta) \sqrt{P_1(1-P_1) + P_2(1-P_2)}}{P_1 - P_2} \cdot 2$$

Where N= minimum sample size, $\alpha = 0.05$, $\beta = 0.80$, $Z_{\alpha} = 1.96$, $Z(1-\beta) = 0.842$ and P_1 and P_2 = prevalence of malaria parasitaemia in HIV-positive and HIV-negative

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INTRODUCTION

About 33 million people are currently infected with Human immunodeficiency virus (HIV) and more than three million people die annually from HIV/AIDS worldwide¹. Seventy percent (70%) of the global HIV positive population live in sub-Saharan Africa¹. Of the over 300 million cases of malaria and one million

patients from previous studies = 32%¹⁵ and 11.6%¹¹ respectively.

A total of 100 newly-diagnosed HIV positive adults 18 years and above as well as 100 age and sex-matched HIV negative controls were recruited from those that presented themselves for HIV counseling and testing (HCT) at JUTH. Ethical clearance was obtained from the Ethics Committee of JUTH. Informed consent was obtained from each participant before enrolment into the study.

DATA COLLECTION

The study participants were consecutively recruited. About four milliliters of blood was obtained from the HIV-infected patients and two milliliters from the control group and dispensed into ethylene diamine tetra-acetic acid (EDTA) containers. Each participant had thick and thin blood film microscopy for malaria parasites done using the Giemsa staining technique according to standard World Health Organisation (WHO) protocol.¹⁶ Malaria parasitaemia was defined as the presence of malaria parasites irrespective of species or parasite density.¹⁶ The HIV-infected subjects had their status confirmed by western blot assay and also had quantification of CD4 T-lymphocytes by flow cytometry (Partec, Germany).

STATISTICAL ANALYSIS

Data analysis was performed using the Epi Info version 3.5.1 statistical software (CDC, Atlanta, GA). Continuous variables were expressed as means (SD) while proportions were used to describe categorical variables. The Chi-squared test was used to compare proportions where appropriate. Probability values <0.05 were considered statistically significant.

RESULTS

The mean age of the HIV-infected patients and controls were 36 ± 9 years and 36 ± 9 years respectively (p=0.96). Their ages ranged from 20 to 60 years. Fifty eight women

(58%) and 42 men (42%) were enrolled in each group. The median CD4 cell count of the HIV-infected patients was 293 (174-512) cells/μL. HIV-infected men tended to have severe immunosuppression (CD4 cell count < 200 cells/μL) more than women (40.5% Vs. 24.1%, p=0.06). All cases of malaria parasitaemia were due to *Plasmodium falciparum*.

Of the 100 HIV-infected adults, 24 (24%) had malaria parasitaemia compared to 9 out of 100 (9%) controls ($\chi^2=8.17$, p=0.04) as shown in Table 1. Further analysis excluding HIV-infected patients with severe immunosuppression resulted in no significant difference in the prevalence of malaria parasitaemia between the remaining HIV-infected patients and the controls (14.5% Vs. 9%, $\chi^2=1.23$, p=0.27) (Table 1).

Table 2 shows the distribution of malaria parasitaemia in HIV-infected patients according to selected socio-demographic characteristics. The association between age and malaria parasitaemia was neither significant for HIV-infected patients (p=0.72) nor the controls (p=0.30). Although the association between malaria parasitaemia and sex did not attain statistical significance, HIV-infected male patients tended to have malaria parasitaemia more than their female counterparts (33.3% Vs. 17.2%, $\chi^2=3.4$, p=0.06) but this trend was not seen in the controls (11.9% for males and 6.9% for females, $\chi^2=0.74$, p=0.39). Participants residing in rural areas had higher prevalence of malaria parasitaemia than urban dwellers both for HIV-infected patients (34.1% Vs. 16.1%, $\chi^2=4.3$, p=0.04) and controls (18.4% Vs. 6.5%, $\chi^2=3.4$, p=0.04).

Further analysis in HIV-infected patients showed that the prevalence of malaria parasitaemia progressively increased at lower CD4 cell counts with the highest prevalence of 45.2 % occurring in those with CD4 cell count <200 cells/μL ($\chi^2=11.5$, p=0.003) as shown in Table 2.

DISCUSSION

Table 1. Prevalence of malaria parasitaemia (MP) in HIV positive and HIV negative patients

HIV status	MP positive		MP negative	
	n (%)	n (%)	χ^2	p-value
HIV Positive	24 (24)	76 (76)	8.17	0.04
HIV Negative	9 (9)	91 (76)		
HIV Positive with high CD4*	10 (14.5)	59 (85.5)	1.23	0.27
HIV Negative	9 (9)	91 (76)		

*High CD4 was defined as CD4 cell count = 200 cells/μL

Table 2. Distribution of malaria parasitaemia (MP) in HIV-infected patients according to selected socio-demographic variables, and immunological status.

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Characteristic	MP positive	MP negative	χ^2	p-value
	n (%)	n (%)		
Sex				
Male	14 (33.3)	28 (66.7)	3.4	0.06
Female	10 (17.2)	48 (82.8)		
Age (Mean \pm SD) years	35.88 \pm 7.36	36.66 \pm 9.68	----	0.72
Residence				
Rural	15 (34.1)	29 (65.9)	4.3	0.04
Urban	9 (16.1)	47 (83.9)		
CD4 cell category (cells/μL)				
< 200	14 (45.2)	17 (54.8)	11.5	0.003
200-499	7 (17.5)	33 (82.5)		
\geq 500	3 (10.3)	26 (89.7)		

The prevalence of malaria parasitaemia among HIV-infected patients in this study was 24% which was significantly higher than the 9% in the controls. This finding is consistent with a prevalence of malaria parasitaemia of 29.4% in HIV-infected adults reported by Nkuo-Akenji and co-workers¹⁷ in Cameroon. Onyenekwe and colleagues¹⁰ in Nnewi, South-east Nigeria also documented comparable rates of 18.9% in HIV-infected patients and 10.6% in the controls although the age of their participants ranged from 2-70 years.

The findings of this study also agree with those of a previous study in Jos¹¹ where the prevalence of malaria parasitaemia was found to be 21% among HIV-infected adults and 11.6% in a mixed control group aged 10-59 years. Higher prevalence rates of malaria parasitaemia in HIV-infected patients than HIV negative subjects can be explained by the fact that HIV infection reduces immune responses that lead to plasmodium clearance notably CD4 cell activity and antimalarial cytokines¹⁸. The mechanisms of natural immunity to malaria parasitaemia are believed to involve activation of a series of innate

pathways such as dendritic and natural killer cell activation, pro-inflammatory cytokine release and counter regulatory cytokines as well as adequate T and B cell responses and cytophilic antibody effector responses all of which are reduced in HIV-infected patients¹⁸. This explanation is further supported by the finding in this study that prevalence of malaria parasitaemia progressively increased at lower CD4 cell categories, an observation that has been corroborated by the few studies in sub-Saharan Africa that have investigated the influence of immune status on prevalence of malaria parasitaemia in HIV-infected patients^{8,9,13}.

Some studies have documented much higher prevalence rates of malaria parasitaemia in HIV-infected adults than we found; 48% by Patnaik *et al*⁹ in Malawi and 46% in Benin City, South-south Nigeria by Akinbo and colleagues¹³. A much lower prevalence rate of malaria parasitaemia of 11.8% has been reported among Ugandan adults by Whitworth and co-workers⁸. The higher prevalence rate found in Malawi could be because the study was carried out during a six month period

identified as the malaria season thus excluding periods of low malaria transmission compared to our study period that spanned both seasons of intense and low transmission. In Benin City, 56% of their HIV-infected subjects had severe immunosuppression (CD4 cell count <200 cells/ μ L) compared to 31% in this study and this may be responsible for the higher rate of malaria parasitaemia in their study. This argument is further supported by an important finding in our study that exclusion of HIV-infected subjects with severe immunosuppression from the analysis reduced the frequency of malaria parasitaemia in HIV-infected patients from 24% to 14.5%. In addition, the fact that Plateau State is on a higher altitude with relatively lower environmental temperatures could result in lower malaria transmission rates compared to Benin City which is a low land with higher temperatures. Reduced malaria transmission at higher altitudes has been documented in a malaria endemic area in Tanzania¹⁹.

Age and sex had no significant relationship with malaria parasitaemia in this study. Similarly, previous studies involving Nigerian adults have not documented any significant association between age or sex and malaria parasitaemia^{10,11,13}. The trend towards a higher prevalence of malaria parasitaemia in male HIV-infected patients in this study may be attributable to the observation that HIV-infected men tended to have severe immunosuppression more than women. The higher rates of malaria infection found in rural residents compared to urban dwellers is not surprising considering the fact that they are more likely to indulge in practices which create favourable breeding sites for mosquitoes²⁰. In addition, malaria control measures are less commonly carried out in rural areas in Nigeria²⁰.

Our study was not without limitations. Since the study design is cross-sectional, a direct effect of HIV on malaria and vice versa cannot be elucidated, only an association between the two can be highlighted. Longitudinal studies to further explore this interaction as well as studies to unravel its clinical relevance are highly needed in regions where both infections are endemic.

In conclusion, HIV infected patients are more likely to develop malaria infection than HIV negative individuals and the risk of malaria infection in HIV-infected patients increases as the degree of immunosuppression worsens. These findings have provided additional information on the burden of malaria in the HIV-infected adult population in Nigeria. This interaction between HIV and malaria will likely have significant public health implications. In essence, HIV is likely to fuel malaria infection in tropical countries where both diseases are endemic. Malaria control measures should be further intensified in HIV-infected populations.

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REFERENCES

1. World Health Organisation. Global HIV/AIDS report. Geneva, WHO 2008.
2. World Health Organisation. Roll Back Malaria Partnership: World malaria report. Geneva, WHO 2008.
3. Federal Ministry of Health. Department of Public Health National AIDS/STDs Control Program. Technical Report. 2005 National HIV/Syphilis seroprevalence sentinel survey among pregnant women attending antenatal clinics.
4. Chandramohan D, Greenwood BM. Is there an interaction between human immunodeficiency virus and Plasmodium falciparum? *Int J Epidemiol.* 1998; 27: 296-301.
5. Verhoeff FH, Brabin BJ, Hart CA, *et al.* Increased prevalence of malaria in HIV-infected pregnant women and its implication for malaria control. *Trop Med Int Health.* 1999; 4: 5-12.
6. Van-Ejik AM, Ayisi JG, Ter-Kuile FO, *et al.* HIV increases the risk of malaria in women of all gravidities in Kisumu, Kenya. *AIDS.* 2003; 17: 595-603.
7. Greenberg AE, Nguyen-Dinh P, Mann JM, *et al.* The association between malaria, blood transfusions, and HIV seropositivity in a paediatric population in Kinshasa, Zaire. *JAMA.* 1988; 259: 545-9.
8. Whitworth J, Morgan D, Quigley M, *et al.* Effects of HIV-1 and increasing immunosuppression on malaria parasitaemia and clinical episodes in adults in rural Uganda: a cohort study. *Lancet.* 2000; 356: 1051-6.
9. Patnaik P, Jere CS, Miller WC, *et al.* Effects of HIV-1 serostatus, HIV RNA concentration, and CD4 count on the incidence of malaria infection in a cohort of adults in rural Malawi. *J Infect Dis.* 2005; 192: 984-91.
10. Onyenekwe CC, Ukibe N, Meludu SC, *et al.* Prevalence of malaria as co-infection in HIV-infected individuals in a malaria endemic area of south-eastern Nigeria. *J Vector Borne Dis.* 2007; 44: 250-4.
11. Uneke CJ, Ogbu O, Inyama PU, *et al.* Malaria infection in HIV-seropositive and HIV-seronegative individuals in Jos, Nigeria. *J Vector Borne Dis.* 2005; 42: 151-4.
12. Onifade AK, Akanni EO, Mewoyeka OO. Incidence of malaria infection among HIV immunodeficiency virus patients in Ondo State, Nigeria. *Middle-East J of Sci Res.* 2007; 2(2): 48-53.
13. Akinbo FO, Okaka CE, Omoregie R, Mordi R, Igbinuwen O. Prevalence of malaria and anaemia among HIV-infected patients in Benin City, Nigeria. *NZ J Med Lab Sci.* 2009; 63: 78-80.

14. Dawson B, Trapp RG. Basic and clinical biostatistics. 4th edn. New York: Lange Medical Books & McGraw-Hill, 2004; 145-6.
15. Goselle ON, Onwuliri COE, Onwuliri VA. Malaria and the effect of malaria parasitaemia on albumin level among HIV/AIDS patients in Jos, Nigeria. *J Med Sci*. 2007; 7: 1187-91.
16. World Health Organisation. Bench aids for the diagnosis of malaria infections. Geneva, WHO 2000.
17. Nkuo-Akenji T, Tevoufouet EE, Nzang F, Ngufor N, Fon E. High prevalence of HIV and malaria co-infection in urban Douala, Cameroon. *Afric J AIDS Research*. 2008; 7: 22935.
18. Renia L, Potter SM. Co-infection of malaria with HIV: an immunological perspective. *Parasit Immunol*. 2006; 28: 589-595.
19. Chandler CI, Drakeley CJ, Reyburn H, Carneiro I. The effect of altitude on parasite density case definitions for malaria in north-eastern Tanzania. *Trop Med Int Health*. 2006; 2: 1178-84.
20. Oladepo O, Tona GO, Oshiname FO, Titiloye MA. Malaria knowledge and agricultural practices that promote mosquito breeding in two rural farming communities in Oyo State, Nigeria. *Malar J*. 2010; 9: 91.