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Prevalence of malaria and anaemia in asymptomatic HIV infected children in Lagos

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ABSTRACT

Malaria and HIV are causes of severe morbidity and mortality in Sub-Saharan Africa. Individuals with HIV/AIDS are at increased risk of clinical malaria and severe illness. Sub-Saharan Africa has a high HIV prevalence. Anemia as a complication of malaria has been associated with increased mortality in HIV-infected children. This study determined the prevalence of malaria in asymptomatic HIV positive children, and the association between malaria and hematologic parameters in the study population. It is a cross sectional study conducted at the Out Patients' Clinic, Nigerian Institute of Medical Research, Lagos. Study population comprised HIV infected children aged 1 year - 14 years. 151 children participated in the study between June and November 2016 after a detailed informed consent process. Malaria parasite density, hemoglobin and CD4 cell counts were determined. The prevalence of malaria parasitaemia among participants was 14.6%. Majority had a CD4 count > 500 cells/µL (85.1%). The prevalence of anemia (Hb < 11.0g/dL) was 29.1% in the study population. No statistically significant association was found between CD4 count and hemoglobin concentration with malaria parasitaemia. This study revealed a low prevalence of malaria and anemia amongst asymptomatic HIV positive children.

KEY WORDS: ***Malaria, Anaemia, CD4, Children, HIV, Prevalence, Lagos***

INTRODUCTION

Malaria, anaemia and HIV are recognized causes of severe morbidity and mortality. The Sustainable Development Goals aim to end poverty. Malaria and HIV/AIDS disproportionately affect poor people particularly in sub-Saharan Africa, thus they have been termed "Diseases of poverty"[1]. Individuals with HIV/AIDS are at increased risk of symptomatic malaria and severe illness. There is an estimated 1.8 million children under the age of 15 years living with HIV worldwide[2]. Sub-Saharan Africa has a high HIV prevalence, with 3 million HIV-infected children[3]. Nigeria has 260,000 HIV positive children aged below 15 years[4].

In HIV positive African children, malaria is a significant deterrent to adequate nutritional development[5]. In malaria endemic areas,

malaria accounts for a significant proportion of anaemia in children[2]. Anaemia is a major cause of morbidity and mortality with malaria[2]. There is also HIV associated anaemia which can either result from complications of the HIV infection, or side effects of antiretroviral agents. It is important to note that as HIV has its effects on malaria, malaria also has its own effects on HIV, and anaemia interacts with both HIV and Malaria, leading to considerable public health and socio economic implications. HIV infection increases the incidence and severity of clinical malaria[1]. Cerebral Malaria-attributed mortality has been noted to be higher in HIV infected children when compared to children not infected with HIV[3]. Anaemia in HIV is said to reduce survival and negatively impact quality of life[6]. Anaemia as a complication of malaria has been association with increased mortality in children infected with HIV[7]. HIV infection can decrease the protection offered by anti-malarial treatment[1]. Acute malaria infection results in an upsurge of viral load which can lead to increased transmission of HIV and more rapid disease progression[1].

In order to prevent the occurrence of malaria, a lot of public health interventions (such as vector control activities/products; use of insecticide treated nets; new diagnostic tools; appropriate medicines and effective surveillance activities) have been put in place in malaria endemic countries to eliminate malaria[8]. These malaria endemic countries have their weakness, because of the lower gross national incomes and lower total domestic government spending per capital for their large number of malaria cases, than countries with fewer cases[9].

The implementation of proper and integrated malaria and anaemia preventive measures could improve HIV-related morbidity and mortality[10]. Knowledge of the magnitude of the problem of malaria and anaemia in HIV infected children will help in focused intervention. The aim of this study was therefore, to determine the prevalence of malaria and anaemia among HIV positive children and the association between malaria and haematological parameters in the study population.

METHODOLOGY

Study design

This cross sectional study was conducted at the Out Patients' Clinic, Nigerian Institute of Medical Research, Yaba, Lagos. The clinic provides comprehensive HIV care and treatment services and has cumulatively enrolled more than 24,000 thousand patients with HIV including adults, pregnant women and children since inception, making it one of the largest HIV care and treatment centres in Nigeria.

Study Power and Sample Size

A sample size of 165 was calculated using (http://www.raosoft.com/samplesize.html) online where the population size is 330 HIV infected children, age ranged from 1 year to 14 years accessing care at the clinic, margin of error of 5%, Confidence interval of 95%; power of 80% and prevalence of malaria in HIV infected children in Nigeria of 11 – 31%. Ten children who had incomplete records were however excluded, thus a total of 155 children were enrolled into the study between June and November 2016, after a detailed informed consent process. The purpose, processes and potential benefits of the study were explained to caregivers and patients old enough to understand and their consent and assent (for children aged 12-14 years) sought before enrolment. Children who had received antimalarial medication in the last one month were excluded from the study.

Collection of Data

Information on socio-demographic characteristics, as well as use of long lasting insecticide treated nets (LLIN) was obtained with the use of an interviewer administered

semi-structured questionnaire. Data on HIV baseline characteristics of the patient such as age at diagnosis, World Health Organization (WHO) clinical stage, initial viral load and CD4 count, as well as use of, and duration on antiretroviral drugs (ARVs) were abstracted from the clinic's electronic data base.

After the questionnaire was filled, a trained phlebotomist collected venous blood into an ethylene diamine tetra acetate (EDTA) bottle labeled with the patient's study number and date of sample collection. Part of the sample was used for the determination of the participant's hemoglobin level and CD4 cell count while the rest was used to prepare thick and thin films for malaria parasite identification and speciation.

Method of Staining for Malaria Parasite Identification

Light microscopy method was used to identify malaria parasites. Blood films for microscopy were prepared by Giemsa stain as described by WHO[12].

Hemoglobin and CD4 Count Measurement Methods

Hemoglobin (Hb) level was determined using the Mindray Auto Hematology Analyzer (BC-5380), which analyzes 27 parameters. The samples in EDTA bottles were placed on racks, which were placed on the machine and the 'run' button, clicked. After a 3-5 minute processing period the result was displayed on the screen and the Hb read off as grams/deciliter (g/dL).

CD4 count was obtained with the Cyflow Counter from Sysmex Partec. About 2ml of blood in EDTA bottle was mixed for 5 minutes on the Invitrogen dynamixer. 20µL of the mixed blood is pipetted into the CD4 tube and mixed with 20 µL of monoclonal antibody. This was incubated at room temperature away from light for 15 minutes. After incubation, 800 µL of no lyse buffer was added to the mixture. The whole was then inserted into the Cyflow machine and the result displayed as cell count per microliter (µL) of blood.

Data Analysis

Study data were entered into a spreadsheet and analysed using statistical package for social sciences (SPSS) version 20. Chi square test was used to compare categorical variables and means were compared with the ANOVA test. Odds ratios were used to compare groups and p value less than 0.05 was taken as significant.

Ethical Consideration

Ethical clearance (Reference number IRB/12/183) was obtained from the Institutional Review Board (IRB) of the Nigerian Institute of Medical Research. Patients and caregivers were assured that participation was entirely voluntary and refusal to participate would not interfere in any way with the usual care at the clinic. Even after parental consent was obtained, any child who refused participation at any point during the study procedure was excluded from the study.

Strict confidentiality was ensured in the handling of patient data as only study personnel, data entry clerks, and statistician had access to such information. Children that were found to have malaria parasitaemia from the study results were managed according to the Nigeria National Malaria Treatment Guidelines with artemisinin combination antimalarial therapy.

RESULTS

There were 155 HIV infected children aged 1-14 years recruited into the study but 151 participated as four children refused blood sample collection despite parental consent. There were 75 males and 76 females (M: F = 1: 1). The mean age of the participants was 8.4 years (±3.1 years). Majority of

participants were Igbo (tribe) (46.4%), Christians (78.8%), lived with both parents (69.9%), and were in primary school (57.6%). About a quarter of participants (22.6%) were either single or double orphans. Majority of primary caregivers were mothers (73.5%), had at least secondary school education (78.6%) and were petty traders (50.0%). Household income for majority of participants (60.6%) was not more than twenty thousand naira, which is about the national minimum wage of eighteen thousand naira (N 18,000.00), (**Table 1**).

Table 1: Sociodemographic Characteristics of Participants

Characteristic	Frequency (%)	Characteristic	Frequency (%)
Sex:		**Parental Status:**	
Males	75 (49.7)	Living Together	102 (67.5)
Females	76 (50.3)	Separated	11 (7.3)
Total	151 (100.0)	Orphaned	33 (21.9)
		No response	5 (3.3)
Ethnic Group:		**Primary Caregiver:**	
Hausa	7 (4.6)	Mother	111 (73.5)
Igbo	48 (31.8)	Father	30 (19.9)
Yoruba	70 (46.4)	Others	10 (6.6)
Others	26 (17.2)		
Religion:		**Caregiver Education:**	
Christianity	119 (78.8)	<Secondary School	31(20.5)
Islam	27 (17.9)	≥ Secondary School	120 (79.5)
Others	5 (3.3)		
Class in School:		**Family Income (N):**	
Primary	87 (57.6)	≤ 20,000	86 (57.0)
JSS*	31 (20.5)	21,000-50,000	27 (17.9)
Other	33 (21.9)	>50,000	29 (19.2)
		No response	9 (6.0)

The prevalence of malaria parasitaemia among participants was 14.6% and the mean geometric malaria parasite density (GMPD) was 988 parasites/µL of blood. Malaria parasitaemia was highest in participants aged 5-9 years (12 of 72 = 16.6%) and least in those aged 10-14 years (7 of 62 = 11.5%). GMPD was highest (1069 parasites/µL of blood) in those aged 10 -14 years. These differences were however not statistically significant (**Table 2**).

Majority of participants (108 [70.1%]) came in with mild disease (WHO clinical stages 1 and 2). Most participants (145 [94.2%]) were on antiretroviral therapy and the median duration on ARVs was 61 months (IQR 32-84 months). Majority had a CD4 count > 500 cells/µL (85.1%) and HIV RNA Viral Load less than 1000 copies/mL (74.7%). **Table 3** shows HIV related characteristics in relation to malaria parasitaemia.

The mean heamoglobin concentration among the study population was 11.5 ± 2.0 g/dL. The mean haemoglobin (Hb) concentration among participants with malaria parasitaemia was 11.2 g/dL, 11.4g/dL and 11.3g/dL in those aged 1-4 years, 5-9 years, and 10-14 years respectively. The prevalence of anemia (Hb < 11.0g/dL) was 29.1% in the study population. It was least in those aged 10-14 years and was same (30.0%) in participants aged less than five years and least 5-9 years. This is illustrated in **table 4**.

Table 2: Socio-demographic Characteristics Associated with Malaria Parasitaemia

Characteristic	All Participants	Malaria neg n (%)	Malaria Pos n (%)	X^2	P value	GMPD
Age Group (yrs):				0.844	0.252	
<5	20	17 (85.0)	3 (15.0) (Ref)			649.0
5-9	70	58 (82.9)	12 (17.1)			1027.8
10-14	61	54 (88.5)	7 (11.5)			1069.7
Total	**151**	**129 (85.4)**	**22 (14.6)**			**988**
Sex:				0.245	0.621	
Male	75	63 (84.0)	12 (16.0)			982.3
Female	76	66 (86.8)	10 (13.2)			994.9
Total	**151**	**129 (85.4)**	**22 (14.6)**			
Parental Status:				1.72	0.18	
Living together	102	**89 (87.3)**	13 (12.7)			
Orphaned	33	**27 (81.8)**	6 (18.2) (Ref)			
Separated	11	**8 (72.7)**	3 (27.3)			
Total	**146**	**124 (84.9)**	**22 (15.1)**			
Primary Caregiver:				2.38	0.12	
Mother	110	91 (82.7)	19 (17.3)			
Other	41	38 (92.7)	3 (7.3)			
Total	**151**	**129 (85.4)**	**22 (14.6)**			
Family Income (N):				2.34	0.67	
≤ 20,000	86	72 (83.7)	14 (16.3)			
21,000-50,000	27	22 (81.5)	5 (18.5)			
>50,000	29	26 (89.7)	3 (10.3)			
Total	**142**	**120 (85.9)**	**22 (14.1)**			

Table 3: HIV-Related Characteristics and Malaria Parasitaemia

Characteristic	All Subjects	Mal neg n (%)	Mal + n (%)	X^2	P value	GMPD
WHO Clinical stage				1.090	0.21	
1 & 2	100	88 (88.0)	12 (12.0)			802.3
3 & 4	43	35 (81.4)	8 (18.6)			1234.9
Total	**143**	**123 (86.0)**	**20 (14.0)**			
ARV Use				2.707	0.126	
Yes	143	123 (86.6)	20 (14.0)			1062.9
No	8	6 (65.7)	2 (25.0)			273
Total	**151**	**129 (85.4)**	**22 (14.6)**			
Hb (g/dL):				0.87	0.49	
< 11	44	38 (86.4)	6 (13.6)			785.2
>11	103	87 (84.5)	16 (15.5)			1050.9
Total	**147**	**125 (85.0)**	**22 (15.0)**			
CD4 (cell/µL):				1.024	0.245	
<200	3	3 (100.0)	0 (0.0) (Ref)			
200-499	18	14 (77.8)	4 (22.2)			577.3
≥500	128	111 (86.7)	17 (13.3)			1056.1
Total	**149**	**128 (85.9)**	**21 (14.1)**			

Table 4: Factors associated with Anemia in study participants

Characteristic	All Participants	Number anemic	X^2	OR	P value
Age Group (yrs):			0.019	0.93 (0.32-2.67)	0.54
<5	20	6 (30.0%)			
5-9	70	21 (30.0%) (Ref)			
10-14	61	17 (27.9%)			
Total	**151**	**44 (29.1%)**			
Sex:			1.08	1.42 (0.72-2.81)	0.19
Male	75	18 (24.0%)			
Female	76	26 (34.2%)			
Total	**151**	**44 (29.1%)**			
WHO Clinical stage			3.06	0.51 (0.24-1.09)	0.04*
1 & 2	100	25 (25.0%)			
3 & 4	43	17 (39.5%)			
Total	**143**	**42 (29.4)**			
ARV Use			1.13	0.33 (.0.03-2.78)	0.16
Yes	143	43 (30.1%)			
No	8	1 (12.5%)			
Total	**151**	**44(29.1%)**			
CD4 (cell/µL):			0.018	1.18 (0.22-5.69)	0.43
<200	3	1 (33.3%)			
200-499	18	5 (27.8%) (Ref)			
≥500	128	38 (29.7%)			
Total	**149**	**44 (29.5%)**			

DISCUSSION

The prevalence of malaria in this study was 14.6%. This is similar to 14.5% reported by a study in Benue State, Nigeria[14]. However, this prevalence is lower than 36.1% and 36.6% reported by Noland *et al*[15] in a study conducted in Abia and Plateau States of Nigeria. This could be attributed to the renewed commitment by the government to decrease the prevalence of malaria by distributing free LLINs, free ACTs for treatment of malaria and more aggressive campaign against malaria by the use of simplified IEC materials. Malaria parasitaemia was highest in participants aged 5-9 years (16.6%), this same age group had the highest prevalence of over 50% in both Abia and Plateau States of Nigeria as reported by Noland *et al*[15]. Malaria prevalence was lowest in those aged 10-14 years (11.5%), this is at variance with the report the report by Mmadu *et al*[16] carried out among hospital attendees in Karu, Nasarawa State, Nigeria, which had the highest prevalence of 29% in age group 2-5 years. The prevalence difference among the different age groups in this study was not statistically significant. The low parasitaemia in the older age group may be due to an acquired immunity against malaria as a result of repeated infections.

GMPD was higher among 10-14 years (1069.7), females (994.9), those with advanced disease (1234.9), those on ARV (1062.9) and those with CD4 ≥500 (1056.1). However, there was no significant difference with their counterparts.

Malaria parasitaemia was higher among the children with CD4 ≥500. This contradicts findings in other studies, which suggests that immunosuppression increases the risk of higher malaria parasitaemia[9]. The occurrence of malaria parasitaemia was equally distributed between males and

females as reported by Noland *et al*[15], this implies an equal exposure to similar environmental conditions by both sexes.

Majority (60.6%) of caregivers of participants had a household income of less than 20,000 naira. About two-thirds (73.5%) of the caregivers were mothers. More than two-thirds of the caregivers had at least a secondary school education which is similar to that reported in a study conducted in Minna, Nigeria[17]. This could be explained by the fact that the study was carried out in a city where acquiring a formal education is highly recommended. More than one fifth (22.6%) of the participants were orphans.

Majority of participants (70.1%) came in with mild HIV disease (WHO clinical stages 1 and 2). Most participants (94.2%) were on antiretroviral therapy and the median duration on ARVs was 61 months (IQR 32-84 months). Majority had a CD4 count > 500 cells/µL (85.1%) and HIV RNA Viral Load less than 1000 copies/ml (74.7%).

The prevalence of anaemia (Hb < 11.0g/dL) was 29.1% in the study population. This is lower than 49.6% reported by Bate *et al* in Southern Cameroun[10] and 67% reported by Tay *et al* in a Ghanaian study[17]. The low prevalence could be as a result of availability and use of anti malarial preventive measures (insecticide treated nets) that has been intensified in our environment. Anaemia was least in those aged 10-14 years (27.9%) and was same in participants aged less than five years and 5-9 years (30.0%). This is not surprising, as both HIV and malaria are known causes of anemia especially in children≤ 5 years of age. Anaemia occurred more in females (34.2%), more in those with CD4 <200 (33.3%), this could be as a result of chronic inflammation or the presence of opportunistic infections in HIV. Anaemia also occurred more among those of ARV (30.1%). The type of ARV the child is using could also be the reason for the occurrence of anemia among those on ART as some have been reported to cause anaemia. Other factors could be responsible for anemia in the participants such as poor nutritional status, hemoglobinopathies, infections and infestations.

There was no statistical significant association between WHO clinical stage, use of anti retroviral, CD4 count and Hb concentration with malaria parasitaemia. Though some studies have reported an increased risk of malaria parasitaemia among children on ART and those with low CD4 count[9].

There was no statistically significant association between both male and female, ARV use and CD4 count with anemia.

The low prevalence of malaria and anemia in this study can be attributed to the fact that majority of the children in the study asymptomatic HIV positive children.

CONCLUSION

This study revealed a low prevalence (14.6%) of malaria and anaemia (29.1%), when compared to prevalence from other similar studies conducted in Nigeria. We recommend sustenance of the national interventions, which would have contributed to the low prevalence rates in this study.

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