Analysis of HIV/Malaria Coinfections among HIV-1 Infected Individuals in Two Tertiary Hospitals in Old Cross River State, Nigeria

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Authors’ contributions

This work was carried out in collaboration among all authors. Author IOO conceived and designed the study, partially financed the whole study, assisted in the collection of samples, the laboratory analysis and contributed principally in writing up the manuscript as well as in the data and statistical analysis of this study. Author UIE procured the materials used, ran the laboratory analysis and drafting of the manuscript which she used as part of her M.Sc. thesis in the Department of Microbiology, University of Port Harcourt, Port Harcourt, Nigeria. Author HCIA wrote the proposal for ethical approval, procured the materials used for sample collection, addressed the subjects, collected samples and participated in the study design and reviewing of the manuscript. Author TIC participated in the laboratory analysis and performed the statistical analysis. All authors contributed equally in writing up this manuscript, editing, proof-reading and approval of the final manuscript for this publication.

ABSTRACT

Aims: Human Immunodeficiency Virus (HIV) and Malaria are the two main global public health threats that dent development in low and middle-income countries. This study evaluated the immunological marker and HIV/Malaria co-infection among individuals infected with HIV-1 in old Cross River State, Nigeria.

Study Design: Cross-sectional study.

Place and Duration of Study: University of Calabar Teaching Hospital (UCTH) and University of Uyo Teaching Hospital (UUTH) between March 2018 and August 2019.
Methods: A total of 417 individuals infected with HIV-1 partook in this study. The age of these individuals ranged from 4-72 years (average age = 39.1 years). Plasma samples were analyzed for HIV and Malaria using Enzyme-Linked immunosorbent Assay. The CD4 count was enumerated using the Partec CyFlow® Counter. Plasma viral loads (PVL) were determined using the Abbott Real-Time HIV-1 assay.

Results: Results showed that 230 (55.1%) of the participants were in the 31-45 years age range. The majority (67.4%) of the HIV-1 infected individuals were females. An overall prevalence of HIV/Malaria coinfection in Old Cross River State, Nigeria was 14.3%, of which Uyo was 6.3% and Calabar was 3.0%. A higher prevalence of HIV/Malaria coinfection was observed among age groups <25 years (17.5%), males (5.1%), singles or divorced/widow/widower (7.7%), those with primary education (7.5%), and students (10.0%). Higher HIV/Malaria coinfection was also observed among those with CD4 cell count <200 cells/μl and 350-499 cells/μl (5.7%) and PVL >5000 copies/mL (7.9%) compared to others with 2.0% prevalence. Of all variables evaluated only marital status (p= 0.033), educational background (p= 0.000) and occupations (p =0.000) were significantly associated.

Conclusions: This study further confirmed the presence of HIV/Malaria coinfection in old Cross River State, Nigeria. This study has added to the voices on the ground to give a better view on the frequency and the pattern of distribution of HIV/Malaria coinfection since limited studies have been done on this in old Cross River State, Nigeria. This, therefore, highlights the need for a well-structured approach to the management of HIV/Malaria coinfection in Nigeria.

Keywords: Antibodies; HIV; coinfections; malaria; Nigeria.

1. INTRODUCTION

Human Immunodeficiency Virus (HIV) and malaria are two main worldwide health threats that affect development in low and middle-income countries [1-2]. In sub-Saharan Africa, HIV and AIDS coinfection with Malaria is very much prevalent [3]. These infections have led to the loss of about 5 million lives yearly, bearing significant humanitarian, economic, and social impact, which is yet to be measured [1-2]. In addition to occurring in the same zone geographically, these infections are also said to be linked with poverty, having a major public health implication [4].

It is a well-known opportunistic infection and also an important factor affecting the increased disease progression to AIDS in HIV-infected persons due to a significantly increased destruction of active CD4 helper T-cells and a quick breakdown of immune functions. *P. falciparum* causes the severe form of malaria while a milder disease which is less severe is caused by *P. vivax, P. ovale, and P. malariae* [5]. Over 50% of the people on earth are vulnerable to the malaria infection and they have estimated over 300 million malaria cases annually in the tropics. In 2016, Nigeria contributed to over 27% of the total malaria cases and 24% of mortality from malaria globally. Some studies have revealed a high occurrence of malaria among people living with HIV [6]. A population-based study showed that those infected with HIV were more likely to get Malaria than those that were not infected with the virus [7].

The high occurrence of both malaria and HIV in the sub-Saharan region indicates that coinfection is relatively common, making it an important health concern due to the synergistic nature of the HIV-malaria partnership. HIV infection exerts influence on malaria by diminishing the response of the immune system to Plasmodium invasion and it’s been maintained by several researchers that malaria increases the replication of the HIV both in vivo and in vitro [6].

Sub-Saharan Africa is hit by most deadly diseases in the world. HIV and malaria are diseases that mostly affect the poor, contributing greatly to the high poverty level in sub-Saharan Africa nations. The young population whose strength contribute to the growth of the local economy are mostly hit by these diseases [8]. The risk and gravity of Malaria disease are amplified by HIV. Infections with HIV and malaria amongst the two most vital global health problems of developing countries including Nigeria, which was said to cause more than 4 million deaths a year [9].

Furthermore, the rate at which malaria is spread is boosted when there is HIV infection. This process activates CD4 cells and increases the production of cytokines which makes the microenvironment suitable for the distribution of HIV among the CD4 cells, thereby increasing
HIV-1 replication. Researches done previously has tried to create a relationship between HIV and malaria, but with difficulties [10]. However, recent researches have proposed that frequent malaria infection culminates in a much faster decline in CD4+ T cells over time. Malaria co-infection with HIV produces regular occurrence of symptomatic malaria [11] and more occurrence of serious or complicated malaria including death in both children and adults [12].

Since 2009, the Centre for Disease Prevention and Control has included Malaria in the list of AIDS-related opportunistic infections. Although not regarded as the major cause of death, malaria ranks third as the most significant cause of ill-health in people living with HIV/AIDS [13]. The synergistic nature of the HIV/malaria partnership makes coinfection a major health concern. Malaria is said to upsurge HIV replication in vitro and in vivo [11]. Additionally, evidence shows that malaria coinfection with HIV triggers the progression of malaria disease, enhances the risk of severe malaria in adults [14] and raises the risk of congenital infection [15]. Furthermore, this dual infection increases the distribution of both diseases, particularly in sub-Saharan Africa [12,16-18].

A previous study [19] investigating the frequency of HIV and Malaria seropositivity amongst undergraduates at a tertiary healthcare Centre in Port Harcourt, Nigeria showed no incidence of coinfection. Consequently, the present study aimed at determining the prevalence of HIV/Malaria coinfections in HIV-1 infected individuals in old Cross River State, Nigeria.

2. MATERIALS AND METHODS

2.1 Study Areas

The study was conducted in the old Cross River States (Akwa Ibom State and Cross Rivers State). Akwa Ibom is one of Nigeria’s 36 states, with a population of over five million people created in 1987 from the former Cross River State and is currently the highest oil- and gas-producing state in the country [20]. The state's capital is Uyo, with over 500,000 inhabitants. It is located in the coastal southern part of the country, lying between latitudes 4°32′N and 5°33′N, and longitudes 7°25′E and 8°25′E. The state is located in the South-South geopolitical zone and is bordered on the east by Cross River State, on the west by Rivers State and Abia State, and the south by the Atlantic Ocean and the southernmost tip of Cross River State [20]. In addition to English, the main spoken languages are Ibibio, Annang, Eket and Oron [21]. Cross River State is a coastal state in southeastern Nigeria [22], bordering Cameroon to the east. It is located in Nigeria’s Delta Region and occupies 20,156 square kilometres. It is located at an elevation of 152 meters above sea level and its population amounts to 3,104,446. Its coordinates are 5°45′0″N and 8°30′0″E in DMS (Degrees Minutes Seconds) or 5.75 and 8.5 (in decimal degrees). It shares boundaries with Benue State to the north, Ebonyi and Abia States to the west, to the east by the Cameroon Republic and to the south by Akwa-Ibom and the Atlantic Ocean [23]. Its capital is at Calabar, and it is named after the Cross River [24], which passes through the state. The state is ethnically diverse, including Efiks, Bekwaras, and Ejaghame inhabitants. The Latitude of Cross River State is 6.167 and the Longitude is 8.6601. Cross River State is connected with a major highway to its sister state Akwa Ibom [20].

2.2 Study Design

A cross-sectional study in old Cross Rivers State, Nigeria was carried out.

2.3 Sample Size Determination

The sample size for this study was determined using the formula: \( N = \frac{Z^2pq}{d^2} \) [25]. Where \( N \) is the desired sample size, \( P \) is the expected prevalence in the target population, \( Q = 1 - P \), \( Z = 1.96 \) standard error, \( d \) is the level of statistical significance (0.05).

For Akwa-Ibom State, a \( p \) value of 6.4% (reported by UNAIDS [26]) was used.

\[
Z = \text{Normal standard distribution that corresponds to 95.0% confidence interval as 1.96.}
\]

\[
p = \text{Prevalence of HIV (6.4% for Akwa-Ibom State as at UNAIDS [26])} = 0.064
\]

\[
q = 1 - p = 1 - 0.064 = 0.936
\]

\[
d = \text{degree of accuracy/precision expected as 0.05}
\]

\[
N = 92 \text{ HIV HIV-positive persons (estimated for Akwa-Ibom State)}.
\]

Hence, the estimated sample size was 92 HIV-positive individuals with an additional 10% sampled to take care of study participants that may be lost to follow-up [25,27], providing a total sample size of 100 for Akwa-Ibom State, Nigeria.
For Cross River State, a p value of 4.4% (reported by UNAIDS, 2016) was used.

\[ Z = \text{Normal standard distribution that corresponds to 95.0% confidence interval as } 1.96. \]

\[ p = \text{Prevalence of HIV (4.4% Cross Rivers State as at UNAIDS [26] sentinel survey) } = 0.044 \]

\[ q = 1 - p = 0.956 \]

\[ d = \text{degree of accuracy/precision expected as } 0.05 \]

\[ N = 65 \text{ HIV-positive persons (estimated for Cross Rivers State).} \]

Hence, the estimated sample size was 65 HIV-positive individuals with an additional 10.0% sampled to take care of study participants that may be lost to follow-up [25,27], providing a total sample size of 75 for Cross River State, Nigeria. However, in this study, in all 417 samples were obtained from all confirmed HIV-1 infected participants. The 417 samples of these cohorts were used for malaria analysis.

### 2.4 Study Population

Four hundred and seventeen (417) HIV-positive patients were selected and enrolled for the study (Table 1). While the entire HIV-positive individuals in old Cross River State were the target population to which the findings of the study was extrapolated. Their ages ranged from 4-72 years (average = 39.1 years). Two hundred and thirty (65.1%) of them were in the 31-45 years age range. The majority (67.4%) of the HIV-1 infected individuals was females and 32.6% were males. The male: female ratio in the present study of 1:2 (Table 1). Over 60.0% of the HIV-1 infected individuals were married (62.8%, n=262), 142 (34.1%) were singles and 13 (3.1%) were divorced/widows/widowers (Table 1). Majority of the study participants had tertiary education (54.4%, n=227), 147 (35.3%) had secondary education, 40 (9.6%) had primary education and 3 (0.7%) had no formal education (Table 1). In terms of occupation, the majority were traders (23.3%), followed by civil servants (15.6%), students (14.4%), business (11.8%) and teaching was 9.6%. About 6.5% were unemployed, 6.0% were artisans, driving and retirees were 3.4% respectively while farmers (2.0%) were the least (Table 1).

#### 2.4.1 Sample collection

Blood samples were collected from HIV-infected individuals in old Cross River State, Nigeria used in this study. Three millilitres (3 ml) of blood were collected from 417. HIV-infected individuals by venipuncture, between June 2018 and August 2019. The blood was allowed to clot and centrifuged at 3000 rpm for 5 minutes. The sera were carefully aspirated into plain bottles and stored at -20°C until analyzed.

### 2.5 Serological Analysis of Malaria

Plasma samples were analyzed for the presence of Malaria *Plasmodium falciparum* using the ELISA kit manufactured by DIA.PRO Diagnostic Bioprobes Srl (Milano) – Italy, according to manufacturer’s specifications.

#### 2.6 CD4 T Cell Count Enumeration

EDTA-treated blood samples were used for CD4 cell count using Partec CyFlow® Counter (Partec GmbH, Munster, Germany). The CD4 cell count was done as stipulated by the Partec CyFlow® Counter manufacturer.

#### 2.7 HIV-1 Viral Load Testing (Abbott Real-Time Assay)

Plasma viral load (PVL) was analyzed using the Abbott Real-Time HIV assay US Protocol.

#### 2.8 Data Analysis

Descriptive statistics were used to describe the characteristics of the study participants. Chi-square test and a multivariate test (logistic regression) were used to fine-tune our findings and to determine relationships between the variables and the prevalence of HIV/Malaria co-infections. P-value was considered significant at 0.05. All analyses were conducted using complex samples analysis of the Statistical Package for the Social Sciences (SPSS), IBM version 22.

### 3. RESULTS AND DISCUSSION

#### 3.1 Results

#### 3.1.1 General characteristics of HIV-infected individuals

Table 1 shows the 417 HIV-infected individuals who partook in this study: 241 (57.8%) from Calabar, Cross Rivers State, Nigeria and 176 (42.2%) from Uyo, Akwa-Ibom State, Nigeria. Clinical characteristics of HIV-infected individuals revealed that the CD4 (cells/μl) count ranged
from 5 – 2139 cells/µl (average = 455.6 cells/µl) (Table 1). Generally, of the 417 samples analyzed for viral loads (VL), 151 (36.2%) had VL less than 40 copies/mL, 102 (24.5%) fell within the range 40-5000 copies/mL, and 164 (39.3%) were within >5001 copies/mL (Table 1).

### Table 1. Socio-demographical and clinical characteristics of HIV-1/malaria coinfected individuals in old cross State, Nigeria

<table>
<thead>
<tr>
<th>Variables</th>
<th>No. tested (%)</th>
<th>Malaria (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Locations</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uyo</td>
<td>176 (58.0)</td>
<td>11 (6.3)</td>
<td>P = 0.232</td>
</tr>
<tr>
<td>Calabar</td>
<td>241 (42.0)</td>
<td>7 (3.0)</td>
<td></td>
</tr>
<tr>
<td><strong>Age groups (years)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25</td>
<td>40 (9.6)</td>
<td>7 (17.5)</td>
<td>P = 0.899</td>
</tr>
<tr>
<td>26-30</td>
<td>46 (11.0)</td>
<td>2 (4.3)</td>
<td></td>
</tr>
<tr>
<td>31-35</td>
<td>64 (15.3)</td>
<td>1 (1.6)</td>
<td></td>
</tr>
<tr>
<td>36-40</td>
<td>94 (21.8)</td>
<td>1 (1.1)</td>
<td></td>
</tr>
<tr>
<td>41-45</td>
<td>72 (17.3)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>46-50</td>
<td>43 (10.3)</td>
<td>1 (2.3)</td>
<td></td>
</tr>
<tr>
<td>51-55</td>
<td>28 (6.7)</td>
<td>1 (3.6)</td>
<td></td>
</tr>
<tr>
<td>56-60</td>
<td>21 (5.0)</td>
<td>1 (4.8)</td>
<td></td>
</tr>
<tr>
<td>&gt;61</td>
<td>12 (2.9)</td>
<td>1 (8.3)</td>
<td></td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>136 (32.6)</td>
<td>7 (5.1)</td>
<td>P = 0.910</td>
</tr>
<tr>
<td>Females</td>
<td>281 (67.4)</td>
<td>11 (3.9)</td>
<td></td>
</tr>
<tr>
<td><strong>Marital status</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>262 (62.8)</td>
<td>6 (2.3)</td>
<td>P = 0.033</td>
</tr>
<tr>
<td>Singles</td>
<td>142 (34.1)</td>
<td>11 (7.7)</td>
<td></td>
</tr>
<tr>
<td>Divorced/Widowed</td>
<td>13 (3.1)</td>
<td>1 (7.7)</td>
<td></td>
</tr>
<tr>
<td><strong>Educational status</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Formal</td>
<td>3 (0.7)</td>
<td>0 (0.0)</td>
<td>P = 0.000</td>
</tr>
<tr>
<td>Primary</td>
<td>40 (9.6)</td>
<td>3 (7.5)</td>
<td></td>
</tr>
<tr>
<td>Secondary</td>
<td>147 (35.3)</td>
<td>7 (4.8)</td>
<td></td>
</tr>
<tr>
<td>Tertiary</td>
<td>227 (54.4)</td>
<td>8 (3.5)</td>
<td></td>
</tr>
<tr>
<td><strong>Occupation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trading</td>
<td>97 (23.3)</td>
<td>5 (5.2)</td>
<td>P = 0.000</td>
</tr>
<tr>
<td>Teaching</td>
<td>40 (9.6)</td>
<td>1 (2.5)</td>
<td></td>
</tr>
<tr>
<td>Civil Servant</td>
<td>65 (15.6)</td>
<td>2 (3.1)</td>
<td></td>
</tr>
<tr>
<td>Public Servant</td>
<td>18 (4.3)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>Business</td>
<td>49 (11.8)</td>
<td>3 (6.1)</td>
<td></td>
</tr>
<tr>
<td>Artisans</td>
<td>25 (6.0)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>Driving</td>
<td>14 (3.4)</td>
<td>1 (7.1)</td>
<td></td>
</tr>
<tr>
<td>Retired</td>
<td>14 (3.4)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>Farming</td>
<td>8 (2.0)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>Student</td>
<td>60 (14.4)</td>
<td>6 (10.0)</td>
<td></td>
</tr>
<tr>
<td>Unemployed</td>
<td>27 (6.5)</td>
<td>0 (0.0)</td>
<td></td>
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<tr>
<td><strong>CD4 counts (cells/µl)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 200</td>
<td>70 (16.8)</td>
<td>4 (5.7)</td>
<td>P = 0.758</td>
</tr>
<tr>
<td>200-349</td>
<td>103 (24.7)</td>
<td>5 (4.9)</td>
<td></td>
</tr>
<tr>
<td>350-499</td>
<td>88 (21.1)</td>
<td>5 (5.7)</td>
<td></td>
</tr>
<tr>
<td>&gt;500</td>
<td>156 (37.4)</td>
<td>4 (2.6)</td>
<td></td>
</tr>
<tr>
<td><strong>Viral load (copies/mL)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 40</td>
<td>151 (36.2)</td>
<td>3 (2.0)</td>
<td>P = 0.120</td>
</tr>
<tr>
<td>40 – 5000</td>
<td>102 (24.5)</td>
<td>2 (2.0)</td>
<td></td>
</tr>
<tr>
<td>5001 &amp; above</td>
<td>164 (39.3)</td>
<td>13 (7.9)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>417 (100.0)</td>
<td>18 (4.3)</td>
<td></td>
</tr>
</tbody>
</table>
3.1.2 Overall prevalence of HIV/Malaria coinfections

Results showed an overall prevalence of HIV/Malaria coinfection was 4.3% for Old Cross River State, Nigeria, 6.3% for Uyo and 3.0% for Calabar, Nigeria. However, these differences were not statistically associated (P=0.232). Table 1 shows the seroprevalence of HIV coinfections with Malaria amongst HIV-1 infected individuals in old Cross Rivers State, Nigeria with their sociodemographic and clinical variables.

3.1.3 Age-specific HIV/Malaria coinfections

Higher HIV/Malaria coinfection was observed among age groups <25 years (17.5%) than in other age-groups. The age-specific prevalence showed that HIV/Malaria coinfections were highest in ages <25 years (17.5%), followed by ages 61 years and above (8.3%), 56-60 years (4.8%), 26-30 years (4.3%), 51-55 years (3.6%), 46-50 years (2.3%) and 31-35 years (1.6%) while 36-40 years had the least prevalence (1.1%), however, these differences were not statistically associated (P=0.899) [Table 1].

3.1.4 Sex-specific HIV/Malaria coinfections

Higher HIV/Malaria coinfection was observed among males (5.1%) than in females (3.9%). The study showed no significant difference (P=0.910) between sex and HIV/Malaria coinfections amongst HIV-1 infected individuals (Table 1).

3.1.5 Marital status-specific HIV/Malaria coinfections

Higher HIV/Malaria coinfection was observed among individuals who were singles or divorced/widow/widower (7.7%) than in married individuals (2.3%). A significant difference (P=0.033) exist between marital status and HIV/Malaria coinfections amongst HIV-1 infected individuals (Table 1).

3.1.6 Educational status-specific HIV/Malaria coinfections

Higher HIV/Malaria coinfection was observed among individuals who had primary education (7.5%) than other educational status (Secondary 4.8%, Tertiary 3.5%). A significant difference (P=0.000) exist between educational status and HIV/Malaria coinfections (Table 1).

3.1.7 Occupation-specific HIV/Malaria coinfections

Higher HIV/Malaria coinfection was observed among students (10.0%) than other occupations. This was followed by drivers (7.1%), business (6.1%), traders (5.2%), civil servants (3.1%) and teachers (2.5%) while other occupations recorded zero prevalence for HIV/ Malaria coinfection. A significant difference (P=0.000) exist between occupation and HIV/Malaria coinfections (Table 1).

3.1.8 CD4-specific HIV/Malaria coinfections

Higher HIV/Malaria coinfection was observed among HIV-1 patients with CD4 T cell count <200 cells/µl and 350-499 cells/µl (5.7%), followed by those with CD4 T cell count 200-349 cells/µl (4.9%) and the least prevalence occurred in those with CD4 T cell count >500 cells/µl (2.6%) as shown in Table 1. These differences were not statistically significant (P=0.758).

3.1.9 Viral loads-specific HIV/Malaria coinfections

Higher HIV/Malaria coinfection was observed among HIV-1 patients with viral loads (VL) above 5000 copies/mL (7.9%) compared to others with 2.0% prevalence (Table 1). No significant difference (P=0.120) exist between Viral load and HIV/Malaria coinfections (Table 1).

3.2 Discussion

Malaria is still a major public health problem especially within the tropical and sub-tropical regions despite a clear decline in its incidence by 30% globally and by 34% in Africa [28-30]. The need to conduct prevalence studies and surveys such as this on an annual basis is to monitor the progress made so far in realizing Sustainable Development Goal (SDG) of combating malaria and HIV [28]. It is also in a way to measure the impact and effectiveness of malaria control programmes in the area [28]. Evidence-based studies in other states in Nigeria have documented a high prevalence of malaria among pregnant women such as 26% in Port Harcourt [31], 40.6% in Abakaliki [32], 40.7% in Cross River State [28], 52.0% reported in Lagos [33] and 99.0% in Enugu [34]. In the same vein, high prevalences as high as 40.06% to 70.8% were also reported among children under five years of age in other previous studies in Nigeria [28,35-38]. Malaria prevalence was reported to be 48.06% in Jos [35], 58.2% in Anambra [36], 64%

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in Abuja [37], 66.3% in Cross River State [28] and 70.8% in Ogun [38]. Previous studies in old Cross River State [39-40] had reported as high as 55.0% and 80.8% prevalence of malaria respectively, in the general population in Cross River State, Nigeria. In the same vein, 12.0% prevalence of malaria was reported in the general population in Akwa Ibom State, Nigeria. Also, in the general population, previous studies [41,42] had reported a total of 3,228 cases of malaria from 1983–2012, with a minimum of 61 and maximum cases of 302. Since these evidenced-based studies in general populations had reported high malaria transmission, it was therefore pertinent to carry out a coinfection study among the HIV population in the settings. It was based on this evidence that this study was aimed at determining the prevalence of HIV/malaria co-infection in old Cross River State, Nigeria.

This study showed that HIV coinfections with Malaria were determined to be 4.3%. The 4.3% coinfection rate reported in this study is dissimilar when compared with the findings of other studies elsewhere in Nigeria. Dada et al. [43] in a study carried out in Akure, Ondo State, Nigeria reported HIV/Malaria coinfection to be 10.3%. This low HIV/Malaria coinfection (4.3%) observed in this study is similar to a study carried out among undergraduate students in Port Harcourt with zero prevalence [19]. A similar value (4.55%) was reported in Akure [44]. Another similar study carried out in Bamenda Cameroon also indicated a low coinfection rate (2.24%) of HIV/malaria [45]. Olusi and Abe [44] carried out a study which was intended to investigate the level of coinfection of HIV and Malaria parasite in Akure, Ondo State, Nigeria, that study revealed that of 4.55% of the pregnant women tested, was infected with HIV and 96.92% were infected with malaria.

Higher HIV/Malaria coinfection was observed among age groups <25 years (17.5%) than in other age-groups. Similarly, higher HIV/Malaria coinfection was also observed among age groups <25 years (10.0%) than in other age-groups. This is slightly different from a study where higher HIV/Malaria coinfection was observed in ages of 20-49 years [43].

Gender has been highlighted as an important risk factor in the frequency of both malaria and HIV disease with women being 50% more at risk of contracting malaria than men [46]. Higher HIV/Malaria coinfection was observed among males (5.1%) than in females (3.9%). Though, the difference was not significant (P=0.05). This finding is similar to another study in Akure, Ondo State, Nigeria which reported HIV/Malaria coinfection to be 10.3% with a higher frequency in females than in males [43]. Also, similar to a study carried out in Bamenda Cameroon of which 6 out of 7 that were coinfected with Malaria were females [44]. In other studies, in old Cross River State, Nigeria [41-42], there were more cases of malaria in males than in females. This simply implies that males are more infected by malaria than their female counterparts probably due to their immunological characteristics [41-42].

Higher HIV/Malaria coinfection was observed among individuals who were singles or divorced/widow/widower (7.7%) than in married individuals (2.3%). Higher HIV/Malaria coinfection was observed among individuals who had primary education (7.5%) than other educational status (Secondary 4.8%, Tertiary 3.5%). This is contrary to many studies which have shown the frequency of coinfection to be higher among those with no formal education [47]. A significant difference (P<0.05) exist between occupation and HIV/Malaria coinfections.

HIV-infected individuals are at an increased risk of clinical malaria, severe illness, hospitalization, and death [48]. Malaria causes anaemia leading to blood transfusions, a procedure that increases the risk for HIV infection where universal blood screening is yet to be achieved [48]. From this standpoint, our study reported higher HIV/Malaria coinfection was observed among HIV-1 patients with CD4 cell count <200 cells/μl and 350-499 cells/μl (5.7%), followed by those with CD4 T cell count 200-349 cells/μl (4.9%) and the least prevalence occurred in those with CD4 cell count ≥500 cells/μl (2.6%). In a related study by Eyong et al. [3], lower CD4 count levels were significantly related to high-density malaria parasitemia among in HIV and AIDS individuals in Bamenda, Cameroon.

Malaria contributes to a temporary increase in viral load among HIV-infected people which may worsen the clinical disease, increase mother-to-child transmission, and augment transmission in adults [48]. Also, based on this premise, 39.3% of the individuals with HIV-1 in this study had a high viral load above 5,000 copies/ml which is indicative of treatment failure, defined by WHO [49] as a persistently detectable viral load exceeding 1000 copies/ml (that is, two consecutive viral load measurements within a
three-month interval, with adherence support between measurements) after at least six months of using ARV drugs. Higher HIV/Malaria coinfection was observed among HIV-1 patients with viral loads (VL) above 5000 copies/mL (7.9%) compared to others with 2.0% prevalence. An important study from Malawi revealed that HIV-1 plasma viral loads were high in malaria-infected individuals than in those not infected with Malaria, and these levels remained higher for up to 10 weeks after treatment [50].

From evidence-based studies in the study area, the trend in malaria prevalence from 1983 to 2012 revealed a 75.5% increase in malaria in old Cross River State, Nigeria. This is owing to the reported cases of malaria reported from 2006-2012 were more significant than those reported in the 1980s [41,42]. The pattern obtained in their study indicates that malaria is still on the increase as it has not been properly tackled in the past three decades. Despite the increasing campaign on malaria and the need for protection against infection, malaria prevalence happens to be on the rise in the study area. However, our findings revealed a low prevalence of malaria among the key HIV population in the same study area. This finding serves to highlight the fact that current interventions seem to be yielding little or no results in reducing the incidence of the disease.

4. CONCLUSION

This study further confirmed the presence of HIV/Malaria coinfection in old Cross River State, Nigeria. Our finding has the potential to contribute to knowledge on the epidemiology of HIV/Malaria coinfection. The malaria prevalence reported in this study group differs greatly from what has been reported previously in the general population in the study area. Despite the low coinfection rate obtained in this study, HIV patients seem to be at higher risk of malaria owing to the suppressed immune system and this knowledge calls for more structured approach on the care of those living with HIV. There is still the need for intensified awareness of Malaria and HIV prevention. Our findings also highlight the need for a well-structured approach to the management of HIV/Malaria coinfection in Nigeria.

CONSENT

All authors declare that 'informed consent was obtained from the patient (or other approved parties) for this study. Consenting HIV-infected individuals accessing HIV clinics at the two tertiary hospitals in old Cross River State, Nigeria who were not on medications for any conditions, were included in the study irrespective of age. Individuals who failed to give their consent were excluded from the study.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed following the ethical standards laid down in the 1964 Declaration of Helsinki." Ethical approval for this study was obtained from the Hospital Research Ethics Committees of Uyo Teaching Hospital (UUTH), Uyo, Nigeria and University of Calabar Teaching Hospital (UCTH), Calabar, Nigeria.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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