1. Introduction

Severe malaria and HIV coinfection is a disastrous syndemism especially in the face of antimalarial resistance and pregnancy. Malaria and HIV are two important global health infectious diseases. Malaria is the fourth leading cause of death of children less than 5 years and pregnant women in developing nations[1]. Malaria cases tend to increase each year because of poor healthcare delivery systems, emergence of drug and insecticide resistance and climate changes[2].

Geographically, Malaria and HIV/AIDS coinfections overlap, primarily in sub-Saharan Africa, Southeast Asia and South America. Pregnant women suffer particularly serious consequences when infected with both HIV/AIDS and malaria. HIV/AIDS can increase the adverse effects of malaria in pregnancy, including anemia, placental malaria infection and low birth weight[3]. HIV and malaria interact synergistically with each other. HIV infection can increase the severity of malaria and the parasite burdens might facilitate higher rates of malaria transmission. Individuals considered semi-immune to malaria in endemic regions can also develop clinical malaria if they are infected with HIV[3].

Malaria infection is associated with heightened CD4+ cell activation and up-regulation of proinflammatory cytokines, providing an ideal microenvironment for the spread of HIV in CD4+ cells and thus for rapid HIV replication[4]. Understanding the human immune response to malaria and HIV leads us to expect...
that either infection might influence the clinical course of the other. The immune deficiency caused by HIV infection should, in theory, reduce the immune response to malaria parasitaemia and therefore increase the frequency and severity of clinical attacks of malaria. So HIV infection affects the clinical presentation, severity and response to treatment of malaria cases[4].

We report the findings of a case-control study by determining the effects of severe malaria/HIV coinfection on the hemoglobin and CD4+ cell counts in pregnant women living in Kaduna State, Nigeria.

2. Materials and methods

The case-control study was conducted in four secondary healthcare facilities in Kaduna State, Nigeria. Blood samples anticoagulated with ethylenediaminetetraacetic acid were collected from consenting pregnant women attending General Hospital Kawo, Yusuf Dantsoho Hospital, Gwamna Awon Hospital and Barau Dikko Hospital, Kaduna State, Nigeria. The selection of health facilities was based on easy accessibility and number of antenatal attendance. Eighteen HIV-infected women with severe malaria parasitaemia (SMP) served as test subjects while 23 HIV-uninfected women with severe malaria served as control subjects. All the test subjects were on first-line antiretroviral therapy (ART). Malaria microscopy and HIV screening were conducted based on standard protocols while antimalarial susceptibility tests (using chloroquine, artesunate, artether and sulfadoxin-pyrimethamine), CD4+ cell counts and hemoglobin concentration were conducted using schizont maturation assay, flow cytometry and methemoglobin methods respectively. Multiple-drug resistant severe malaria parasitemia (MDRSMP) was defined by resistance against three or more antimalarial drugs.

2.1. Determination of CD4+ cell count and hemoglobin concentration

CD4+ cell count in whole blood was determined using Partec™ Cyflow analyzer model SL3 based on manufacturer’s instruction. As described by Cheesborough[5], hemoglobin concentration was determined using methemoglobin method.

2.2. Parasite identification and counts

The parasite species were identified by Giemsa stained thin blood films and the parasite count was made against white blood cells per field on microscope slides as described by Cheesborough[5]. Severe malaria was defined by parasite counts > 10000/μL of blood.

2.3. Ethical approval and informed consent

This study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the ethical research committee of the Kaduna state Ministry of Health, Nigeria. Written informed consent was obtained from all participants.

2.4. Statistical analysis

Mean ± SD was derived from test and control subjects. Chi-square, student’s t-test and Pearson’s correction were used to determine significance between variables and study groups using SPSS software version 20 (California Inc., USA). A two sided P < 0.05 at 95% confidence interval was considered statistically significant.

3. Results

Eight (44.4%) women with SMP/HIV coinfections had MDRSMP. None of the control subjects had MDRSMP. There was statistical association between MDRSMP in test and control subjects (Table 1). Women with SMP had significantly low hemoglobin concentration [(7.1 ± 1.8) g/dL] and low CD4+ cell counts [(209.0 ± 43.0) cells/mm3] when compared with the control counterparts [(10.8 ± 2.2) g/dL and (431.0 ± 57.4) cells/mm3] (P < 0.05) (Table 2). SMP/HIV coinfection was significantly correlated with low hemoglobin concentration (r = −0.254, P = 0.03) but not with CD4+ cell counts (r = −2.44, P = 0.075) (Table 3).

Table 2
Comparison of hemoglobin concentration and CD4+ cell counts of test and control subjects.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Test subjects (n = 18)</th>
<th>Control subjects (n = 23)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>7.1 ± 1.8</td>
<td>10.8 ± 2.2</td>
<td>&lt; 0.000 1*</td>
</tr>
<tr>
<td>CD4+ cell count (cells/mm3)</td>
<td>209.0 ± 43.0</td>
<td>431.0 ± 57.4</td>
<td>&lt; 0.000 1*</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD. *: Significant difference as determined by unpaired student’s t-test.

Table 3
Correlation between hemoglobin concentration and CD4+ cell counts in test and control subjects.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Test subjects (n = 18)</th>
<th>Control subjects (n = 23)</th>
<th>r</th>
<th>P</th>
<th>r</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>−1.25</td>
<td>0.030</td>
<td>-0.254</td>
<td>0.125</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD4+ cell count (cells/mm3)</td>
<td>−2.44</td>
<td>0.075</td>
<td>0.016</td>
<td>0.913</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

r: Pearson’s correlation.

SMP in test subjects was significantly correlated with low hemoglobin concentration but not with CD4+ cell counts. However, SMP in control subjects was not significantly correlated with low

\[1^*: \text{Significant association as determined by Chi-square test.}\]
hemoglobin concentration and CD4⁺ cell counts.

4. Discussion

The present study has yielded some important findings in regard of malaria and HIV infections among pregnant women in Nigeria. The increased risk for severe malaria in HIV-infected persons already has been reported from areas in Nigeria[6,7].

In our study, despite the pregnant women with SMP/HIV coinfection were on first-line ART, the mean CD4⁺ count was < 350 cells/mm³ while the mean CD4⁺ cell count of subjects with severe malaria without HIV infection was > 350 cells/mm³. This is in conformity with previous reports[8,9]. The major reason for this observation may be due to the fact that patients present themselves very late for medical consultation. The part of healthcare workers with fear of stigmatization and inadequate counselling favour late consultations and inappropriate management of SMP/HIV co-infected patients. More so, the relatively low CD4⁺ cells count in the test subjects could also be due to ART resistance, which consequently enables the HIV to be in full replication without being checkmated hence resulting in the depletion of CD4⁺ cells.

SMP/HIV co-infected patients had anemia thus confirming several other literatures[7,10,11]. Anemia remains a major indicator profuse hemolysis and bone marrow suppression caused by malaria and HIV respectively. However, it should be noted that anemia could be multifactorial, iron deficiency and malnutrition, which could be concomitant causes[6,12].

Findings from this study showed significant correlation between hemoglobin concentration and CD4⁺ cell count in SMP/HIV co-infected patients. This is in accordance with a report by Kakisingi et al.[12]. The low CD4⁺ cells count in the test subjects could be connected with progressive immune deterioration caused by dual pathogens[13].

The rate of antimalarial resistance in subjects with SMP/HIV coinfection was relatively higher than those with SMP without HIV infection. This is contrary to reports by Byakika-Kibwika et al.[14], Tagoe and Bouchie[13] where they reported HIV infections were not a significant risk factor for antimalarial resistance. The difference could be due to the nature of study design and the sample size.

Although the present study has yielded some important findings in regard of malaria and HIV coinfections among pregnant women, its design is not without limitations. First, as a case-control design nature does not allow us to make rigid inferences from these findings. The second limitation concerns the non-exclusion of confounded variables (e.g. nutrition status) that could interfere with hemoglobin value and the absence of real follow-up due to the difficulty to enroll patients.

SMP/HIV coinfection in pregnant women exists in the study area. In the absence of prompt and appropriate clinical interventions, SMP/HIV coinfection may likely lead to severe anemia and progression to AIDS. Malaria infected pregnant women especially those with HIV coinfections, which should be periodically and closely monitored for presence of antimalarial and ART resistance.

Conflict of interest statement

We declare that we have no conflict of interest.

References


