Assessment of Altered Plasma Lipid Pattern in Plasmodium Falciparum Malaria Infected and Non Infected Individuals

ESAN AYODELE JACOB*

Department of Haematology and Blood Transfusion Science, Federal Medical Centre, P.M.B 201 Ido-Ekiti, Nigeria

*Corresponding author: ayodelejacob4u@gmail.com

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Abstract This study aimed to assess blood lipid profile status in pre, post anti-malaria drug treatment in Plasmodium falciparum malaria parasite infected patients and control individuals. Two hundred and two blood samples were collected pre-treatment and post anti-malaria drug treatment. Lipid profile was estimated using CHOD-PAP method; Thick blood film was made. Post treatment HDL was significantly lower compared to pre treatment and control. Pre treatment LDL was significantly higher compared to post treatment and control. Pre treatment triglyceride was significantly lower compared to post treatment and control. Certain lipids are increased while some are decreased with malaria infection/treatment, the rapidly growing malaria parasite requires large amounts of lipids for increase in surface area and volume of its internal membranes, certain serum lipid fractions may favour the onset and/or severity of malaria infection.

Keywords: malaria parasite, lipid profile and anti-malaria therapy


1. Introduction

The rapidly growing malaria parasite requires large amounts of lipids for increase in surface area and volume of its internal membranes, certain serum lipid fractions may favour the onset and/or severity of malaria infection. Very little is known about mechanism involved in lipid changes related to malaria. Hypercholesterolemia and hypertriglyceridemia was observed in both uncomplicated and complicated malaria [1,2,3] whereas Kittl et al., [4] have shown no correlation between severity of malaria attacks and extent of HDL – cholesterol decrease. Human serum HDL is necessary for P. falciparum in vitro culture. Cholesterol is synthesized in the liver which happens to be the major site of plasmodium infection and this raises some questions whether there is any relationship between the cholesterol synthesis by the liver and the plasmodium infection of the liver. Although, the parasite has ways that enables it to thrive and multiply using nutrients from the host, they still cannot synthesize majority of their own lipids and cholesterol in vivo. In view of this, one would have to expect that the serum lipid levels to be low compared with the uninfected group. Liver ensures homeostasis of lipid and lipoprotein metabolism, hepatocellular damage often associated with severe and acute P. falciparum infections impairs these processes, leading to alterations in plasma lipid and lipoprotein patterns [5,6]. The alterations in serum lipid profile of malarious subjects could be attributable to the level of haemolysis in malaria, which is proportional to severity of infection [7]. Since the erythrocyte membranes are predominantly lipid in composition, the liberation of membrane lipids following sustained haemolysis accounted for the observed alterations in the serum lipid profile of patients presenting this disease [8]. Furthermore, parasitized parenchyma and Kupffer cells compromise lipid metabolism engendering distortions in lipoprotein particles synthesized by the liver with associated alterations in plasma lipid profile [9]. Hyperlipidemia, a hallmark of malarial infection which may results in depletion of natural antioxidants and facilitates the production of reactive oxygen species (ROS) which has the ability to react with all biological molecules like lipids, proteins, carbohydrates, DNA and exert cytotoxic effects on cellular components [10]. Thus increased ROS and impaired antioxidant defense contributes for initiation and progression of micro and macro vascular complications in malaria [11,12].

2. Materials and Methods

2.1. Subjects and Study Design

This study was conducted at Federal Medical Centre, Ido-Ekiti, Ekiti State Nigeria; between November 2012
and March 2013. Subjects were *Plasmodium falciparum* malaria infected adult individuals; presented with signs and symptoms of malaria infection. This was confirmed using malaria rapid kit test and microscopy detection of malaria parasite. Two hundred and two blood samples were collected (5 ml) on lithium heparin twice from each malaria infected individuals; grouped as pre-treatment (at presentation) and post anti-malaria drug treatment. One hundred and two (102) blood samples from apparently healthy individuals were collected as control; both *Plasmodium falciparum* malaria infected subjects and controls were within the age 15-64 years of both sex. Patient’s consent was sort for through an informed consent form; also ethical approval was obtained from the hospital. Structured questionnaire was used to obtained demographic characteristic and other relevant information for study.

### 2.2. Sample Collection

Five millimeters (5 ml) of blood sample was collected from each subject on the first day of visiting hospital as baseline sample after the patient has been clinically diagnosis for malaria infection, another 5 ml of blood sample was collected on the second or third day after taking anti-malaria drugs. 4 ml of blood sample was collected on lithium heparin bottle to assay lipid profile and 1 ml of blood sample was dispensed into di-potassium ethylenediaminetetracetic acid (K2EDTA) vaccutainer bottles for malaria parasite detection on thick blood film.

### 2.3. Methodology

Lipid profile majorly consist of high density lipoproteins (HDL), low density lipoproteins (LDL), triglycerides and cholesterol. Lipid profile was estimated using CHOD-PAP method; The procedures were as described by the manufacturer of the kit (randox); Low density lipoproteins was calculated by Freidewald formula. Thick blood film was made from EDTA blood sample and stained with Giemsa’s staining technique for malaria parasite detection; observed under microscopy using x40 and x100 objectives lenses, the procedure was described by Monica Cheesbrough [13].

### 3. Statistical Analysis

Data obtained were analyzed for mean and standard deviation; significant test was done by ANOVA Level of significance was considered as <0.05.

### 4. Results

**Table 1:** shows comparison of HDL, LDL, triglycerides and total cholesterol. The mean HDL in post treatment was significantly lower compared to pre treatment and control (p<0.001). The mean LDL in pre treatment was significantly higher compared to post treatment and control (p<0.001). The mean triglyceride in pre treatment was significantly higher compared to post treatment and control (p<0.001). The mean total cholesterol in pre treatment was significantly lower compared to post treatment and control (p<0.001). Multiple comparisons between pre treatment and post treatment show that HDL, LDL, triglycerides were significantly higher in pre treatment compared to post treatment while total cholesterol in pre treatment was lower compared to post treatment levels. Multiple comparisons between pre treatment and control show that LDL and Triglyceride were significantly higher in pre treatment compared to control while HDL and total cholesterol were significantly lower in pre treatment compared to control. LDL and Triglyceride were significantly higher in post treatment compared to control while HDL and total cholesterol in post treatment were significantly lower compared to control. Figure 1 shows the prevalence of *P. falciparum* malaria parasite infection according to sex distribution. The frequency for male and female were 129 and 73 respectively in malaria infected subjects.

<table>
<thead>
<tr>
<th>GROUPS</th>
<th>HDL-C mg/dL</th>
<th>LDL-C mg/dL</th>
<th>TG mg/dL</th>
<th>TC mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Treatment (N = 202)</td>
<td>28.75± 6.51</td>
<td>17.72± 1.25</td>
<td>22.02± 1.55</td>
<td>96.88± 19.81</td>
</tr>
<tr>
<td>Post-Treatment (N = 202)</td>
<td>27.47± 3.44</td>
<td>12.21± 0.86</td>
<td>17.61± 1.24</td>
<td>102.37± 12.31</td>
</tr>
<tr>
<td>Control (N=102)</td>
<td>42.08± 3.66</td>
<td>6.89± 0.68</td>
<td>11.63± 1.15</td>
<td>124.03± 10.29</td>
</tr>
<tr>
<td>F</td>
<td>329.36</td>
<td>27.40</td>
<td>41.42</td>
<td>106.41</td>
</tr>
<tr>
<td>(P-value)</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>(Pre-Treatment VS (Post Treatment) p-value)</td>
<td>0.04*</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
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<tr>
<td>(Pre treatment) VS (Control) p-value</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
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<tr>
<td>(Post Treatment) Vs (Control) p-value</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
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<td>&lt;0.001*</td>
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P<0.05 significance, P>0.05 no Significant, F (P-value) = mean ± SD of parameters compared using ANOVA.
5. Discussion

Lipoproteins are major lipid component in plasma and certainly targets for oxidative stress, it appears that the parasites take advantage of the oxidative stress to increase its pathogenicity. The result of blood lipid profile; high density lipoprotein, low density lipoprotein, triglycerides and total cholesterol obtained in this present study were lower compared to control subjects, although the values were within the normal range. In the pretreatment, high density lipoprotein, low density lipoprotein and triglycerides were higher while total cholesterol was lower compared to post treatment. Similar to this present study, Chikezie and Okpara [14] reported that, in moderate malaria infection, serum levels of low density lipoprotein and high density lipoprotein were lower than in control subjects. These observations suggested the critical role of oxidized lipoproteins, especially low density lipoprotein on the pathogenesis of malaria. In addition, moderate malaria infection was associated with reduced serum levels of very low density lipoprotein and high density lipoprotein that was in conformity with this present study. Findings of Baptisa, [7] is in consistent with this present study, he stated, that in malaria endemic areas, when plasma levels of cholesterol, triglycerides, HDLc and LDLc were analyzed in children infected with P. falciparum, investigators have found significantly low levels of lipid profile. Similar to this present study, Djoumessi, [15] reported low levels of the cholesterol in patients infected with malaria as compared to normal healthy controls. In accordance to this present study, Ogboho et al., [16] reported that, there were significant decreases in total cholesterol, HDL and VLDL when compared with the values from control group. He explained that the reduction in total cholesterol may be as a result of significant reduction in HDL, probably due to oxidative modification. The increased oxidative stress in malaria, which accounts for the degradation of the lipoproteins, may originate from several sources including intracellular of parasitized erythrocytes and extracellular of haemolysed erythrocytes or host immune responses. Similarly, Nilsson-Ehle, [17] and Mohanty, [3] reported that, during malaria infection, the levels of low density lipoproteins (LDL) and high density lipoproteins (HDL) are decreased while triglycerides are moderately increased. Mohanty et al., [3] accounted that, plasma levels of high density lipoproteins, low density lipoproteins, total cholesterol and triglycerides were measured in 60 patients with P. falciparum malaria (37 severe cases and 23 mild) and in 83 healthy individuals, to study malaria-induced changes in plasma lipids. Triglyceride levels were lower in the patients than in the control which was consistent with this present study. Faucher et al., [5] stated that, in low-level malaria infection, the levels of total cholesterol, low density lipoproteins (LDL) and high density lipoproteins (HDL) are reduced while triglyceride levels are increased. These events may be related to the oxidation, and they are in consistent with the fact that host response to acute infection increases lipoprotein oxidation in vivo. In malaria infection, alteration of lipid metabolism during acute infection may result from acute phase response [18]. The acute phase response is associated with changes in lipid metabolism including a moderate increase in serum lipids. Triglyceride levels were lower in the patients than (37 severe cases and 23 mild) and in 83 healthy subjects. These observations suggested the critical role of oxidized lipoproteins, especially low density lipoprotein on the pathogenesis of malaria. 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