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Original Research Article**Biochemical indices of liver functions in infected malaria patients in Nigeria****Adelakun Ayodele. A, Adediji Isaac. O^{*}, Motayo Babatunde and Akinwande Kazeem**¹Department of Chemical Pathology, LAUTECH Teaching Hospital, Ogbomosho, Oyo State, Nigeria.²Department of Medical Laboratory Science, Babcock University, Ilisan- Remo, Ogun State, Nigeria.³Department of Medical Microbiology and Parasitology, Federal Medical Centre, Abeokuta, Ogun State, Nigeria.⁴Department of Chemical Pathology, Federal Medical Centre, Abeokuta, Ogun State, Nigeria.***Correspondence Info:**

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E-mail: adedijisaac20@yahoo.com**Abstract****Introduction:** Malaria is a tropical disease, which has hepatocellular involvement and is a significant cause of morbidity and mortality especially among children.**Objective:** This study investigated the biochemical indices of liver function in children infected with malaria and compared their results with healthy children (age and sex-matched).**Methodology:** Fifty patients (age: 5.1 ± 1.9 years) were enrolled from the Pediatrics' clinic of a tertiary health institution in Ogun state, Nigeria. Fifty age- and sex- matched apparently healthy children, from the same geographical location were selected as control. Examination of a thick blood film was done to confirm the presence of *Plasmodium falciparum* trophozoite in patients and its absence in controls. The *in vitro* determination of the plasma activities of aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), plasma total and conjugated bilirubin was performed using standard methods. Data obtained were statistically analyzed using student's t-test where P of less than 0.05 was considered significant.**Results:** The plasma activities of AST (34 ± 28 vs 10 ± 4 U/L) and plasma levels of total bilirubin (1.1 ± 0.7 vs 0.6 ± 0.2 mg/dL) were significantly higher in malaria patients compared with controls ($p < 0.001$). There was no significant difference in the plasma activities of ALT and ALP as well as concentration of conjugated bilirubin when compared with controls.**Conclusion:** This study concluded that abnormal biochemical indices of liver functions observed in malaria patients does not conclusively imply liver disease, it could be as a result of intravascular haemolysis.**Keywords:** *Plasmodium falciparum*, Malaria, Bilirubin, Liver enzymes**1.Introduction**

Malaria is a parasitic infection that is commonly spread through the bite of *Plasmodia* infected vector, female *Anopheles* mosquitoes. Other means of transmitting the infection are through blood transfusion[1] and congenital transmission[2]. Malaria is the most important of the parasitic diseases of humans, with over 1 billion cases and between 1-3 million deaths each year, most of whom are children below the age of 5 years (CDC). There are four different species of *Plasmodium* that can cause

malaria; viz *Plasmodium falciparum*, *P. vivax*, *P. malariae*, and *P. ovale*. Malaria caused by *P. falciparum* is the most dangerous form of malaria[3]. The largest proportion of this morbidity and mortality occurs in sub-Saharan Africa; in most African countries, 75% of cases were due to *P. falciparum*, whereas in most other countries with malaria transmission, other less virulent plasmodial species predominate[4][5]. Almost every malarial death is caused by *P. falciparum*[5][6].

When the parasites reach densities of about 50/ μ L of blood, the symptomatic stage of the infection begins, which is mainly characterized by headache, fatigue, abdominal discomfort, muscle aches and fever[7]. Malaria leads to systemic manifestations with effects on major organs such as kidneys and liver[8][9]. There could also be pulmonary complications resulting from malaria infection[5]. Renal impairment is common among adults with severe *falciparum* malaria but rare among children[4][10]. Mild and severe forms of haemolytic jaundice are also common and they are associated with *P. falciparum* infections however, severe haemolytic jaundice is more common in adults than children, and these result from hemolysis, hepatocyte injury, and cholestasis[10]. Malaria as a result of *P. falciparum* infection causes clinical jaundice (plasma total bilirubin >3mg/dL) in about 2.5 – 5.3% of infections in endemic areas[9][11]. A number of histological changes in the liver in *P. falciparum* malaria which include reactive Kupffer cells, retention of haemozoin pigment and minimal parasitized red blood cell (PRBC) sequestration has been reported[12][13]. Hepatic involvement in *P. falciparum* malaria is therefore a common presentation, and presence of jaundice is one of the indicators of severe malaria as defined by World Health Organization in 2008[6].

Jaundice in *falciparum* malaria may vary from mild to severe and is associated with high incidence of complications and mortality[14]. In clinical diagnosis, plasma activities of AST, ALT and ALP are useful diagnostic markers of liver diseases. AST is abundant in the liver, cardiac muscle, skeletal muscle and erythrocytes, relative to ALT[15], whereas bilirubin is a breakdown product of haemoglobin metabolism[16].

Since raised plasma activities of AST and elevated plasma level of unconjugated bilirubin could be as a result of haemolysis as well as liver disease. Therefore, an increase in either, in a case of malaria should be investigated.

This study was aimed to determine if there would be any increase in plasma activities of liver enzymes and plasma level of bilirubin in patients presenting with malaria and to compare the findings of these parameters with those from age- and sex-matched apparently healthy individuals.

2.0 Materials and Methods

2.1 Subjects

A total of 100 subjects were recruited which included 50 children aged 3 to 7 years (28 males and 22 females), presenting with acute malaria at the Pediatric Out-patient Unit of Federal Medical Centre,

Abeokuta, Nigeria. During the period of the investigation, subjects were differentially diagnosed not to have superimposed infections or clinically significant renal and hepatic conditions. Fifty apparently healthy age- and sex- matched apparently healthy subjects were selected as controls. All the subjects belonged to the same socioeconomic class of the society.

2.2 Sample collection and analysis

Blood sample (5mL) was collected by venepuncture into lithium heparin container. A drop of the whole blood was used for microscopic examination of malaria parasite by thick blood film and was stained with 10% Giemsa solution[17]. The remainder was spun to obtain plasma for the determination of plasma activities of aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), as well as plasma bilirubin concentration. Randox enzymatic kit was used for the *in vitro* determination of the plasma activities of ALT and AST using the colorimetric method of Reitman and Frankel[18]. Randox enzymatic kit was used for the *in vitro* determination of plasma activities of ALP, using the colorimetric method of Gesellschaft[19]. Plasma total and conjugated bilirubin concentrations were determined using the Jendrassik-Grof method[20].

2.3 Statistical Analysis

Statistical analysis was done using the statistical package for social sciences (SPSS) version 13.0. Results were expressed as mean \pm standard deviation. Student's t-test was used to compare means between patients and controls where P of less than 0.05 was considered significant.

3. Results

Table 1 shows the biochemical indices of liver functions in malaria infected patients compared with control subjects between the age range of 3-7 years. Plasma activities of AST and plasma levels of total and unconjugated bilirubin were significantly higher in malaria patients compared with controls subjects. However, no significant difference was observed in plasma activities of ALT, ALP as well as plasma levels of conjugated bilirubin in malaria patients when compared with controls.

Table1: The table of biochemical indices of liver functions in malaria patients and control subjects

Parameter	Patients (N=50)	Controls (N=50)	P-Value
AST(U/L)	34 \pm 28	10 \pm 4	< 0.001*
ALT(U/L)	9 \pm 6	9 \pm 4	NS
ALP(U/L)	200 \pm 77	188 \pm 38	NS
T.BIL(mg/dL)	1.1 \pm 0.7	0.6 \pm 0.2	<0.001*
C.BIL(mg/dL)	0.3 \pm 0.2	0.3 \pm 0.1	NS
U.BIL(mg/dL)	0.8 \pm 0.5	0.3 \pm 0.1	<0.001*

*Significantly different from comparable control subjects; NS= Not significant.

AST= Aspartate Transaminase, ALT= Alanine Transaminase, ALP= Alkaline Phosphatase, T.BIL= Total bilirubin, C.BIL= Conjugated bilirubin, U.BIL= Unconjugated bilirubin

4. Discussion

Jaundice is a common finding in malaria. Jaundice in severe *P.falciparum* malaria is multifactorial; these may be due to destruction of parasitized red blood cells[4][21].

The results of the present study observed an increase in plasma activities of AST as well as increase in the plasma levels of total bilirubin concentration in malaria patients. The observed increase in AST could be attributed to the destruction of erythrocytes during the induced intravascular haemolysis of parasitized red cells and haemolysis of non-parasitized red cells (innocent bystanders). The results support the study by Anand *et al* that observed increased plasma activities of AST and raised plasma levels of unconjugated bilirubin in patients with malaria[22].

Furthermore, excessive destruction of erythrocytes usually characterizes *falciparum* malaria infection thus contributing significantly to a rise in the plasma level of unconjugated bilirubin which was also observed in the present study. Ignatus *et al* revealed that in malaria parasitemia especially by *P.falciparum*, large numbers of erythrocytes are infected and they are eventually destroyed by the spleen, thus resulting in haemolytic anaemia and there is also increased plasma level of total bilirubin (dominant unconjugated fraction) without any significant elevation of the liver enzymes[23]. However, in malaria hepatopathy, there is derangement of liver functions in individuals with malaria[26]. Uzuegbu *et al* observed an increase in ALT and most of the subjects in that study had hepatomegaly and this can be regarded as a complication of severe malaria infection[24]. In patients with malarial hepatopathy, Devarbhavi *et al* observed that plasma conjugated bilirubin was elevated in contrast to unconjugated bilirubin which is raised in malaria infected individuals due to haemolysis[25]. Liver enzymes (both AST and ALT) may be elevated 2-3 times normal in patients with malarial hepatopathy[25][26][27]. In liver diseases, increased plasma activities of AST are usually accompanied by rise in ALT. However, when AST is solely increased in the plasma, this could be as a result of skeletal muscle disease or haemolysis[18].

5. Conclusion

The findings of this study revealed that abnormal levels of plasma AST and plasma

unconjugated bilirubin observed in malaria patients does not conclusively imply liver disease, this could be as a result of *P.falciparum* induced intravascular haemolysis and it is not all the cases of malaria infections that are associated derangement of liver functions. However, liver involvement may be dependent on the load of parasitemia. It is of great importance to know that liver functions should be assessed and impairment should be managed properly in the course of malaria to prevent complications. There should also be post treatment analysis of these biochemical indices of liver functions purposely for comparison and to fully elucidate the involvement of liver in *P.falciparum* malaria infection.

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