



## EFFECT OF MALARIA INFECTION ON HEPATIC AND RENAL FUNCTIONS IN PREGNANT WOMEN ATTENDING ANTENATAL CLINIC AT GENERAL HOSPITAL DUTSE, JIGAWA-NIGERIA

<sup>1</sup>Muhammad Shamsiyya Sani., <sup>2</sup>Balogun Joshua Babalola and <sup>2</sup>Dogara, Musa Mustapha

<sup>1</sup>Department of Biological Sciences, Faculty of Science, Federal University Gusau Zamfara state Nigeria.

<sup>2</sup> Department of Biological Sciences, Faculty of Science, Federal University Dutse, P.M.B.7156, Jigawa State, Nigeria.

\*Corresponding Authors Email: [joshufeli@gmail.com](mailto:joshufeli@gmail.com); +2348068607137

### ABSTRACT

The effect of malaria infection on hepatic and renal functions in pregnancy was investigated. Three malarious and non-malarious pregnant women of age ranges 15 to 40 years with a mean (SD) of 23.5 (6.6) years and a median (IQR) of 20.5 (18.3 to 27) years were enrolled. Liver enzymes (AST, ALT and ALP) and Kidney (UCE) functions were determined using Randox standard assay kits. The levels of alkaline phosphatase (ALP) and albumin were significant as malaria infected pregnant women had significantly lowered levels of ALP and albumin compared to controls (21.3 vs 26.1 IU/L,  $P = 0.03$  and 4.8 vs 6.0 g/dl  $P = 0.02$ ). There was no significant difference between malaria infected pregnant women and their non-malarious counterparts ( $P > 0.05$ ) in their renal functions. There was no significant difference in mean concentrations of urea, creatinine, sodium, potassium and chloride regardless of the severity of malaria. Usually in pregnancy markers of liver function decrease due to expansion of extracellular fluid except alkaline phosphatase which is elevated due to its placental origin. Results of this study showed decreased level of ALP which could possibly be an indication that the parasite has not reached its hepatic stage. The severity of gestational malaria depends on the initial immunity of the pregnant woman. The impact of malaria on pregnancy and conversely, the impact of pregnancy on malaria, are two factors which must be put into consideration during gestational malaria.

**Keywords:** Malaria, Renal and Hepatic Functions, Pregnant Women, Jigawa

### INTRODUCTION

Malaria is one of the most important causes of morbidity and mortality in the world. The disease is transmitted by female *Anopheles* mosquitoes which carry infective sporozoite stage of *Plasmodium* parasite in their salivary glands, which is transmitted from person to person through the bite of the mosquito. Pregnant women and children under five years are particularly vulnerable to the disease due to their weaker immune systems (WHO, 2000). An estimated 25 million women become pregnant in malaria-endemic areas of sub-Saharan Africa, with over 10,000 maternal and about 200,000 infant deaths per year as a result of *P. falciparum* infection (Broen *et al.*, 2007 and Rogerson *et al.*, 2007). Malaria suppresses responses to immunogens, and placental malaria impairs materno-foetal antibody transfer, which potentially reduces the benefits of maternal immunization strategies (Duffy 2003; Metenou *et al.*, 2007 and Steketee *et al.*, 2001). Also, parasites-infected red blood cells (IRBCs) sequestration in the placenta is a key feature of infection by *P. falciparum* during pregnancy and is frequently associated with severe adverse outcomes for both mother and baby such as spontaneous abortion, preterm delivery, low birth weight and infant death, as well as severe anaemia for both mother and infant (Tuteja, 2007; Guyatt and Snow, 2004 and Van de Broek and Letsky, 2000). Pregnancy increases the frequency and severity of most infectious diseases but its effect on malaria seems worse

(Rogerson *et al.*, 2007; Desai *et al.*, 2007). Several theories have been put forward to explain this increased risk including changes to the cellular immune responses that otherwise should offer protection, and increased attractiveness of the pregnant woman to mosquitoes. The former is believed to result from the increased level of circulating maternal steroids in pregnancy (Okpere, 2004). This was the subject of the extensive research by (Bouyou *et al.*, 2005) in which they summarized that a sustained increase in cortisol level underlies the increased susceptibility of pregnant women to malaria (Bouyou *et al.*, 2005).

Lindsay *et al.* (2000) found that pregnant women attracted twice the number of anopheles mosquito compared to their non-pregnant counterparts (Lindsay *et al.*, 2000). This they believed may be connected to certain physiological and behavioral changes that occur in pregnancy including increased volume of exhaled air and release of volatile substances (Lindsay *et al.*, 2000). These substances may be detected by the mosquitoes hence leading to increased attractiveness of the pregnant woman to mosquito (Lindsay *et al.*, 2000). Cerebral malaria, acute renal failure and severe hemolysis, complications of malaria that are rare in adults in endemic areas, may be seen in pregnancy (Okpere, 2004). Hence the need to look into malaria infection in pregnancy, this study might give some insight into management of malarious pregnancy in Jigawa State and Nigeria at large.

## MATERIALS AND METHODS

### Ethical approval

Ethical clearance for this study was obtained from the State Ministry of Health Jigawa State, and the consent of patients involved in the study was sought and obtained via signing of the consent forms.

### Collection of Obstetric Data

With the aid of a questionnaire, team of resident nurses obtained sociodemographic characteristics and obstetric history (age, parity, gravidity and gestational age) from one hundred and three (103) women, who came for antenatal clinic and gave informed consent for this study. Histories of treatment of malaria during preceding week of any anti malaria chemotherapy were obtained from the patients cards.

### Inclusion Criteria

1. Subjects (test) were not on antimalarial drug and exclude those who had other infections.
2. Those from whom informed consent was obtained.

### Exclusion Criteria

1. Patients on drugs that affect lipid metabolism and liver enzymes were excluded.
2. Patients presented with clinical symptoms such as fever, headache, body weakness and nausea but without parasites obtained in blood smear were excluded as well as those who refused consent.

### Sample Collection and Processing

With the help of qualified medical personnel, 5ml of blood was collected by venipuncture from each participating pregnant woman. 2ml of blood was immediately transferred into bottle containing ethylene diamine tetra acetic acid (EDTA) that was used for hematological study, while the remaining 3ml of blood was transferred into a plain bottle that was allowed to clot and serum was later obtained. The level of electrolytes, total protein creatinine, urea and liver enzymes were determined from the serum. The parasitaemia was determined by microscopy.

### Kidney function test

Kidney function test was done by determining the level of creatinine, urea and electrolytes in the serum of the study subjects using Randox test kit according to the manufacturer's instructions.

### Liver Function Test

#### Determination of serum ALT, AST and ALP

Serum ALT, AST and ALP were used to determine the liver function in the samples using the calorimetric method with standard assay kits obtained from Randox. Values obtained were compared to the standard value range.

### Statistical Analyses

The differences among the groups were analyzed by the one-way analysis of variance. Inter-group comparisons were done using Duncan's multiple range tests with 95% confidence intervals.

## RESULTS AND DISCUSSION

### Results

Malaria is known to have devastating effects on mortality in tropical and subtropical regions with the effect being magnified in people with weakened immunity such as those in pregnancy, out of which only a fractions have access to effective interventions (Wagbatsoma and Omoike, 2008).

Reports on the levels of urea and creatinine among pregnant malaria patients are varied. Of the hepatic parameters assessed, levels of alkaline phosphatase (ALP) and albumin were found to be statistically different between the two groups (Figure 1): malaria infected pregnant women had significantly lowered levels of ALP and albumin compared to controls (21.3 vs 26.1 IU/L,  $P = 0.03$  and 4.8 vs 6.0 g/dl  $P = 0.02$ ). With regards to renal function, there was no statistically significant difference between malaria infected pregnant women and their non-malarious counterparts ( $P > 0.05$ ). It is known that in pregnancy all markers of liver function decrease due to expansion of extracellular fluid except alkaline phosphatase which is elevated due to ALP of placental origin. However the results of this study showed a decrease in the level of ALP this could possibly be an indication that the parasite has not reached its hepatic stage, as changes in serum ALP activity can be used as a potential biomarker in assessing the integrity of the hepatic

drainage system during acute malaria infection *falciparum* (WHO 2006).

Table 1 shows the levels of renal and hepatic function parameters in relation to the degree of parasitaemia. The result showed that mean concentration levels of urea, creatinine, sodium, potassium and chloride were similar (i.e., no statistically significant difference) regardless of the severity of

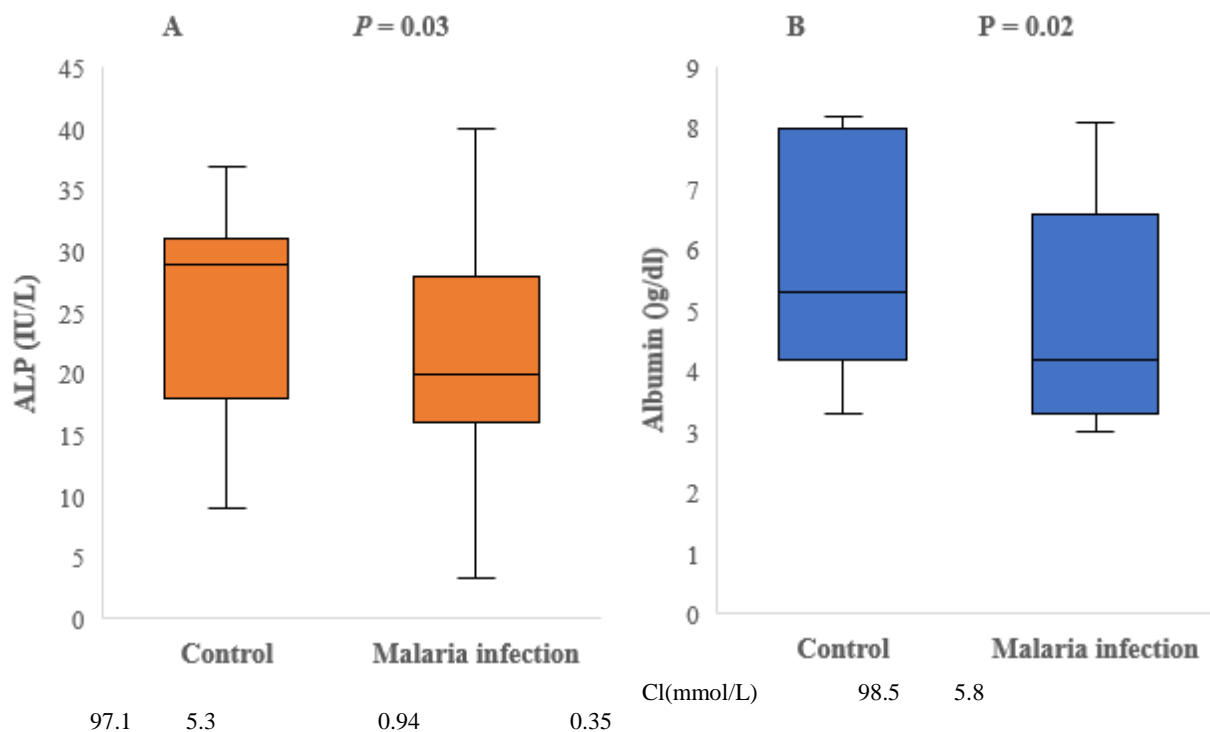
malaria infection. This disagrees with Afrifa *et al.* (2017), which observed statistical increase in levels of renal parameters. However, studies by Ugwuja and Ugwu (2011) revealed decreasing levels of the parameters under consideration among malaria pregnant mothers, which is in consonant with the findings in this study.

**Figure 1 Levels of ALP and albumin between malaria infected and non-infected (controls) pregnant women.** Box represents median with 25 and 75 percentiles

Table 2 shows Levels of hepatic and renal function parameters in relation to the degree of parasitemia, which was not significant (P>0.05), this disagrees with the findings of Mishra *et al.* (2016) which found increased levels of Transaminases and Alkaline Phosphatases in malaria infected pregnant women.

**Table 1: Levels of hepatic and renal function parameters between malaria infected and non-infected (controls) pregnant women**

Parameter	Control (n = 15)		Malaria infected (n = 88)		t	P-value
	mean	SD	mean	SD		
AST (IU/L)	18.3	5.4	16.7	5.0	1.10	0.28
ALT (IU/L)	29.8	9.6	28.0	7.7	0.81	0.42
ALP (IU/L)	26.1	8.1	21.3	7.9	2.17	0.03*
TP (g/dl)	5.4	1.8	6.1	1.8	1.39	0.17
Alb (g/dl)	6.0	1.8	4.8	1.7	2.44	0.02*
Ur (mmol/l)	3.0	2.4	3.6	2.6	0.82	0.42
Cr (µmol/l)	63.1	36.6	61.2	30.8	0.22	0.83
Na (mmol/L)	140.0	7.6	140.5	7.0	0.25	0.80
K (mmol/L)	3.8	0.8	4.0	0.7	0.97	0.34



SD: Standard deviation, AST: Aspartate transaminase, ALT: Alanine transaminase  
 ALP: Alkaline phosphatase, TP: Total protein, Alb: Albumin, Ur: Urea, Cr: Creatinine  
 Na: Sodium K: Potassium Cl: Chloride \*Significant at P < 0.05

**Table 2: Levels of hepatic and renal function parameters in relation to the degree of parasitemia.**

Parameter	Control (n = 15)	Degree of Parasitemia			
		+	++	+++	
		(n = 31)	(n = 25)	(n = 32)	
AST (IU/L)	18.3 (5.4)	17.3 (5.0)	16.6 (5.1)	16.3 (5.1)	
ALT (IU/L)	29.8 (9.6)	28.9 (6.9)	28.3 (7.8)	26.8 (7.9)	
ALP (IU/L)	26.1 (8.1)	22.7 (8.5)	21.3 (7.7)	20.1 (7.5)	
TP (g/dl)	5.4 (1.8)	5.9 (1.9)	6.5 (1.7)	6.1 (1.7)	
Alb (g/dl)	6.0 (1.8)	4.8 (1.7)	4.6 (1.6)	5.0 (1.8)	
Ur (mmol/l)	3.0 (2.4)	3.4 (2.5)	3.1 (1.4)	4.3 (3.2)	
Cr (µmol/l)	63.1 (36.6)		57.3 (32.9)	59.2 (29.3)	66.5 (31.5)
Na (mmol/L)	140.0 (7.6)		138.0 (6.2)	140.8 (6.7)	142.7 (7.3)
K (mmol/L)	3.8 (0.82)	4.1 (0.67)	3.9 (0.58)	4.0 (0.81)	
Cl (mmol/L)	98.5 (5.9)	98.1 (5.8)	97.4 (4.6)	95.8 (5.0)	

Values are mean (standard deviation)

+: Mild parasitemia      ++: Moderate parasitemia      +++: Severe parasitemia

Significant difference was assessed using One-Way ANOVA at  $P < 0.05$

P-values: AST = 0.63, ALT = 0.61, ALP = 0.10, TP = 0.35, Alb = 0.09, Ur = 0.24. Cr = 0.68,

Na = 0.06, K = 0.57, Cl = 0.26

AST: Aspartate transaminase, ALT: Alanine transaminase, ALP: Alkaline phosphatase

TP: Total protein, Alb: Albumin, Ur: Urea, Cr: Creatinine, Na: Sodium      K: Potassium

Cl: Chloride

## CONCLUSION

Based on the findings of this study in Dutse, Jigawa State, malaria has no significant impact on renal biochemical (most importantly urea and creatinine) and hepatic (especially AST, ALT and ALP) profiles. This could be due the fact that as at when the study was conducted majority of the malaria positive pregnant women had no hepatic stage in them. We recommend that further study be carried out with larger samples and especially during raining season, when mosquitoes are breeding in their numbers, to confirm if our findings are consistent.

## CONFLICT OF INTEREST

There was no conflict of interest among the Authors .

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