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*Original Article:*

# Renal and Hepatic Dysfunction in Malaria Patients in Minna, North Central Nigeria

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**Abstract:**
Information on kidney and liver involvement in malaria in Africa is still very scanty. Kidney and liver functions were assessed in 70 malaria patients using serum levels of creatinine and urea and urinary protein levels as test indicators of kidney function and serum levels of bilirubin, aspartate aminotranferase (AST or SGOT), alanine aminotransferase (ALT or SGPT), and alkaline phosphatase (ALP) as indicators of liver function. Descriptive analysis of results obtained showed that 67.14% of patients had creatinine level above the 126µmole/L which is considered the upper limit of the normal range. Three cases (4.29%) had creatinine levels well above 265µmoles/L. The serum concentrations of creatinine, urea, protein, conjugated and total bilirubin, AST, ALT, and ALP in malaria patients were significantly higher ($p<0.05$) than those of malaria free individuals. We conclude that renal dysfunction, acute renal failure and liver dysfunction are clinical features of malaria in Minna, North Central Nigeria.
**Key Words:** Malaria, Transferases, Creatinine, Bilirubin, Hepatic dysfunction, Renal dysfunction.

## Introduction:

Malaria is a devastating disease in humans caused by a protozoan, plasmodium species. It accounts for an estimated 2-3 million deaths annually across well over 100 countries.(1) Out of the species of plasmodium parasite, *Plasmodium falciparum*, *P. vivax, P malaria*e and *P. ovale* that cause malaria in humans, *P. falciparum* is responsible for most deaths and most of the severe complications although renal involvement is also known to be caused by *Plasmodium malariae*.(2-5) Infection due to*P. falciparum* accounts for 80% of malaria cases in Nigeria.

Cases of malaria associated renal and hepatic impairment have been reported from different parts of malaria endemic countries.(6-11) The severity of malaria associated renal impairment in a particular area is largely a function of the disease prevalence and other aetiological factors prevailing in the area. (12) The same is likely to be true of hepatic dysfunction.

Unfortunately information on the association of malaria with impairment of renal and hepatic functions in malaria patients in Nigeria is very scanty. This information is very necessary because malaria is highly endemic in Nigeria, and the mortality rate is quite high, especially in children. Renal failure (serum creatinine >3 mg/dl) and jaundice (bilirubin >3mg/dl) may be indicative of severe malaria(12), which will require special attention. Although largely unreported, cases of inadequate treatment of malaria in Nigeria may be quite high, especially among the urban and rural poor. The main reasons for this are two-fold. First of this is the high level of self medication arising from difficulties inherent in the healthcare delivery system which make reporting to hospitals and clinics very unattractive and in many cases people report to hospitals as a last resort. Secondly, a great majority of Nigerians, and indeed the urban and rural poor in many countries of sub-Saharan Africa, use local herbs and plants as the main source of medicines and not as complementary medicine as is generally believed. While some of these may be very effective, others are not. The implication of all this is that the impairment of organ functions which would otherwise be transient, present only during the duration of the disease, will gradually progress to chronic organ dysfunction with the attendant disastrous consequences.

Both kidney and liver are very vital organs in the body and any impairment of their functions if not detected early and managed properly may have devastating consequences.

In Nigeria, malaria accounts for 30-50% of outpatients in health institutions across the country. 8-10% of admitted children are due to malaria, with mortality rate of as much as 0.3 million annually, most of them children below the age of 5 years. It therefore becomes very necessary to constantly evaluate the extent of renal and hepatic impairment in malaria cases to ensure proper management of malaria infection with its associated complications. We report here that renal impairment and hepatic dysfunction are not uncommon in malaria cases in Minna, Northern Nigeria and acute renal failure is also a clinical manifestation of malaria in Minna.

## Materials and Methods:

**The Study Subjects:** The study was done at the General hospital, Minna, Nigeria. The study population comprised of a total of 142 individuals. This was made up of 72 (40 females and 32 males) malaria free individuals, who served as controls, and 70 (35 females and 35 males) confirmed (presence of malaria parasites) malaria patients. The patients consisted of 18 children (ages <18) and 52 adults (ages ≥18) while the controls were made up of 3 children and 69 adults.

**Materials:** ***Serum samples:*** Serum samples were collected between October and December 2006, from 70 malaria patients who reported at the Minna General hospital. Serum samples were similarly collected from 70 healthy (no malaria parasites detectable) individuals.

**Methods**

- ***Determination of urea level in serum:*** The diacetylmonoxine method of Kaplan(13) was used.
- ***Determination of creatinine level:*** Serum creatinine concentration was determined as described by Thomas(14)
- ***Serum bilirubin (total and conjugated) level:*** Serum levels of conjugated and total bilirubin were determined according to the method described by Kaplan(13)
- ***Serum electrolytes (sodium and potassium):*** Flame photometry as described by Overman and Davis(15) was used to determine the levels of sodium and potassium in the serum.
- ***Serum concentration of alkaline phosphatase (ALP):*** The concentration of ALP was determined as described by Burtis and Ashwood(16)
- ***Glutamate-pyruvate transaminase (SGPT/ALT) and Aspartate aminotransferase (SGOT/AST):*** The serum concentrations of ALT and AST were determined according to the method of Wilkinson et al(17)
- ***Estimation of protein level in urine:*** The conventional Biuret method(18) was used in the estimation of urinary protein level.

**Results:**

Impairment of renal function as a result of malaria infection was assessed by measurement of serum concentrations of creatinine, urea, protein, sodium, and potassium, in both malaria patients and malaria free individuals while hepatic function was assessed by measurement of bilirubin, AST, ALT and ALP. Data obtained showed that 67.14% of patients (47 out of 70) had creatinine level above the 126µmole/L which is considered the upper limit of the normal range (Table 1). Three cases (4.29%) had creatinine levels well above 265µmoles/L and all three were female children aged 13, 10, and 5 years. The average creatinine level of children with malaria was 182.9µmoles/L while that of adults was 146.8µmoles/L (Fig. 3.). This difference was however not statistically significant ($p = 0.07$).

**Table 1. Descriptive analysis of serum creatinine, urea, bilirubin, AST, ALT, and ALP.**

| Parameters & normal values | Control | | | Patients | | | |
|---|---|---|---|---|---|---|---|
| | | | | Children <18 years | | Adults ≥18years | |
| | Male [N=32] Mean ±SD | Female [N=40] Mean ±SD | | Male [N=8] | Female [N=10] | Male [N=27] | Female [N=25] |
| | | | | No/% of patients | No/% of patients | No/% of patients | No/% of patients |
| Creatinine 72-126µmoles/L | 95.31±20.38 | 90.42±22.89 | >126µmoles/L | 5/7.14 | 8/11.43 | 21/30 | 13/18.57 |
| | | | ≥265µmoles/L | 0/0 | 3/4.29 | 0/0 | 0/0 |
| Urea 3.0-6.0mmoles/L | 4.88±1.92 | 5.20±2.48 | >6mMoles/L | 3/4.29 | 4/5.71 | 15/21.43 | 15/21.43 |
| Total bilirubin 3.0-20.0µmoles/L | 11.39 ±4.18 | 11.83 ±4.38 | >20.0 µmoles/L | 1/1.43 | 1/1.43 | 2/2.86 | 4/5.71 |
| | | | ≥51 µmoles/L | 0/0 | 0/0 | 0/0 | 1/1.43 |
| Conjugated bilirubin 2.0-14.0µmoles/L | 6.27±2.89 | 6.73±3.05 | >14µmoles/L | 1/1.43 | 0/0 | 1/1.43 | 3/4.29 |
| AST (SGOT) 0-45iu/L | 8.92±7.01 | 8.30±5.17 | >45iu/L | 0/0 | 0/0 | 0/0 | 1/1.43 |
| ALT(SGPT) 3-60iu/L | 13.67 ±7.16 | 13.68 ±5.65 | >60iu/L | 0/0 | 0/0 | 0/0 | 0/0 |
| ALP 35-71iu/L | 48.14±13.57 | 48.71±13.04 | >71iu/L | 4/5.71 | 11/15.7 | 18/25.71 | 17/24.29 |

The average serum levels of aspartate aminotransferase (AST) and glutamate-pyruvate transaminase (ALT) in adults were 13.14iu/L and 20.03iu/L respectively while the corresponding values in children were 8.55iu/L and 16.22iu/L. One way ANOVA showed significance difference ($p = 0.001$ for AST and $p = 0.026$ for ALT) between children and adult in each case (Fig. 3.).

Except for sodium and potassium, the serum concentrations of creatinine, urea, protein, conjugated and total bilirubin, AST, ALT, and ALP in malaria patients were significantly higher ($p<0.05$) than those of malaria free individuals (Fig. 1,2 and 4).

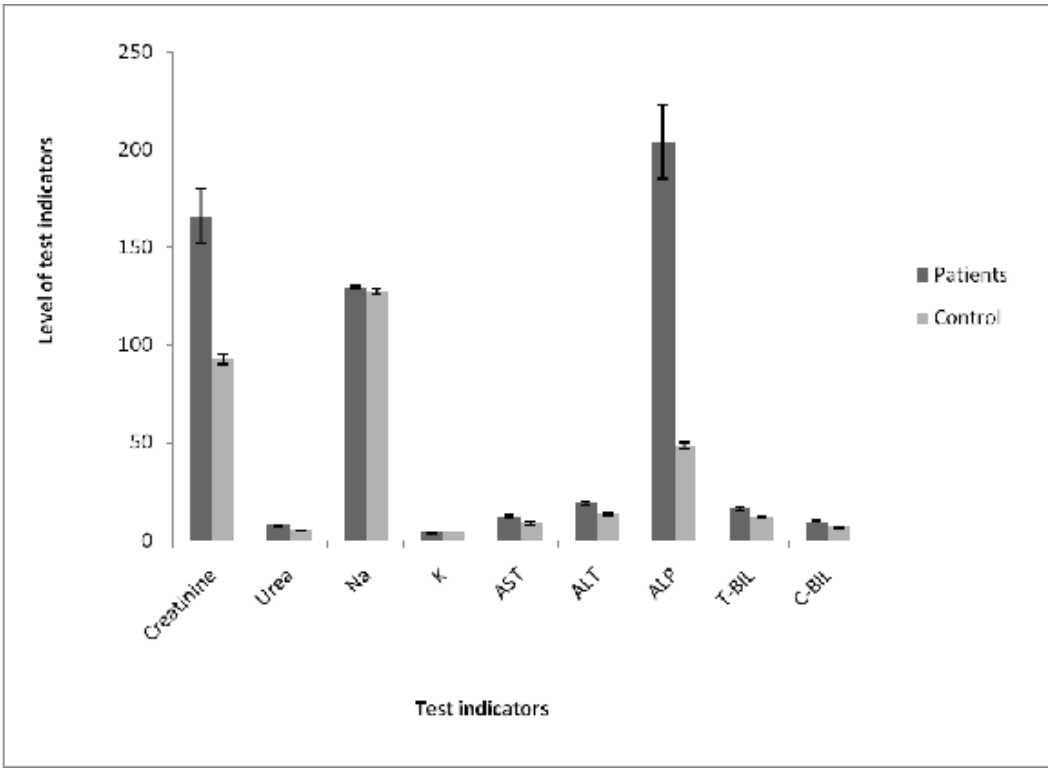


**Figure 1: Serum levels of some biochemical parameters in malaria patients and healthy individuals**
Na = Sodium, K = Potassium, AST (SGOT)= Aspartate aminotransferase, ALT (SGPT)= Glutamate-pyruvate transaminase, ALP = Alkaline phosphatase, T-BIL = Total bilirubin, C-BIL = Conjugated bilirubin

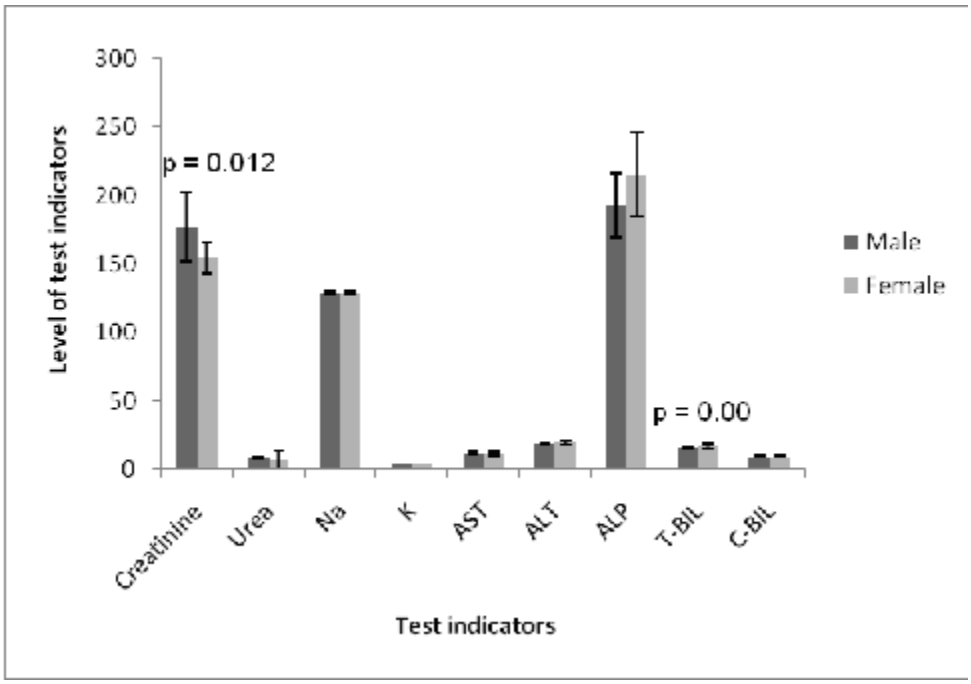


**Figure 2: Some serum biochemical parameters of male and female malaria patients. The test indicators carry the same meaning as in Figure 1 above.**

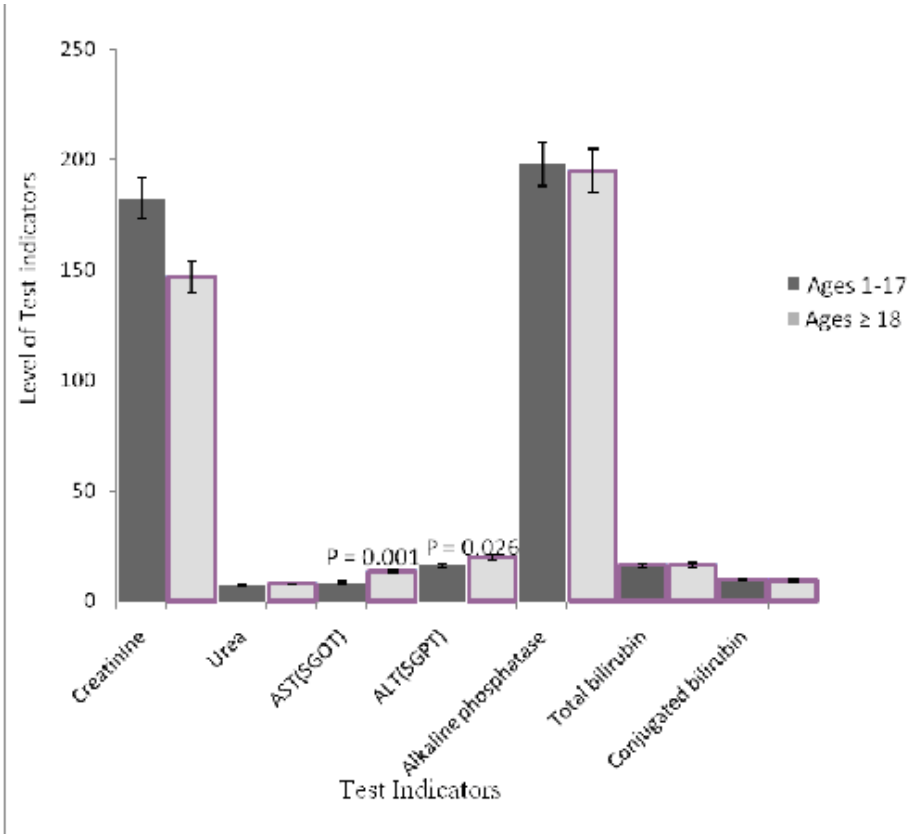


**Figure 3: Some serum biochemical parameters of children (ages 1-17 years) and adult (ages ≥ 18 years) malaria patients**

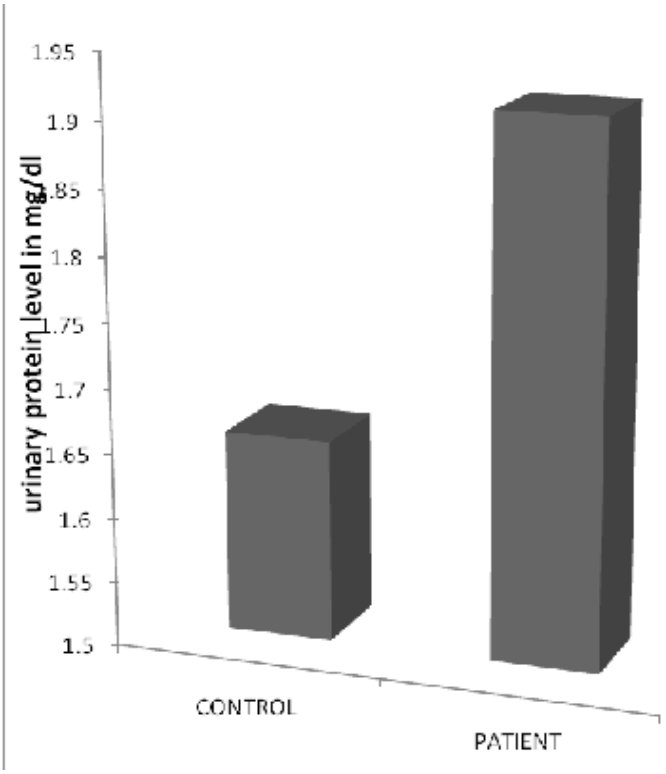


**Figure 4: Urinary protein levels of malaria patients and healthy individuals**

**Discussion:**

Malaria-associated renal and hepatic dysfunctions are complications of malaria and are increasingly becoming problems of great concern in malaria endemic countries like Nigeria. This study has shown that as high as 67.14% of the patients have serum creatinine levels above the upper limit of 126µ-moles/L while 52.86% have serum urea levels above the upper limit of 6mmoles/L (Table 1.). According to the World Health Organization,(12) serum creatinine level above 265 µmoles/L is an indication of acute renal failure (ARF). In the present study, 4.29% of the patients had creatinine levels well above 265 µmoles/L and could therefore be said to have ARF. If serum creatinine level >176.8 µmoles/L is used as an indication of renal failure as reported by Naqvi et al, (19) then the cases of ARF in our study is as high as 34.29%. Most reports show that ARF occurs in 1-5% of patients(2-4,12,20-22) although incidence of up to 60% has been reported.(2) All 3 cases of the ARF reported here occurred in female children of ages 13, 10 and 5 years. Reports of malaria-associated renal dysfunction in this region based largely on urinary protein levels have earlier been published.(7,11) Doubtful as the use of urinary protein level as indicator of kidney dysfunction may be, results of the present study have reinforced the conclusion contained in these earlier reports, more so when the 67.14% of patients with renal dysfunction obtained in this study is not far from the 52% (7) and 69.5% (11) obtained in these earlier studies. However, the observed higher incidence of renal dysfunction in females compared to males in these earlier reports was not the case in the present study (Fig. 2), although all three cases of acute renal failure occurred in females.

Hepatic dysfunction in malaria has been reported from parts of South East Asia.(10,22,23) Hepatic dysfunction is evident in this study as 11.43% and 7.15% of patients have serum levels of total bilirubin and conjugated bilirubin respectively above the upper limits of 20µmoles/L and 14µmoles/L respectively (Table 1). A comparative analysis between children and adults did not show any significant difference except in the levels of the transaminases (AST and ALT) in which the levels in the adults were significantly ($p < 0.05$) higher than the values in the children. These transaminases are marker enzymes for liver toxicity. The liver being the major site of drug metabolism, the higher level of these enzymes in adults compared to children may have been due to more prolonged use of drugs by adults leading to progressive damage of the liver in adult patients. Hyperbilirubinaemia (serum bilirubin ≥51 µmoles/L) of unconjugated type was observed in a patient (1.43%). The same patient was the only one with elevated level of AST. A large proportion of patients (71.41%) had levels of alkaline phosphatase (ALP) above the upper limit of 71 iu/L. While elevated levels of serum ALP are an indication of liver disease, it is difficult for us to say that the elevated levels of the enzyme observed in this study is due to malaria since the other parameters – bilirubin, AST, and ALT levels – do not have corresponding high levels. This however has raised an important question that needs to be addressed and that question is: What are the effects of malaria, antimalarials, and other drugs administered during malaria treatment on kidney and liver function indicators? A well designed experiment to provide answer to this question may lead to very significant findings and contribute immensely to our knowledge of the pathophysiology of malaria.

**Conclusion:**

We conclude that renal dysfunction and acute renal failure are a feature of malaria in Minna, North Central Nigeria. Impairment of liver function is also a manifestation of malaria in this area.

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