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Original Paper

Plasmodium Falciparum-Induced Kidney and Liver Dysfunction in Malaria Patients in Freetown, Sierra Leone

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ABSTRACT

This study was undertaken to investigate the effect of *Plasmodium falciparum* infection on kidney and liver function parameters in malaria patients in Freetown, Sierra Leone. Blood samples taken from 64 malaria patients and 64 non-malaria volunteers at Abanita and Blue Shield Hospitals, Freetown Sierra Leone between January to April, 2009 were examined. Changes in serum biochemical parameters were analysed using normal range values as baseline. Serum bilirubin, alkaline phosphatase (ALP), alanine aminotransferase (ALT) and aspartate aminotransferase (AST) concentrations were significantly elevated in falciparum malaria patients compared to their non-malaria counterparts which is an indication of defective liver function. Most of patients with falciparum malaria also have significantly high serum concentrations of urea, creatinine, sodium and potassium showing alteration in kidney function. This study suggests that malaria parasites could be responsible for derangement of kidney and liver functions in patients and could therefore contribute to organ damage in affected individuals if not treated.

Keywords: Kidney function, Liver function, Malaria, *Plasmodium falciparum*

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INTRODUCTION

Malaria is the most significant parasitic disease of human accounting for 300-500 million clinical cases annually (Amador and Patarroyo, 1996; Hart, 2004). It is defined as the presence of one or more complications in patient showing high parasitaemia of *Plasmodium falciparum* in their peripheral blood film (Yokoto and Calisei, 2006). The World Health Organization (WHO) estimates that 300-500 million cases of malaria occur and more than one million people die of malaria each year, especially in developing countries (WHO, 2000; Kilama and Ntoumi, 2009). In Africa, a child dies from malaria every 30 second. Malaria is responsible for about 48% of the total outpatient morbidity in Sierra Leone, 60% of children hospital referrals and a national mortality of 38% of all reported cases (Snow *et al*., 2005).

Malaria affects almost all organ systems but acute kidney and liver injury are the most dreaded complications of severe malaria. Renal involvement varies from mild protenuria to severe ozotemia associated with metabolic acidosis. The most common renal lesion of malaria is acute renal failure due to acute tubular necrosis and mild proliferatiave glomurulonephropathy (Mahakur *et al*., 1983). Various authors have reported close relationship between incidence of severe malaria and liver damage characterized by jaundice (Mishra *et al*., 1992; Dondorp and Day 2007). Jaundice results from intravascular haemolysis of parasitized erythrocytes, hepatic dysfunction and possibly an element of micro-angiopathic haemolysis associated with intravascular coagulation (Tredger and Sherwood, 1997).

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The aim of this study is to determine the occurrence of kidney and liver malfunction due to malaria infection in patients admitted at Abanita and Blue Shield Hospitals, Freetown Sierra Leone.

METHODOLOGY

Screening Test for Malaria Parasites

Sixty four (64) malaria patients and sixty four (64) non-malaria volunteers (aged between 20 and 40 years) who attended Abanita and Blue Shield Hospitals in Freetown Sierra Leone between January and April 2009 were examined. About one thousand (1000) patients (malaria and non-malaria) attended the Hospitals between this period and the study population was randomly selected using non-probability sampling method. Their blood was screened for malaria parasites to determine level of parasitaemia. Blood was taken directly from the patient's finger and used to prepare thin blood films.

The blood films were stained using Giemsa stain for the detection of normal parasitaemia and for determination of species. The prepared thin blood films were allowed to air dry and then fixed with 70% methanol for one minute. The stain was infiltrated under the slide and stain for 45min. After the end of the staining time, slides were rinsed briefly with tap water and allowed to drain in a vertical position. A field was selected (using the X10 objective) where the RBCs are in an evenly distributed monolayer followed by the X100 oil immersion objective. A minimum of 500 RBCs were counted and number of infected RBCs recorded. The percent of infected RBCs (parasitaemia) was determined by enumerating the number of infected RBCs in relation to the number of uninfected RBCs as follows:-

$$\% \text{ Parasitaemia} = \frac{\text{No of infected RBCs}}{\text{No of RBCs counted}} \times 100$$

Measurement of Kidney and Liver functions Parameters

Blood was collected by venepuncture into a clean plain sample bottles and allowed to clot for the preparation of serum. The clotted blood was centrifuged at 3000 rpm for 5 minutes after which the clear supernatant (serum) was separated from the pellet and kept frozen till required. All serum parameters were determined using Randox test kits with the aid of UV scam spectrophotometer. Serum bilirubin concentration was determined by the dimethyl sulphoxide principle described by Tietz *et al*. (1994) while the Para-Nitrophenyl phosphate (PNPP) method was used for determination of serum ALP concentration (Cathala *et al*., 1975). Serum ALT concentration was determined by the pyruvate method while AST concentration was measured using the oxaloacetate method (Christen and Metzler, 1985). Determination of urea concentration in blood was done by the use of Bertha lot method while creatinine level in blood was determined by the use of Jaffe method as described by Tietz *et al*. (1994). Serum sodium and potassium were measured using the flame photometer.

RESULTS

Table 1 show the parasite density of *Plasmodium falciparum* in the volunteers examined. Sixty-four (64) volunteers had parasitaemia in the range of 0.0001- 0.0005% and are regarded as non-malaria subjects while 64 participants with percentage parasitaemia in the range of 0.1 and 5.0 are regarded as having malaria in accordance with WHO standard. Figure 1 shows the level of elevation of urea, creatinine, sodium and potassium in the serum of malaria and non-malaria subjects. 32% of patients with falciparum malaria had high serum urea while urea was elevated in16% of their non-malaria counterparts.

Table 1: Parasite Density of *Plasmodium falciparum* in Malaria and Non-Malaria Volunteers

% Parasitaemia	No of Volunteers	Age range	Mean weight (kg)	Clinical Correlation
0.0001 - 0.0005	64	20-40	53	No malaria
0.1-0.9	14	20-40	58	Malaria
1.0 -1.9	20	20-40	60	Malaria
2.0-5.0	30	20-40	56	Malaria

The percentage of malaria patients with high serum creatinine was 36% compared to 18% in non-malaria patients. 30% of malaria patients had increased serum sodium concentration compared to 14% in non malaria volunteers. The percentage of malaria patients with elevated serum potassium was 34% while only 18% of non-malaria subjects had elevated serum potassium.

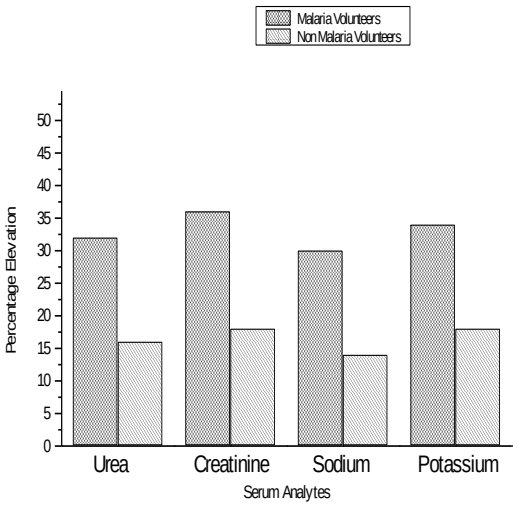

Figure 1: Elevation of Serum Analytes in Malaria and Non Malaria Volunteers

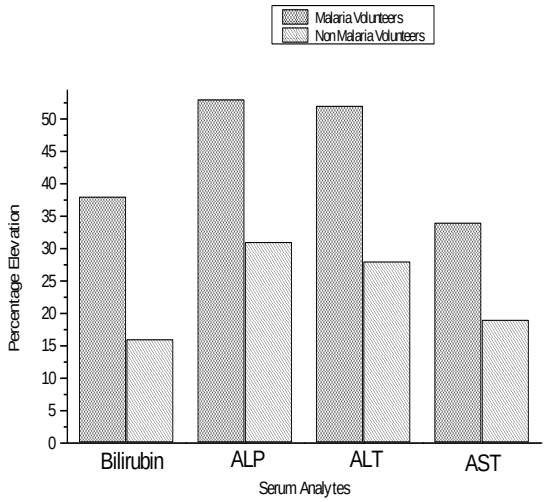

Figure 2: Elevation of Serum Analytes in Malaria and Non Malaria Volunteers

Figure 2 shows the level of elevation of bilirubin, ALP, ALT and AST in the serum of volunteers. 38% of patients with falciparum malaria had high serum bilirubin which was observed in 16% of their non-malaria counterpart. The percentage of malaria patients with high serum ALP is 53% compared to 31% in non-malaria volunteers. Elevated ALT was observed in 52% of malaria patients compared to 28% in non-malaria subjects. The percentage of malaria patients with elevated AST is 34% while only 19% of their non-malaria counterparts had elevated serum AST.

DISCUSSION

The significant increase observed in the serum urea and creatinine of malaria patients compared to their non- malaria counterpart in this study is an indication of impairment of renal function. This might be due to increased synthesis from the damaged kidney cells caused by malaria parasites (Orth and Ritz, 1998). Serum urea has been reported to increase in acute and chronic intrinsic renal disease (Cameron and Greger, 1998) and also when there is decreased effective circulating blood volume with decreased renal perfusion (Orth and Ritz, 1998). Increase in serum creatinine has also been reported to arise from intrinsic renal lesions, decreased perfusion of the kidney, or obstruction of lower urinary tract malaria infection (Cameron and Greger, 1998).

The observed elevation in serum sodium and potassium in malaria patients is an indication that the parasites might have altered renal function in the patients. Elevated serum sodium levels have been attributed to intravascular haemolysis which is associated to renal failure. Intravascular haemolysis of parasitized and non parasitized red blood cells has been considered as an important factor in causing mild to moderate kidney failure in man (Halpperin and Kamel, 1998).

The entry of merozoites of *P. falciparum* into the RBC depends on a specific receptor, thrombospondin. The parasite attaches to this receptor and taken into the RBC by invagination where it then matures. This leads to alteration of RBC membrane and reduction in its deformability (Sitprija 1988). It also enhances adherence of the RBC to endothelial cells and occlusion of microcirculation in organs (Rajapurkar, 1994). This interference with microcirculation leads to ischemic acute tubular necrosis in the kidney (Mahakur *et al*., 1983).

The observed elevation of serum bilirubin level in malaria patients in this study indicate increased red blood cell haemolysis. Elevated serum bilirubin has been associated with hepatocellular damage, biliary tract obstruction, haemolysis and neonatal jaundice (Renner, 1995).

Yokoto and Calisei (2006) also observed elevated serum bilirubin in malaria patient swhich they attributed to intravascular haemolysis and associated renal failure. Majority of the patients showed elevation in serum activities of the three enzymes (ALP, ALT and AST) indicating liver damage. Elevation of serum ALP activity has been attributed to hepatobiliary diseases (Moss and Rosalki, 1996) while Increase in serum ALT and AST activity has been reported in conditions involving necrosis of hepatocytes (Macfarlane *et al*., 2000).

The observed derangement in liver function in malaria patients in this study may result from alteration in blood flow through the organs as parasitised red blood cells adhere to endothelia cells, blocking the sinusoids and obstructing the intrahepatic blood flow. Many workers have also reported histopathological changes in malaria patients which include hepatocyte necrosis, cholestasis, bile stasis and granulomatous lesions (Mishra *et al*., 1992; Saissy *et al*., 1994; Marsh *et al*., 1995). The bile stasis might result due to impairment of bilirubin transport which may lead to reticulo-endothelial blockage and disturbance of hepatocyte microvilli (Trager and Jensen, 1976). Baheti *et al*. (2003) and Saissy *et al*. (1994) investigated histopathological changes of the liver in malaria patients and observed kupffer cell hyperplasia, malaria pigmentation, portal infiltration and liver cell necrosis all of which are indications of hepatic cell alteration.

CONCLUSION

This study shows that malaria infection caused derangement in kidney and liver activities characterized by alteration in their functions. Therefore, adequate prevention and control measures should be employed for management of falciparum malaria so as to reduce incidence of tissue damage arising from malaria infection. Use of antioxidants and protease inhibitor may offer clinical benefit by preventing organ complications due to endothelial apoptosis.

REFERENCES

Amador R and Patarroyo ME (1996). Malaria Vaccines. *J Clin Immunol*.**16**: 183-189.

Beheti R, Laddha P and Gehlot RS (2003). Liver Involvement in Falciparum Malaria: A Histo-pathological Analysis. *J Indian Acad Clin Med*. **4**: 35-38.

Cameron JS and Greger R (1998). Renal Function and Testing of Function. *Oxford Textbook of Clinical Nephrology*. Davison AM, Cameron JS, Grunfeld JP, Kerr DNS, Rits E, Winearl GC. Eds. Pp: 36-39.

Cathala G, Prunell C and Dehapple A (1975). Alkaline Phosphatase. *J Biochem*. **290**: 6046-6053.

Christen P and Metzler DE (1985). *Aminotransferases*. Wiley Interscience Inc. New York. Pp 49-60

Halpperin ML and Kamel KS (1998). Electrolyte Quinter: Potassium. *Lance*t. **352**: 135-140.

Dondorp AM and Day NP (2007). The Treatment of Severe Malaria. *Trans R Soc Trop Med Hyg.* **101**: 633–634.

Hart DH (2004). *The Origin of Malaria: Mixed Message From Genetic Diversity* (2nd Edition). McDonald Publishers, New York. Pp: 15-22.

Kaplan MM (1972). Alkaline Phosphatase. *N Engl J Med*. **280**: 200-202.

Kilama W and Ntoumi F (2009). Malaria: A Research Agenda for the Eradication Era. *Lancet.* **374**:1480–1482.

Macfarlane I, Bomford A and Sherwood RA (2000). *Liver Diseases and Laboratory Medicine*. ACB Ventures Publications London. Pp: 134-138.

Mahakur AC, Panda SN, Nanda BK, Bose TK, Satpathy SR and Misra Y(1983). Malaria Acute Renal Failure. *J Assoc Phys India*. **31**:613-616.

Marsh K, Forster D, Waruiru C, Mwangi I, Winstanley M, Marsh V, Newton C, Winstanley P, Warn P, Peshu N, Pasvol G and Snow R (1995). Indicators of Life threatening Malaria in African Children. *N Engl J Med*. **332**:1399-1404.

Mishra SK, Mohanty S and Das BS (1992). Hepatic Changes in *Plasmodium falciparum* Malaria. *Indian J Malaria*. **29**: 167-171.

Moss DW and Rosalki SBv(1996). *Enzyme Tests in Diagnosis*. 2nd Edition. Edward Arnold. London. Pp: 201-213.

Orth SR and Ritz E (1998). The Nephritic Syndrome. *N Engl J Med*. **338**: 1202-1211.

Renner EL (1995). Liver Function Test. *Balliere J. Clin Gastroenterology* **9**: 661-772.

Rajapurkar MM (1994). Renal Involvement in Malaria. *J Postgrad Med*. **40**:13-134.

Saissy JM, Vitris M, Diatta B, Kempf J, Adam F and Sarthou JL (1994). Severe Malaria in African Adults Living in a Seasonal Endemic Area. *Intensive Care Med*. **20**:437-441

Sitprija V (1988). Nephropathy in Falciparum Malaria. *Kidney Internatn.* **34**:867-869

Snow RW, Guerra CA, Noor AM, Myint HY and Hay SI (2005). The Global Distribution of Clinical Episodes of *Plasmodium falciparum* Malaria. *Nature*. **434**: 214–217.

Tietz NW, Pruden EL and Siggaard-Andersen O (1994). In: *Tietz Textbook of Clinical Chemistry* (Burtis C.A. and Ashwell E.R. eds.) W.B Saunders Company London. Pp: 1354-1374.

Trager WJB and Jensen T (1976). Human Malaria Parasite in Continuous Outline. *Malaria Research* **5**: 673-675.

Tredger JM and Sherwood RA (1997). The Liver: New Functional, Prognostic and Diagnostic Tests. *Ann Clin Biochem*. **34**: 121-141.

World Health Organization, Division of Control of Tropical Diseases (2000). Severe Falciparum Malaria. *Trans R Soc Trop Med Hyg*. **94**:1-90

Yokoto USC and Calisei T (2006). Malaria Parasite and their Relationships with their Host. *Malaria Res.* **44**: 265-273.