GLOBAL JOURNAL OF MEDICAL SCIENCES VOL. 2, NO. 2: 2003: 103 - 106
COPYRIGHT(C) BACHUDO SCIENCE CO LTD. ISSN 1596 - 2911. PRINTED IN NIGERIA.


# SERUM UREA AND CREATININE LEVELS IN NIGERIAN HUMAN MALARIA PATIENTS

E. C. ONYENEKE, A. M. OGHENEJODE, E. O. ALUMONAH, C. J. OKONKWO and N. A. OKPOGBA.

(Received 30 September 2001; Revision accepted 15 May 2003)

ABSTRACT

Serum urea and creatinine levels were determined in malaria patients infected with *P. falciparum*. Serum urea levels decreased significantly ($P<0.05$) in both mild (4.10 ±1.10 mmol/L) and moderate (4.40 ±1.40 mmol/L) parasitaemia when compared to control subjects (5.50 ±1.40 mmol/L). On the other hand, serum creatinine levels decreased in mild parasitaemia (82.00 ±16.87 µmol/L) but increased significantly in moderate (94.30 ± 24.14 µmol/L) and severe parasitaemia (113.90 ± 46.30µmol/L; $P<0.05$. Control; 88.30 ± 11.87 µmol/L). The relationship of the results to protein metabolism and kidney function is discussed.

**KEYWORDS:** Malaria, Serum urea and creatinine, Nigeria)

## INTRODUCTION

Malaria remains one of the most significant infectious diseases (Schlagenhauf and Steffen, 1994), which has plagued mankind for thousands of years (WHO, 1992). It is by far the most important insect-borne disease that infects humans (Veeken, 1992). There are some 300-500 million clinical cases of malaria each year, 90% of them in Africa (Freedman, 1991) and 1.5-3 million deaths, one million of them, African children under the age of five (WHO, 1992). Malaria is holoendemic in parts of Africa, Asia and South and Central America and causes huge mortality and morbidity (Walton *et al*, 1986).

The physiology of severe *Plasmodium falciparum* is characterized by anaemia, jaundice, liver failure, acute renal failure and sometimes even death (Hall, 1977). Malarial infection leads to increased glucose consumption (Sherman and Tanigoshi, 1974; Kreier, 1980). Amino acids and ATP depletion is observed as infected erythrocytes take them up (Peters, 1987; Wernsdorfer and McGregor, 1988). There is significant increase in the total lipid levels (Ononogbu and Onyeneke, 1983), which is contributed mainly by the phospholipid fraction. In infants, albumin concentration falls while there could be deficiency in certain vitamins (Thurnham *et al*, 1983). Parasitaemia leads to a significant decrease in sodium levels but increase in potassium levels and these changes are dependent on the degree of parasitaemia (Alumanah *et al*, 1994). The activities of certain enzymes such as Glucose – 6 – phosphate dehydrogenase, acetyl cholinesterase and lactate dehydrogenase were also found to be raised during pathological infection. (Wernsdorfer and McGregor, 1988).

A common pathological change also observed in human and animal malaria is fatty infiltration in liver parenchyma cells (Fletcher and Maegraith, 1966) and this often leads to alteration in the metabolism of certain metabolites in the liver. In chronic cases, there is severe organ damage affecting the kidney, liver, brain and gastro-intestinal tract (Wernsdorfer and McGregor, 1988). This condition leads to variations in the overall metabolism of the system and in most cases leads to death. Significant variations have been observed in many metabolites (Kreier1980; Ononogbu and Onyeneke 1983; Alumanah *et al* 1994) either as a result of the inability of the liver to catabolize or transform them or the inability of the kidney to function properly. It is in this regard that the authors examined the serum levels of urea and creatinine during malarial infection in Nigerian patients.

## MATERIALS AND METHODS

Blood samples were collected from 150 malaria patients of both sexes who reported at Universities of Benin, Nigeria and Nnamdi Azikiwe Teaching Hospitals in Nigeria. The patients were tested for infection and parasitaemia, with only 126 of them testing positive as carriers of the parasite. Degree of infection was determined by the degree of parasitaeamia following examination of Giemsa – stained blood smears for parasites. The parasite was identified as *Plasmodium falciparum*. The degrees of infection were categorized as mild,

E. C. ONYENEKE , Department of Biochemistry, University of Benin, Benin-City, Nigeria
A. M. OGHENEJODE, Department of Biochemistry, University of Benin, Benin-City, Nigeria.
E. O. ALUMONAH. Department of Biochemistry, University of Nigeria, Nsukka, Nigeria
C. J OKONKWO, Dept. of Human Biochemistry, College of Health Science, Nnamdi Azikiwe University, Nnewi, Nige
N. A. OKPOGBA, Dept. of Human Biochemistry, College of Health Science, Nnamdi Azikiwe University Nnewi, Niger

moderate and severe. All patients were of Nigerian origin.

Venous blood (5.0ml) samples was collected by venipuncture and immediately added to a non-heparinized container. They were allowed to stand for 1 hour to retract and later centrifuged at 10,000g for 5 mins at 4°C. The supernatant serum was collected into venoject tubes.

Twenty healthy volunteers were used as controls, with their blood smears showing no *P. falciparum*. These volunteers were also not known to suffer any patho-physiological conditions that affect serum urea and creatinine levels. All data were statistically analyzed by Duncan and t-Tests.

Serum urea and creatinine levels were estimated using Ames Sera-pak ® automated method (Ames, 1981). Values were read off using Chemistry Analyzer RA-50 (Technicon Ames) at 37°C against control and standard sera (Ames SERA-CHEK ™)

## RESULTS

Serum levels of urea and creatinine were determined in one hundred and twenty-six malarial patients and the results are as shown in Table 1.

Serum urea levels were found to decrease significantly ($P<0.05$) in both mild (4.10 ± 1.10 mmol/L) and moderate parasitaemia. (4.40 ± 1.40mmol/L) when compared to the control (5.50 ± 1.40mmol/L). Values of creatinine obtained for females were also found to be lower than that of their corresponding male counterparts (mild: female – 3.93 ±1.18; male – 4.20 ± 1.17mmol/L; moderate: female –3.75 ± 1.64; male –5.00 ± 0.84mmol/L). During severe parasitaemia, the serum urea levels did not differ significantly (5.70 ± 3.13mmol/L) when compared to the control However, the values obtained for females (3.75 ± 1.64mmol/L) were found to be significantly lower ($P<0.01$). On the other hand, male subjects showed significantly raised levels of urea (7.40 ± 3.20mmol/L; $P<0.01$) for the same degree of parasitaemia.

Serum creatinine levels were found to decrease in mild parasitaemia (82.00 ± 16.87 µmol/L) but increased significantly in moderate (94.30 ± 24.74µmol/L) and severe parasitaemia (113.90 ± 46.30 µmol/L; $P<0.05$). Values obtained for females were lower than that recorded for males in mild, moderate and severe parasitaemia and they were significant for the corresponding values when compared to the control.

**Table 1: Mean Serum Urea and Creatinine Levels in Malaria Patients**

| Degree of Parasitaemia | Samples size (N) | Urea (mmol/L) | Creatinine (µmol/L) |
|---|---|---|---|
| **Control** | | | |
| Pooled sample | 20 | 5.50 ±1.04 | 88.30 ± 11.87 |
| Females | | (3.3-7.5) | (61-107) |
| | 10 | 5.35 ± 0.81 | 80.70 ± 8.94 |
| | | (4.1 – 6.8) | (61 - 90) |
| Males | 10 | 5.71 ± 1.17 | 95.20 ± 8.97 |
| | | (3.3-7.5) | (81 - 107) |
| **Mild** | 48 | 4.10 ± 1.10* | 82.00 ± 16.87* |
| Pooled sample | | (1.8-6.4) | (59-135) |
| Females | 30 | 3.93 ± 1.18** | 74.40 ± 13.25* |
| | | (1.8-6.4) | (59-104) |
| Males | 18 | 4.20 ±1.17** | 87.57 ± 17.99* |
| | | (2.6-6.2) | (61 - 135) |
| **Moderate** | 52 | 4.40 ± 1.40* | 94.30 ± 24.74* |
| Pooled sample | | (1.9-6.5) | (54-129) |
| Females | s19 | 3.75 ± 1.64** | 76.75 ± 22.65 |
| | | (1.9-6.2) | (54-109) |
| Males | 33 | 5.00 ± 0.84 | 108.40 ± 15.69** |
| **Severe** | | (4.0-6.5) | (82-129) |
| Pooled sample | 26 | 5.70 ± 3.13 | 113.90 ± 46.30* |
| | | (2.2-11.3) | (60-207) |
| Females | 11 | 3.55 ± 0.93** | 87.0 ± 22.06 |
| | | (2.2-4.8) | (60-117) |
| Males | 15 | 7.40 ± 3.20** | 133.0 ± 46.13** |
| | | (3.3-11.3) | (88-207) |

Values represent mean ± SEM. * $P< 0.05$. **$P< 0.01$. Numbers in parenthesis represent the range values.

## DISCUSSION

*Plasmodium falciparum*, the most serious form of malaria is responsible for over 90% of infection among Nigerians (WHO, 1992).

Various pathological and physiological changes are known to be associated in animals with malaria infection. These include hypertrophy or enlargement of spleen and liver, appearance of hemozoin pigments, anaemia due to destruction of erythrocytes, and liberation of toxic substances in plasma (Riley and Deegan, 1960). These changes are reversible when anti-malarial drugs were used except in terminal stages (Lee *et al*, 1988). The amount, specific gravity, colour and total solids of urine are generally increased in malaria. There is increased excretion of nitrogen and at first decreased elimination of phosphates. Infected erythrocytes take up amino acids at a greater rate than uninfected cells and thus there is a decrease in the accumulation of free amino acids (Wernsdorfer and McGregor, 1988). Urea is the end product of protein metabolism and the principal form in which nitrogen is excreted by the body. Urea is formed in the liver and excreted by the kidneys. During malarial attack, a decrease in the plasma protein levels has been observed (Raphael, 1983) and albumin concentration falls (Thurnham *et al*, 1983). Protein deficiency is very high, and this is due to the fact that there is excessive body protein catabolism in fever, one of the symptoms of malaria.

Episodes of acute malaria infection are thought to cause an increase in the levels of serum urea and creatinine (Phillips, 1984).

The results obtained in the present study show that serum urea levels in females decreased significantly ($P< 0.05$) in both mild and moderate parasitaemia, but increased in males ($P< 0.01$) only in severe parasitaemia when compared to the control. Values obtained for females were also found to be lower than their male counterparts.

Creatinine is found in muscle and blood and is excreted in the urine. It is a nitrogenous end product of muscle metabolism, the production of which is a function of total muscle mass and is therefore fairly constant within a given individual. It is freely filtered by the renal glomeruli (Marima-Matarira, 1985). Elevated serum creatinine is a result of failure of the kidney to perform some of its function of clearing the body of waste products of metabolism. Renal failure results in high serum creatinine levels (Marima- Matarira, 1985), and this would occur as one of the complications under severe falciparum malaria.

Severe parasitaemia causes fatty infiltration in the liver parenchymal cells (Fletcher and Maegraith, 1966), and this often leads to alterations in the metabolism of certain metabolites in the liver.

In Thailand, Phillips (1984) showed that about a third of the adult patients with cerebral malaria had elevated levels of urea and creatinine. Serum creatinine levels were found from this study to decrease significantly during mild parasitaemia (82.00 ± 16.87µmol/L) but increased significantly in both moderate (94.30 ± 24.74 µmol/L; $P< 0.05$) and severe parasitaemia (113.90 ± 46.30 µmol/L; $P< 0.05$) when compared to control subjects (88.30 ±11.87 µmol/L).

Our results thus corroborates earlier studies by Delmont *et al* (1994) and Phillips (1984) who indicated elevated levels in serum creatinine and urea in patients with severe falciparum malaria. Both urea and creatinine are derived ultimately from dietary protein, but their differing metabolic pathways suggest that their rates of excretion are relatively independent, although urea levels are useful indices of the rate of protein breakdown while production of creatinine is a function of total muscle mass. This work therefore complements earlier studies using animal malaria.

## REFERENCES

Alumanah, E.O., Onyeneke, E. C., Garuba, H. I. and Onoagbe, I. O., 1994. Plasma Electrolyte Levels in Human Malaria. J. Innov. Life Sci., 1:14-19

Ames., 1981. Ames Division, MILES Ltd., Stoke Court, Stoke Poges, Bucks England, Monograph 6510ADI and 6740ADI

Delmont, J., Broqui, P., Poullin P. and Bourgeade, A., 1994. Harbour Acquired Plasmodium facilparum malaria. The lancet, 344 (891): 330.

Fletcher, K. A. and Maegraith, B.G., 1966. Some Aspects of the Pathogenesis of malaria, Bull. Soc. Path. Expt., 59:626-634

Freedman, O. D., 1991. Imported Malaria here to stay. WHO Epidemiology Record., 22:239-42.

Hall, A.P., 1977. The Treatment of Severe Falciparum Malaria. Trans. R Soc. Trop. Med. Hyg., 71:367-379.

Kreier, J. P., 1980. Malaria. Acad. Press N.Y. 3: 111-162

Lee, P., Duke, V. G., and Ye, Z., 1988. X-ray Micro Analysis of Plasmodium falciparum and Infected Red Blood Cells: Effects of Qunighaosu and Chloroquine on Potassium, Sodium and Phosphorus Composition. Ann. J. Trop. Med. Hyg., 39 (2): 157-165.

Marima – Matarira, H.T., 1985. Urea, Creatinine and Electrolytes in Zimbabwean Males.Cent. Afr. J.Med. 31 (12): 21.

Ononogbu, I.C. and Onyeneke, E.C., 1983. Plasma Lipid Changes in Human Malaria. Tropenmed. Parasitol., 34:193-6

Peters, W., 1987 Chemotherapy and Drug Resistance in Malaria. Acad. Press, Lond. (1): 47-63

Phillips, R.E., 1984. Failure of Chloroquine Erythromycin and Chloroquine TetracyclineCombinations in the Treatment of Chloroquine Resistant Falciparum Malaria in Eastern Thailand..Lancet 1:300-302

Raphael, S., 1983. Lynchs Medical Laboratory Technology W.B. Saunders company, Toronto pp 514

Riley, M. V. and Deegan, T., 1960. The Effect of Plasmodium berghei Malaria on Mouse Liver Mitochondria. Biochem. J., 76: 41-56

Schlagenhauf, P. and Steffen, R., 1994. Standby Treatment of Malaria in Travellers: A Review. J. Trop. Med. Hyg., 97 (3) : 151-155

Sherman, I.W. and Tanigoshi, L., 1974. Glucose Transport in the Malarial (Plasmodium Lophurae) Infected

Thurnham, D. I., Oppendheimer, S. J. and Bull. R., 1983. Riboflavin Status and Malaria in infants in Papua New Guinea. Trans. Roy. Soc. Trop. Med. Hyg., 77:423-424

Veeken, H. B., 1992. Insecticide - Impregnated Bed Nets for Malaria Control: A Review of Field Trails. Bull. Organ. 70 (3): 293-96 WHO IRLTH

Walton, J., Beeson, P. and Bodley, R., 1986. Oxford companion to Medicine. Oxford University Press, p5.

Wernsdorfer, H.W. and McGregor, I., 1988. Malaria: Principles and Practice of Malariology. Churchill Livingstone, Edinburgh, Lond. Melbourne N.Y. (I): 61-67 and (II) 1263: 709-753.

WHO., 1992. World Health Organisation Guidelines for the Dagnosis and Treatment of Malaria in Africa. Afro. Techn. Papers. (22)1:3-33