Malaria is a disease caused by a parasite (*Plasmodium falciparum*) that lives part of its life in humans and part in mosquitoes, and it remains one of the major killers of humans worldwide, threatening the lives of more than one-third of the world population. This study determined the effect of malaria infection on the kidney function and lipid profile of malarial patients and normal individuals. This was done by carrying out tests on markers of kidney function – creatinine and electrolytes (Sodium, Potassium, Chloride and Bicarbonate ions) – and also on the concentration of LDL- and HDL-cholesterol, triacylglycerol and VLDL as marker for lipid profile estimation. The results obtained by us showed that there was no significant difference (P < 0.05) in either of the tested electrolytes of malaria infected patients when compared with normal individuals. The only significant variations were found in urea and creatinine. Urea concentration was significantly higher (41.70 ± 6.11 a) in malaria patients when compared with normal individuals (30.00 ± 21.21 b), while creatinine concentration was significantly lower (0.863 ± 0.233 b) in malaria patients when compared with normal individuals (1.00 ± 0.707 a). In malaria infected patients, the serum status of total and HDL-cholesterol and VLDL was higher than in normal individuals. The high value of urea in malaria infection cases was attributed to excess breakdown of red blood cells and low urea clearance through the kidney. The low level of creatinine could be due to either an increase in its clearance or decreased muscular activities that occur in malaria infection.

**Keywords:** Malaria parasite, urea, creatinine, cholesterol, triacylglycerol.

**INTRODUCTION**

Malaria is a life-threatening parasitic disease transmitted through the bite of a female anopheles mosquito (1). It is a disease that can be treated in just 48 hours,
yet it can cause fatal complications if diagnosis and treatment are delayed (2). Malaria is caused by *Plasmodium vivax*, *Plasmodium falciparum*, *Plasmodium ovale* and *Plasmodium malariae*.

Approximately 50% of the Nigerian population experience at least one episode of malaria yearly (3). Typically, malaria produces fever, headache, vomiting and other flu-like symptoms. If drugs are not available for treatment or the parasites are resistant to them, the infection can progress rapidly to become life-threatening (4, 5). Malaria parasites are developing unacceptable levels of resistance to one drug after another and many insecticides are no longer useful against mosquitoes transmitting the disease (6). Sodium ion (Na\(^+\)) is the major cation of extracellular fluid and as such it plays a central role in the maintenance of the normal distribution of water and osmotic pressure in various fluid compartments (7). On the other hand, potassium ion (K\(^+\)) is the major intracellular cation, with an average cellular concentration in the cell tissue of 150 mmol/L (8). In addition to water balance, these electrolytes play an important role in pH maintenance, heart regulation and muscle function, electron transfer reactions as well as serving as cofactors for enzymes (9).

Since Na\(^+\) and K\(^+\) have been shown to be highly indispensable in water homeostasis, which is fundamental to the survival of all organisms, it is necessary to estimate the levels of these electrolytes and kidney function in all cases of falciparum malaria (10) and in severe malaria infection for better management of such patients.

Hepatocellular damage often associated with severe and acute malaria parasite infections impairs biochemical processes, leading to alterations in lipid and lipoprotein patterns (11). Likewise, hyperbilirubinemia, increased plasma levels of aspartate transferase (AST) and alanine transferase (ALT) activities are strong evidence of gross hepatocytic dysfunction in patients with *P. falciparum* infection (12, 13).

Relationships between serum lipid profile and severity of malaria and other parasitic infections in human have drawn the attention of various research authors and have been proposed as a basis for diagnosis and severity of the disease (14). The present study seeks to investigate the serum lipid profile and kidney function of individuals with malaria infection.

**MATERIALS AND METHOD**

**BLOOD SAMPLE COLLECTION**

Blood samples of malaria patients were obtained from Michael Okpara University of Agriculture, Umudike Staff Clinic in Umuahia, Abia State, Nigeria. For the test group, prior to blood collection, our team had visited the hospital and
informed the medical doctor about the research. After diagnosing patients for malaria, the medical doctor asked for their approval to take a blood sample for research purposes. Those who agreed have duly completed and signed a consent form, and provided their blood samples to our team. Blood samples were spun at 3000 rpm for 10 minutes to obtain serum using a Bench top centrifuge (800B).

CONTROL GROUP

For the control group, which comprised individuals of Michael Okpara University of Agriculture Umudike, the study advert made public the subjects nominated from those who replied to the announcement. A two days seminar was organized for them, providing thorough details on the purpose of the research work. Afterwards, each participant received an informed consent form and all those who returned it correctly filled and signed were screened for enrolment. Prior to biochemical analysis, malaria test (Rapid Diagnostic Test) was carried out on controls to ensure they do not carry the malaria parasite. Members of the control group were also screened to ensure that two weeks before the experimental day they were not on any anti malaria therapy. Enrolment criteria included being older than 18 years and absence of any known disease, alcohol and tobacco consumption, and pregnancy (in females).

DETERMINATION OF SERUM UREA CONCENTRATION

The method of Chaney and Marbach (15) was used. It is based on the principle that urea in the serum is hydrolyzed to ammonia in the presence of urease. The ammonia is then measured spectrophotometrically by Berthelot’s reaction.

DETERMINATION OF SERUM CREATININE CONCENTRATION

The method of Taussky (16) was used. Creatinine reacts with picric acid in alkaline medium to form a red complex of creatinine picrate.

DETERMINATION OF POTASSIUM ION

Potassium is determined colorimetrically in human serum and plasma using the method AOAC (17).

DETERMINATION OF SODIUM ION

The determination of sodium is based on the Teco Sodium kit by the method of AOAC (17).
DETERMINATION OF CHLORIDE ION

Chloride ion procedure is a direct method based on a modification of Skeggs et al., (18). Chloride ions form a soluble, non-ionized compound with mercuric ions and displace thiocyanate ions from non-ionized mercuric thiocyanate. The released thiocyanate ions react with ferric ions to form a colour complex that absorbs light at 480 nm. The intensity of the colour produced is directly proportional to the chloride ion concentration.

DETERMINATION OF BICARBONATE ION

The determination of bicarbonate ion was based on the Teco bioassay bicarbonate kit, which is also based on the method described by Tietz et al. (19).

TOTAL CHOLESTEROL ESTIMATION

The serum total cholesterol was determined using the enzymatic method of Allain et al. (20).

HIGH DENSITY LIPOPROTEIN ESTIMATION

The high density lipoprotein (HDL) cholesterol was estimated using the method of Grove (21).

TRIACYLGLYCEROL CONCENTRATION ESTIMATION

Serum triacylglycerol (TAG) was estimated via the colorimetric method of Tietz (22).

LOW DENSITY LIPOPROTEIN ESTIMATION

The low density lipoprotein (LDL) cholesterol was estimated using the method of Assmann et al. (23).

VERY LOW DENSITY LIPOPROTEIN ESTIMATION

Very low density lipoprotein (VLDL) cholesterol was estimated using the following formula: VLDL = total cholesterol – (HDL + LDL).

STATISTICAL ANALYSIS

Statistical analysis was carried out using the Student T test at 95% confidence level.
RESULTS AND DISCUSSION

The mean value of urea concentration was significantly increased \((P < 0.05)\) in malaria patients (test) when compared with normal individuals (controls), thus giving the value 41.70 as serum urea concentration for the test group and 30.00 for the control group. The mean value for creatinine was significantly decreased \((P < 0.05)\) in test patients when compared to controls, thus giving the value 0.86 as serum creatinine concentration for the test group and 1.00 for the control group.

![Urea and creatinine concentration](image)

Fig. 1 – Mean urea and creatinine concentrations in the sera obtained from malaria patients and normal individuals.

The mean value for sodium ion did not reveal any significant change \((P < 0.05)\) in test patients when compared to controls, thus giving the value 139.50 as serum sodium ion concentration for the test group and 140.00 for the control group. The value for potassium ion did not reveal any significant change \((P < 0.05)\) in test patients when compared to controls, thus giving the value 4.15 as serum potassium ion concentration for the test group and 4.00 for the control group. Bicarbonate ion concentration did not reveal any significant change \((P < 0.05)\) in test patients when compared to controls, thus giving the value 26.80 as serum bicarbonate ion concentration for the test group and 25.50 for the control group. The value for chloride ion did not reveal any significant change \((P < 0.05)\) in test
patients when compared to controls, thus giving the value 105.40 as serum chloride ion concentration for the test group and 103.50 for the control group.

Fig. 2 – Mean sodium, potassium, bicarbonate and chloride ion concentrations in the sera obtained from malaria patients and normal individuals.

The mean value for cholesterol did not reveal any significant change (P < 0.05) in test patients when compared to controls, thus giving the value 213.00 mg/dL as serum cholesterol concentration for the test group and 210.00 mg/dL for the control group. The mean value for triacylglycerol did not reveal any significant change (P < 0.05) in test patients when compared to controls, thus giving the value 144.70 mg/dL as serum triacylglycerol concentration for the test group and 150.00 mg/dL for the control group. The mean value for low density lipoprotein significantly decreased (P < 0.05) in the malaria patients when compared with normal individuals, thus giving the value 53.7 mg/dL as serum low density lipoprotein concentration for the test group and 130.0 mg/dL for the control group. The mean value for high density lipoprotein significantly increased (P < 0.05) in malaria patients when compared with normal individuals, thus giving the value 109.1 mg/dL as serum high density lipoprotein concentration for the test group and 60.0 mg/dL for the control group. The mean value for very low density lipoprotein significantly increased (P < 0.05) in malaria patients when compared with normal individuals, thus giving the value 37.2 mg/dL as serum very low density lipoprotein concentration for the test group and 22.5 mg/dL for the control group.
FIG. 3 – Mean cholesterol, triacylglycerol, LDL, HDL and VLDL concentrations in the sera obtained from malaria patients and normal individuals.

**DISCUSSION**

Malaria is a life-threatening parasitic disease transmitted through the bite of a female anopheles mosquito. It causes fatal complications if diagnosis and treatment are delayed. The present study shows the effect of malaria parasite infection on kidney function of individuals. Kidney function tests are routine tests that are used for the detection and management of renal impairments.

Urea was significantly higher ($P < .05$) in malaria patients when compared to normal individuals, which agrees with the work of Barber (24). Urea is a waste product of chain breakdown of amino acids that make up proteins, and these amino acids are metabolized and converted in the liver to ammonia, carbon dioxide, water and energy (25). Ammonia is excreted from the body in the form of urea through the kidney of living organisms and it is the major organic component of human urine. This increase in urea can be attributed to excessive haemolysis by malaria parasites during their erythrocyte life cycle stage, which further results in the breakdown of globin protein of hemoglobin and its amino acid monomers that are further converted to urea (26). As a result, a decreased glomerular filtration rate of the kidney may be seen, thereby increasing urea concentration in the blood.

Creatinine was observed to be significantly lower ($P < 0.05$) in malaria patients when compared with normal individuals. Creatinine is the breakdown product of creatine phosphate in muscles and is fairly constant in its production rate by the body. It only varies depending on the muscle mass of the body (27). The creatinine is removed mainly through the kidney by the process of glomerular
filtration, but also via proximal tubular secretion; the difference in creatinine concentration can be attributed to the various muscle sizes or decreased muscular activity of the malaria patients and normal individuals.

According to the result of this present study, there was no significant effect of malaria parasite on the serum electrolytes of malaria patients when compared to normal individuals, which is in agreement with the work of Kakkilaya (28). This implies that impairment in the normal electrolyte function may not be attributed as a part of the pathophysiology that occurs in malaria infection.

Sodium ion is one of the electrolytes that control blood pressure and blood volume; it is also needed for proper functioning of the nerves and muscle. From this study, there is no significant difference (P < 0.05) in sodium ion concentration between malaria patients and normal individuals, which agrees with a report of Stephen (29), who claimed that sodium ion concentration was not affected in plasmodium infection.

Potassium ion is the electrolyte that is necessary for the normal functioning of the heart, kidney and other organs. In this study, there was no significant difference in potassium concentration of malaria patients when compared with normal individual, which is also in accordance with Stephen’s results (29) that indicate that potassium ion concentration is not affected in plasmodium infection.

Bicarbonate ion is a major element in our body, which is secreted by the stomach and is necessary for digestion. Bicarbonate is present in all body fluid and organs; it plays a major role in acid-base balance in the human body. According to this study, there was no significant difference in malaria patients when compared with normal individuals, which suggests that blood bicarbonate ion concentration may not be affected in malaria infection.

Chloride ion is a major anion that is important in the control of proper hydration, osmotic pressure and acid-base balance (30). In our study, there was no significant difference in malaria patients when compared with normal individuals, which suggests that blood chloride levels may not be affected in malaria infection.

In the present study, the serum status of total cholesterol, HDL and VLDL in malaria infected patients were higher than those in normal individual. This finding is consistent with data reported in other studies that showed elevated levels of lipoproteins like HDL, total cholesterol and VLDL in patients suffering from malaria infection (31). Cholesterol is synthesized in the liver, which happens to be the major site of plasmodium infection, and this raises some questions whether there is any relationship between cholesterol synthesis by the liver and plasmodium infection of the liver. Although the parasite has ways that enable it to thrive and multiply using nutrients from the host, they still cannot synthesize majority of their own lipids and cholesterol in vivo.
However, the evidence of higher concentrations of serum lipids in the infected group, despite the requirement of lipids for the parasite growth could be explained from the findings which demonstrate that the Plasmodium genome includes gene-encoding enzymes for phospholipids metabolism (32) allowing *de novo* synthesis of phosphatidylcholine via the Kennedy Pathway (*de novo* synthesis of phosphatidylethanolamine and phosphatidylcholine) and necessitating only the uptake of the small choline molecule. In addition, the parasite genome contains genes similar to those for type II fatty acid synthesis pathway. The protein products of these genes are located within the apicoplast and allow for the production of fatty acids, some of which are unique to the parasite (33). Thus, the parasite may be able to meet many of its lipid requirements from its own biosynthetic pathways.

The decrease in serum LDL concentrations of malaria patients when compared with normal individuals that was observed in our study has been reported by other authors (34), who found no significant change in plasma cholesterol during and after malaria infection.

Serum cholesterol plays an important role in atheromatous disease. In conditions with elevated concentrations of oxidized LDL particles, especially small LDL particles, cholesterol promotes atheroma plaque deposits in the walls of arteries, a condition known as atherosclerosis, which is a major contributor of the disease. In contrast, HDL particles have been the only identified mechanism by which cholesterol can be removed from atheroma. Therefore, an increased concentration of HDL, as shown by our research, correlates with lower rates of atheroma progression, even regression. In this study, higher HDL-cholesterol than LDL-cholesterol was observed. There is a universal trend that lower total cholesterol levels correlate with lower rate of atherosclerotic event. However, the primary association of atherosclerosis with cholesterol has always been specific with cholesterol transport patterns, but not on total cholesterol level. For instance, if total cholesterol can be low, yet made up primarily of small LDL and small HDL particles and atheroma growth rates are often high. In contrast, however, if the number of LDL particles is low and a large percentage of the HDL particles is high, then atheroma growth rates are usually low, even negative, for any given total cholesterol concentration.

CONCLUSION

Malaria remains a public health problem in developing countries like Nigeria, especially in rural areas like Umudike, where the sanitary conditions are poor; early diagnosis and treatment can considerably reduce the malaria morbidity and mortality rate.
Among all studied parameters, it was observed that the parasite affects the mopping up of excess urea from the blood by reducing its clearance rate; it also increases the clearance rate of creatinine from the kidney. Therefore, for proper management and possibly treatment of malaria, target should be channeled towards increasing the rate at which the kidney can mop up urea. For the lipid profile, it was concluded that its concentration in malaria patients was not altered when compared with that measured in normal individuals.

REFERENCES


