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Effects of Malaria Parasitaemia on Electrolytes (NA, K, CL, HCO3) and Some Liver Enzymes (AST and ALT) in Patient Attending University of Maiduguri Teaching Hospital

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ABSTRACT

Malaria is a life threatening disease, with nearly half of the world's population being vulnerable to the infection. The parasitic infection, when untreated or improperly treated, is characterized by fatal complications such as chronic kidney disease, liver disease and death. This study was designed to analyze blood electrolytes and liver enzymes of malaria patients attending UMTH, Maiduguri. Standard methods were used to determine malaria density, Na^+, K^+, Cl^- and HCO_3^-) ALP, AST and ALT. Majority of the malaria patients (39.4%) are within the age group of 25 to 31 years. One hundred and sixty one (89.4%) out of 180 malaria patients have malaria density of (+) while 19 (10.6%) have malaria density of (++).The mean value of chloride of 102.29 ± 6.89 mmol/L in malaria patients was significantly lower than that of control subjects of 103.07 ± 5.81 ($p< 0.05$). The mean value of ALT of 10.35 ± 4.33 U/L in male malaria patients was significantly higher than that of female malaria patients of 8.87 ± 4.13 ($p< 0.05$). The mean values of Na^+, K^+, Cl^-, HCO_3^-, ALP, AST and ALT in malaria patients with (+) showed no statistical difference compared to malaria patients with (++) ($p> 0.05$). The mean values of HCO_3^- of 20.65 ± 1.39 mmol/L, 20.72 ± 1.50 mmol/L, 21.20 ± 1.31 mmol/L, 21.23 ± 1.34 mmol/L and 22.14 ± 1.07 mmol/L for 18-24 years, 25-31 years, 32-38 years, 39-45 years and 46-52 years, respectively showed statistically significant difference. It is concluded that majority of malaria patients who are males and adults, seek medical attention at early stage of malaria infection and at the point of enrolment where the malaria infection have little or no effects on electrolytes and liver enzymes. This is an indication of effectiveness of awareness and control measures against malaria infection. However, as emphasized by previous authors, efforts are still needed toward control measures and eradication of malaria infection in this region.

1. INTRODUCTION

1.1. Background

Malaria is an infectious disease that causes an estimated 2 – 3 million deaths and 300 – 500 million clinical cases in the world. The majority of whom are young children in sub-Saharan Africa (Snow et al, 1999). Malaria is a potentially life-threatening disease in the tropics as it affects over 400 million people, with an estimated mortality of 10,000 women of reproductive age and over one million infants and young children each year (Barbain, 1989; Mishra et al, 2003). Malaria is transmitted by the female Anopheles mosquitoes (Ayuba, Barlas, &Lubbad, 2000). The world health organization (WHO) in 2010, estimated that malaria infects over 200million people and kills up to 800,000 worldwide, with over 90% of the death in sub-Saharan Africa.

There are four species of plasmodium that infect humans; *Plasmodium Falciparum, Plasmodium vivax, plasmodium malariae and Plasmodium ovale.* P. falciparum is the major human parasite responsible for high morbidity and mortality, and the infection is associated with fever, a high number of parasites in the blood, and pathogenesis, including severe anemia, body weight loss and cerebral malaria in humans (Breman et al., 2001). Severe malaria which is defined as the presence of one or more complications in a patient showing asexual parasitaemia of plasmodium falciparum in peripheral blood film (PBF), is almost exclusively caused by P. falciparum infection and usually

arises 6 – 14 days after infection (Trampuz et al, 2003). Consequences of severe malaria include coma and death if untreated. Young children and pregnant women are especially vulnerable. Splenomegaly (enlarged spleen), severe headache, cerebral ischemia, hepatomegaly (enlarged liver), hypoglycemia and hemoglobinuria with renal failure may occur. Renal failure is a feature of black water fever, where hemoglobin from lysed red blood cells leaks into the urine. Severe malaria can progress extremely rapidly and cause death within hours or days (Trumpuz, et al., 2003).

Renal impairment is common in severe malaria in non-immune adults and the microscopic pathology is acute tublar necrosis: glomerulonephrities is rare. In some cases acute tublar necrosis may be precipitated by intravascular hemolysis (Myer et al., 2001). Hepatic injury causing jaundice and raised liver enzyme levels in the blood has been reported in severe plasmodium falciparum infection. Hepatocyte necrosis has been demonstrated in liver biopsies of these patients (Kochar et al., 2003). According to WHO, jaundice is one of the cardinal manifestations of severe malaria in adults. The causes contribution to jaundice may include destruction of parasitized RBCs leading to intravascular haemolysis, immune haemolysis due to the adherence of circulating antigen-antibody complexes to the surface of erythrocytes, malnutrition, shock, or disseminated intravascular coagulation leading to microangiopathichaemolysis and hepatic dysfunction.

Although jaundice in patients with malaria is caused by intravascular hemolysis; these reports indicate direct hepatic injury as an additional problem. The term “malarial hepatitis” has been used to describe hepatic injury.

1.2. Statement of the Problem

Malaria is a global problem, each year more than 300 million cases are diagnosed and more than 1.5million die of the disease in sub-sahara Africa (WHO, 2012). The effects of the infection are particularly apparent in young children and pregnant women.

In an environment like ours where insecticide treatment net compliance is low and drainage system is poorly managed, risk of malaria parasitaemia could be high. This study will be designed to determine the effect of malaria parasitaemia on electrolytes and liver enzymes.

1.3. Objectives of the Study are to;

A. determine the effects of malaria parasite on the serum levels of sodium, potassium, chloride and biocarbonate,
B. estimate the serum activity of the liver enzymes AspartateaminoTransferase (AST), AlanineaminoTransferase (ALT), and
C. estimate the effect of electrolytes and liver enzymes on malaria densities.

1.4. Significance of the Study

The study is expected to give a better understanding of the electrolytic pattern in malaria infection. The knowledge of the derangement in biochemical parameters in malaria parasitaemia will help in the treatment and management of complications that accompany both acute and chronic malaria.

1.5. Scope of the Study

The scope of this study was limited to the effect of Malaria Parasitaemia on electrolyte (Na, K, CL, HCO_3) and liver enzyme (AST and ALT). The study comprised of one hundred and eighty (180) patients including both adults and children with clinical features of malaria and confirmed for the presence of the parasites in their blood (parasitaemia), and one hundred and twenty five (125) malaria-free individuals as control. The sample collection was conducted from September 2017 to march 2018.

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2. LITERATURE REVIEW

2.1. Malaria

Malaria is a mosquito-borne infectious disease caused by the genus *Plasmodium*. It is widespread in tropical and subtropical regions, including parts of the Americas, Asia, and Africa. Each year, there are approximately 350-500 million cases of malaria, killing between one to three million people, the majority of whom are young children in sub-Saharan Africa (Snow *et al*., 2005). Ninety percent of malaria-related deaths occur in Sub-Saharan Africa and is commonly associated with poverty, and can indeed be a cause of poverty and a major hindrance to economic development (Tauil, 2006).

Five species of the *Plasmodium* parasite can infect humans; the most serious forms of the disease are caused by *Plasmodium falciparum.* Malaria caused by *Plasmodium vivax, Plasmodium ovale and Plasmodium malariae* causes mild disease in humans that is not generally fatal. A fifth species, *Plasmodium knowlesi,* is a zoonosis that causes malaria in macaques but can also infect humans (WHO*,* 2011).

Malaria is naturally transmitted by the bite of a female *Anopheles* mosquito. When a mosquito bites an infected person, a small amount of blood is taken, which contains malaria parasites. These develop within the mosquito, and about one week later, when the mosquito takes its next blood meal, the parasites are injected with the mosquito's saliva into the person being bitten. After a period of between two weeks and several months (occasionally years) spent in the liver, the malaria parasites start to multiply within red blood cells, causing symptoms that include fever, and headache. In severe cases the disease worsens leading to hallucinations, coma, and death (WHO, 2011*).*

2.1.1. Epidemiology

Malaria causes about 250 million cases of fever and approximately one million deaths annually (WHO, 2005). The vast majority of cases occur in children under 5 years old, (Akanbi, *et al.,* 2009). Pregnant women are also especially vulnerable, despite efforts to reduce transmission and increase treatment, there has been little change in which areas are at risk of this disease since 1992, indeed, if the prevalence of malaria stays on its present upwards course, the death rate will double in the next twenty years since precise statistics are unknown, because many cases occur in rural areas where people do not have access to hospitals, as a consequence, the majority of cases are undocumented (Hay *et al.,* 2004).

Malaria is presently endemic in a broad band around the equator, in areas of the Americas, many parts of Asia, and much of Africa. However, it is in sub-Saharan Africa where 85-90% of malaria fatalities occur (Guyatt, H.L. and Snow, R.W. 2004). The geographic distribution of malaria within large regions is complex, and malaria afflicted and malaria-free areas are often found close to each other. In drier areas, outbreaks of malaria can be predicted with reasonable accuracy by mapping rainfall. Malaria is more common in rural areas than in cities this contrary to dengue fever where urban areas present the greater risk (Van Benthem*et al.,*2005). In Africa malaria is present in both rural and urban areas, though the risk is lower in the larger cities, but the global endemic levels of malaria have not been mapped since the 1960s (Van Benthem*et al.,*2005*).*

Individuals in all continents are potentially at risk, but the greatest suffering falls to people in tropical countries. The degree of endemicity varies between countries and even between different areas in the same country. In regions of high endemicity, the greatest suffering is borne by children less than 5years of age whereas in areas of low endemicity, the disease affects all age groups. The patterns of pathology also differ with changes in the degree of endemicity. In areas of high endemicity, although individuals after 5 years of age continue to harbor malaria parasites, the frequency of the disease is greatly reduced, this is called clinical immunity. Pregnant women, even if previously clinically immune, have a significantly enhanced risk for a pathogenic process that has a major effect on the fetus and newborn, particularly during the first pregnancy (Akanbi, *et al.,* 2009).

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2.1.2. Life Cycle of Malaria Parasite

The parasite's primary (definitive) hosts and transmission vectors are female mosquitoes of the *Anopheles* genus, while humans and other vertebrates are secondary hosts. Young mosquitoes first ingest the malaria parasite by feeding on an infected human carrier and the infected *Anopheles* mosquitoes *carry Plasmodium* Sporozoites in their salivary glands. A mosquito becomes infected when it takes a blood meal from an infected human, for example once ingested the parasite, gametocytes taken up in the blood will further differentiate into male or female gametes and then fuse in the mosquito gut (WHO*,* 2011). This produces an ookinate that penetrates the gut lining and produces an oocyst in the gut wall. When the oocyst ruptures, it releases sporozoites that migrate through the mosquito's body to the salivary glands, where they are then ready to infect a new human host. This type of transmission is occasionally referred to as anterior station transfer, the sporozoites are injected into the skin, alongside saliva, when the mosquito takes a subsequent blood meal (WHO, 2011).

Only female mosquitoes feed on blood, thus males do not transmit the diseases. The females *Anopheles* mosquito prefer to feed at night, and they usually start searching for meal at dusk, and will continue throughout the night until taking a meal. Malaria parasites can also be transmitted by blood transfusions, although this is rare (Augustijn, *et al.,* 2007).

2.1.3. Pathophysiology of Malaria

Pathogenesis relates to the various host and parasite factors that are responsible for causing pathology. Malaria is a disease caused by repeated cycle of growth of the parasite *Plasmodium* in the erythrocyte. Various cellular and molecular strategies allow the parasite to evade the immune response for many cycles of parasite multiplication (Snow *et al.,* 2005).

The most pronounced changes related to malaria involve the blood and the blood-firming system, the spleen and the liver. Secondary changes can occur in all the other major organs, depending on the type and severity of the infection. The pathological changes are more profound and severe in case of P. *falciparum* malaria. Severe malaria is a complex multisystem disorder with many similarities to sepsis syndrome (Snow *et al.,* 2005).

2.1.4. Effect of Malaria on the Liver

Enlargement of the liver occurs early in malaria. The liver is enlarged after the first paroxysms, when it is usually firm and may be tender. It is oedematous, coloured brown, grey or even black as a result of deposition of malaria pigment. Hepatic sinusoids are dilated and contain hypertrophied Kupffer cells and parasitized red cells. Small areas of centrilobular necrosis may be seen in severe cases and these may be due to shock or disseminated intravascular coagulation. Prolonged infection may be associated with stromal induration and diffuse proliferation of fibrous connective tissue. However, changes of cirrhosis are not seen. Liver damage may result from an alteration in vascular flow through the organ as the parasitized RBCs adhere to endothelial cells, blocking sinusoids and obstructing intrahepatic blood flow (Ghoda, 2002). In *falciparum* malaria, in addition to the involvement of the mesenchyma, the hepatocytes may also be involved, causing functional changes as well as malarial hepatitis (Kochar*et al.,* 2003).

Malarial hepatitis is characterized by hyperbilirubinemia with elevation of conjugated bilirubin, increased levels of transaminases AspartateaminoTranferase, (AST) and AlanineaminoTranferase, (ALT) and Alkaline phosphatase. Being part of the severe *falciparum* infection, it may be associated with renal failure, anaemia or other complications. *Falciparum* malaria patients may present with history of yellowish discoloration of eyes and urine with mild jaundice, which is fairly common in malaria and may be seen in 20-40% of the cases. Deeper jaundice with serum bilirubin of more than 3 mg/l is seen in severe P. *falciparum* malaria. Liver involvement in severe *falciparum* malaria is due to impairment of local microcirculation associated with hepatocellular damage (Devarbhavi, *et al.,* 2005).

In patients with repeated attacks of malaria, liver also enlarges significantly along with a large and hard spleen. However, there is no functional abnormality of the liver in these patients. Malaria is not a proven cause for cirrhosis of the liver, but the liver function abnormalities are reported to be related to the grade of parasitaemia, fever, duration of illness, nutritional status, or associated medical problems. The term malaria hepatitis has been used to describe this condition (Ghoda, 2002).

2.2. Liver Enzymes

Damage to tissue can release different types of enzymes based on their location. For example, mild inflammation of the liver reversibly increases the permeability of the cell membrane and releases cytoplasmic enzymes such as Lactate Dehydrogenase (LD) Alkaline Phosphatase (ALP), ALT, and AST, while cellular death (necrosis) will release mitochondrial sources of ALT and AST (Beers et al., 1999). Distribution of these enzymes within specific types of hepatic tissues varies. ALP are more concentrated in the biliary ducts or tissues of the small ducts (canaliculi), while AST, ALT, and LD are found mainly in structural (parenchymal) hepatic cells. Multiple forms of enzymes, called isoenzymes, are distributed in several different tissues types (Ebele*et al.,* 2010).

2.2.1. AST and ALT

The transaminases are two closely related enzymes of clinical significance, particularly in the assessment of liver function. Among the duo, AspartateaminoTransferase (AST) is known to exist in two electrophoretically distinct forms; a cationic isoenzyme associated with the mitochondria and the anionic form associated with the cytoplasm (Calbreath*et al.,* 1992). Tissue levels of AST are highest in the heart and liver. Significant amount are also found in skeletal muscle and kidney, with lower levels in pancreas, spleen and lung. Low levels of AST are also found in erythrocytes. AlanineaminoTransferase (ALT) is present in varying concentrations in the liver, heart, skeletal muscle, kidney, pancreas, spleen, lung and red blood cells (Sherman *et al.,* 2004). Both enzymes increase in many disorders related to the liver damage; hence they have been proven to be sensitive indicators of liver-cell injury (Pratt and Kaplan, 2000). In particular, patients with viral hepatitis present with marked increases in the serum activities of both ALT and AST frequently before clinical symptoms of the disease become apparent (Schiff *et al.,* 1999). ALT is more elevated than AST in various necro-inflamantory conditions of the liver, reflecting its greater efficiency as a liver disease marker (Rosenthal and Haight, 1989).

2.3. Effect of Malaria on the Kidney

Malaria can cause varied problems in the kidneys, commonly seen as albuminuria during the acute attack. Acute diffuse malarial nephritis with hypertension, albuminuria and oedema may also be rarely seen, and in *P.malariae* infection, nephritic syndrome may be seen (Quartan malaria nephropathy). This immune complex mediated nephropathy develops weeks after the malarial illness and is characterized by albuminuria, oedema and hypertension. It may be progressive and may require treatment with steroids or immune suppressants (Hanson *et al.,*2009).

In severe *P.falciparurn*malaria, acute renal failure may develop in 0.1-0.6% of the patients. Microcirculation disorders, anoxia and subsequent necrosis of the glomeruli and renal tubules are responsible for this serious complication. Renal involvement in severe malaria is one of the three commonest causes of death in adults with severe malaria (White &Looareesuwan 1987), but the pathogenesis of malaria-associated acute renal failure (MARF) is less well characterized than the syndrome of cerebral malaria. MARF occurs in 1-4% of hospitalized adults and older children, but is very unusual in younger children (White &Looareesuwan 1987). The clinical presentation of renal dysfunction is usually acute oliguric or anuric renal failure, with hypercatabolism and associated acidosis (Sitprija*et al.,* 1988). Clinically, patients show a mixture of pre-renal and renal failure with associated acidosis suggesting acute tubular necrosis (ATN) (Mishra *et al.,* 2007).

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2.4. Electrolytes

Electrolytes are classified as either anions, negatively charged ions or cations, positively charged ions. The four major electrolytes are sodium (Na'), Potassium (K^+), Chloride (Cl^-), Bicarbonate (HCO_3^-). Sodium and Potassium are cations, with sodium in greater concentration extracellularly and potassium in greater concentration intracellularly, while Chloride and Bicarbonate are anions. Control of cation concentration is maintained by the Na-K-ATPase pump (Jasani*et al.,* 2012).

2.4.1. Sodium

Sodiumis the major cation of extracellular fluid, representing almost one-half of the osmotic strength of plasma. It therefore plays a central role in maintaining the normal distribution of water and osmotic pressure in the extracellular fluid compartment. Extremely high or low sodium concentrations in plasma will cause severe osmotic pressure changes that can induce serious consequences to several organs. The most immediate effect is swelling on the brain and potential coma (Kumar *et al.,* 1998).

2.4.2. Potassium

Potassium is the major intracellular cation, and is also controlled by the Na-K ATPase pump. Potassium maintains cardiac rhythm and contributes to neuromuscular conduction. Imbalances in potassium level, as indicated by hyperkalemia or hypokalemia, will cause cardiac arrhythmias and neuromuscular weakness (Kumar *et al,.* 1998).

2.4.3. Chloride

Chloride is extracellular anions that helps maintain electrical neutrality with sodium. Chloride contributes to the maintenance of acid-base balance by participating in the *isohydric shift*. The isohydric shift describes the maintenance of hydrogen ion concentration as shifting of hydrogen ion occurs between fluid spaces. The shift refers to the buffering of H^+ with $HCO3^-$ and other buffers intracellularly and movement to extracellular fluid spaces (Kumar *et al.,* 1998).

2.4.4. Bicarbonate

Bicarbonate is the major component of the extracellular buffer system, and is controlled by renal tubular cells and erythrocytes, the previously described metabolic component of the buffer system. Bicarbonate ion is produced from carbon dioxide as it reacts with water in the plasma. Some bicarbonate is found in cells (intracellularly), where it maintains electrical neutrality in conjunction with potassium. Bicarbonate may move to extracellular fluid in order to buffer if, forming H_2CO_3 (Kumar *et al,.* 1998).

2.5. Effect of Malaria on Electrolytes

Hyponatraemia is common in acute childhood illness, being found in as many as 31% of cases of pneumonia, 50% of cases of meningitis and many other conditions associated with either pulmonary or cerebral pathology. It is also common in severe malaria, and studies in adults and children have, as in childhood pneumonia and meningitis, stressed that the possible cause may be the syndrome of in-appropriate antidiuretic hormone secretion (SIADH) (English *et al.,* 1994).

However, the diagnosis of SIADH is one of exclusion and the presence of renal impairment and hypovolaemia in particular are incompatible with the diagnosis. Renal impairment is said to be uncommon in children with malaria although mild renal impairment has been described in Indian children with non-severe malaria (Maitland *et al.,* 2004). In adults, acute renal failure is a common serious complication of malaria and hypovolaemia, possibly caused by dehydration, one of many factors that have been implicated in its pathogenesis (English *et al.,* 1994). Recent work in Malawian children described metabolic acidosis that often resolved with administration of intravenous fluids, implying that dehydration, a recognized cause of metabolic acidosis, is found in childhood malaria (Taylor *et al.,* 1993).

Reduced level of plasma bicarbonate may be caused by the exhaustion of bicarbonate reserve to revert the metabolic acidosis caused by the elevated plasma urea and creatinine, Rajpurkar (1994) also reported that hypervoleamia and replacement with only glucose containing intravascular solution might also cause low bicarbonate level.

The aberrant in serum potassium level is one of the common laboratory abnormalities seen in the patients with malaria. Brooks *et al* reported the correlation of the serum potassium and the haemolysis of red blood cell in the patients infected with malaria, which brought the complications. Acidosis is now recognized as an important component of severe malaria syndrome and a predictor of fatal outcome. Alterations in plasma potassium concentrations are commonly associated with acidosis. However, Maitland *et al* noted that the abnormality of potassium was often not apparent on admission. Of interest, no previous study on the correlation of the serum potassium and the percentage of parasitaemia was established (Hanson 2009).

Acidosis is an important contributor to death from severe *falciparum* malaria. In adult patients, acidosis results from metabolic, circulatory, and renal dysfunction, whereas in children, metabolic factors appear to predominate (Day *et al*., 2000). Metabolic acidosis results from abnormal microcirculatory perfusion and anaerobic glycolysis due to sequestration of parasitized erythrocytes, also, cellular dysfunction consequent on release of host and parasite-derived toxic mediators. Arterial bicarbonate and venous and cerebrospinal fluid concentrations of lactate have been shown to be powerful prognostic indicators in patients with severe malaria (Day *et al.,* 2000).To assess the respective roles of respiratory status, renal dysfunction, and glycolytic abnormalities in acidosis in severe malaria and specifically in the pathogenesis of cerebral malaria.

In severe malaria, unidentified anions other than lactate are the most important contributors to metabolic acidosis, a major causes of death.The strong anion gap is a powerful prognostic indicator in patients with severe malaria (WHO 2000).

2.6. Diagnosis of Malaria

Diagnosis of malaria involve identification of malaria parasite or its antigens products in the blood of the patient. Although this seems simple, the efficacy of the diagnosis is subject to many factors. The different forms of the four malaria species; the different stages of erythrocyticschizogony; the endemicity of different species; the population movements; the inter-relation between the levels of transmission, immunity, parasitaemia, and the symptoms; the problems of recurrent malaria, drug resistance, persisting viable or nonviable parasitaemia, and sequestration of the parasites in the deeper tissues; and the use of chemoprophylaxis or even presumptive treatment on the basis of clinical diagnosis can all have a bearing on the identification and interpretation of malaria parasitaemia on a diagnostic test.The diagnosis of malaria is confirmed by blood tests and can be divided into microscopic and non-microscopic tests (Cheesebrough, 1998).

2.6.1. Microscopic Tests

For nearly a hundred years, the direct microscopic visualization of the parasite on the thick and thin blood smears has been the accepted method for the diagnosis of malaria in most settings, from the clinical laboratory to the field surveys. The careful examination of a well-prepared and well-stained blood film currently remains the “gold standard” for malaria diagnosis.

The microscopic test involve staining and direct visualization of the parasite under the microscope.

A. Peripheral smear study
B. Quantitative Buffy Coat (QBC) test (Cheesebrough, 1998).

2.6.2. Peripheral Smear Study for Malarial Parasites – The MP Test

Light microscopy of thick and thin stained blood smears remains the standard method for diagnosing malaria. It involves collection of a blood smear, its staining with Romanowsky stains and examination of theRed Blood Cells for intracellular malarial parasites. Thick smears are 20-40 times

more sensitive than thin smears for screening of *Plasmodium* parasites, with a detection limit of 10-50 trophozoites/l. Thin smears allow one to identify malaria species (including the diagnosis of mixture infections), quantify parasitaemia, and assess for the presence of schizonts, gametocytes, and malarial pigment in neutrophils and monocytes. The diagnostic accuracy relies on the quality of the blood smear and experience of laboratory personnel (Trampuz*et al.,* 2003).

The level of parasitaemia may be expressed either as a percentage of parasitized erythrocytes or as the number of parasites per microliter of blood. In non-*falciparum* malaria, parasitaemia rarely exceeds 2%, whereas it can be considerably higher (>50%) in *falciparum* malaria. In non-immune individuals, hyperparasitaemia (>5% parasitaemia or > 250, 000 parasites/l) is generally associated with severe disease (Moody *et al.,* 2000).

In *falciparum* malaria, parasitized erythrocytes may be sequestered in tissue capillaries resulting in a falsely low parasite count in the peripheral blood ('visible' parasitaemia). In such instances, the developmental stages of the parasite seen on blood smear may help to assess disease severity better than parasite count alone. The presence of more mature parasite forms (>20% of parasites as late trophozoites and schizonts) and of more than 5% of neutrophils containing malarial pigment indicates more advanced disease and a worse prognosis. One negative blood smear makes the diagnosis of malaria very unlikely (especially the severe form); however, smears should be repeated every 6-12 hours for 48 hours if malaria is still suspected (Moody *et al.,* 2000).

The smear can be prepared from blood collect by venipuncture, finger prick and ear lobe stab. In obstetric practice, cord blood and placental impression smears can be used. Sometime no parasites can be found in peripheral blood smears from patients with malaria, even in severe infections. This may be explained by partial antimalarial treatment or by sequestration of parasitized cells in deep vascular beds. In these cases, parasites, or malarial pigment may be found in the bone marrow aspirates. Presence of malarial pigment in circulating neutrophils and monocytes may also suggest the possibility of malaria (Torres, 2003).

2.6.3. Non-Microscopic Tests

Several attempts have been made to take the malaria diagnosis out of the realm of the microscope and the microscopist. Important advances have been made in diagnostic testing, including fluorescence microscopy of parasite nuclei stained with acridine orange, rapid dipstick immunoassay, and polymerase Chain Reaction assays (Trampuz*et al.,* 2003). These tests involve identification of the parasitic antigen or the antiplasmodial antibodies or the parasitic metabolic products. Nucleic acid probes and immunofluorescence for the detection of *Plasmodia* within the erythrocytes; gel diffusion, counter-immunoelectrophoresis, radio immunoassay, and enzyme immunoassay for malaria antigens in the body fluids; and hemagglutination test, indirect immunoflourescence, enzyme immunoassay, immunochromatography, and Western blotting for anti-plasmodial antibodies in the serum have all been developed. These tests have found some limited applications in research, retrograde confirmation of malaria, investigation of cryptic malaria, transfusion blood screening, and investigation, of transfusion acquired infections (Cheesebrough, 1998).

3. METHODOLOGY

3.1. Location of the Study

The study was carried out at University of Maiduguri Teaching Hospital (UMTH), Maiduguri, Borno State, Nigeria. The UMTH serves as a referral centre, catering for the needs of the entire North-East. Maiduguri is located on latitude $11^{o}51$N and longitude $13^{o}09$E, altitude 305m and with an annual rainfall of 650mm. It is inhabited by about 908,645 people (2006 census) and lies in the Sudan-Sahelian zone with marked seasonal variation in transmission of malaria (Rose *et al.,* 2002). The cumulative prevalence of malaria in Maiduguri is about 27.26% (Samdi*et al.*, 2005) which can be described as mesoendemic (WHO, 2003).

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3.2. Ethical clearance

The ethical permission was obtained from the ethics and research Committee of the University of Maiduguri Teaching Hospital in order to carry out the research.

3.3. Subjects

The study group comprised of one hundred and eighty (180) patients with clinical features of malaria and confirmed to have the parasite in their blood (parasitaemia). These patients were from the outpatient department who have been referred to the parasitology laboratory for malaria parasite investigation at the Hospital. The control group was made up of one hundred and twenty five (125) malaria-free individuals.

3.3.1. Inclusion Criteria

All the test subjects were confirmed as malaria patients, having positive malaria parasitaemia by Giemsa Stained thick blood film microscopy.

3.3.2. Exclusion Criteria

Subjects who present with clinical symptoms of malaria but found negative for malaria parasitaemia or thick blood film were excluded from the study as well as subjects with history of hepatitis or renal impairment. Subject with abnormal electrolyte and liver enzymes were excluded from the control group of the study.

3.4. Sample Collection and Preparation

Two specimen bottles, anticoagulant bottles containing K_2 EDTA and plain bottles were used for sample collection. Thick blood films for malaria parasite quantification were made either from the anticoagulated blood sample or from the drop remaining on the needle after sample collection. Blood samples (3 – 5ml) were collected by clean venepuncture from the antecubital fossa into already labeled bottles, without undue pressure to either the arm or the plunger of the syringes. Samples in the plain tubes were allowed to clot and the clotted samples centrifuged at 4000rpm for 5min to obtain the sera for the biochemical investigation. The serum supernatants was separated into sterile bottles and analysed immediately. When immediate analysis is not possible, the samples were stored in the refrigerator and analysis carried out within four (4) days (Ananad*et al.,* 1992).

3.4.1. Parasitological Examination

The presence and relative parasite count of *Plasmodium falciparum*in each blood sample was determined from Giemsa stained thick films after staining for 30 minutes. A slide was scored as negative when 100 high power fields (at 1000 x magnification) have been examined thoroughly without seeing any parasites.

Classification of the degree of parasite:

The malaria parasite density was graded as follows:

1 parasite/field: low density (+)

2 – 9 parasites/field: Medium density (++)

> 20 parasites/field: High density (+++)(Choesbrough, 1998).

3.5. Electrolytes

The sodium and potassium in the samples were analyzed using flame emission spectrophotometric method (Tietz*et al.,* 1996). The chloride was estimated using the Schales and Schales method while the Bicarbonate was estimated by titrimetric method of Davidson and Henry (1979).

3.5.1. Sodium and Potassium Estimation

Principle of Flame Emission Spectrophotometry

Using compressed air, diluted serum is sprayed in droplets into a non-luminous gas flame which becomes coloured by the characteristic emission of sodium and potassium metallic ions in the sample. Using a light filter, the light of wavelength corresponding to the metal being estimated, is selected. The amount of the light emitted depends on the concentration of metallic ions present in the sample.

Procedure:

1 in 100 dilution of serum was made with de-ionized water in universal container (100l of serum in 10ml of de-ionized water), mixed and aspirated into the flame analyzer at a wavelength of 589nm for Na+ and 756nm for K+, having calibrated the machine with a standard solution containing 140mmol/L Na+ and 4.3 mmol/L K+ in de-ionized water.

3.5.2. Chloride and Bicarbonate Estimation

3.5.2.1. Chloride

Principle:

This method involves titrating chloride ions with mercuric ions, forming soluble but non-ionized mercuric chloride. The end point is reached when excess mercuric ions form a complex with the indicator diphenylcarbazone producing a violet colour.

Procedure:

To 1.8ml of de-ionized water, 200l of serum and 2 drops of the indicator diphenylcarbazone was added and titrated with 2ml of mercuric chloride (standardized). On addition of the mercuric nitrate, solution changes from salmon pink to deep purple. The end point was reached with the yield of sudden but permanent change from pale yellow to violet. The volume of the mercuric nitrate consumed (titre) was then be noted.

Calculation:

$$\frac{\text{Titre of test}}{\text{Titre of standard}} \times 100 \text{ mmol/1} = \text{conc. Of chloride (mmol/l)}$$

3.5.2.2. Bicarbonate

Principle:

When serum is mixed with 0.01N HCL, there is a loss of acidity due to the bicarbonate in the serum. This decrease in acidity can be determined by titrating against standard 0.01N NaOH.

Procedure:

To 2.0ml of de-ionized water, 100l of serum and 2 drops of the indicator, phenol red, were added. 1ml of bicarbonate acid (0.01N HCL) was then be added and titrated (Back Titration) with 1ml of the base, 0.01N NaOH. The end point was reached with the neutralization of the acid giving an orange colour. The volume of the base remaining is then noted.

Calculation: 0.1ml represents 5mmol/l

3.6. Estimation of Serum AST and ALT

AST and ALT were estimated using Dinitrophenyl hydrazine coupling colorimetric technique (Reitman and Frankel, 1957).

3.6.1. AspartateaminoTranferase(AST)

Principle:

When AST is incubated at 37^0C for exactly 30minutes in a pH 7.5 buffered substrate containing aspartate and -ketoglutarate, it catelyses the transfer of amino acid group from aspartate to ketogluterate, forming oxaloacetate and glutamate. The oxaloacetate reacts with 2, 4-dinitrophenylhydrazine to form 2, 4- dinitrophenylhydrazone, which in alkaline pH is red brown, and

the intensity is proportional to the enzyme activity in the serum. The absorbance of the colour produced is measured in a colourimeter at 456nm wavelength.

Equation of the reaction

L-Aspartate + α-ketoglutarate $\xrightarrow{AST}$ L-glutamate + Oxaloacetate

Oxaloacetate + 2, 4-dinitrophenylhydrazine $\xrightarrow{\text{alkaline pH}}$ 2,4-dinitrophenylhydrazone

Procedure

1. Into clean test tubes placed in a rack and arranged in a water bath regulated at 37^0C, 0.5ml of AST reagent l was dispensed.
2. 100l of distilled water was dispensed into the test tube marked blank while 100l of test serum was dispensed into the other test tubes with controls in the appropriate positions.
3. The contents of the test tubes were properly mixed and incubated for 30 minutes in the water bath
4. 0.5ml of AST reagent ll (2-4dinitrophenyl hydrazine) was dispensed into all the test tubes and was incubated for 20 minutes at 25^0C.
5. 5.0ml of sodium hydroxide (colour developer) was pipetted into the test tubes to stop the reaction.
6. It was then be mixed and read at 546nm wavelength against the reagent blank after 5minutes.
7. The concentration was determined using a table provided by the manufacturers

3.6.2. AlanineaminoTransferase (ALT)

Principle:

When ALT is incubated at 37^0C for exactly 30minutes in a pH 7.5 bufferd substrate containing L-alanine and-ketoglutarate, it catalyses the transfer of amino acid group from L-alanine to ketogluterate, forming pyruvate and L-glutamate. The pyruvate reacts with 2, 4-dinitrophenylhydrazine to form 2, 4-dinitrophenylhydrazone, which in alkaline pH is red brown, and the intensity is proportional to the enzyme activity in the serum. The absorbance of the colour produced is measured in a colourimeter at 546nm wavelength.

Equation of the reaction

L-Alanine + α-ketoglutarate $\xrightarrow{ALT}$ L-glutamate + Pyruvate

Pyruvate + 2,4-dinitrophenylhydrazine $\xrightarrow{\text{alkaline pH}}$ 2,4-dinitrophenylhydrazone

Procedure

1. Into clean test tubes placed in a rack and arranged in a water bath regulated at 37^0C, 0.5ml of ALT reagent l was dispensed.
2. 100l of distilled water was dispensed into the test tube marked blank while 100l of test serum was dispensed into the other test tubes with controls in the appropriate positions.
3. The contents of the test tube was properly mixed and incubated for 30 minutes in the water bath.
4. 0.5ml of ALT reagent ll (2-4dinitrophenyl hydrazine) was dispensed into all the test tubes and was incubated for 20 minutes at 25^0C
5. 5.0ml of sodium hydroxide (colour developer) was pipetted into the test tubes to stop the reaction.
6. It was then mixed and read at 546nm wavelength against the reagent blank after 5minutes.

The concentration was determined using a table provided by the manufacturers.

3.7. Data Analysis

The data obtained from this study was subjected to descriptive statistic using statistical package IBM SPSS Statistics version 20.0 software. The mean ± Standard deviation were used to describe the treatment means across the age groups of the study. Also frequencies were used to present the result. Statistical comparison was performed using student's t-test (paired-sample tests) and analysis of variance (ANOVA) for multiple groups. The results were considered significant at p-value < 0.05.

4. RESULTS

This study included one hundred and eighty (125) malaria patients attending University of Maiduguri Teaching Hospital, Nigeria and one hundred and twenty-five (125) non-malaria control subjects comprising of students, hospital and University staff.

Table 4.1 shows socio-demographic characteristics of malaria patients in University of Maiduguri Teaching Hospital, Nigeria and Control subjects. The study subjects and control participants were not gender and number-matched. Seventy percent (70%) and sixty percent (60%) of malaria patients and control subjects, respectively were male. Majority of the malaria patients (39.4%) and control subjects (44.0%) are within the age group of 25 to 31 years while the less percentage of 3.9 and 3.2, respectively are within the age group of 46 to 52 years. One hundred and sixty one (89.4%) out of 180 malaria patients have malaria density of (+) while 19 (10.6%) have malaria density of (++).

Table 4.2 depicts the mean values of electrolytes and liver enzymes of malaria patients in University of Maiduguri Teaching Hospital, Nigeria and control subjects. The mean value of chloride of 102.29 ± 6.89 mmol/L in malaria patients was significantly lower than that of control subjects of 103.07 ± 5.81 ($p< 0.05$). The mean values of Na^+, K^+, HCO_3^-, ALP, AST and ALT in malaria patients showed no statistical difference compared to the control subjects ($p> 0.05$).

Table 4.3 summarizes the mean values of electrolytes and liver enzymes of malaria patients in University of Maiduguri Teaching Hospital, Nigeria in relation to gender. The mean value of ALT of 10.35 ± 4.33 U/L in male malaria patients was significantly higher than that of female malaria patients of 8.87 ± 4.13 ($p< 0.05$). The mean values of Na^+, K^+, Cl^-, HCO_3^-, ALP and AST in malaria patients showed no statistical difference compared to the control subjects ($p> 0.05$).

Table 4.4 shows the mean values of electrolytes and liver enzymes of malaria patients in University of Maiduguri Teaching Hospital, Nigeria in relation to malaria density. The mean values of Na^+, K^+, Cl^-, HCO_3^-, ALP, AST and ALT in malaria patients with (+) showed no statistical difference compared to malaria patients with (++) ($p> 0.05$).

Table 4.5 gives the mean values of electrolytes and liver enzymes of malaria patients in University of Maiduguri Teaching Hospital, Nigeria in relation to age group. The mean values of HCO_3^- of 20.65 ± 1.39 mmol/L, 20.72 ± 1.50 mmol/L, 21.20 ± 1.31 mmol/L, 21.23 ± 1.34 mmol/L and 22.14 ± 1.07 mmol/L for 18-24 years, 25-31 years, 32-38 years, 39-45 years and 46-52 years, respectively showed statistically significant difference. However, the mean values of Na^+, K^+, Cl^-, ALP, AST and ALT in malaria patients showed no statistical difference in relation to age ($p> 0.05$).

Table 4.1: Socio-demographic characteristics of malaria patients in University of Maiduguri Teaching Hospital, Nigeria and Control subjects.

Variables	Malaria Patients		Control Subjects	
	Frequency (N)	Prevalence (%)	Frequency (N)	Prevalence (%)
Gender				
Female	37	29.6	65	52.0
Male	88	70.4	60	48.0
Total	**125**	**100.0**	**125**	**100.0**

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Age Group (years)				
18-24	37	29.6	32	25.6
25-31	50	40.0	55	44.0
32-38	28	22.4	22	17.6
≥ 39	10	8.0	16	12.8
Total	**125**	**100.0**	**125**	**100.0**
Malaria Density				
(+)	111	88.8	-	-
(++)	14	11.2	-	-
Total	**125**	**100.0**	**-**	**-**

Keys: + = Malaria density of 1-10 malaria parasites per high power field and ++ = Malaria density of 11-100 malaria parasites per high power field.

Table 4.2: Mean Values of Electrolytes and Liver Enzymes of Malaria Patients in University of Maiduguri Teaching Hospital, Nigeria and Control Subjects.

Variables	**Malaria Patients** (N = 125)	**Control Subjects** (N = 125)	**t**	**p-value**
Na^+ (mmol/L)	136.70 ± 5.75	135.15 ± 5.63	2.074	0.040*
K^+ (mmol/L)	4.03 ± 0.55	4.47 ± 3.69	-1.335	0.1.84
Cl^- (mmol/L)	102.29 ± 6.89	103.07 ± 5.81	-1.068	0.2.87
HCO_3^- (mmol/L)	20.70 ± 1.48	20.97 ± 1.34	-1.425	0.1.57
ALP (U/L)	36.38 ± 13.06	39.80 ± 14.68	-1.858	0.066
AST (U/L)	14.61 ± 9.62	14.12 ± 11.66	0.358	0.721
ALT (U/L)	10.16 ± 4.64	10.34 ± 5.15	-0.305	0.761

Legend: Paired sample student t-test was used to analyze mean electrolytes parameters between malaria patients and control subjects.

Keys: ALP = Alkaline phosphatase, AST = Aspartate transaminase, ALT = Alanine transaminase, SD = Standard deviation, N = frequency, * = statistically significant comparison; p-value ≤ 0.05 = statistically significant and p-value >0.05 is not statistically significant.

Table 4.3: Mean Values of Electrolytes and Liver Enzymes of Malaria Patients in University of Maiduguri Teaching Hospital, Nigeria in Relation to Gender.

Variables	**Female Malaria Patients** (N = 37)	**Male Malaria Patients** (N = 88)	**F**	**p-value**
	Mean ± SD	Mean ± SD		
Na^+ (mmol/L)	135.59 ± 5.68	137.17 ± 5.75	1.970	0.163
K^+ (mmol/L)	3.92 ± 0.32	5.08 ± 0.62	2.020	0.158
Cl^- (mmol/L)	102.68 ± 5.65	102.13 ± 7.38	0.165	0.685
$HCO3^-$ (mmol/L)	20.62 ± 1.23	20.74 ± 1.57	0.63	0.687
ALP (U/L)	38.24 ± 14.89	35.60 ± 12.22	1.065	0.304
AST (U/L)	15.25 ± 8.30	14.34 ± 10.56	0.228	0.634
ALT (U/L)	8.76 ± 4.17	10.75 ± 4.72	4.962	0.028*

Legend: Paired sample student t-test was used to analyze mean electrolytes parameters between male and female malaria patients.

Keys: ALP = Alkaline phosphatase, AST = Aspartate transaminase, ALT = Alanine transaminase, SD = Standard deviation, N = frequency; * = statistically significant comparison; p-value ≤ 0.05 = statistically significant and p-value >0.05 is not statistically significant.

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Table 4.4: Mean Values of Electrolytes and Liver Enzymes of Malaria Patients in University of Maiduguri Teaching Hospital, Nigeria in Relation to Malaria Density.

Variables	Malaria Patients with (+) (N = 111)	Malaria Patients with (++) (N = 14)	F	p-value
	Mean ± SD	Mean ± SD		
Na^+ (mmol/L)	136.71 ± 5.79	136.64 ± 5.71	0.002	0.967
K^+ (mmol/L)	4.05 ± 0.57	3.88 ± 0.32	1.228	0.270
Cl^- (mmol/L)	102.20 ± 7.00	103.00 ± 6.15	0.167	0.683
$HCO3^-$ (mmol/L)	20.76 ± 1.50	20.29 ± 1.27	1.269	0.262
ALP (U/L)	35.31 ± 11.64	44.93 ± 19.84	7.076	0.009*
AST (U/L)	14.46 ± 9.38	15.79 ± 11.70	0.235	0.629
ALT (U/L)	10.34 ± 4.54	8.71 ± 5.36	1.538	0.217

Legend: Paired sample student t-test was used to analyze mean electrolytes parameters between malaria patients with (+) and malaria patients with (++).

Keys: ALP = Alkaline phosphatase, AST = Aspartate transaminase, ALT = Alanine transaminase, SD = Standard deviation, N = frequency, + = Malaria density of 1-10 malaria parasites per high power field and ++ = Malaria density of 11-100 malaria parasites per high power field; * = statistically significant comparison; p-value ≤ 0.05 = statistically significant and p-value >0.05 is not statistically significant.

Table 4.5: Mean Values of Electrolytes and Liver Enzymes of Malaria Patients in Maiduguri, Nigeria in Relation to Age Group.

Variables	18-24 years (N = 37)	25-31 years (N = 50)	32-38 years (N = 28)	≥ 39years (N = 10)	F	p-value
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD		
Na^+ (mmol/L)	137.35 ± 5.01	135.74 ± 5.91	137.96 ± 5.87	135.60 ± 6.38	1.201	0.313
K^+ (mmol/L)	3.94 ± 0.38	4.06 ± 0.66	4.10 ± 0.44	4.03 ± 7.4	0.535	0.659
Cl^- (mmol/L)	101.68 ± 6.31	102.32 ± 8.07	102.86 ± 6.50	102.80 ± 3.33	0.176	0.912
HCO_3^- (mmol/L)	20.65 ± 1.44	20.52 ± 1.61	21.04 ± 1.26	20.90 ± 1.52	0.803	0.495
ALP (U/L)	38.59 ± 16.38	35.96 ± 11.04	35.36 ± 13.24	33.20 ± 7.25	0.621	0.603
AST (U/L)	15.08 ± 14.11	14.26 ± 6.89	15.04 ± 8.04	13.40 ± 4.84	0.120	0.948
ALT (U/L)	10.03 ± 5.63	10.54 ± 4.99	10.21 ± 2.50	8.60 ± 3.47	0.494	0.687

Keys: ALP = Alkaline phosphatase, AST = Aspartate transaminase, ALT = Alanine transaminase, SD = Standard deviation, N = frequency; * = statistically significant comparison; p-value ≤ 0.05 = statistically significant and p-value >0.05 is not statistically significant.

5. DISCUSSION

Malaria is a life threatening disease, with nearly half of the world's population being vulnerable to the infection (Mishra *et al*., 2002). Malaria still has an alarming burden in Sub-Saharan Africa and Nigeria in particular (World Malaria Report, 2011). Malaria is characterized by fatal complications when untreated or improperly treated (Gali*et al*., 2018); some of the malarial complications include but not limited to blood electrolytes imbalances, chronic kidney disease (CKD), liver disease and death (Gali*et al*., 2018). Sex, age and malaria density have been reported to perturb blood electrolytes and liver enzymes (Hassan *et al*., 2008; Rathod, 2014; Adelakun*et al*., 2015).

In this study, one hundred and eighty (180) malaria patients attending the UMTH were grouped based on sex, age and malaria density; their blood electrolytes (Na^+, K^+, Cl^- and HCO_3^-) and liver

enzymes (ALP, AST and ALT) were analyzed and compared with one hundred and twenty five (125) control subjects. Our study revealed that most of malaria patients (70%) were male; majority (39.0%) of the malaria patients are within the age of 21-35 years. The preponderance of them has low malaria density (+). This study is consistent with findings from previous extensive research (Kotepui*et al*., 2015). This possibly may be due to higher hospital attendance among the group of individuals.

This study compared the blood electrolytes parameters (Na^+, K^+, Cl^- and HCO_3^-) and liver enzymes (ALP, AST and ALT) of malaria patients with those of the control subjects. There was little or no difference between the electrolytes parameters in malaria patients compared to the control subjects. This is in concordance with findings by Jasmin*et al.* (2012) but however, opposed to findings by Idogun and Airauhi (2009) who reported hyponatraemia and hypokalaemia in malaria patients. The mean value of Cl^- of malaria patients was significantly lower than the mean value of Cl^- of control subjects of with p-value 0.052. This is in variance with study by Singh *et al.* (2015). There were however, no significant differences in mean values of Na^+, K^+ and HCO_3^- compared with mean values of control subjects with p-values 0.369, 0.203 and 0.387, respectively. Plasma electrolytes play vital role in water homeostasis, which is a must for survival of all individuals, it is therefore imperative to determine their levels in all cases of malaria (Bradley *et al*., 1996). The maintenance of osmotic pressure and water distribution in the various body fluid compartment is a primary function of the four major electrolytes, the sodium (Na^+), potassium (K^+), chloride (Cl^-) and bicarbonate (HCO_3^-) (Idogun and Airauhi, 2009). In addition to water homeostasis, these electrolytes play important role in the maintenance of pH, proper heart and muscle function, oxidative-reduction reactions and as co-factors for enzymes (Idogun and Airauhi, 2009).

Our findings revealed that there was no significant difference in the electrolyte status of female malaria patients compared to male malaria patients. This is in agreement with report from Uzuegbu (2011). This present study also showed that malaria density had no significant effects on the electrolytes of the malaria patients. This finding however disagree previous reports (Maitland, 2005; Sitprija, 2008; Idogun and Airauhi, 2009). When compared in relation to age of malaria patients, our study showed little or no difference in mean values of electrolyte parameters. While HCO_3^- concentration differ across the age groups (p-value =0.031), there were no significant difference in Na^+, K^+ and Cl^- of the malaria patients (p-values 0.213, 0.120 and 0.652, respectively).

Our study revealed that there were no significant differences in mean values of liver enzymes ALP, AST and ALT of malaria patients compared with those of the control subjects with p-values 0.292, 0.848 and 0.559. This finding disagrees with previous reports by Osaretin*et al*. (2013) and Ratnendra*et*al. (2017) which showed significantly different levels of ALP, AST and ALT in malaria infection. However, the present study showed a significantly increased ALT concentration in male malaria patients compared with the female malaria patients (p-value = 0.035). This is in concordance with previous study (Ratnendra*et*al., 2017). The study further depicted that there were no significant differences in the concentrations of ALP and AST in malaria patients in relation to gender (p-value > 0.05). This present study also showed that malaria density had no significant effects on the liver enzymes of the malaria patients. Kochar*et al.* (2003) observed that patients of malaria hepatitis had linear increase in AST and ALT levels with increasing bilirubin level. Other previous studies, as opposed to our study, have also documented liver dysfunction in Plasmodium falciparum malaria (Anad*et al*., 1992; Premaratna*et al*., 2001). An increase in levels of liver enzyme (ALT) could be due to leakage from hepatic cells that were killed or injured by the auto immune progress and/or by abnormal cell activation induced by the parasites (Ratnendra*et*al., 2017). This finding supports previous report (Guthrow*et al*., 2007) as judged by the changes in liver function markers, there appears to be a measure of liver dysfunction and compromise in P. falciparum malaria infected patients, which seems to be more severe among male patients irrespective of age .

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6. SUMMARY/CONCLUSION/RECOMMENDATION

6.1. SUMMARY

The major findings from this study are enlisted below:

1. Majority (70.0%) of malaria patients attending UMTH are male.
2. Majority of malaria patients (39.4%) are 25-31 years of age.
3. Most of the malaria patients (89.4%) have malaria density of (+).
4. Cl^- levels are significantly lower in malaria patients than control subjects.
5. ALT levels are significantly higher in male than in female malaria patients.
6. There are no significant differences in values of electrolyte parameters and liver enzymes in malaria patients in relation to malaria densities.
7. There is a significant difference in concentration of HCO_3^- in malaria patients in relation to age.

6.2. CONCLUSION

The findings from this study can lead to a conclusion that majority of malaria patients who are males and adults, seek medical attention at early stage of malaria infection and at the point of enrolment where the malaria infection have little or no effects on electrolytes and liver enzymes. This is an indication of effectiveness of awareness and control measures against malaria infection. However, as emphasized by previous authors, efforts are still needed toward control measures and eradication of malaria infection in this region.

6.3. RECOMMENDATION

1. The electrolytes and liver enzymes status of malaria patients are direct indications of body fluid homeostasis and liver function. These underline the need to be analysed for all malaria patients.

The malaria density, electrolytes and liver enzymes of children of ages less than 5 years, pregnant women and the elderly should be examined, since they are among most vulnerable group of people.

2. Broader study covering Internally Displaced Persons (IDPs) and villages is recommended.

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