*Original article*

# Malaria parasitaemia and disorders of plasma electrolytes

Idogun ES[1], Airauhi LU[2]

[1] *Department of Chemical Pathology*; [2] *Department of Medical Microbiology*, *University of Benin Teaching Hospital*, *Benin-city*, *Edo-State*, *Nigeria*

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**Abstract**

**Objective**: To assess the plasma electrolyte status of patients with diagnosis of malaria but without the symptoms of diarrhea, vomiting or altered sensorium and correlation of the plasma electrolyte changes and the degree of parasitaemia. **Methods**: All the participants were adults, who met the clinical case definition of malaria but without the symptoms of diarrhea, vomiting or other medical illness. Blood slides were screened microscopically for malaria parasite and the parasite positive patients were grouped into A (mild), B (moderate) and C (heavy) malaria parasiteamia, depending on the malaria parasite count per high power microscopic field. Plasma sodium, potassium and chloride were estimated using the ion selective electrode method, while bicarbonate ions were determined by simple titration method. **Results**: A total of 200 subjects were studied which comprised of 150 patients and 50 controls. The mean plasma sodium was significantly lower in patients with heavy parasitaemia[group C, (128.8 ± 1.2) mmol/L] compared to those with mild and moderate parasitemia[(133.5 ± 2.8) mmol/L and (133.5 ± 3.5) mmol/L, $P < 0.0001$]. The mean plasma chloride was lowest in those patients with heavy parasitaemia (group C) than those patients of group A and B ($P < 0.0001$). Patients in group C also had significant hypokalaemia[(3.2 ± 0.5) mmol/L] when compared to those in groups A and B[(3.6 ± 0.3) mmol/L and (4.1 ± 0.6) mmol/L respectively, $P < 0.0001$]. **Conclusion**: A disorder of plasma electrolytes in malaria patients that had no symptoms of diarrhea and vomiting was reported. And the severity of hyponatraemia and hypokalaemia correlate with the severity of the patients' malaria parasitaemia. This data should alert clinicians on the need to assess electrolytes status of patients with malaria even without the symptoms of fluid loss, especially when malaria parasitaemia is heavy.

**Keywords**: Malaria; Parasitaemia; Plasma electrolytes; Disorders

## INTRODUCTION

This study was provoked by the authors' observation that some patients diagnosed with malaria had plasma electrolyte imbalance even when they had no symptoms of frank fluid losses like vomiting and diarrhea. Malaria is the major cause of mortality and morbidity in the tropical and subtropical regions of the world[1]. It is estimated that 300 – 500 million persons suffer from malaria every year and more than one million die each. Majority of these cases and deaths particularly those in children occur in Sub-Saharan Africa[1]. In normal physiology, maintenance of water homeostasis is paramount to life for all organisms. The maintenance of osmotic pressure and water distribution in the various body fluid compartment is a primary function of the four major electrolytes, sodium ($Na^+$), potassium ($K^+$), chloride ($Cl^-$), and bicarbonate ($HCO_3^-$). In addition to water homeostasis, these electrolytes play important role in the maintenance of pH, proper heart and

Correspondence to: Dr. Idogun E. Sylvester, Department of Chemical Pathology, University of Benin Teaching Hospital, P. M. B. 1111, Benin-City, Edo-State, Nigeria.
Tel: +2348023185483
E-mail: sylvesteridogun@yahoo.co.uk

muscle function, oxidation-reduction reactions and as co-factors for enzymes. Indeed, there are almost no metabolic processes that are not dependent on or affected by electrolytes[2].

Till date, the causes of electrolyte disorders in malaria infection are mainly attributed to fluid and electrolyte losses through diarrhea and vomiting that sometimes characterize malaria infection particularly in children and non-immune individuals. Although experimental findings have shown that the erythrocytes membrane integrity and function alters with malaria infection and that ions metabolism generally alter when red cells are parasitized by malaria parasites[3,4]. As the malaria parasite (*Plasmodium falciparum*) grows within its host erythrocyte, it induces the increase in the permeability of the erythrocyte membrane to a range of low-molecular-mass solutes, including $Na^+$ and $K^+$. This results in a progressive increase in the concentration of $Na^+$ in the erythrocyte cytosol at the expense of the plasma sodium ion concentration[3,4]. The parasite cytosol has a relatively low $Na^+$ gradient across the parasite plasma membrane such that these movements may be sufficient to alter plasma levels of sodium and potassium ions[3].

In this study, we selected a group of patients with laboratory confirmed *Plasmodium* infection but without clinical symptoms/complications such as diarrhea, vomiting and loss/altered sensorium. The objective of this study was to correlate the degree of parastaemia with plasma electrolyte status, with the aim of establishing the relationship between blood parasitaemia and plasma electrolyte disorders. It is hoped that the results will add to the epidemiological data that exists concerning electrolyte disorders in malaria infections since electrolyte disorders contribute significantly to the high morbidity and mortality of malaria patients.

## MATERIALS AND METHODS

This study was conducted from August 2006 to July 2007 in Benin-City in southern part of Nigeria. Malaria is endemic in this part of the country and transmission is all year round. The herd immunity of this community is high.

Malaria was defined as a febrile illness accompanied by *P. falciparum* trophozoite stage parasitaemia and clinical features for which no other cause(s) could be found.

The patients were randomly selected from the hospital patients presenting with clinical signs and symptoms compatible with case definition of malaria. The blood samples were drawn and sent to the microbiology laboratory for malaria parasite investigation and for electrolyte and urea investigations in chemical pathology laboratory of the hospital.

All the participants were adults, who met the clinical case definition and without other medical illness. All those who presented with diarrhea and vomiting or those with case definition of severe malaria were excluded. Also excluded were patients on diuretic drug therapy for other medical conditions.

Blood films were stained with Giemsa and blood slides screened microscopically for malaria parasite. The criterion for smear positivity was the demonstration of trophozoites of malaria. Parasite counts per microlitre of blood were calculated by recording the number of parasites present per high power field and multiplying the number by 500[5]. Less than 5 malaria parasites present per high power field was classified as mild (group A), 5 – 10 malaria parasite present per high power field as moderate (group B), ⩾10 malaria parasite per high field as heavy parasiteamia (group C), and the controls was group D.

Blood for electrolytes and urea were collected in specimen bottles with lithium heparin as anticoagulant and centrifuged at 3 000 rpm for 10 mins. Thereafter, the plasma was harvested with clean Pasteur pipettes into plasma bottles and was stored frozen until analyses were carried out in batches.

Plasma electrolytes, sodium, potassium and chloride were estimated using the ion selective electrode methodology ( humalyte electrolyte equipment manufactured by Human, Germany) [6]. while bicarbonate ions were determined by simple titration method[7]. Urea was quantified by the urea enzymatic method[8].

### Ethical consideration

Ethical approval was obtained from the hospital research ethical committee. All the participants gave approval after due explanation by the researchers.

### Statistics analysis

Statistical analysis was performed with Instat graph pad soft ware version 3.0. Means and standard deviations were determined for quantitative data and frequency determined for categorical variables. Student-*t* test was

used to test for significant association and analysis of variance was used to compare multiple means. $P$ value $\leqslant 0.05$ was considered statistically significant.

## RESULTS

A total of 200 subjects were studied which comprised of 150 patients and 50 controls. The study population was divided into three depending on the degree of malaria parasitaemia. Group A (mild), group B (moderate) and group C (heavy) parasitaemia while group D represent the controls. Each group comprised of 50 patients and a total of 55 males and 95 females were studied. The age range was 19 – 60 years. There was no significant difference in the mean ages of the controls and those of the patients ($P < 0.05$, Table 1). The plasma sodium was significantly lower in patients with severe parasitaemia[group C, (128.8 ± 1.2) mmol/L] compared to those with mild and moderate parasitaemia [(133.5 ± 2.8) mmol/L and (133.5 ± 3.5) mmol/L, $P < 0.0001$]. Plasma chloride disorder was similar to that of sodium, being lowest in those patients with severe parasitaemia (group C) than those patients of group A and B. Patient in group C also had significant hypokalaemia when compared with those in group A and B as well as the controls ($P < 0.0001$). The correlation of plasma level of sodium and potassium to the degree of parasitaemia showed negative relationship although not significant statistically ($r = -0.87, P = 0.33$ and $r = -0.44, P = 0.71$, for sodium and potassium respectively). Also the plasma chloride disorder showed a negative correlation but was not statistically significant ($r = -0.90$, $P = 0.12$). However, plasma bicarbonate and urea did not show any pattern of change when compared with the degree of parasitaemia (Table 1).

**Table 1** The plasma electrolytes of the patients and control and malaria parasitaemia in the patients

| Variable | A($n$ = 50) | B ($n$ = 50) | C($n$ = 50) | D($n$ = 50) |
|---|---|---|---|---|
| Age(years) | 34.30 ± 11.50 | 37.60 ± 11.20 | 37.50 ± 7.10 | 34.90 ± 11.20 |
| Sodium(mmol/L) | 133.50 ± 2.80 | 133.50 ± 3.50 | 128.80 ± 1.60 | 134.80 ± 3.80 |
| Chloride(mmol/L) | 93.90 ± 7.90 | 91.50 ± 6.50 | 86.80 ± 8.90 | 95.30 ± 7.70 |
| Potassium(mmol/L) | 3.60 ± 0.30 | 4.10 ± 0.60 | 3.20 ± 0.50 | 4.40 ± 0.70 |
| Bicarbonate(mmol/L | 25.00 ± 6.90 | 29.10 ± 3.80 | 27.50 ± 8.40 | 27.20 ± 4.80 |
| Urea(mmol/L) | 6.40 ± 2.70 | 7.30 ± 3.30 | 7.60 ± 5.00 | 5.00 ± 2.50 |
| Malaria parasite count/hpf | 2.18 ± 0.94 | 6.12 ± 1.00 | 11.18 ± 1.08 | 0 |
| Malaria parasite density/$mm^3$ | 1 090.00 ± 470.00 | 3 060.00 ± 500.00 | 5 590.00 ± 540.00 | 0 |

## DISCUSSION

Malaria remains one of the commonest diseases in Africa and sub-sahara Africa that causes high mortality and morbidity especially amongst children. Malaria claims millions of lives in Africa and sub-sahara Africa[9]. Malaria is often associated with abnormalities of fluid, electrolyte, and acid base balance. These can occur in any patient with malaria but are more common in severe falciparum malaria, extremes of age and in patients with high degree of fever and vomiting and diarrhea[10]. We report hyponatraemia and hypokalaemia in a group of uncomplicated malaria cases. The hyponatraemia is more severe in patients with heavy malaria parasitaemia. Our findings are consistent with other studies[11,12]. The pathophysiology of the hyponatraemia in malaria could be traced to diarrhea and vomiting as well as fluid losses through hyperpyrexia which sometimes characterized severely parasitized patients. Although, hyponatraemia is hardly severe but it could cause muscular weakness, vomiting, anorexia and cramps seen in patients with malaria. Experimental study has shown that fluid, electrolytes and mineral perturbation are prevalent features of tropical diseases especially malaria[12]. Hemodynamic alterations, fever, nitrogen wasting, and changes in membrane transport and acid-base balance contribute to these perturbations. We attempt to establish that it is not only when a patient presents with diarrhea and vomiting that electrolyte disorders occur in malaria but patients with heavy parasitaemia may present with electrolyte disorders especially hyponatraemia and hypokalaemia as shown in this study. Models

of malaria have been used to show that common hemodynamic changes in this tropical disease include decreased systemic vascular resistance, increased cardiac output and increased secretion of anti diuretic hormone (ADH)[12]. Other mechanisms of the hyponatraemia include the entry of sodium ions into cells and re-setting of osmoreceptors[12]. Hypokalaemia in malaria have also be reported by other authors[12-14]. The pathophysiology of the hypokalaemia apart from fluid losses through diarrhea and vomiting may be traced to hyperventilation and pyrexia during malaria infection which leads to a shift in potassium ions from the intracellular space to the extra cellular space[14].

Disorder of bicarbonate that have been reported more frequently is acidosis, but in this study we found significant variations in the plasma bicarbonate status of patients with malaria but these variations did not correlate with the degree of parasitaemia of the patients. Although it is expected that fever could cause hyperventilation which may induce respiratory alkalosis and a high plasma bicarbonate level, we did not find this expected relationship probably because of the diverse nature of the clinical presentations that are commonly seen in patients in endemic malaria zone like ours.

We report a disorder of plasma electrolytes in malaria patients that had no symptoms of diarrhea and vomiting and the degree of hyponatraemia and hypokalaemia correlate with the patients' malaria parasitaemia. This data should alert clinicians on the need to assess electrolytes status in patients with malaria even without the symptoms of fluid loss, especially when malaria parasitaemia is heavy.

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