ASSESSMENT OF TRACE ELEMENTS LEVELS IN CHILDREN WITH MALARIA

ABSTRACT

Malaria is a mosquito-borne infectious disease of humans and other animals caused by parasitic protozoans of the genus *Plasmodium*. Trace elements are dietary mineral that are in very minute quantities and they play significant roles in some biochemical processes leading to modifications of the causes of many diseases and also influence susceptibility to infection by malaria parasite in particular. The primary aim of this research is to assess the trace elements levels i.e selenium, copper, iron and lead in children with malaria. A total of eighty (80) subjects were recruited from University of Benin Teaching Hospital, Benin City, Edo State for this study. Fifty (50) malaria children from age 0-7years and thirty(30) non-malaria children serving as control. The samples were collected and analysed by standard method. The means and standard deviations in µg/dl of iron, copper, selenium and lead in male children with malaria are 161.19±54.62,145.59±55.32, 0.33±0.12 and 0.066±0.03 and when compared and tested statistically with their corresponding control values as 170.59±106.39, 156.39±93.58, 0.37±0.23, and 0.07±0.12 respectively, the difference was significant ($p<0.05$).The means and standard deviations in µg/dl of iron, copper, selenium and lead in females children with malaria are 232.86±192.62, 142.88±82.86, 0.479±0.414 and 0.06±0.04 and when compared and tested statistically with their corresponding control values as 241.38±123.78, 213.24±141.12, 0.497±0.255 and0.11±0.09 respectively, the difference was significant ($p<0.05$). Malaria parasite therefore has a damageable effect on the concentration of trace elements (iron, copper and selenium and lead) in children living in Edo State as a case study. In view of the importance of interest of these micronutrients, the significant variation has to be attended to check nutritional recovery in infected children, and to avoid worsening the pathological state during supplementation of these micronutrients. This implies that there may be need to supplement children with malaria with adequate micronutrients as this may be necessary in solving the menace of malaria morbidity in children.

Keywords: malaria morbidity, Malaria parasite, susceptibility to infection, nutritional recovery

INTRODUCTION

Malaria is a mosquito-borne infectious disease of humans and other animals caused by parasitic protozoans (a type of unicellular microorganism) of the genus *Plasmodium*. Commonly, the disease is transmitted via a bite from an infected female *Anopheles* mosquito, which introduces the organisms from its saliva into a person's circulatory system. In the blood, the protists travel to the liver to mature and reproduce. Malaria causes symptoms that typically include fever and headache, which in severe cases can progress to coma or death. The disease is widespread in tropical and subtropical regions in a broad band around the equator, including much of Sub-Saharan Africa, Asia, and the Americas.

"Trace elements are dietary mineral that are in very minute quantities (less than 0.01%) of the mass of the organism. They are useful for proper growth, development, maintaining and recovering the health of the organism. They have several roles in living organisms. Some are essential components of enzymes where they attract substrate molecules and facilitate their conversion to specific end products. Some donate or accept electrons in reactions of reduction and oxidation, which results in the generation and utilization of metabolic energy. Some trace elements impart structural stability to important biological molecules.Finally, some trace elements control important biological processes through such actions as facilitating the binding of molecules to receptor sites on cell membranes, altering the structure or ionic nature of membranes to prevent or allow specific molecules to enter or leave a cell, and inducing gene expression resulting in the formation of proteins involved in life processes" (John and Duffus, 2002). The trace elements of interest in this study are copper, iron and selenium

"Copper is essential to all living organisms as a trace dietary mineral because it is a key constituent of the respiratory enzyme complex cytochrome c oxidase. In molluscs and crustacea copper is a constituent of the blood pigment hemocyanin, which is replaced by the iron-complexed haemoglobin in fish and other vertebrates. The main areas where copper is found in humans are liver, muscle and bone" (Johnson and Larry 2008).

"The metabolism of all living organisms requires iron. Iron is a part of heme, which is the active site of peroxidases that protect cells from oxidative injury by reducing peroxides to water. Heme is also the active site of electron transport in cytochromes.When iron levels are insufficient, proliferation of bacteria or nucleated cells stops" (Carlsson *et al.*,2008).

"Selenium is a chemical element with symbol(Se) and atomic number 34. Selenium salts are toxic in large amounts, but trace amounts are necessary for cellular function in many organisms, including all animals. Selenium is a component of the antioxidant enzymes glutathione peroxidase and thioredoxin reductase (which indirectly reduce certain oxidized molecules in animals and some plants). It is also found in three deiodinase enzymes, which convert one thyroid hormone to another" (Gram *et al.*, 1995).

For centuries, lead toxicity has been one of the most significant preventable causes of neurologic morbidity from an environmental toxin. Lead is ubiquitous in our environment but has no physiologic role in human systems. Its effects are pervasive yet often subtle, with consequences ranging from cognitive impairment in children to peripheral neuropathy in adults. Currently, three forms of lead nephropathy are recognized. The first is acute lead poisoning resulting from acute massive exposure to lead, which causes classic symptoms, including colic, encephalopathy, anaemia, neuropathy, and Fanconi syndrome. The second is chronic lead nephropathy which is a slowly progressive interstitial nephritis resulting from excessive cumulative exposure to lead and is frequently associated with hypertension and gout. The third is lead-induced hypertension.

Furthermore, the Global use of micronutrients in health care delivery has taken centre stage due to the realization of their importance in disease management. Malaria is among the diseases plaguing a good population of the developing world and the cost implication for the management is very high. Free radicals are generated in malaria, so, a balance between minerals and antioxidants is imperative to maintain membrane integrity and function. Protection of red cell

membranes from free radical-mediated oxidative stress is crucial to their management. Minerals such as copper, iron, chromium, magnesium, selenium have been found to relieve oxidative stress associated with them.

MATERIALS AND METHOD

Study Population

The subjects used in this study were from the University of Benin Teaching Hospital located in Ugbowo, Benin city, Edo state, Nigeria. A total of eighty (80) subjects were recruited for this study, fifty (50) malaria children and thirty(30) non-malaria children which served as control.

Sample Collection

Blood samples were collected from each subjects from the antecubital vein using sterile disposable syringe and needle into accurately pre-lebelledEDTA containersfor both malaria and non malaria children.The blood samples were centrifuged with laboratory centrifuge within two hours of collection and the plasma separated into clean dry plain container which are labelled corresponding to the initial blood samples container.Samples were kept frozen until time of analysis.

Determination Of Trace Elements

The trace elements (Fe, Cu, Se, and Pb) were determined with atomic absorption spectrophotometer (AAS), using direct method.

Statistical Analysis

Mean, standard deviation and student's t-test were used at 95% confidence level.

RESULTS

The results of this study showed that the plasma levels of iron, copper, selenium and the heavy metal in the children with malaria vary considerably compared with the non malaria children (control group) and when tested statistically there was a significant difference ($P<0.05$) between the test and control subjects (Table 1).

Also, the results obtained shows that the plasma levels of iron, copper, selenium and the heavy metal in male children with malaria vary considerably compared with the non malaria children. And when tested statistically there was a significant difference ($P<0.05$) between the test and control subjects (Table 2)

The results also showed that the plasma levels of iron, copper, selenium and the heavy metal in female children with malaria vary considerably compared with the non malaria children. And

when tested statistically there was a significant difference (P<0.05) between the test and control subjects (Table 3).

Furthermore, the results showed that the plasma levels of iron and selenium increased in females subjects when compared with the males subjects. And also copper plasma level showed a slight decreased in female subjects when compared with male subjects. The plasma level of lead shows no difference between males and females subjects (Table 4).

Table 1: The plasma levels of Iron, Copper, Selenium and Lead in Malaria subjects and non-malaria subjects.

Parameters (µg/dl)	Malaria subjects (n=50)	Non-malaria subjects (n=30)	t-value	P-value	Remark
Iron	185.17±170.68	196.62±112.15	-0.33	P<0.05	S
Copper	161.28±70.13	178.21±108.82	-0.85	P<0.05	S
Selenium	0.39±0.32	0.41±0.23	-0.30	P<0.05	S
Lead	0.063±0.03	0.08±0.18	-0.30	P<0.05	S

Table 2: The Plasma levels of iron, copper, selenium and lead in Male Malaria Subjects and non-Malaria Subjects.

Parameters (µg/dl)	Malaria subjects (n=28)	Non-malaria subjects (n=22)	t-value	P-value	Remark
Iron	161.19±54.62	170.59±106.39	-0.39	P<0.05	S
Copper	145.59±55.32	156.39±93.58	-0.51	P<0.05	S

Selenium	0.33±0.12	0.37±0.23	-0.77	P<0.05	S
Lead	0.066±0.03	0.07±0.12	-0.17	P<0.05	S

Table 3: The plasma levels of Iron, Copper, Selenium and Lead in Female malaria subjects and Non-Malaria Subjects

Parameters (µg/dl)	Malaria subjects (n=22)	Non-malaria subjects (n=8)	t-value	P-value	Remark
Iron	232.86±192.62	241.38±123.78	-0.11	P<0.05	S
Copper	142.88±82.86	213.24±141.12	-1.64	P<0.05	S
Selenium	0.479±0.414	0.497±0.255	-0.11	P<0.05	S
Lead	0.06±0.04	0.11±0.09	-1.62	P<0.05	S

Table 4: The plasma levels of Iron, Copper, Selenium and Lead in males and females children with malaria.

Parameters (µg/dl)	Male subjects (n=28)	Female subjects (n=22)
Iron	161.19±54.62	232.86±192.62
Copper	145.59±55.32	142.88±82.86

Selenium	0.33±0.12	0.479±0.414
Lead	0.066±0.03	0.06±0.04

DISCUSSION

Micronutrient plays significant roles in some biochemical processes leading to modifications of the causes of many diseases and also influence susceptibility to infection by malaria parasite in particular.

This study shows that the level in µg/dl of iron, copper, selenium, and lead (mean and standard deviation) in males and females children with malariavary considerably compared with the non malaria children. And when compared with that of control subjects the difference was significant ($p<0.05$).The results obtained showed a decreased level of plasma iron, copper, selenium and lead when compared with the control subjects.

The decrease in plasma iron may have been due to the use of this nutrient by *plasmodium parasite,* insufficient supply of iron in the diet, impaired absorption of iron and acute or chronic blood loss in children with malaria.This result is in line with the work of Nussemblatt and Semba, (2002).

The decreased level of plasma copper may be partly due to its use by *Plasmodium* to fight the oxidant flow generated in course of infection. This result is in agreement with the work of Shankar,(2000).

"Selenium is know to act as an antioxidant and peroxynitrite scanger when incorporated into selenoproteins" (Gramm *et al.,*1995). "It is the main element in glutathione peroxidase (an active enzyme against oxidative stress) that reduces formation of free radicals and peroxidation of lipoproteins. The low concentration of selenium in serum could potentially expose the subjects to oxidative stress which is known to be associated with the pathogenesis of diseases such as malaria infection" (Burk, 2000).

The decreased in the lead level is in agreement with the work of Forrer *et al.*, (2001) who shows that lead is absorbed more easily if there is iron deficiency and inadequate micronutrient in the diet thus resulting to its reduction in this subjects.

The reduction of iron, copper and selenium serum concentration in this study agreed with the work of Nussemblatt and Semba, (2002) who associated malaria infestation to essential nutrients concentration in children. In their opinion, variability in concentrations of these nutrients in population suffering from malaria is assigned majorly to *Plasmodium* infection (Zeba *et al*.,

2008). The micronutrient reduction may be due to reduce intake, increased demands by children and infants and increased loss due to *Plasmodium falciparum* infection.

"Anaemia is associated with *Plasmodium* manifestation by a direct destruction and ineffective erythropoesis and the effect of nitric oxide which can inhibit the enzyme methionine synthase in infected children but also would take place in nutritional deficiency of these trace elements. The cohabitation of these two aspects (parasite manifestation and nutritional deficiency of trace elements) creates damage in the health of infected children" (Wongsrichanalai *et al*., 2002).

The plasma levels in µg/dl (means and standard deviation) of iron and selenium showed an increased in females subjects when compared with the males subjects. And also copper plasma level showed a slight decreased in female subjects when compared with male subjects. Gender-related changes seen in this research might rely on a specific source of exposure in one sex or due to difference in physiological factors or metabolic pathway. This results is in line with the work of Avino *et al.*, (2011).The plasma level of lead shows no difference between males and females subjects.

From the results of this study, it is evident that malaria has a damageable effect on the plasma levels of iron, copper and selenium in the blood. The malaria parasites trap micronutrients for their metabolism thereby leading to deficiency in serum concentration of this nutrient in malaria parasitized children. For the heavy metal (lead), it is evident that deficiency in micronutrients result in decrease in lead level in malaria subjects.

Conclusion

In view of the outcome of this research work, malaria parasite lowers the concentration of micronutrients. It is therefore recommended that malaria parasitized children and infant in Edo State, Nigeria as a case study be placed routinely on antioxidant vitamins to manage the micronutrient deficiencies seen in these children. There is also the need of insecticide treated bed nets intermittent preventive treatment and effective case management of malaria illness among children and infants. There should be adequate enlightenment of the public especially those living in the rural areas about the effects of malaria on micronutrients, so as to promote the prevention of *plasmodium* infections. It is also recommended to supplement children with malaria infection with adequate micronutrients which may also be essential in preventing malaria mortality and morbidity among young children.

Ethical Approval:

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

Consent

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

REFERENCES

Avino, P., Capannesi, G., Manigrasso, M., Sabbioni, E. and Rosada. A. (2011): Element assessment in whole blood, serum and urine of three Italian sub-population by *INAA Micro-chemical Journal*, vol. 99, no.2, pp.548-555.

Burk, R.F.(2000): Selenium, an antioxidant. Nutri Clin Car.;5:75-79.

Carlsson, M., Cortes, D., Jepson, S. and Kansstrup,T.(2008): Severe ironintoxication treated with exchange transfusion. *Arch Dis Child*.;**93(**4):321- 322.

Forrer, R., Gautchi, K. And Lutz, H. (2001): Simultaneous measurement of trace elements in human serum and their reference ranges by ICP-MS. Biological Trace Elements Resources.; 80:77-93.

Gram, H. J., kapft, A. and Bratter,P.(1995): The neccesity ofb selenium. pp.60-68.
Johnson, M.D. and Larry, E. (2008): "Copper"*Merck Manual Home Health Handbook*.

Nussemblatt,V.and Semba,K. (2002): Micronutrient malnutrition and pathogenesis of malarial anemia. *Acta. Tropica*. **82**: 321-337.

Shankar, A.H. (2000): Nutritional modulation of malaria morbidity and mortality. *J. Infect*., **182**: S37-S53.

Wongsrichanalai, C., Pickard, A., Wernsdorfer, W. and Meschnick, S. (2002). Epidemiology of drug-resistant malaria. *Lancet*. **2** (4): 209-218.

Zeba, A.N., Sorgho, H., Rouamba, N., Zongo, I., Rouamba, J., Guiguemdé, R.T., Hamer, D.H., Mokhtar, N. and Ouedraogo, J.B. (2008): Major reduction of malariamorbidity with combined vitamin A and copper and ironsupplementation in young children in burkina faso. A randomized double blind trial. *Nutr. J.* 7 : page 7.