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Variations in levels of selected micronutrients during malaria infection: A study from Ado-Ekiti, Ekiti, Nigeria

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ABSTRACT

Background

Malaria infection has been a global issue most especially in tropical and subtropical regions. Disease progression to severe malaria as a result of alteration in micronutrients could worsen the illness. The study aimed to determine whether there are variations in the levels of selected micronutrients (Iron, copper, magnesium, and zinc), malaria parasite density and packed cell volume (PCV) during malaria infection.

Material and methods

A total of one hundred young adults between the ages of eighteen and twenty two years were investigated. Blood samples were collected from fifty malaria subjects and fifty apparently non-infected subjects. Malaria detection was by microscopy while the parasite density was estimated using WHO standard procedure. Analysis of selected micronutrients (copper, iron, magnesium and zinc) was carried out using direct measurement on atomic absorption spectrophotometer and PCV was estimated using Micro-haematocrit method.

Results

The results showed that the levels of the micronutrients were significantly higher ($p<0.05$) in malaria subjects compared with controls. Significant positive relationships between copper, magnesium and zinc were found at $p<0.01$ and $p<0.05$.

Conclusion

The study concluded that there are significant variations in the levels of the micronutrients during malaria infection.

Keywords

Copper, iron, magnesium, malaria, micronutrients, zinc

Introduction

Malaria is highly endemic in both tropical and subtropical regions and may cause up to one million deaths each year, especially in Africa if proper treatment is not administered [1]. Malaria has been claiming a significant number of lives worldwide which may be approximately one million yearly [2]. According to an estimate by the World Health Organization (WHO) in 2015, it was shown that there were 214 million new cases of malaria worldwide and about 182 million Nigerians were said to be at risk of infection [1].

Children under the age of five years are particularly susceptible to malaria illness, infection and death. Globally in 2015 alone, it was estimated that malaria killed about 306, 000 children under age five which included 292, 000 children in the African Region. Furthermore between 2000 and 2015, the death rate among children under age five fell by 65% and 71% worldwide and Africa respectively [3]. Malaria shows non-specific symptoms at first which are similar to those of a minor systemic viral illness. The symptoms range from fatigue, abdominal discomfort, headache, lassitude to muscle and joint aches which are usually followed by chills, perspiration, anorexia, fever, vomiting as well as worsening malaise. Malaria in young children may also present with poor feeding, cough and lethargy [3]. Full recovery is expected at the early stage of the disease provided that prompt and effective anti-malarial treatment is given if there is no evidence of vital organ dysfunction. It should be noted that parasite burden often continues to increase if ineffective or poor-quality medications are given or if there is delayed treatment particularly in Plasmodium falciparum malaria [3]. Disease progression to severe malaria may take days or few hours and usually occurs with one or more of the following: metabolic acidosis, severe anaemia, hypoglycaemia, acute renal failure or acute pulmonary oedema and coma (cerebral malaria). It is worth noting that severe malaria is fatal in majority of cases if left untreated.

Malaria has continued to thrive in Nigeria despite several efforts to put malaria under control as a result of local weather conditions which often allow transmission to occur throughout the year. In addition, scarce resources and socio-economic instability have hindered efficient malaria control [1]. Although in other areas of the world, malaria is a less prominent cause of deaths, but it can cause substantial disease and incapacitation especially in rural areas of some countries like South America and South Asia.Therefore, since malaria infection is endemic in Nigeria and Africa at large and drug resistance is also a recurring problem as well as loss of appetite for food which is a factor that could affect the levels of micronutrients in the body during malaria infection; the study aimed to determine whether there are changes in the levels of some selected micronutrients (Iron, copper, magnesium, and zinc), malaria parasite density and packed cell volume (PCV) in young adults infested with malaria.

Material and methods

Study Period

The present study was undertaken in Ado-Ekiti during the period of March 2017-June 2017.

Study design and the participants

The study was conducted among young adults who are students of a tertiary institution and living in a community setting. A total of one hundred students between the ages of eighteen and twenty two years were investigated. Blood samples were collected from fifty malaria subjects and fifty apparently non-infected subjects. The fifty malaria subjects comprised of twenty five males and twenty five females.

Data collection

Blood samples were collected using vein puncture from the brachial vein for detection of malaria parasite, malaria density counts, PCV and for the analysis of copper, iron, magnesium and zinc. The detection of malaria parasite was done using thick smear described by [4]. Malaria parasite density was carried out and the estimation of packed cell volume (PCV) was by micro-haematocrit method [5, 6]. Analysis of micronutrients (copper, iron, magnesium and zinc) was carried out using direct measurement on atomic absorption spectrophotometer [7].

Inclusion criteria

All the subjects who were confirmed to have malaria without any disease and apparently healthy subjects without malaria infection (control) were included in the study.

Exclusion criteria

Individuals who were unable to give history properly or no responsible attendant was found, were excluded. Patient with history of other illnesses were set up as exclusion criteria. Sickle cell patients were also excluded to avoid study bias.

Ethical committee approval

The ethical approval to commence the study was obtained from the Ethical Committee of the College of Medicine and Health Sciences, Afe Babalola University, Ado-Ekiti, Ekiti state. The nature and aim of study was explained to each participant using an informed consent form and the subjects gave their consents before blood specimen were collected from them. This research is performed in accordance with the latest version of the Declaration of Helsinki.

Data management and statistical analysis

Data generated from the research was analyzed statistically using the statistical package for social sciences (SPSS) version 20. Independent sample t-tests and correlation were employed as tools to analyze the data. The results were recorded as Mean ± Standard deviation (SD). Significant values at $p < 0.05$ or 0.01 were considered.

Results

The level of PCV decreased significantly at $p<0.05$ in the malaria subjects compared with control. The levels of serum copper and magnesium showed significant increase ($p<0.05$) in the malaria subjects compared with control. There was no significant variation in age, PCV, iron, serum copper, magnesium and zinc in the malaria subjects when the males and females were compared but there was significant increase in malaria parasite density when the male subjects were compared with the female. There were significant positive correlations in the levels of copper, magnesium and zinc while there was significant negative correlation in the levels of PCV compared with copper.

Table 1: Age, PCV and micronutrients levels in malaria and control subjects (mean±SD)

Variables	Test (N=50)	Control (N=50)	P values
Age	20.10 ± 1.78	20.26 ± 1.66	0.643^{X}
PCV (%)	35.06 ± 3.68	37.02 ± 5.15	0.031*
Copper (ppm)	2.43 ± 0.82	1.96 ± 0.69	0.002†
Magnesium (ppm)	27.61 ± 2.59	25.32 ± 2.75	0.000†
Zinc (ppm)	1.47 ± 0.55	1.26 ± 0.49	0.054^{X}
Iron (ppm)	2.37 ± 1.21	3.11 ± 3.33	0.149^{X}

*P<0.05 †P<0.01 ^{X}P>0.05

Table 1 expedites that PCV is significantly lower in malaria subjects while Copper and Magnesium are significantly higher in the malaria subjects compared with control subjects.

Table 2: Age, PCV and micronutrient levels in male and female malaria subjects.

Variables	Male (N=25)	Female (N=25)	P values
Age	20.52±1.50	20.00±1.80	0.2740
PCV (%)	35.88±4.46	34.24±2.54	0.1160
Copper (ppm)	1.78±0.64	2.13±0.70	0.0670
Magnesium (ppm)	24.61±3.37	26.03±1.73	0.0670
Zinc (ppm)	1.21±0.42	1.32±0.55	0.4370
Iron (ppm)	2.51±1.34	2.24±1.07	0.4230

Table 2 expedites that the parameters were not significantly higher/lower in both sexes during malaria infection.

Discussion

The involvement of trace elements in the protection of malaria has been an important subject in numerous studies. Most of these micronutrients such as zinc, copper, and selenium serve as antioxidants and are intertwined in their actions.

The findings of the research showed that malaria infection caused significant decrease in packed cell volume (PCV) in those infested which might have occurred as a result of direct destruction of the red cells or as a result of ineffective erythropoiesis. However, the malaria infection did not affect packed cell volume (PCV) and iron levels irrespective of gender which is in agreement with a report where it was shown that there was no significant difference in PCV and haemoglobin (Hb) [8]. Another study in Tanzania also showed that iron deficiency is protective against severe Plasmodium falciparum infection and deaths in young children. However, it was stated that it could cause other detrimental conditions like poor growth, metabolic disorders and delayed development which could lead to death [9]. Hence, Malaria risk is influenced by physiologic iron status [9]. This is because iron is an essential component of haemoglobin which function to transport and stock oxygen in organisms thereby playing a role in oxidative metabolism including cellular proliferation and other physiological processes [10-12].

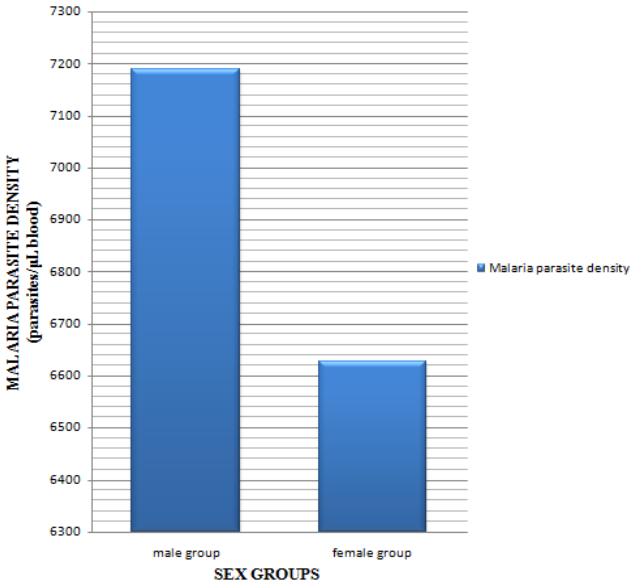

Figure 1: Malaria parasite density in male and female malaria subjects.

Table 3: Relationship between parameters in malaria subjects.

Variables	r value (p value)				
	PCV	Copper	Magnesium	Zinc	Iron
PCV	1.000	-0.31 (0.03)*	-0.23(0.11)	-0.17(0.25)	0.03(0.86)
Copper	-0.31 (0.03)*	1.000	0.36 (0.01)*	0.39(0.01)†	-0.05(0.73)
Magnesium	-0.23(0.11)	0.36*(0.01)	1.000	0.49 (0.00)†	0.11(0.47)
Zinc	-0.17(0.25)	0.39(0.01)†	0.49 (0.00)†	1.000	0.10(0.49)
Iron	0.03(0.86)	-0.05(0.73)	0.11(0.47)	0.10(0.49)	1.000

*Correlation is significant at the 0.05 level (2-tailed)
†Correlation is significant at the 0.01 level (2-tailed)

It was also observed that the packed cell volume (PCV) is increased in male subjects compared with female subjects (though not statistically significant). This may be due to the physiological state of the females and erythropoietic actions as females go through menstruation and it could also be due to the direct effect of sex hormones (both oestrogen and androgen) on erythropoiesis [13].

The results of this study also showed that malaria infection affected the levels of micronutrients as increase in the levels of magnesium was observed. This is in agreement with the reports of a similar work carried out in Ado- Ekiti on pregnant women as well as another report where it was shown that increase in magnesium occured in patients suffering from Plasmodium falciparum and Plasmodium vivax infections [14-16]. This might be due to haemolysis arising from the destruction of the red cells by the malaria parasites [16]. The results of this study also showed an increase in copper levels which is in conformity with the report that copper increased in malaria group compared to control group [17]. This might be due to inflammatory response of the host against the parasites; as copper has a role in immune function [18, 19]. The findings of this study also showed an increase in zinc levels when the results of the test were compared with the control (though not statistically significant) which does not agree with some findings where it was shown that there is significant decrease in serum level of zinc [14, 20]; but conforms with another report where it was shown that higher level of zinc was seen in the malaria infected samples than that of the uninfected samples [21]. This might be due to the movement of zinc from plasma to lymphocytes and liver during the acute phase response which might be due to its role in immune function [14, 22]. There are two possibilities to the above; since zinc is an intracellular element, its plasma level can be affected by haemolysis; and the release of zinc into the serum also occurs during clotting (micro-haemolysis). However, deficiency of zinc can be beneficial for malaria cases since the zinc available in the circulation would reduce the metabolism of microorganisms during infection because zinc aids in their growth [23].

The results of this study did not show that magnesium, copper and zinc levels were affected based on gender in the malaria subjects. The relationship between the levels of these micronutrients (magnesium, copper and zinc) in malaria infection may be physiological. This may be the reason why a slight decrease in magnesium levels was observed in the male group of the malaria subjects when compared with the female group which conforms to the report which showed that male patients had a slightly lower serum magnesium level than female patients in malaria infection [24]. A decrease (not statistically significant) in copper levels was also observed in the male group of malaria subjects compared to the female group which conformed to another report where higher serum and brain copper levels were observed in females compared with males [25]. This is due to the fact that males have low copper levels normally irrespective of the presence of malaria infection. According to the finding; the effect of gender on the serum and brain copper levels in mice and human subjects were investigated and the study agrees with the reason why copper dietary allowance is increased for males and it also agrees with the reason why Alzheimer's disease is mostly seen in the older female than their male counterparts [19, 25]. Also, a decrease (not statistically significant) in zinc levels was observed in male group compared with female group which is in conformity with previous reports where it was shown that higher concentrations of zinc was seen in females than in males [26, 27]. Zinc level is influenced by modifications that occur at different stages of puberty in males and it is directly influenced by gender variations [28]. Zinc, copper and magnesium showed positive significant correlations in the malaria subjects which do not agree with a previous finding that zinc and copper compete with each other as antagonist in order to properly regulate the physiological pathways in the body [29]. Copper and packed cell volume (PCV) also showed negative significant correlation in the malaria subjects which does not agree a finding where it showed that increase in copper causes increase in blood volume and vice versa [30].

Conclusion

It was observed in the study that malaria infection affected the micronutrient levels as evident by increase in magnesium, copper and zinc levels in the malaria subjects. There were positive correlations between the levels of zinc, magnesium and copper. Thus, there is need to monitor the levels of the micronutrients since there were significant changes in micronutrient levels for proper management as this will affect the overall wellbeing of the subjects.

Abbreviations

Packed cell volume (PCV), haemoglobin (Hb) World Health Organization (WHO),

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Authors' contribution

Conceptualization was done by AO, OD and BO. Data curation was done by AO, OD, BO, OO and FO; AO, OD, BO, OO and FO did the formal analysis. Investigation and methodology were done by OD, OO and FO. Project administration was by AO, OD, BO, OO and FO. Resources were by AO, OD, BO, OO and FO.

Competing interests

The authors declare no conflicts of interest.

Limitations & future scope of the study

The present study was confined to young males and females. They belong to same geographical area. So further studies are recommended with larger sample size.

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