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RESEARCH ARTICLE

MALARIA PARASITE DENSITY AND THE LEVEL OF COPPER IN PREGNANT WOMEN IN NNEWI (SOUTH EAST NIGERIA)

[1]Ozougwu, C. P, *[2]Aniagolu, M.O and [3]Ezeokeke, E.A

[1]Department of Chemical Pathology, Enugu State University of Science and Technology Teaching Hospital Enugu
[2]Department of Clinical Chemistry, College of Medicine, Enugu State University of Science and Technology Enugu
[3]Department of Medical Biochemistry, College of Medicine, Enugu State University of Science and Technology Enugu

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ABSTRACT

Malaria during pregnancy continues to be a major health problem in endemic countries with clinical consequences including death of both mother and child and attendant derangement in trace elements. This study is aimed at evaluating the relationship between the trace element copper and malaria density in pregnant women with malaria. The patients are pregnant women attending ante natal clinic of Nnamdi Azikiwe University Teaching Hospital Nnewi, Anambra, South East, Nigeria. The controls are pregnant women without malaria, non-pregnant women with malaria and non-pregnant women without malaria. The concentration of copper was determined by atomic absorption spectrophotometry while the malaria density was determined by counting the parasites against white cells. From results, copper showed a significant increase in pregnant women with malaria 13.63±6.22µmol/L compared to pregnant women without malaria 12.49±3.62µmol/L, non-pregnant women with malaria 7.29±2.83µmol/L and non-pregnant women without malaria 5.26±1.41µmol/L ($F=102.6$; $p<0.05$). Copper has a moderate negative correlation with parasite density ($r=0.32$; $p=0.003$).

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INTRODUCTION

Malaria is an important public health problem in developing countries. Plasmodium falciparum a pathogenic agent remains a major cause of morbidity and mortality to mother and child (Jeffrey and Pia, 2012). There are about 300 million cases of malaria each year, 9 of 10 cases occur in Africa. Women and children are most at risk (WHO, 2011). About 30 million African women are pregnant yearly, for these women; malaria is a threat both to themselves and their babies (Menendez *et al.,* 2000; WHO, 2011). In Malaria endemic areas, malaria during pregnancy may account for up to 15% of maternal anemia, 5-14% of low birth weight, 30% of preventable low birth weight (WHO, 2011). Pregnant women are particularly vulnerable to malaria as pregnancy reduces a woman's immunity to malaria infection and increasing the risk of illness, severe anemia and death for the unborn child.

Corresponding author: **Ozougwu, C. P,**
Department of Chemical Pathology, Enugu State University of Science and Technology Teaching Hospital Enugu
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Maternal malaria increases the risk of spontaneous abortion, still birth, premature delivery and low birth weight (WHO, 2003). Pregnancy is a period of increased metabolic demands with changes in a woman's physiology and requirements of a growing feotus (Broughton, 2007). Insufficient supplies of essential vitamins and micronutrients can lead to a state of biological competition between the mother and conceptus which can be detrimental to the health status of both (King, 2003). Some authors have associated malaria acquisition and its severity to the concentration of micronutrients in pregnant mothers, the protection against acute infection through a moderated deficiency in iron (Nyakeriga *et al.,* 2004); the reduction of risk of fever and clinical malaria episodes through a zinc supplementation (Zeba*et al.,* 2008) and the copper associated with zinc, which the reduction of the ratio copper/zinc is an increasing factor of the oxidative stress (Mezzetti *et al.,* 1998). Deficiencies of specific antioxidant activities associated with the micronutrients iron, selenium, copper, zinc and manganese can result in poor pregnancy outcomes including fetal growth restriction (Fall *et al.,* 2003), pre eclampsia and associated risk of diseases in adulthood,

including cardiovascular diseases and type 1 diabetes (Lykke *et al.,* 2009). Another consequence of oxidative stress resulting from antioxidant deficiency is the development of malaria anemia (Kremsner *et al.,* 2000). Micronutrients are known to be integral part of antioxidants and have been found to influence host cellular and humoral immunological functions (Spallhoiz *et al.,* 1990). Cell mediated immunological response to malaria is found to decrease during pregnancy (Riche *et al.,* 2000). These antioxidants have been shown to provide protection against oxidative stress induced by malaria (Adelekan *et al.,* 1997). Copper is essential for embryonic development. Maternal dietary deficiency can result in both short term consequences including early embryonic death and gross structural abnormalities, and long term consequences such as increased risk of cardiovascular disease and reduced fertilization rates (Fall *et al.,* 2003).

Background of study

Malaria during pregnancy continues to be a major health problem in endemic countries with clinical consequences including death of both mother and child. Research shows that maternal mortality is twice in pregnant women with malaria than among non-pregnant patients with severe malaria. Trace elements are known to be an integral part of antioxidant and have been found to influence host cellular and humoral immunological functions. These essential factors are very important in the body in order for the immune system to cope with the challenges imposed by infectious agents. This study is therefore aimed at evaluating the relationship between trace element copper andmalaria parasite density in pregnant women.

Aim and Objectives

To determine the relationship between the concentration of copper and malaria density in pregnant women in Nnewi. The objectives are as follows:

- To determine the relationship between the concentration of copper and malaria density in pregnant women.
- To determine the level of copper in pregnant women with malaria.

MATERIALS AND METHODS

This study was conducted at NnamdiAzikiwe University Teaching Hospital, Nnewi. Ethical approval for this study was issued by the ethics committee of NnamdiAzikiwe University Teaching Hospital, Nnewi. Four Hundred and sixty women were used for the study, out of this, One Hundred and Sixty pregnant women served as the test subjects, One Hundred pregnant women without malaria, One Hundred women without malaria, One Hundred women with malaria served as control. These women were selected using simple random sampling technique. The pregnant women among them were selected from their clinic while the non-pregnant women were apparently healthy women within Nnewi town. The scope, nature, aims and objectives of the study were explained to the participants for their consent. Women with malaria were later grouped according to parasite density (Melaine*et. al.,* 2010).
Women with established medical risk factors for oxidative stress such as AIDS, diabetes, tuberculosis, smoking and alcohol consumers were excluded from the study.

A volume 6ml of venous blood was collected from each of the participants, 2ml was dispensed into an EDTA container for total white cell count, a drop of blood from the syringe was placed on a clean grease free slide that has been labeled for a thick film while the remaining blood was dispensed into a plain tube. It was allowed to clot at room temperature for approximately one hour and then centrifuged at 2500 RPM for 10 minutes to separate the serum. The serum samples were analyzed for, copper. The thick film was left to air dry before staining.

Statistical Analysis

This was done using graph pad prism version 5. The results were presented as mean ± standard deviation. The statistical methods utilized for the analysis were one way analysis of variance, students "t" test, and correlation.

RESULTS

Copper in Pregnant Women with Malaria and Control subjects (Mean±SD): Pregnant with malaria, pregnant without malaria, non-pregnant women with malaria and non-pregnant women without malaria have mean serum copper level of 13.63±6.22µmol/L, 12.49±3.62µmol/L, 7.29±2.83µmol/L and 5.26±1.41µmol/L respectively.

Table 1. Copper in Pregnant Women with Malaria and Controls subjects (mean±SD)

	COPPER µmol/l
Pregnant Women With Malaria n=160	13.63 ± 6.218
Pregnant Women Without Malaria n=100	12.49±3.62
Non-Pregnant Women With Malaria n=100	7.294±2.83[a,b]
Non Pregnant Women Without Malaria n=100	5.262±1.41[a,b,c]
F-Value	102.6
P-Value	< 0.0001**

NB:a; p<0.05 compared with pregnant women with malaria
b; p<0.05 compared with pregnant women without malaria
c; p<0.05 compared with non-pregnant women with malaria

Table 2. Copper and parasite density in pregnancy (Mean±SD)

	COPPER µmol/l
<2000/µl n=44	15.88±6.340
2000-10000/µl n=96	13.07±6.80[a]
>10000/ µl n=20	13.10±2.92
F-Value	3.131
P-Value	0.0464**

NB: **; significant difference between the means (p<0.05)
a; p<0.05 compared with parasite density <2000/µl

Table 3. Copper level and parasite density in non-pregnancy (Mean±SD)

	COPPER µmol/l
< 2000/µl n=23	5.59±3.21
2000-10000 n=51	7.72±3.04 [a]
>10000 n=26	8.00±0.45 [a]
F-Value	6.662
P-Value	0.0019**

NB: **; significant (p<0.05) difference between the means
a; p<0.05 compared with parasite density <2000/µl
b; p<0.05 compared with parasite density 2000-10000/µl

Table 4. Copper level and Parasite Density in Pregnant and Non Pregnant Women (Mean±SD)

	< 2000/µl		2000 -10000/µl		>10000/µl	
	Pregnant women	Non pregnant women	Pregnant women	Non pregnant women	Pregnant women	Non pregnant women
Copper	15.88± 6.34	5.51 ± 3.21	13.07± 6.80	7.72 ± 3.04	13.10 ± 2.92	8.00 ± 0.45
P-Value	< 0.0001**		< 0.0001**		< 0.0001**	

The result shows a statistically significant difference between the means (F=102.6; p<0.0001). Further analysis shows no significant increased level in pregnant women with malaria compared to pregnant women without malaria (p>0.05), significant higher level in pregnant women with malaria when compared with non-pregnant women with malaria (p<0.0001) and a significant higher level in pregnant women with malaria when compared to non-pregnant women without malaria (p<0.0001), (Table 1).

Table 1. Copper level and Parasite Density in Pregnant and Non Pregnant Women (mean ± SD)

	R	P
Copper	-0.32	0.003

Copper and Parasite Density in Pregnancy (Mean±SD)

Copper, parasite Density of <2000/µl, 2000 – 10000/µl and >10000/µl has copper level of 15.88±6.34µmol/L, 13.07±6.80µmol/L and13.10±2.92µmol/L respectively. The result shows a significant difference between the means (F=3.131; p<0.05). There is a decrease in copper level as the malaria parasite density increases (Table 2).

Copper leveland Parasite Density in Non-Pregnancy (Mean±SD): Parasite Density of <2000/µl, between 2000-10000/µl and > 10000/µl showed copper levels of 5.51±3.21µmol/L, 7.716±3.04µmol/L and 8.003±0.45µmol/L respectively. The result shows a significant difference between the means (F=6.662; p=0.0019). There is a progressive increase in copper level as the malaria parasite density increases (Table.3). Pregnant women with parasite density <2000/µl has copper level of 15.88±6.340µmol/L while non-pregnant women has 5.509±3.214µmol/L. There is a statistically significant higher level of copper in pregnant women than in non-pregnant (P<0.0001). At parasite density level between 2000-10000/µl, pregnant women (13.07±6.801µmol/l) has a statistically significant higher level of copper compared to non-pregnant women (7.716±3.041 µmol/L), (p <0.0001). At parasite density level >10000/µl, pregnant women (13.10± 2.919µmol/L) has a statistically significant higher level compared to non-pregnant women (8.003±0.4511µmol/L), (p < 0.0001) (Table 4).

Correlation between Trace Elements and Parasite Density in Pregnancy

Copper has a moderate negative correlation with parasite density (r=0.32; p= 0.003), (table.5). This means that copper levels decrease with an increase in parasite density.

DISCUSSION

Copper is an essential micronutrient and is required for the formation of many enzymes with important role in the human body. It is essential for embryonic development where deficiency can result in both short term consequences including early embryonic death and gross structural abnormality and long term consequences like increased risk of cardiovascular diseases and reduced fertilization rates (Fall *et al.,* 2003). During pregnancy, many changes occur in copper levels and transport in both mother and fetus. The serum copper increases in early pregnancy and continues to rise reaching levels approximately twice those found in non-pregnant women (Alvarez *et al.,* 2007). This is reflected in this study where there is a significant increase in copper level in pregnancy compared to non-pregnant women up to approximately twice that in non-pregnant women. The cause of increased copper concentration during pregnancy is still a subject of controversy. The elevation has been ascribed to increased estrogen and progesterone levels (Sato and Henkin, 1973).

This assumption is further strengthened by the observation that administration of estrogen and intake of estrogen containing oral contraceptives produce an increase in serum copper concentration (Carruthens*et al.,* 1967). Nwagha*et al.,* (2011) also reported a significant increase in copper during pregnancy which they also attributed to increase in blood estrogens and decreased biliary excretion which is common in pregnancy. In contrast, Borglin and Heukenskjold (1967) noted a lack of relationship between increase and production of estrogen and other hormones and variation in serum copper content. In the present study, there is a slightly higher level of copper in pregnant women with malaria compared with pregnant women without malaria though not significant. Pregnant women with malaria have the highest copper level compared with all the groups. Non-pregnant women with malaria have a significant higher level compared with non-pregnant women without malaria. From this study, this shows that increase in copper level is seen in malaria. Saira*et al.,* (2013) also reported an increase in copper level in malaria. It is suggested to be a result of resistance reaction of maternal organism against the continuously invading metabolic products from the fetus and the parasite into the maternal circulation. Also while malnutrition or malabsorption in the body due to falciparum malaria can cause decreased serum zinc. It has been notified that zinc and copper are always in a competition to repel each other out from their absorption sites in the digestive tract; a diet which is excessive in one of these minerals may result in a deficiency in the other. According to this hypothesis, one can assume elevated copper levels in malaria within low level of zinc (Saira*et al.,* 2013). From this study, it is observed that as parasite density increases, there is a reduction in copper level both in pregnant and non-pregnant women. This is attributed to the uptake of copper from the blood by the malaria parasite (Asaolu and Igbaakin, 2009).

Conclusion

Copper levels increase in pregnancy and in malaria infection while a higher increase in malaria parasite density decreases its serum level.

Recommendation

High copper levels observed during pregnancy means that copper supplementation should not be undertaken in normal pregnancy except in severe malaria cases.

Conflict of interest

Authors' declare no conflict of interest.

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