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Research Article

Effect of *Plasmodium falciparum* Infection on Serum Levels of Calcium, Magnesium, Zinc and Iron Among Adult Sudanese Patients

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Abstract

Background: The effect of *Plasmodium falciparum* infection on the elements (Ca, Mg, Zn and Fe) was determined in adult Sudanese patients. **Materials and Methods:** This study included 75 normal healthy volunteers as control group, 75 infected patients with *Plasmodium falciparum*. Diagnosis was done by immunochromatographic test specific for *Plasmodium falciparum* as well as by thick and thin blood film. The serum specimens were used to measure magnesium (Mg) and iron (Fe) concentrations using a Hitachi 912 Chemistry Analyzer as per manufacturer's procedure. The calcium (Ca) and zinc (Zn) levels were measured by atomic absorption spectrometry. **Results:** In the present study, significant decrease in levels of Mg, Fe and Ca was observed in infected patients when compared to controls ($p = 0.000$). This study showed that whenever the density of the parasites in the blood increased, there was a significant reduction of Fe, Zn and Ca concentration ($p < 0.05$). The Mg and Fe in infected males increased significantly ($p = 0.033$ and $p = 0.000$, respectively) while Zn levels decreased significantly in infected males when compared to infected females ($p = 0.000$). **Conclusion:** It was concluded that *Plasmodium falciparum* infection reduced Mg, Fe and Ca significantly when compared to non-infected control. The levels of serum Fe and Zn were significantly decreased as increasing in the parasitaemia.

Key words: Calcium, magnesium, iron, zinc, malaria, *Plasmodium falciparum*

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Malaria infection is still a major health problem in the developing countries although there has been a gradual decrease in the number of mortality in the past 10 years and many countries were able to reduce malaria cases by 50%¹. Malaria is transmitted to human through the stings of infected mosquitoes and can often be fatal if not treated promptly with proper medication². Malaria is endemic to over 100 nations and territories in Africa, the Middle East, Asia, the South Pacific and Latin America. Every year, 300-500 million people suffer from malaria, causing death to be about 1-2.7 million infected persons. About 90% of these deaths take place in sub-Saharan Africa, particularly among children younger than 5 years. *Plasmodium falciparum* is by far the deadliest of the four human malarial species *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium malariae* and *Plasmodium ovale*³.

Calcium (Ca), iron (Fe), magnesium (Mg), zinc (Zn) and inorganic phosphate (Pi) are essential trace elements and the plasma contents of these nutrients change during the course of most infection. It was also demonstrated that some trace element concentrations change in malaria patients. However, it is not exactly known yet whether the causes of these changes are as a result of specific deficiency from dietary inadequacies and imbalances or a part of defense strategies of an organism that are regulated by acute-phase proteins⁴.

Although, required in very small amounts, elements such as Ca, Pi, Mg, Zn and Fe are vital for maintaining health. Also referred to as macro and micro-minerals, these elements are part of enzymes, hormones and cells in the body⁵. However, data about significant variation of these micronutrients in course of infections in developing countries, where problems of malnutrition and infection were encountered, should be kept under surveillance⁴.

The aim of this study is to assess the effects of *Plasmodium falciparum* infection on the elements (Ca, Mg, Zn and Fe) in the adult Sudanese patients.

MATERIALS AND METHODS

This study was a cross-sectional study carried between August, 2013 and December, 2014 in Khartoum State and Gadarif State, in Al-Ajyal Hospital, Health Care Center of Dr. Omar, Popularity Health Center and Samira Private Specialty Hospital. The study included 75 normal healthy volunteers (37 females and 38 males) as control group with mean age of 26.35 ± 5.56 years; 75 infected patients with *Plasmodium falciparum* (30 females and 45 males) with

mean age of 25.69 ± 7.14 years. All patients presented with symptoms suggestive of malaria for duration ranged between 6 h and 1 day. The diagnosis was confirmed by immunochromatographic test (ICT) specific for *Plasmodium falciparum* as well as thick and thin blood film. Patients taking drugs that are known to interfere with estimation and/or cause major hormonal disorders and those who refused to participate in this study were excluded.

Sampling: This study was approved by the ethical committee of Omdurman Islamic University. Informed consent was obtained from all study participants. Pre-prepared questionnaire including data concerning patients and their illness information was used. Before commencement of standard treatment, 7 mL of venous blood samples were obtained from each participant using standard smear, also ICT test was carried out. After 15 min, serum specimens were collected in the plane container after centrifugation at 3000 rpm for 5 min. The serum stored frozen (-20°C) in a tightly sealed tube for only 2 weeks and then analyzed. Specimens were allowed venipuncture technique in serum separator tubes. Immediately, blood film was prepared including thick smear and thin to room temperature and then mixed thoroughly by gentle inversion before assaying. Then Fe, Mg, Zn and Ca concentrations were measured.

Methods: Serum Fe and Mg concentrations were estimated by standard laboratory method on a Hitachi 912 Chemistry Analyzer (Roche Diagnostics, Germany) as per manufacturer's procedure. The Ca and Zn levels were estimated using Atomic Absorption Spectrometer (Shimadzu's AA-6200, Japan) as described by Baloch *et al.*⁶ and Onem *et al.*⁷. Blood slides were stained with 5% Giemsa stain. The parasitaemia densities were estimated by counting parasites against 200 white blood cells. Parasites densities were classified into three groups: Parasite density $< 2000 \mu\text{L}^{-1}$ (1+parasitaemia), parasite density between 2000 and 40000 μL^{-1} (2+parasitaemia) and parasite density $> 40000 \mu\text{L}^{-1}$ ($\geq 3+$ parasitaemia) as described by Seyrek *et al.*⁴.

Statistical analysis: Statistical analysis was performed using Statistical Package for Social Sciences software computer program version 11.0 (SPSS, Chicago, IL, USA). Statistical significance and differences from control and test values were evaluated by student's t-test. The $p < 0.05$ was considered as statistically significant. Values are expressed as the Mean \pm Standard Deviation (SD).

RESULTS

Table 1 shows significant decrease in levels of Mg, Fe, Zn and Ca in infected patients when compared to non-infected controls.

Table 2 shows that Fe and Zn levels were significantly decreased with increasing parasitaemia. The Mg levels were significantly changed between high and moderate parasitaemia as well as between low and high parasitaemia. The Ca levels showed a significant change between low and moderate parasitaemia as well as between high and moderate parasitaemia.

The results in male patients and female patients were compared in Table 3. The Mg and Fe in males were increased significantly while Zn levels were decreased significantly in males when compared to females.

DISCUSSION

Malaria infection develops via two phases: One that involves the liver (Exoerythrocytic phase) and one that involves red blood cells or erythrocytes (Erythrocytic phase)⁸.

Results of the present study showed that Mg, Fe, Zn and Ca were significantly reduced in the serum of infected patients ($p = 0.000$) much less than the control group. This reduction observed between the two groups of participants (malaria infected patients and controls) could be essentially due to clinical manifestations of malaria: Fever, pulse acceleration,

sweating and shivering. This is justified by the fact that in the course of infection, nutrients move from circulation to the tissues causing a reduction from circulation⁹. Reduction in Ca observed in malaria cases is caused by the clinical manifestation of malaria, which affects neuromuscular excitability, nerve conduction and muscular contraction¹⁰.

Also in this study, according to parasite density, serum concentration for Mg decreased significantly in high parasitaemia when compared to moderate parasitaemia as well as low parasitaemia ($p < 0.05$). This study showed that whenever the density of the parasites in the blood increased, it led to a significant reduction of Fe, Zn and Ca concentration between the three groups ($p < 0.05$). Akanbi *et al.*¹¹ stated that during the acute-phase response, Zn is redistributed from plasma to lymphocytes and to the liver, causing decreased Zn plasma concentrations. Zlotkin *et al.*¹² reported that malaria is a leading cause of Fe deficiency with other micronutrition substances. Luong and Nguyen¹³ also found that losses in Ca can be caused during digestive and renal problems following malaria. This renal insufficiency in malaria infection can cause an increase in urinary excretion of minerals such as Ca.

Serum concentrations of Mg and Fe in the present study were decreased significantly in infected females less than in infected male patients ($p < 0.05$). This finding was in line with that reported by Manser and Khan¹⁴ who studied the concentrations only in normal persons. The concentration of Zn in the serum of female patients was increased significantly when compared to male patients ($p < 0.05$). In normal persons,

Table 1: Comparison of trace elements between infected and control groups (Mean \pm SD)

Parameters	Control (n = 75)	Infected (n = 75)	t-value	p-value
Age (years)	26.350 \pm 5.56	25.690 \pm 7.14	0.6316	0.528
Mg (mg L ⁻¹)	21.281 \pm 6.10	13.607 \pm 5.71	7.9540	0.000*
Fe (mg L ⁻¹)	347.620 \pm 25.25	166.330 \pm 20.61	48.1700	0.000*
Zn (mg L ⁻¹)	877.250 \pm 22.78	848.610 \pm 26.33	7.1240	0.000*
Ca (mg dL ⁻¹)	9.850 \pm 1.31	7.570 \pm 2.08	8.0330	0.000*

* $p < 0.05$ control, Mg: Magnesium, Fe: Iron, Zn: Zinc, Ca: Calcium, SD: Standard deviation

Table 2: Results of trace elements in infected subjects according to parasitaemia (Mean \pm SD)

Parameters	Low parasitaemia (1+)	Moderate parasitaemia (2+)	High parasitaemia ($\geq 3+$)
Mg (mg L ⁻¹) ^{b,c}	15.22 \pm 6.05	13.92 \pm 5.51	11.68 \pm 2.88
Fe (mg L ⁻¹) ^{a,b,c}	225.00 \pm 21.21	172.45 \pm 20.44	101.54 \pm 12.25
Zn (mg L ⁻¹) ^{a,b,c}	889.45 \pm 14.66	860.25 \pm 32.54	796.12 \pm 24.12
Ca (mg dL ⁻¹) ^{a,b,c}	8.89 \pm 2.33	7.44 \pm 4.01	6.38 \pm 1.85

a: $p < 0.05$ compared with the low parasitaemia, b: $p < 0.05$ compared with the moderate parasitaemia, c: $p < 0.05$ compared with the high parasitaemia

Table 3: Results trace elements of infected subjects according to sex (Mean \pm SD)

Parameters	Male patients (n = 45)	Female patients (n = 30)	t-value	p-value
Mg (mg L ⁻¹)	14.351 \pm 3.65	12.863 \pm 1.09	2.165	0.033*
Fe (mg L ⁻¹)	177.67 \pm 30.88	154.990 \pm 18.45	3.611	0.000*
Zn (mg L ⁻¹)	801.20 \pm 52.14	896.020 \pm 32.89	8.846	0.000*
Ca (mg dL ⁻¹)	7.57 \pm 2.08	8.120 \pm 3.00	0.938	0.351

* $p < 0.05$ compared with the female patients, SD: Standard deviation, Mg: Magnesium, Fe: Iron, Zn: Zinc, Ca: Calcium

Zn level in males is higher than females¹⁵. On the other hand, serum Ca was decreased insignificantly in male patients more than female patients ($p < 0.05$). From the present study, it was revealed that there was a significant reduction in Ca values. This is due to the fact that vitamin D will be reduced in infections and subsequently lowered Ca level. The reduction of vitamin D in males when compared to females was assigned by Tekin *et al.*¹⁶.

CONCLUSION

In conclusion, *Plasmodium falciparum* infection reduces serum level of Ca, Mg, Zn and Fe in the adult Sudanese patients. The Ca, Zn and Fe levels were significantly decreased as increasing in the density of *Plasmodium falciparum* parasites in the blood. Comparing to infected females, levels of Mg and Fe in male patients were increased while Zn levels were decreased.

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SIGNIFICANT STATEMENT

- Malaria infection is still a major health problem in the developing countries
- The plasma levels of essential trace elements change during the course of most infection
- Although, required in very small amounts, elements such as Ca, Pi, Mg, Zn and Fe are vital for maintaining health.
- The results of the present study revealed a reduction in serum levels of trace elements
- The findings of the study suggests that supplementation of trace elements in patients infected with *Plasmodium falciparum* is essential to reduce mortality and morbidity

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