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Cortisol and uncomplicated *Plasmodium falciparum* malaria in an area of unstable malaria transmission in eastern Sudan

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ABSTRACT

Objective: To investigate the levels of serum cortisol in patients with uncomplicated *Plasmodium falciparum (P. falciparum)* malaria in an area of unstable malaria transmission in eastern Sudan. **Methods:** The concentrations of cortisol were measured in sera of 25 patients with uncomplicated *P. falciparum* malaria (at presentation, 24 h and 7 d later) and 25 healthy volunteers using radioimmunoassay gamma counter. **Results:** There was no significant difference in mean (SD) of total cortisol levels in patients with malaria in comparison with the control group; 602.2 (369.6) *vs.* 449.2(311.7) ng/mL, P=0.12. In patients with uncomplicated *P. falciparum* malaria, the mean (SD) presenting cortisol levels were significantly higher in comparison to the levels on day 7; 602.2 (369.6) *vs.* 373.6(139.1) ng/mL, P=0.009. In the patients with uncomplicated *P. falciparum* malaria (on presentation) cortisol levels were not correlated with initial temperature or the presenting parasitaemia. **Conclusions:** Thus, cortisol levels were not significantly different between the patients and the controls.

1. Introduction

There are almost 515 million episodes of clinical *Plasmodium falciparum (P. falciparum)* malaria infections[1]. Malaria is the major health problem in Sudan, where it causes up to 7.5–10 million cases and 35 000 deaths every year[2]. Understanding the pathogenesis of malaria is essential–yet not completely understood for the understanding of the disease as whole and may be vital for the development of the future vaccine. There are many hypotheses that could explain susceptibility and pathogensis of malaria. There are few reports on the endocrine changes (especially hypothalamous/pituitary/adrenal axis) during the acute phase of uncomplicated *P. falciparum* malaria[3–6]. The present work was conducted to investigate the levels of serum cortisol in patients with uncomplicated *P. falciparum* malaria in an area of unstable malaria transmission in eastern Sudan[7].

2. Materials and methods

The study was conducted in New Half, eastern Sudan during the period of September–November 2006, where consecutive 25 patients presented (before the mid-day) with uncomplicated *P. falciparum* malaria were approached to participate in the study. Healthy volunteers (25) that matched for age were taken as control. After an informed consent was taken, pre-tested questionnaires were filled to gather the socio-demographic characteristics, the basic medical history. The patients were examined clinically and their temperature was recorded.

Blood films were prepared, stained with giemsa and 100× oil immersion fields were examined for malaria. The parasite density was counted against 200 leucocytes, assuming 8 000 leucocytes/ μ L. All the slides were double-checked blindly and only considered negative if no parasites were detected in 100 oil immersion fields. Then 5 ml of blood was taken for haemoglobin levels, biochemical tests, and centrifuged immediately and the sera kept at -20 ℃ till analyzed by radioimmunoassay gamma counter (Riostad, Germany). RIA KIT (RK-240MACED040501) of IZOTOP (Budapest) was used for analysis of cortisol levels. The entire samples were analyzed by the same person, who is blind about the clinical findings of the patients. The patients were treated with artesunate-sulfadoxine-pyrimethamine which is the first line treatment for malaria in Sudan.

2.1. Ethical clearance

The study received ethical clearance from the Research Board at the Faculty of Medicine, University of Khartoum.

2.2. Statistical analysis

Data were entered into a computer database and SPSS

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software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. The means (age, weight, temperature, and hemoglobin and other biochemical tests) were compared between the patients and controls using student *t*-test, when the data was normally distributed and by Mann-Whitney test if the data was not normally distributed. Cortisol levels between the patients and the controls were compared using student *t*-test, which also used to compare the cortisol levels in patients at presentations and day 1 and day 7. Correlations between parasitemia, temperature and cortisol levels were determined. *P* value$<$0.05 was considered as significant.

3. Results

There were no significant differences in the age, weight, urea and creatinine levels between the patients (at presentations) and the controls, but the haemoglobin level was significantly low in the patients (Table1).

Table 1

Comparison of different presenting variables between the patients with uncomplicated *P. falciparum* malaria and the controls.

Variable	Patients with malaria	Controls	*P* value
Age (years)	18.08(11.10)	15.60(2.80)	0.62
Weight (kg)	45.05(19.60)	47.40(5.90)	0.57
Hemoglobin (g/dL)	11.90(1.70)	13.10(1.70)	0.02
Urea (mg/dL)	27.80(7.90)	27.50(7.60)	0.88
Creatinine (mg/dL)	0.95(0.26)	0.89(0.40)	0.40
Total cortisol (ng/mL)	602.20(369.60)	449.20(311.70)	0.12

There was no significant difference in mean (SD) of total cortisol levels in patients with malaria in comparison with the control group; 602.2 (369.6) *vs*. 449.2(311.7) ng/mL, *P*=0.12 (Table 1).

In patients with uncomplicated falciparum malaria, the mean of the total cortisol level was significantly higher on presentation (day 0) than in day 7; 602.2 (369.6) *vs*. 373.6(139.1) ng/mL, *P*=0.009. There was no significant difference in the cortisol levels on presentation and 24 h later; 602.2 (369.6) *vs*. 491(323.3) ng/mL, *P*=0.12.

In infected patients; there were no correlations between the cortisol levels and parasite density (*r*=0.149, *P*=0.51) or the presenting temperature (*r*=0.308, *P*=0.175).

4. Discussion

There was no significant difference in mean of total cortisol levels in patients with malaria in comparison with the control group. Interestingly, we have recently failed to document significant difference in the cortisol levels-even prolactin too-between pregnant women with uncomplicated *P. falciparum* malaria and the controls in the same area of the study[6]. However, it has been reported that cortisol levels were significantly higher in patients with *P. falciparum* malaria than in the control[3,5]. The significantly higher levels of serum cortisol in the infected patients previously reported indicated an intact hypothalamous/pituitary/adrenal axis in these reports. Activation of this axis in malaria might be as results of release of cytokines and/or results of stress generated by the disease itself as it has been observed earlier that cytokines level was associated with basal and peak levels of ACTH[4].

In patients with uncomplicated falciparum malaria, the mean of the total cortisol level was significantly higher on presentation (day 0) than in day 7. This is in agreement with the other reports[5]. But, our study failed to demonstrate significant difference in the cortisol levels on presentation and 24 h later.

In infected patients; there were no correlations between the cortisol levels and parasite density or the presenting temperature. Recently we have observed a positive correlation between the cortisol levels and parasite density in pregnant women presented with uncomplicated *P. falciparum* malaria in the same area of the study, but there were no significant correlations between the total cortisol levels and temperature[6]. However, Libonati and colleagues have reported a positive correlation between cortisol and the parasitaemia in patients with uncomplicated *P. falciparum* malaria[5]. Furthermore, a positive correlation between cortisol levels and parasite load has been reported in primigravidae infected with *P. falciparum* malaria[8]. This is expected as pregnancy is a unique situation where the immunomodulation is mediated by cortisol and other steroidal hormones as estrogen and progesterone[9].

Thus, our findings are totally different from the previous reports. Large sample-sized studies in this area and other areas of unstable malaria transmission are urgently needed.

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgments

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