

MEASUREMENT OF CREATINE KINASE LEVEL IN SUDANESE CHILDREN WITH CEREBRAL MALARIA, CENTRAL REGION, SUDAN

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ABSTRACT

Background: Malaria is a global disease, and it is a major health problem in Sudan, associated with many complications that increase morbidity and mortality. **Objective:** This study was aimed to measure the creatine kinase (CK) level in Sudanese children with cerebral malaria. **Materials and Methods:** This is prospective cross-sectional hospital based study, was done in sixty three children with cerebral malaria (CM) from Kosti, Rabak, Sinnar, Singa, Rufaa and Medani Teaching hospitals, central region Sudan, during May-October, 2012. Fifty two with cerebral malaria and eleven children affected with uncomplicated malaria. The age of children was ranged between (2-12 years). Data was collected through, clinical evaluation form and designed questionnaire of pediatricians and cerebral malaria was confirmed microscopically, serum concentration of creatine kinase, was measured by spectrophotometer. **Results:** The mean levels of CK is increased in children with cerebral malaria ten hours after admission (488.99 u/L) but decreases 24-48 hours after admission (227 μ /L), and also decreases in those with uncomplicated malaria ($p=0.001$). **Conclusion:** Children with elevated urea levels on admission or those who experienced mean low level of creatine kinase subsequently were more likely to die.

KEY WORDS

Creatine Kinase, Cerebral malaria, Central Sudan.

INTRODUCTION

Malaria continues to be a major health problem in Sub-Saharan Africa. In general, the disease is endemic in more than 90 countries and is responsible for about 500 million cases and more than 1 million deaths each year (1). In Sudan, malaria was determined as one of the most devastating problem that led to loss of 2,877,000 DALYs in the year 2002 and was identified as a common cause of fever (2, 3). Cerebral malaria (CM) is estimated to affect more than 785000 children who are younger than 9 years in sub-Saharan Africa every year, the case fatality rate even with optimal therapy, is 15-30% (4). Children who survive CM may be left with permanent

neurological sequence, including seizures, acquired language disorders, motor deficits and problems with memory and attention (5). Skeletal muscle damage is common in malaria. In order to investigate the relationship between serum creatine kinase (CK) and myoglobin levels, muscle histology, and renal function of plasmodium falciparum malaria, serum creatine kinase levels were estimated in patients with uncomplicated malaria. Muscle appears to be an important site for P-falciparum sequestration, which could contribute to metabolic and renal complication (6). Cerebral malaria (CM) is a serious complication of plasmodium falciparum infection that contributes significantly to morbidity and mortality worldwide.

Primarily young children develop a diffuse potentially rapidly invisible encephalopathy associated with loss of consciousness, seizures and few localizing neurological sign; other complication as severe anemia or respiratory distress increase the tragic outcome (7). Pathophysiology of malaria infection needs two phases to complete the disease picture: one that involves the liver (exoerythrocytic phase), and one that involves red blood cells or erythrocytes (erythrocytic phase). When an infected mosquito pierces a person's skin to take a blood meal, sporozoites in the mosquito's saliva enter the bloodstream and migrate to the liver where they infect hepatocytes, multiplying asexually and asymptotically for a period of 8–30 days (8). In humans, malaria is caused by *P. falciparum*, *P. malariae*, *P. ovale*, *P. vivax* and *P. knowlesi*. (9,10). Among those infected, *P. falciparum* is the most common species identified (~75%) followed by *P. vivax* (~20%)(11) Although *P. falciparum* traditionally accounts for the majority of deaths,(12) recent evidence suggests that *P. vivax* malaria is associated with potentially life-threatening conditions about as often as with a diagnosis of *P. falciparum* infection (13). The histopathological hallmark of cerebral malaria is engorgement of cerebral capillaries and venules with parasitised red blood cells (PRBCs) and non-parasitised RBCs (NPRBCs)(14). Some authors think that cerebral malaria has features of a diffuse encephalomyelitis (15). There are several serious complications of malaria. Infection with *P. falciparum* may result in cerebral malaria, a form of severe malaria that involves encephalopathy. It is associated with retinal whitening, which may be a useful clinical sign in distinguishing malaria from other causes of fever (16) Splenomegaly, severe headache, hepatomegaly (enlarged liver), hypoglycemia, and hemoglobinuria with renal failure may occur (17). No documented data was found to estimate the creatine kinase level among Sudanese children infected with cerebral malaria. So, this study aimed to measure the creatine kinase (CK) level.

MATERIALS AND METHODS

This is cross-sectional study was carried out in central Sudan Gezira irrigation scheme and cities nearby

where malaria is endemic. The study population was children diagnosed as case of malaria who are admitted to teaching hospitals of major cities in this region, selected randomly that include: Kosti, Rabak, Sinnar, Singa, Rufaa and Wad Medani teaching hospitals. The study was conducted during the period between May – October 2012. The sample of this was taken by simple random sample from the pediatrics wards of the selected hospitals. Sixty three child were selected, then the divided into two strata, fifty two of them are eligible to WHO criteria of cerebral malaria, and eleven (11) child affected with un complicated malaria, their age was ranged between (2- 12 years). Cerebral malaria was diagnosed clinically by pediatrician and confirmed microscopically by blood film for malaria using Giemsa stain. First 2ml of venous blood sample were taking from all patients; after 4-10 hours of the onset of admission, and second blood sample was taken after 24 hours of the onset of the admission.

The first blood sample was used to measure hemoglobin (Hb), and to estimate total white blood cell count (TWBC), blood glucose, serum urea and creatine kinase (CK) levels. The second venous blood sample was used to analyze creatine kinase (CK) level. The personal data, history of presenting complain and family history was taken by designed questionnaire. All biochemical measurements were analyzed by photometric method using spectrophotometer device. Clinical examination and findings were achieved by pedestrians in the ward. Children with CM were enrolled if they were admitted to these hospitals and met the World Health Organization criteria for cerebral malaria (CM) which include; coma (Blantyre coma scale 2 or Glasgow coma scale 8), *P. falciparum* on blood smear, and no other cause for coma. Children were considered to have uncomplicated malaria (UM) if they had signs and symptoms of malaria (fever, chills, vomiting, and headache), *P. falciparum* infection on blood smear, and no evidence of malaria complications (e.g., seizures, respiratory distress, severe anemia, or coma) or other acute illness.

All steps of this study were implemented after taking the informed consent by the child's parent and pediatricians.

Statistical analysis was considered as frequency and means for all parameters and outcomes using the SPSS Software program for windows, version 11 to find

the mean difference between two groups at p -value ≥ 0.05 for confidence interval (C.I) = 95%.

RESULTS

Table (1): Mean of Serum Urea, Blood glucose and Creatine Kinase (CK) levels in Sudanese children with cerebral malaria, Central Sudan

Parameter	Mean	Reference values
Serum urea	35.8 mg/dL	15-45 mg/dL
Random blood glucose level	98.8 mg/dL	60-110 mg/dL
CK(4-10)hrs after admission	488.99 μ /L	†
CK(24-48)hrs after admission	227 μ /L	†

† Reference values have not been established for patients that are less than 6 years of age

Table (2): Mean of hemoglobin (Hb) and white blood cell count (WBCC) in Sudanese children with cerebral malaria, Central region, Sudan:

Parameter	Mean	Reference values
Hemoglobin(Hb)	8.23 mg/dL	12-16 mg/dL
WBCs Count	4700/ mm ³	>1100/ mm ³

Table (3): The outcome of Sudanese children with Cerebral Malaria (CM) by means of some hematological and biochemical tests, central region, Sudan.

Outcome of CM	No.	Mean Hb Level	Mean TWBC	Mean blood glucose	Mean Blood urea	Mean C.K Level
Recovered	43	8.85 mg/dL	3.6 mm ³	98.6 mg/dL	35.5 mg/dL	472 μ /L
Died	9	18.1 mg/dL	3.16 mm ³	96.2 mg/dL	61.2 mg/dL	1679 μ /L
Total	52					

Table (4): Mean \pm Std of Creatine Kinase (CK), Hemoglobin (Hb) and Blood urea Levels among children with cerebral malaria (CM) and children with un complicated malaria (UCM) of Sudanese children, Central region, Sudan.

Parameter	CM (n=43) mean \pm Std	UCM (n= 9) mean \pm Std	P-value
CK (μ /L)	740 \pm 488.99	192 \pm 198.55	0.001 *
Hb (mg/dL)	8.23 \pm 1.46	11.11 \pm 1.08	0.000 *
Blood urea(mg/dL)	35.83 \pm 13.67	26.18 \pm 4.94	0.025 *

* significant mean difference

Figure (1): Shows the Frequency (%) of family history of epilepsy and convulsion of Sudanese children suffered malaria and admitted to pediatrics ward, central region, Sudan.

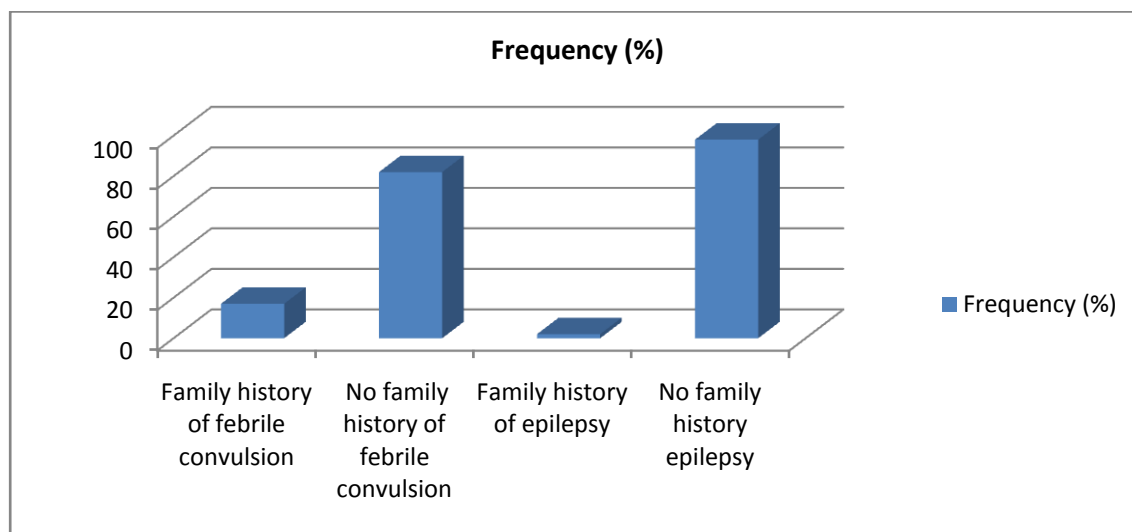
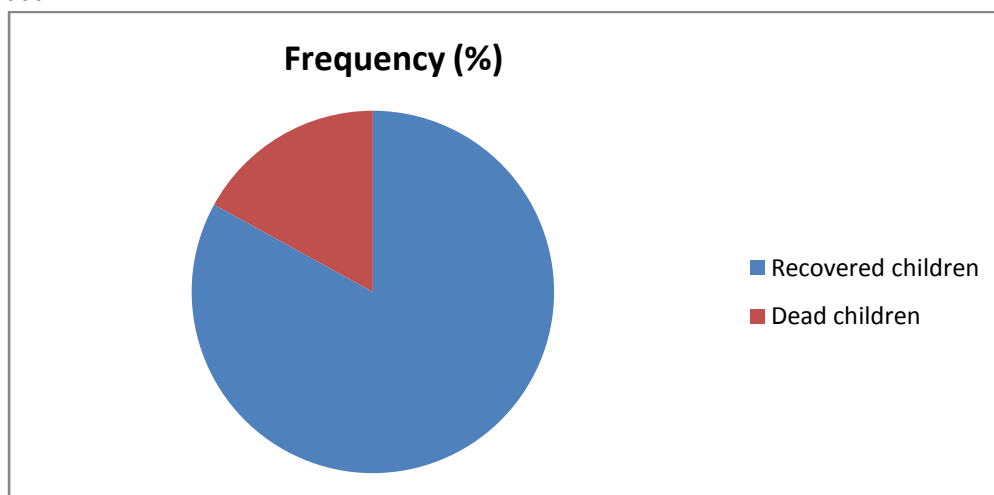


Figure (2): Shows the outcome of Sudanese children suffered malaria and admitted to pediatrics wards, central region, Sudan



DISCUSSION

Cerebral malaria is notable disease among children in central Sudan, where malaria is endemic resulting in raising the prevalence of mortality and morbidity (**Figure 2**). Because CM is severe illness; it characterized by wide range of metabolic disorders elicits spectrum changes in the blood biochemistry among study children (**Table 3**). In general, the function of enzymes is to accelerate biological reactions involved in all chemical transformation reaction in the body (18, 19). Creatine kinase is one of enzymes indeed.

Regarding the effect of cerebral malaria on the activity of creatine kinase enzyme, scientific background confirmed that there is no clear role of creatine kinase in malaria infection, but it may be due to the decrease in the ATP levels that due to loss of heat energy in malarial fever. In the present study the mean levels of CK increased in children with Cerebral Malaria whereas it decreases in those with uncomplicated malaria ($p=0.001$). The mean level of CK is increased in children with Cerebral Malaria ten hours after admission ($488.99 \mu\text{L}$) but decreases 24-48 hours after admission ($227 \mu\text{L}$).

Regarding the manifestations of cerebral malaria as convulsion, blood glucose level, hemoglobin levels (**Table 4**) of this study are similar to the results of studies in African children with cerebral malaria (20) Sudanese children like African children growing up in malaria's endemic areas, concludes that severe *falciparum* malaria usually manifests as seizures, impaired consciousness, or metabolic acidosis presenting as respiratory distress or severe anaemia (20). But, African children rarely develop renal failure or pulmonary edema.

A combination of clinical and laboratory abnormalities particularly low hemoglobin level can identify a group of children with cerebral malaria who are most at risk of dying and require intensive care and also they are candidates for especial forms of therapy.

Both groups in the study showed normal values for serum urea, blood glucose level.

Children with elevated urea levels on admission or those who experienced mean low level of creatine kinase subsequently were more likely to die.

Most of children in the study (**Figure 2**) haven't history of febrile or epileptic convulsions.

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