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Assessment of Renal Function Tests, copper and selenium levels in Homozygous Sickle Cell Disease Patients at Aljazeera state in Sudan

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ABSTRACT

This is a case control study. It was conducted at Madani educational Hospital in Aljazeera state. The aim of the present study is to evaluate Serum urea, creatinine, Na, K, copper and selenium levels in sickle cell disease patients. A total of 70 sickle cell disease patients were enrolled in this study, in addition to 30 healthy' children as a control group age and sex matched apparently healthy control subjects. Blood samples collected from participants were analyzed for trace elements using atomic absorption spectrophotometer. The results of the present study showed a significant increase in the mean of serum urea levels in patients when compared with control group (58.76 ± 10.19) versus (34.27 ± 7.13) mg/dl respectively with (*P-value* 0.00). Result of creatinine indicated insignificant increase when compared mean of patients with mean of control group (0.87 ± 0.22) versus (0.42 ± 0.07) mg/dl with (*P-value* 0.07). Also there was insignificant difference in the serum Na and K in mean of patients comparing with mean of control group (138.77 ± 6.47) versus (139.5 ± 2.93) m.mol/l (*P-value* 0.5), (4.28 ± 0.74) versus (3.91 ± 0.34) m. mol/l (*P-value* 0.10). In the current study there was significant increase in the mean of serum copper levels when compared mean of patients with mean of control group (1.61 ± 0.22) versus (1.03 ± 0.23) mg/ L (*P-value* 0.00) but in the mean of serum selenium levels there was a significant decrease (64.91 ± 3.780) versus (85.40 ± 8.82) (*P-value* 0.00). Conclusively, assessment of trace element levels is vital in the management of sickle cell disease. and thereby improving the chances of survival in sickle cell disease.

Keywords: Homozygous sickle cell diseases, renal function tests, copper, selenium.

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INTRODUCTION

Sickle cell disease (SCD) is an inherited blood disorder that affects red blood cells. People with sickle cell disease have red blood cells that contain mostly hemoglobin S, an abnormal type of hemoglobin. In certain situation, these red cells become sickle and have difficulty in passing through blood vessels^{1,2}. Although sickle cell disease is present from birth, symptoms are rare before the age of 3 to 6 months since a large percentage of the erythrocyte hemoglobin is of the fetal type (Hb F). As more Hb S replaces Hb F in the subject, the main symptoms; episode of anemia, pains and infections and associated crisis become manifested due to irreversible sickling of the erythrocytes when Hb S molecules polymerizes invariably leading to vaso-occlusion in the small capillaries³. In the United States, SCD affects about 72,000 people and 2 million are carriers⁴. In Africa, more than 200,000 infants are born yearly with SCD⁵. The highest prevalence of SCD in Sudanese is among the population from the Western Sudan it is believed that the sickle cell gene has brought to Sudan through immigrants from West African tribes, especially from Hausa and Bargo^{6, 7}. Sickle cell traits present with varied clinical problems including increased urinary tract infection, gross hematuria, complication of hyphema, splenic infarction with altitude hypoxia or exercise, and life threatening complications of exercise, exertional heat illness (excretional rhabdmyolysis, heat stroke or renal failure) or idiopathic sudden death Based on prevailing symptoms renal disorder in the present study considered to test creatinine, Urea, Na,K in sickle cell anemia patient⁸. Patients with sickle cell disease (SCD) are at increased risk of serious morbidity and mortality. The essential metals are well known for their biochemical role in biological systems and in the human body, but can be toxic when present in excess. Trace elements are essential inorganic molecules found in minute quantities of milligram or microgram per kilogram of body weight. Trace elements include copper, selenium, zinc, manganese, chromium, magnesium, fluorine, cobalt, iron and iodine. Some such as lead, cadmium, arsenic, aluminum and nickel are classified as pharmacologically beneficial and toxic hence monitoring of dosage is required⁹. People with sickle cell disease suffer from micronutrients deficiency but preliminary research on dietary habits, show that food and nutrients intake by sickle cell patients meet or exceed recommendation and is not significantly different from healthy controls. This suggests that high errates of nutrients deficiency may be due to increased needs of many nutrients in sickle cell patients¹⁰. The global use of micronutrients in health care delivery system has taken central stage due to the realization of their importance in disease management. Since (SCD) is among the disease plaguing a sizeable population of the developing world and the cost implication of its management is very high and is characterized by anemia and immunological disturbances, including the generation of free

radicals; balance between minerals and anti-oxidants is imperative in maintaining red cell membrane integrity and function¹¹. And because protection of red cell membrane from free radical mediated oxidative stress is crucial to the management of SCD, minerals such as Copper, Zinc, Iron, Chromium, Magnesium, Selenium, Vanadium as well as Vitamins like Vitamins A, C, E, folate (folic acid) and Vitamin B complex will be of great benefit towards relieve of oxidative stress associated with RBC cell membranes¹².

MATERIALS AND METHOD

This study was conducted on known patients with homozygous sickle cell disease (HbSS), diagnosed by physicians depending on the laboratory investigation. The laboratory tests for the biochemical parameters were conducted in order to assess the biochemical status and changes in patients with sickle cell disease. These tests include; trace elements tests (serum copper, selenium) and renal function tests (serum urea, creatinine, sodium and potassium).

Study Design

This is a case control study with sequential recruitment of study participants with sickle cell disease and those without the disease (apparently healthy) with genotype AA or AS who served as control.

Study Subjects

A total of 70 sickle cell disease patients and 30 apparently healthy controls were recruited for this study from the sickle cell center, Aljazeera state after obtaining ethical clearance from an ethical review board and appropriate informed consent from the subjects as well as their parents/guardian. The recruited participants were appropriately age and sex matched.

Sample Collection/Analysis

Venous blood samples (5 mls) were collected from each subject into a plain container. The labeled samples were spun in a bucket centrifuge at a speed of 2500rps to separate serum from red cells. The serum obtained was stored in a chest freezer at a temperature of -20C. Serum traces elements (copper and selenium) levels were determined by atomic absorption spectrophotometer technique as described by Kaneko (1999). Serum (urea, creatinine, sodium, potassium,) levels were determined by photometric method and flame photometric method respectively. As is usual in flame photometry serious errors can be caused by the presence of other substances in the sample. In the case studied for purposes of illustration it is shown that these interference errors can be reduced to the order of $\pm 6\%$ by the addition of excess ammonium phosphate.

Data Analysis

Data obtained was analyzed using SPSS version 17 statistical soft ware package. Results were expressed as mean \pm SD and a P value of <0.05 was considered significant.

RESULT AND DISCUSSION

Table 1: Age and sex distribution of the studied patients

Age group	Male		female		total	
	NO	%	NO	%	NO	%
< 2	13	21.3	9	22.5	22	22
2- 9	40	66.7	23	57.5	63	63
10-16	7	7	8	20	15	15

In this table showed the age subgroups and sex distribution for SCD patients which indicated tremendous increases in the number and percentage of the disease among male and female in the age between 2-9years (N40, 66.7 % - N23, 57.5 %), While that in age group between 10-16 years (N7, 7 % - N8, 20 % respectively).

Table 2: Serum renal function tests levels in sickle cell disease patients

Renal function test	Patients N = 70	Controls N = 30	P-Value
Urea (mg/dl)	58.76 ± 10.19*	34.27 ± 7.13	0.00
Creatinine (mg/dl)	0.87 ± 0.22*	0.42 ± 0.07	0.07
Na+ (m.mol/l)	138.7 ± 6.4	139.5 ± 2.9	0.5
K +(m.mol/l)	4.28 ± 0.7	3.9 ± 0.3	0.10

Values are expressed as Mean ± SD, P < 0.05 is considered significant compared with control.

Table 3: Serum trace element levels in sickle cell disease patients

Trace elements	Patients N = 70	Controls N = 30	P- Value
Cu (mg/l)	1.61 ± 0.22*	1.03 ± 0.23	0.00
Se (mg/l)	64.91 ± 3.78*	85.40 ± 8.82	0.00

Values are expressed as Mean ± SD, P < 0.05 is considered significant compared with control.

The result of the present study showed that the concentration of urea in the blood of sickle patient was significantly raised, while that of Creatinine concentration was found insignificantly raised. Elevated levels of urea are generally observed in pre renal, renal and post renal condition.¹³ Increase in serum creatinine signifies renal function impairment and its clearance are significantly reduced. The renal impairment may be due to intrinsic renal lesion, decreased perfusion of kidney or by obstruction of the lower urinary tract. Raised concentration in urea and creatinine suggest that pathogenicity of sickling might result renal impairment. Results of the present study also showed the significant differences between the mean levels of Na+ and K+ between the study groups but were within the normal reference range. Deficiencies of some essential trace elements are important in red blood cell maintenance, body growth and development. Have been observed in sickle cell disease^{3, 11} in the present study the significantly low serum selenium level is in agreement with the report of³. Selenium plays an important role as a cofactor for the reduction of antioxidant enzyme such as glutathione peroxidase, an enzyme which helps react with potentially harmful

oxidizing agents in substances like hemoglobin. High levels of glutathione function in the blood are associated with longevity. Deficiency of selenium can thus be attributed to the mortality in sickle cell disease³. In this study, an increase in plasma copper was observed in SCD subjects. Copper is known to be essential in the proper functioning of different metal enzymes which include ceruloplasmin involved in iron metabolism. Deficiency of copper is known to cause anemia. Studies have suggested that the copper containing enzyme, ceruloplasmin may have specific role, probably related to its function in mobilization of stored iron in the liver which makes iron available for hemoglobin synthesis. However, it has been observed that in copper deficiency induced anemia, in spite of elevated iron level in the liver, the rate of hemoglobin synthesis remain significantly reduced¹⁴. In this study, an increase in plasma copper was observed in SCD subjects. Zinc and copper competes with each other for similar binding sites on proteins and in zinc deficient tissues increase in copper has been observed previously¹⁵.

CONCLUSION

The result of the present study concludes that renal function impairment common in sickle cell patients while the abnormality of electrolytes present insignificantly in sickle patients. The finding of studies state the abnormality play a significant role in sickle cell patients physiopathology and can be used to management of the disease. Also the disorders in some essential trace elements occur in sickle cell disease. The present study recommends in addition intermittent renal function tests assessment are needed to be monitored.

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