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Assessment of Liver Enzymes, Zinc and Magnesium Levels in Homozygous Sickle Cell Disease Patients at Aljazeera State, Sudan

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ABSTRACT

Assessment of serum liver enzyme and trace element levels was carried out in a total of hundred (100) subjects comprising seventy (70) sickle cell disease patients attending Madani learning hospital comparatively with thirty (30) apparently healthy persons as control subjects. Blood samples were collected from participants, they were analyzed for trace elements using atomic absorption spectrophotometer. The enzymes activities for serum glutamic oxaloacetic transaminases (SGOT), serum glutamic pyruvic transaminases (SGPT), and Alkaline phosphatase (ALP) were measured using the kinetic tests depending on the reaction with the substrates (2,4-dinitrophenylhydrazine and P. Nitro phenyl). The mean serum level of Magnesium, Zinc, in sickle cell disease patients were 13.1000 ± 1.89 mg/L, 0.40883 ± 0.095 mg/L respectively. Serum magnesium, zinc levels were significantly lower ($p < 0.05$) in sickle cell disease patients when compared with the control. While liver enzymes were in a significant difference ($P < 0.01$). SGOT reported low activity while ALP reported higher activity between the study groups. Serum trace elements levels was not age or sex dependent, as similar pattern of serum trace elements was observed in both male and female sickle cell disease patients. The age and sex distribution for SCD patients indicated tremendous increases in the number and percentage of the disease among males and females in the age between 2-9 years (66.7%, 57.5%) respectively. Seventy (70) patients with homozygous sickle cell (SS) disease, with both sexes. Their age ranged between 6 months to 17 years. Thirty persons (30) were used as control. Freshly obtained blood samples from patients and control were used to estimate biochemical parameters which include; liver function test (SGOT & SGPT and alkaline phosphatase), and trace element (Zinc, Magnesium). Different analytical (colorimetry, spectrophotometer) methods were used to determine biochemical parameters indicated above. Serum trace elements (Zinc, Magnesium) was significantly low ($P < 0.05$) in SCD patients compared with the control. SGOT reported Significant low activity ($P < 0.01$) in-reverse to ALP which reported higher activity between the study group, while the SGPT has shown low significant activity ($P < 0.01$)

Keyword: In Homozygous Sickle Cell Disease, liver enzymes, zinc, magnesium.

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INTRODUCTION

Sickle cell disease (SCD) is an inherited blood disorder caused by abnormal properties conveyed to sickle cell erythrocyte by mutant sickle cell hemoglobin (HbS) and is common in people of African origin. However, it also found that in other ethnic groups (Embury, 1996)¹. 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 (Platt, 2000; Platt et al., 2004)². Sickle cell anemia (SCA) is a chronic hemolytic anemia that occurs in persons homozygous for sickle cell gene. It represents a model of molecular disease from the level of gene structure and action to the ultimate clinical syndrome in the patient (Behrman and Vaughan, 1996)³. In Sudan in 1982, Saha and Samuel studied sickle cell gene and liver functions in Sudanese population and they found that the carriers of sickle cell trait had a higher level of SGOT, SGPT compared to those with Hb and homozygous sickle cell hemoglobin. Furthermore, In 1992 Mohamed et al studied the serum variables in ninety Sudanese patients with sickle cell disease, they found that Serum SGOT, SGPT serum were notably raised. These controversial outcomes reported so far as well as the lack of clear cut study at Aljazeera state Sudan, led us to assess the serum levels of Zinc, Magnesium and liver enzymes in diagnosed patients with homozygous sickle cell disease. This study was conducted to evaluate biochemical changes which could be useful as laboratory tools to assess the disease severity in patients with homozygous sickle cell disease. Trace elements are essential inorganic molecules found in minute quantities of milligram or microgram per kilogram of body weight. Trace elements include zinc, copper, selenium, 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 required (Burtis et al., 2008)⁴. People with sickle cell disease suffer from many micro nutrient deficiency but preliminary research on dietary habits show that food and nutrient intake by sickle cell patients meet or exceeds recommendation and is not significantly different from healthy controls. This suggests that higher rates of nutrient deficiency may be due to increased needs of many nutrients in sickle cell patients. (Tagney et al., 1989)⁵. The global use of micronutrients in health care delivery system has taken central stage due to the realization of their importance in disease management. Sickle cell disease is among the disease plaguing a sizeable population of the developing world and the cost implication of its management is very high. Sickle cell disease is characterized by anemia and immunological disturbances. Free radicals are generated in sickle cell disease; hence balance between minerals and antioxidants are imperative in maintaining red cell membrane integrity and function (Okpuzor and Okochi, 2009)⁶. Protection of red cell

membrane from free radical mediated oxidative stress is crucial to the management of sickle cell disease. Minerals such as copper, zinc, magnesium as well as vitamins like vitamin homozygous sickle cell disease.

MATERIALS AND METHOD

This study was conducted on known patients with homozygous sickle cell disease (HbSS) Diagnosed by physicians depending on the laboratory investigations. 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 Zinc, Magnesium) and liver enzymes tests (serum transaminases (SGOT and SGPT) and alkaline phosphatase). Seventy SCD patients attending Madani learning Hospitals during May 2007-January 2009, these subjects were divided into six age groups (Table II). Thirty subjects were included as control group. A questionnaire was designed to obtain information about; age, sex, tribe, weight, height, education, occupations, and family history. After a written consent obtained from all study subjects, 5 ml venous blood samples were collected, transferred to plain centrifuge tube, allowed to stand for ½ hour to clot and after the retraction of the clot, serum was separated using bench centrifuge at 5000 for 10 minutes. 1ml of the sera was analyzed immediately for enzymes SGOT, SGPT, ALP. The rest of the sera were kept frozen at -20 C° until analyzed. Determination of Serum trace elements (Zinc and Magnesium) levels were performed using Atomic absorption Spectrophotometry techniques described by (Yamashita *etal.*, 1989)⁹ and (Johnsen and Eliason R, 1987)⁷ respectively. The enzymes activities for serum glutamic oxaloacetic transaminases (SGOT), serum glutamic pyruvic transaminases (SGPT), and Alkaline phosphatase (ALP) were measured using the kinetic tests depending on the reaction with the substrates (2,4-dinitrophenylhydrazine and P. Nitrophenyl). The detailed analysis was described before. Different variables are presented as mean ± standard deviation. Analysis of variance (ONE WAY ANOVA) was applied for comparison between different groups. The confidence limit was 95%, the p value considered significant at a value less than 0.05. Statistical analysis was done using SPSS programme under windows (IBM) computer system. The study protocol was approved by the University of Gezira review board of the Faculty of Medicine (Medani, Sudan).

RESULTS AND DISCUSSION

The clinical manifestations of sickle cell disease (SCD) patients showed an increase in the percentage of pain crisis and chronic anemia followed by recurrent infections such as Malaria. (Table 1) showed the groups age and sex distribution for SCD patients which indicated a tremendous increases in the number and percentage of the disease among males and females in the age between 2-9 years (66.7%, 57.7%) respectively. The serum levels of

enzymes showed a significant difference ($P < 0.01$), SGOT reported low activity while ALP reported higher activity between the study groups (Table 2). As shown in (Table 3), there was a reduction in serum Mg and Zn levels. This reduction was however, significant ($P < 0.05$) for serum Mg ($11.03 \pm 1.77 \text{ mg/L}$) and Zn ($120.85 \pm 10.29 \text{ } \mu\text{g/dl}$) levels when compared with the control. This was also the same result in cases of male and female sickle cell disease patients. However, in male sickle cell disease patients the reduction in the serum zinc concentration was not significant ($P > 0.05$) when compared with the control. This profile was also observed in male and female sickle cell disease patients. However, among the different sickle cell age groups which were examined there, was no statistically significant difference in serum trace elements.

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
10-17	7	7	8	20	15	15

Table 2: Serum liver enzyme levels in sickle cell disease patients

Liver enzymes	Patients N = 70	Controls N = 30	Significance
SGOT (U/L)	15.889 ± 8.6595	11.060 ± 2.9520	*
SGPT (U/L)	7.433 ± 2.9803	11.360 ± 4.1347	*
ALP (U/L)	149.674 ± 22.1215	92.850 ± 26.3501	**

Values are expressed as Mean \pm SD, $P < 0.01$ is considered significant compared with control. (** = $P < 0.01$)

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

Trace Elements	Patients N = 70	Controls N = 30	Significance
Mg (mg/l)	13.1000 ± 1.89370	18.8067 ± 1.00479	*
Zn (mg/l)	0.40883 ± 0.095101	0.76817 ± 0.152868	*

Values are expressed as Mean \pm SD, $P < 0.05$ is considered significant compared with control. (* = $P < 0.05$)

In most African countries, the outlook for patients with SCD continues to be poor. Today there is no doubt that general survival is improving with more medical care and improvement of environmental and social factors. It was known that sickle cell disease was characterized by chronic haemolysis. These results can be used as a reliable guide to estimate the haemolytic anaemia which was found in all studied patients as well as sickle cell disease in homozygous patients. The recent studies have measured some hepatic enzymes (SGOT, SGPT, ALP) activities and reported increased activity of SGOT and increase in ALP, while SGPT activity as an important indicator for RBCs destruction (Saha et al 1982 Su)¹⁰ reported no difference between the two groups, however all activities fall within the reference range.

This result was found to be in consistent with (Saha et al 1982 su)¹⁰. The deficiencies of trace elements such as zinc and magnesium are important in red blood cell maintenance, body growth and development have been observed in sickle cell disease (Durosinmi et al, 1993; Okpuzor and Okochi, 2009)^{6,11}. Significantly low serum magnesium and zinc concentration was obtained from comparison of sickle cell disease patients and the control subjects. In a study conducted by Defrancheschi et al, (1997)¹², low concentration of serum magnesium level has been noted in patients with sickle cell disease, this in turn is thought to contribute to red blood cell dehydration and a concomitant increase in the symptoms of sickle cell disease. The significantly low serum zinc level is in agreement with the report of Prasad and Cossack, (1993)¹³ and Prasad, (2002)¹⁴ who related zinc deficiency in sickle cell disease to manifestations such as growth retardation, hypogonadism in males, hyperammonemia, abnormal dark adaptation and cell mediated immune disorder. Zinc deficiency can also be the result of the adverse effect of hydroxyurea which increase zinc excretion as reported by Silliman et al.. (1993)¹⁵.

CONCLUSION

This study highlights the liver enzymes variable in patients with homozygous sickle cell disease at Aljazeera state Sudan; which can be added to parameters used for diagnosis of SCD in addition measurement of serum zinc and magnesium as supportive tests to diagnose SCD. The study recommended dietary supplementation with essential trace elements such as Mg and Znadjuvant in sickle cell disease therapy.

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