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HYPERTRIGLYCERIDEMIA IN SUDANESE CHILDREN WITH SICKLE CELL DISEASE

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ABSTRACT

Sickle cell disease (SCD) is the most common serious genetic disorder in Sudan; which characterized by red cells rigidity and abnormal viscoelasticity of cell membrane, that affect the plasma lipid profile. The aim of this study was to evaluate lipid profile in children with HbSS in Gaafer Ibn Oof children's Hospital in Khartoum, Sudan. This case control study was done in 100 children; 50 of them were with sickle cell disease (HbSS) and another 50 were healthy children (HbAA), who were age and sex matched; served as control. The mean age of the children with SCD was (7.6±4.27years), versus (7.15±4.19 years) in control subjects. After overnight fasting; serum lipid profile was done using automated chemical analyzer. The mean triglycerides in SCD group was (151.6±5.6 mg/dl), versus (124.3±4.0 mg/dl); with P value (0.001), total cholesterol was (102.9±5.0mg/dl), versus (140.8±4.6mg/dl); with P value (0.000), HDL was (25.2±1.3mg/dl), versus (35.1±1.6 mg/dl); P value (0.000), LDL was (46.8±3.9 mg/dl), versus (54.6±1.5 mg/dl), VLDL was (30.3±1.3mg/dl) versus (24.9±0.8mg/dl) and atherogenic index was (1.21±0.55) versus (1.15±0.42); respectively. In SCD group; serum triglycerides significantly increased; while total cholesterol and high density lipoproteins significantly decreased. **Conclusion**: hypertriglyceridemia is predominant in Sudanese children with sickle cell disease; while total cholesterol and high density lipoproteins significantly reduce; these lipid abnormalities could represent a cardiovascular risk factor for the children with sickle cell disease.

KEYWORDS: triglycerides, cholesterol, lipoproteins, serum, sickle cell disease, Sudan.

INTRODUCTION

Sickle-cell disease (SCD) is a wide-spread inherited hemoglobinopathy that is due to a point mutation in the globin chain.[1] The glutamic acid is replaced with valine; in position six on the β-chains of hemoglobin (Hb).[2,1] Sickle cell denotes all genotypes containing at least one sickle gene[3,4], it is found at a low frequency in all populations, the highest prevalence occurring in people of African and African-Caribbean origin[3]. The prevalence of SCD is very high in some areas like central Africa, Mediterranean region, Eastern countries and in certain part of India.[5,6] In Africa; more than 200,000 infants are born yearly with SCD.[7] The genotypes of HbSS, AS (HbAS) and (HbSS); were most common among the western Sudanese tribes, HbSS was present in 1% of Sudanese subjects.[8] In Nigeria, HbSS and HbSc (a milder-variant) are the main forms of SCD.[9] The sickle cell disease is the commonest monogenic disorder in India, affects all the major organs of the body.[10] SCD is now the most common serious genetic condition in England, affecting more than 1 in 2,000 live births.[3] Hemoglobin (S) occurs in high frequency in areas endemic with plasmodium falciparum including those from Africa, India, the Mediterranean area and Saudi Arabia.[11] SCD causes a wide spectrum of clinical manifestations including hemolysis and anemia.[1] Sickle cell disease is a significant cause of morbidity and mortality among black individuals and descendant of Africans.[12,6] The problems in sickle cell disease typically begin around 5 to 6 months of age.[13] In sickle cell anemia; the red blood cells change from their usual biconcave shape to sickle shape, and become stiff rather than soft and flexible.[14] Patients with sickle cell disease have high frequency of hypocholesterolaemia.[15] Less degree of hemolysis is associated with an insignificant reduction in plasma lipids and lipoproteins.[10] In SCD patients' total cholesterol, high-density lipoprotein-cholesterol (HDL-C), and low-density lipoprotein-cholesterol (LDL-C) were significantly decreased.[16,17] While; serum triglyceride levels are significantly

elevated.[16] Sickle cell anemia is associated with defective lipid homeostasis.[17] The pathophysiology of the hypocholesterolemia remains obscure; although several mechanisms described; the intense erythropoiesis causes increase cholesterol utilization.[18] Cardiovascular risk as indicated by atherogenic index is higher in SCD patients.[15] Earlier researchers believed that, lipid profile in patients with sickle cell anemia poses an uncertain threat for coronary vascular disease.[10]

Lipid metabolism may be altered in sickle cell disease patients; hence present study was carried out to compare the serum lipid profile in sickle cell disease children (HbSS) compared with normal children (HbAA).

PATIENTS AND METHODS

The aim of this case control study was to evaluate lipid profile in children with HbSS (homozygous) attending Gaafer Ibn Oof children's hospital in Khartoum, Sudan, for routine follow up. These children were diagnosed with HbSS, clinically assessed by a physician. Fully hematological analysis were performed for them and confirmed with hemoglobin electrophoresis. This study included 50 (HbSS) children who had not received blood transfusion in the last three months. Another 50 age and sex matched normal children with (HbAA) were served as control. After overnight fasting; 5 milliliters of venous blood were collected from each subject in a plain container in sterile conditions. Serum was separated after centrifugation at 3000 RPM for 10 minutes, and then stored at -20°C; till the time of biochemical analysis using automated chemical analyzer (Mindray-BS380). Total cholesterol, triglycerides (TG), low density lipoprotein (LDL) and high density lipoprotein (HDL) were measured parallel with control samples from Biosystem Company (Spain). Very low density lipoproteins (VLDL) was calculated using Friedewald formula (VLDL=TG/5). Serum atherogenic index was calculated by; log (TG/HDL-C).

ETHEICAL CONSIDERATIONS

Ethical approval for the study was obtained from ethical committee from National Ribat University and Federal Ministry of Health. Informed consents were taken from all the children participated in the study and from their parents. The study was done in the period from January 2014 to February 2015; in Gaafer Ibn Oof Children's Hospital, and National Ribat University, Khartoum, Sudan. The precision and accuracy of all methods used in this study were checked by commercially prepared control sera obtained from Biosystem- Spain.

STATISTICAL ANALYSIS

Data was analyzed by IBM, SPSS version 20.The results were expressed as mean ± standard deviation and student T test was used to calculate the level of significance. P value ≤ 0.05 was considered significance.

RESULTS

This study revealed that; the mean age of the children with sickle cell disease was (7.6±4.27years), versus (7.15±4.19 years) in control subjects. In the study group 23(46%) were males, and 27(54%) were females; while in control group 24(48%) were males and 26(52%) were female. The mean serum triglycerides level in the schoolchildren with sickle cell disease was (151.6±5.6mg/dl), versus (124.3±4.0mg/dl) in the healthy children, with significant difference; P value (0.001), serum total cholesterol was (102.9±5.0mg/dl), versus (140.8±4.6mg/dl) in healthy control group, with significant difference; P value (0.000), serum HDL was (25.2±1.3mg/dl), versus (35.1±1.6mg/dl) in the normal children, with significant difference; P value (0.000), serum LDL was (46.8±3.9mg/dl), versus (54.6±1.5mg/dl) in the healthy children with insignificant difference and serum VLDL was (30.3±1.3mg/dl) versus (24.9±0.8mg/dl) in the control group. Atherogenic index in the sickle cell disease group was (1.21±0.55) versus (1.15±0.42) in the healthy children.

Table (1) Descriptive table of the gender distribution in the children with sickle cell disease and their control

Subjects	Males	Females	Total
Sickle cell disease patients	23(46%)	27(54%)	50
Controls	24 (48%)	26(52%)	50
Total	47	52	100

Table: (2). Comparative study of lipid profile of the children with sickle cell disease and their control group

Items	Patients (No=50) (mean±std)	Control (No=50) (mean±std)	P value
Age (years)	7.6±4.27	7.15.0±4.19	
Triglyceride (mg/dl)	151.6±5.6	124.3±4.0	0.001
Cholesterol (mg/dl)	102.9±5.0	140.8±4.6	0.000
HDL (mg/dl)	25.2±1.3	35.1±1.6	0.000
LDL (mg/dl)	46.8±3.9	54.6±1.5	
VLDL(mg/dl)	30.3±1.3	24.9±0.8	
Atherogenic index (TC/HDL ratio)	1.21±0.55	1.15±0.42	

DISCUSION

The common sickle cell syndromes result when the gene for sickle hemoglobin is inherited from both parents. Sudan as one of central Africa countries experiences high rate of sickle cell disease; especially in western Sudan. The disease is mainly distributed in nomads with low medical services. The increase in red blood cells destruction and sickling of erythrocytes that occurs with sickle cells disease leads to a chronic hemolytic anemia, which may potentially result in alterations of many metabolites as mentioned earlier by Myfanwy et al (1998)[19]; as well as other clinical problems including fever and acidosis of the blood.[11] In the present study serum triglycerides levels significantly elevate in the children with sickle cell disease, this finding is consistent with that previously reported by Suzana et al, (2010)[16] and Mokondjimobe and group (2012).[23] Hypertriglyceridemia can be a risk factor for coronary artery disease as recorded by Gotto (1998)[21]; because it is known that hypertriglyceridemia correlates significantly with markers of hemolysis like; lactate dehydrogenase, arginase, endothelial activation, soluble vascular cell adhesion molecule-1, and amino-terminal brain natriuretic peptide; as concluded by Suzana et al, (2010).[16] The abnormal viscoelastic properties of oxygenated sickled cells; irreversibly corelate to abnormal property of the red cell membrane which affect the plasma lipid profile as mentioned by Nnodim et al (2012).[14] In this research serum cholesterol significantly decreases in Sudanese children with sickle cell disease; this finding is in agreement with that reported in Senegal by Diatta et al (2014)[20], and in Iran by Rahimi et al (2006)[22], and in other places like; Suzana and group in (2010)[16], Kehinde et al (2014)[17] and Mokondjimobe et al (2012).[23] The hemolytic stress leads to increase of erythropoiesis which in turn associated with reduction in plasma lipids and lipoproteins as recorded by Saket et al (2013).[10] High density lipoprotein or the good cholesterol also significantly reduced in children with sickle cell anemia, this conclusion is consistent with that reported in Senegal by Diatta et al (2014).[20] In the present study the serum astherogenic index or (TC/HDL) ratio; increases among the children with sickle cell anemia, when compared to normal healthy children, the increase of this index is one of cardiovascular diseases predictors. In sickle cell disease alteration in the lipid metabolism becomes pronounced; especially in vaso-occlusive crisis as reported by Kehinde et al (2014).[17] The pathophysiology of the hypocholesterolemia remains obscure, although several mechanisms have been proposed[18]; such as intense erythropoiesis that causing increased cholesterol utilization, increased cholesterol uptake by the reticuloendothelial system, liver injury secondary to iron overload and plasma dilution due to anemia as suggested by Kehinde et al; (2014).[17] and Shalev et al (2007).[18] In general sickle cell disease is a wide-spread inherited hemoglobinopathy disease associated with many clinical and health manifestations including cardiovascular risk in early age of life.

CONCLUSION

In Sudanese children with sickle cell disease; serum triglycerides significantly increase, while cholesterol and high density lipoproteins significantly decrease; these lipid abnormalities could represent a cardiovascular risk for sickle cell disease patients. Longitudinal studies in large populations are suggested to provide pathophysiological basis of lipid and lipoproteins disorders in sickle cell disease.

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