Serum Lipid Profile In Sickle Cell Disease Patients In Raipur District, Chhattisgarh

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Abstract: Background: The sickle cell disease is commonest monogenic disorder in India, affects all the major organs of the body. In India the rates of cardio vascular disease (CVD) among urban population have risen continuously and the major risk factor includes lipid abnormalities. 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 patients (HbSS) with normal person (HbAA) Method: A cross sectional study was done in 34 HbSS patients and age and sex matched normal 31 HbAA controls. Total Cholesterol (TC), High Density Lipoprotein (HDL), Low Density Lipoprotein (LDL), Triglyceride (TG) and Very Low Density Lipoprotein (VLDL) estimation was done. Mean, Standard deviation, Students T test analysis were used for analysis of results. Result: Mean value of TC, HDL and LDL were insignificantly lower than normal controls whereas TG and VLDL were insignificantly higher in both gender. Conclusion: Less degree of hemolytic stress leads to blunted rate of erythropoiesis which in turn is associated with an insignificant reduction in plasma lipids and lipoproteins. It appears that lipid profile in patients with sickle cell anemia poses an uncertain threat for coronary vascular disease.

Key words: Sickle cell disease, Hypocholesterolemia, Total cholesterol, Cholesterol

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Introduction: Although advances in supportive therapies have greatly increased the life expectancy of individuals with sickle cell disease in technologically advanced countries, the morbidity and mortality of this disorder remain high. Sickle cell disease is an inherited hemoglobinopathy occurring in many parts of the world including Indian sub–continent[1]. In India it is prevalent in tribal population and in Chhattisgarh the highest frequency of the sickle cell gene occurred among the Scheduled Tribes and Scheduled Castes and Other Backward Classes[2].

The cause of SCD is an A – to - T transversion in the codon for amino acid composition 6 in the Beta hemoglobin gene. Because of this mutation, a Valine residue replaces the normal Glutamic acid (glu6val) and HbS Beta-globin chains are substituted for normal HbA beta-globin chains[3,4]. In the deoxygenated state, the solubility of sickle cell hemoglobin (HbS) is decreased and, therefore, it precipitates as bundles of long fibers causing sickling of red cell. During oxygenation de-sickling occurs, but some cells become irreversibly sickled cells and do not regain the normal red cell shape. The cell membrane becomes fragile due to the constant reversal of sickling and de-sickling phenomenon and is eventually lysed. The homozygous state has been defined as an incapacitating disease in which the hematological and several biochemical parameter values are abnormal[5].

Cardio Vascular Disease (CVD) is the world's leading killer accounting for 29.2 % deaths of the total number of global deaths in 2003. It is postulated that serum lipid profile, that is a group of tests on cholesterol and its linked lipoproteins is used as an indicator for development of CVD in SCD patients. Out of all the fractions, multistep development of atherosclerosis is related to high levels of LDL-C and TG whereas decreased levels of HDL- C.

For above reason plasma lipid profile TC, HDL, LDL, TG and VLDL is evaluated in SCD patients to provide contributory information for concurrent occurrence of CVD which is an important cause of mortality in these cases.

Materials and Method: Study Design: After ethical clearance from Pt. J. N. M. Medical College, Raipur, a cross sectional study was carried out along with the mobile unit of sickle cell project in Raipur District Chhattisgarh following informed consent. The 34 subjects homozygous sickle cell disease patients having haemoglobin (HbSS) from 15 to 35 years were taken for study and compared with age and sex

matched controls. These subjects and controls were evaluated for sickling by solubility test in mobile unit & positive test results were confirmed for Trait (HbAS) or Disease (HbSS) by performing Hemoglobin Electrophoresis.

Blood sample collection: In all subjects, 5 ml of overnight fasting venous samples are collected from all subjects from which 3 ml is collected in plain bottles & allowed to clot for estimation of lipid profile and 2 ml in EDTA bottles for Hb electrophoresis by cellulose acetate.

Estimation of Lipid profile: The plasma lipid profile was measured by Automated method by the iLab 650 Automated Machine. The iLab 650 Automated Machine measured serum lipid profile - TC, and TG concentration by enzymatic essay, HDL-C by calorimetrically. In the iLab 650 automated machine the calculation of VLDL- C was done by VLDL–C = Triglyceride / 5 and LDL - C calculation by the following Friedewald Equation LDL–C = TC - HDL-C – (TG / 5)[6].

Statistical analysis: The result were expressed as mean ± standard deviation and student T test was used to calculate the level of significance. A p-value of 0.05 or less was considered statistically significant.

Result: Table 1 showed the level of lipid profile in sickle cell disease and controls. The mean plasma Total cholesterol, HDL-C and LDL-C were insignificantly (p>0.05) lower than their normal matched controls. Mean value of serum TG and VLDL-C were insignificantly higher than normal matched HbAA person.

Table 1: Concentrations of Lipids in the serum of Men and Women with Sickle Cell Disease and Controls

	Males			Females		
Parameters	SCD (n* = 23)	Controls (n = 17)	p-value	SCD (n = 11)	Controls (n = 14)	p-value
Total cholesterol (mg/dl)	162.52 ± 16.65	165.59 ± 21.27	p>0.05	169.73 ± 13.24	174.57 ± 20.99	p>0.05
HDL-cholesterol (mg/dl)	33.35 ±4.43	34.47 ± 3.24	p>0.05	32.64 ± 4.82	37.00 ± 3.37	p>0.05
LDL-cholesterol (mg/dl)	103.83 ± 15.45	107.53 ± 19.36	p>0.05	112.55 ± 13.41	114.57 ± 19.75	p>0.05
Triglyceride (mg/dl)	125.61 ± 34.30	117.29 ± 30.39	p>0.05	123.55 ± 19.49	121.07 ± 18.69	p>0.05
VLDL (mg/dl)	25.35 ± 6.75	23.47 ± 6.06	p>0.05	24.64 ± 3.88	24.21 ± 3.77	p>0.05

Data expressed as mean and SD, *Number of Subjects,

Discussion: Some of the workers have shown that the plasma total cholesterol of SCD, was significantly lower in comparison to normal control [5,7,14].

It has been postulated that the hypocholesterolemia in SCD might be due to increased cholesterol utilization and decreased circulation. Hemolytic stress could be associated with a significant reduction in plasma lipid concentration [8,9].

Metabolism of lipids and lipoproteins is being altered in patients with sickle cell anemia. Decreased red cell volume in these patients leads to increased plasma volume and dilution of plasma constituents including lipids and lipoproteins[11,13] , or the down regulation of cholesterol biosynthesis[10,15]. which occurs through the rate-limiting enzyme of β-

hydroxymethyl – glutaryl - CoA reductase or decrease dietary intake of cholesterol[10,11] or decrease activity of lecithin: cholesterol acyltransferase (LCAT)[10].

Another suspected cause was increase in the rate of exchange between plasma cholesterol and RBC membrane cholesterol[16]. Increased hepatobiliary excretion of cholesterol and bile salts, increased conversion of cholesterol to bile salts, decreased reabsorption of cholesterol and bile salts in the small intestine, and down regulation of cholesterol biosynthesis pathway was put forward the explanation for hypocholesterolemia in SCD[15]. In an another explanation for the reduced cholesterol concentration in hemolytic anemia could be either due to liver function abnormalities or due to decrease endogenous production[11,13]. It is also proposed that hypocholesterolemia in SCD might be induced by HbS gene[12].

A possible explanation for the statistically insignificant decrease of plasma cholesterol and other parameters in this study design is probably lower level of hemolytic stress because SCD cases are on steady state. There is markedly derangement in levels of Hb and erythropoietin. As a result of above findings there is decreased rate of erythropoiesis which is the main factor for increased cholesterol utilization.

In previous work and established projects the cholesterol levels were significantly low because cholesterol was utilized in excess in erythropoietic activity. How ever it is also hypothesized that cholesterol is largely conserved by entero-hepatic circulation, at least in healthy symptomless individuals. RBCs membraneis synthesized by recycled cholesterol from hemolysed RBCs.

Due to fore mentioned causes it can rightly be explained why there is less decrease in levels of plasma cholesterol and there is no statistically significance in plasma TC, HDL, LDL, Triglyceride and VLDL in SCD cases as a result of low levels of hemolytic burden and blunted erythropoiesis.

For the study we have concluded that levels of triglycerides is elevated but there is associated decrease in the levels of TC, HDL and LDL fractions. Though lipid monitoring is an important guide to cardiac markers but past work and studies offer an uncertain explanation regarding genetic protection offered by HbS gene against occurrence of CVD in some races and population and positive association of increased TG and LDL leading to risk of CVD in SCD cases.

Conclusion: Finally to recollect the result there is decrease in levels of TC and LDL and there is also associated decrease in HDL and increase in TG levels all of which are not significant. So we can say that there is uncertain threat for development of CVD.

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