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Investigating the correlation between clinical & biochemical parameters with lipid abnormalities in sickle cell disease

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Abstract
Background: *Sickle cell disease (SCD) is an inherited hemoglobinopathy occurring in many parts of the world including Indian sub–continent. In SCD, there is many pathological changes occurring in body and it leads to many clinical complications and alteration in biochemical parameters which may lead to worsen SCD. Thus on this background this study of the correlation between clinical & biochemical parameters with lipid abnormalities in sickle cell disease was planned.*
Methods: *This prospective observational study was conducted from February 2016 to October 2017 at MGM Medical College and MY Hospital Indore, MP, which included 50 SCD patients and 50 healthy, age, and sex matched controls.*
Results: *In this study, total bilirubin was between 1-3mg/dl in 27 patients in which increased and normal triglycerides (TG) were found in 11 and 16 patients respectively and total bilirubin more than 3mg/dl was found in 7 patients with increased TG and 7 patients with normal TG. A 'p value' for total bilirubin was found to be 0.146 i.e. there is no effect of increased triglycerides on total bilirubin. Total bilirubin was in between 1-3mg/dl in 27 patients and all patients had decreased total cholesterol (TC) and bilirubin level more than 3mg/dl was found in 14 patients out of which 13 patients had decreased TC. A 'p value' for total bilirubin is found to be 0.026 i.e. there is significant effect of decreased cholesterol on total bilirubin. A 'p value' for LDH is found to be 0.724 i.e. there is no effect of decreased cholesterol on LDH. LDH was between 140-280U/L in 7 patients with increased TG and 6 patients with normal TG and LDH was more than 280U/L in 16 patients with increased TG and 17 patients with normal TG. A 'p value' for LDH is found to be 0.546 i.e. there is no effect of increased TG on LDH.*
Conclusions: *On the basis of our study, it can be concluded that in sickle cell disease patients, decreased total cholesterol can be associated with clinically significant increased in total bilirubin levels and there is no effect of increased TG on bilirubin levels. Further studies in large number of patients in advised to include or exclude above findings.*
Keywords: *Lactate dehydrogenase, Sickle cell anemia, Total Cholesterol, Triglycerides.*

Introduction

Sickle cell disease (SCD) is an inherited hemoglobinopathy occurring in many parts of the world including Indian sub–continent.[1] In India it is prevalent in tribal population. The problem in sickle cell disease typically begins around 5 to 6

months of age. 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 betaglobin chains.[2,3]

Abnormal lipid homeostasis has been reported in SCA as well as other haematological disorders such as β-thalassemia and this has been suggested to have the potential to alter membrane fluidity and function of red blood cell (RBC) in individuals with SCA.[4-6] Earlier studies reported significant increase in plasma triglyceride (TG) levels and concurrent significant decrease in plasma levels of total cholesterol (TC), high-density lipoprotein-cholesterol (HDL) and low-density lipoprotein-cholesterol (LDL) in SCA subjects.[7] Several inconclusive mechanisms such as heightened erythropoiesis (causing increased cholesterol utilization), defective liver function (due to iron overload) and defects in post-absorptive plasma homeostasis of fatty acids have been put forward to explain the pathogenesis of this SCA-associated lipid abnormalities.[8]

Hypertriglyceridemia can be a risk factor for coronary artery disease as recorded by Gotto; 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.[9] On the above mentioned background this study investigating the correlation between clinical & biochemical parameters with lipid abnormalities in sickle cell disease was planned.

Methods

This prospective observational study was conducted from February, 2016 to October, 2017 at MGM Medical College and MY Hospital Indore, MP, which included 50 SCD patients and 50 healthy, age, and sex matched controls.

Clinical History of the Patients: The information of patients regarding to study as name, age, gender, weight, marital status, occupation, address and disease related history was achieved by the conversation and questionnaire with the patients.

Laboratory Examination: Blood sample of the patients was collected for the laboratory examination such as Haemoglobin electrophoresis, total blood count, lipid profile, LDH etc. These tests were done in the laboratory of MGM Medical College and MY Hospital, Indore, MP.

Inclusion Criteria: All SCD patients who were diagnosed and with/without treatment for SCD and not on any lipid lowering drugs.

Exclusion Criteria: All patients on lipid lowering drugs for coronary artery disease, cerebro-vascular accident or any other cause of hyperlipidemia.

Statistical Analysis: For the present study, statistical analysis required was done by the statistician accordingly the appropriate tests were applied. For analysis, statistical software SPSS latest version 20.0 was used. A p value of <0.05 was considered as statistically significant.

Results

This prospective observational study was conducted from February, 2016 to October, 2017 at MGM Medical College and MY Hospital Indore, MP, which included 50 SCD patients and 50 healthy age and sex matched controls. Our result of this study is as following:

As shown in table 1, total bilirubin was between 1-3mg/dl in 27 patients in which increased and normal TG were found in 11 and 16 patients respectively and total bilirubin more than 3mg/dl was found in 7 patients with increased TG and 7 patients with normal TG. A ‘p value’ for total bilirubin was found to be 0.146 i.e. there is no effect of increased triglycerides on total bilirubin.

Table 1: Association between total bilirubin and triglycerides

Total bilirubin(mg/dl)	Increased TG	Normal TG	Total	P value
0.2-1	3	0	3	0.146
1-3	11	16	27	
>3	7	7	14	

As shown in table 2, LDH was between 140-280U/L in 7 patients with increased TG and 6 patients with normal TG and LDH was more than 280U/L in 16 patients with increased TG and 17 patients with normal TG. A 'p value' for LDH is found to be 0.546 i.e. there is no effect of increased TG on LDH.

Table 2: Correlation between lactate dehydrogenase and triglycerides level

LDH(U/L)	Increased TG	Normal TG	Total	P value
<140	0	1	1	0.546
140-280	7	6	13	
>280	16	20	36	

As shown in table 3, LDH was found to be more than 280U/L in 35 patients with decreased TC and LDH between 140-280U/L in 12 patients with decreased TC. A 'p value' for LDH is found to be 0.724 i.e. there is no effect of decreased cholesterol on LDH.

Table 3: Correlation between lactate dehydrogenase and total cholesterol

LDH(U/L)	Decreased TC	Normal TC	Total	P value
<140	1	0	1	0.724
140-280	12	1	13	
>280	35	1	36	

As shown in table 4, a total bilirubin was in between 1-3mg/dl in 27 patients and all patients had decreased total cholesterol (TC) and bilirubin level more than 3mg/dl was found in 14 patients out of which 13 patients had decreased TC. A 'p value' for total bilirubin is found to be 0.026 i.e. there is significant effect of decreased cholesterol on total bilirubin.

Table 4: Association between total bilirubin and total cholesterol

Total bilirubin(mg/dl)	Decreased TC	Normal TC	Total	P value
0.2-1	2	1	3	0.026
1-3	27	0	27	
>3	13	1	14	

Discussion

We found a significant decrease in TC levels in SCD patients compared to control. HDL cholesterol in SCD patients is significantly lower than that of control subjects. It is the same for other authors' studies.[9] Serum LDL cholesterol levels in SCD is significantly lower than the controls. Some of the workers have shown that the plasma total cholesterol of SCD, was significantly lower in comparison to normal control. 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. Metabolism of lipids and lipoproteins is being altered in patients with SCD. Decreased red cell volume in these patients leads to increased plasma volume and dilution of plasma constituents including lipids and lipoproteins or the down regulation of cholesterol biosynthesis.[10]

The reduction of HDL concentration and n-3 polyunsaturated fatty acids in serum phospholipids of sickle cell anemia has been reported in Nigeria. Also, a significant decrease of polyunsaturated fatty acids in erythrocyte of SCD patients was found[11]. It was suggested that the elongation and desaturation of fatty acids are disrupted in sickle cell disease. Another suspected cause was increase in the rate of exchange between plasma cholesterol and RBC membrane cholesterol. 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. There is markedly derangement in levels of Haemoglobin and erythropoietin. As a result of above findings there is increased 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. However it is also hypothesized that cholesterol is largely conserved by entero-hepatic circulation, at least in healthy symptomless individuals. RBCs membrane is synthesized by recycled cholesterol from hemolysed RBCs. Triglyceride-rich VLDL-C particles availability may play an important role in lipid oxidization in SCD patients. The increase of triglycerides probably contributes to an increase in the hepatic production of VLDL-C, increasing the number of receptors for LDL-C that is extensively metabolized, decreasing its serum levels.

In this study, total bilirubin was between 1-3mg/dl in 27 patients in which increased and normal triglycerides (TG) were found in 11 and 16 patients respectively and total bilirubin more than 3mg/dl was found in 7 patients with increased TG and 7 patients with normal TG. A ‘p value’ for total bilirubin was found to be 0.146 i.e. there is no effect of increased triglycerides on total bilirubin. Total bilirubin was in between 1-3mg/dl in 27 patients and all patients had decreased total cholesterol (TC) and bilirubin level more than 3mg/dl was found in 14 patients out of which 13 patients had decreased TC. A ‘p value’ for total bilirubin is found to be 0.026 i.e. there is significant effect of decreased cholesterol on total bilirubin. A ‘p value’ for LDH is found to be 0.724 i.e. there is no effect of decreased cholesterol on LDH. LDH was between 140-280U/L in 7 patients with increased TG and 6 patients with normal TG and LDH was more than 280U/L in 16 patients with increased TG and 17 patients with normal TG. A ‘p value’ for LDH is found to be 0.546 i.e. there is no effect of increased TG on LDH.

Conclusions

On the basis of our study, it can be concluded that in sickle cell disease patients, decreased total cholesterol can be associated with clinically significant increased in total bilirubin levels and there is no effect of increased TG on bilirubin levels. Further study in large number of SCD patients and controls may help to confirm or exclude the above findings.

Disclosure

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Conflict of interest: Not declared
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