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Frequency of S447X lipoprotein lipase and -514C>T hepatic lipase gene polymorphism amongst Indian sickle cell patients

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ABSTRACT

Study states the lipoprotein lipase and hepatic lipase gene polymorphism may be associated in cardio vascular disease. Thus our aim was to evaluate the frequency of LPL and HL polymorphism in Indian sickle cell patients and their clinical outcomes. We had evaluated 162 sickle patients and 170 controls to compare the frequency. Study reported the similar frequency amongst patients and controls. Their was no clinical association of these gene variant and cardiac risk factor in sickle patients.

KEYWORDS

LPL;
HL;
SCD;
Polymorphism.

INTRODUCTION

Lipoprotein lipase is a glycoprotein enzyme that plays a key role in hydrolyzing triglycerides in chylomicrons and very low density lipoproteins (VLDL) as the first step in their metabolism[1,2]. Human PHP-LPL is catalytically active in a monomeric form, and its apparent molecular weight is 61,000[3], whereas there is a report that human LPL is catalytically active in a dimeric form[4]. Major cause of morbidity and mortality accounts coronary artery disease. Recent research indicate the alterations in lipid metabolism, including high LDL (low density lipoprotein) and low HDL (high density lipoprotein) cholesterol, high triglycerides levels, high apoB levels, high lipoprotein (a) (Lp (a) levels, are all important risk factors for CAD. All these lipid abnormalities themselves have genetic determinants[5,6]. Hepatic lipase (HL) is a lipolytic enzyme that contributes to the regulation of plasma triglyceride (TG) levels and synthesized by hepatocytes and found localized at the surface of liver sinusoid capillaries. Increased levels of TG may increase the risk of developing coronary heart disease, and studies suggest that mutations in the HL gene may be associated with elevated TG levels and increased risk of coronary heart disease. It is secreted and bound to the hepatocyte surface and readily released by heparin. It is a member of the lipase super family and is homologous to lipoprotein lipase and pancreatic lipase[7-9]. There is a paucity of data of these variants. In this study, the frequency of these mutations was assessed in Asian Indian origin SCD patients.

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MATERIALS AND METHOD

Subjects were sickle cell patients who attended the out patients department; All India Institute of Medical Sciences (AIIMS), New Delhi, India. This study was done in the Department of Hematology and it was approved by the institutional ethical committee. About 5 ml blood sample was collected from the patients after taken their informed consent. The complete blood count and the red cell indices were measured by an automated cell analyzer (SYSMEX K-4500, Kobe Japan). The quantitative assessment of Hb F, Hb A, Hb A2 and Hb S and the diagnosis of the sickle homozygous and the sickle beta thalassaemia patients was done by high performance liquid chromatography (HPLC-Bio-Rad-VariantTMBio Rad, CA, USA). DNA extraction was performed by the phenol-chloroform method. Genotyping of S447X and -514C>T was done according to published literatures[10,11]. Statistical analysis was performed using GraphPad statistics software. Yates chi-square test was used to assess the intergroup significance. A p-value of <0.05 was considered as statistically significant.

RESULT AND DISCUSSION

Study subjects were sickle cell patients [SA,45; SS,50; SB,70 (mean age 15.25±1.8 years)] while 170 age and sex match controls were recruited to compare the frequency. Out of 162 Sicklers 136 were normal for LPL and 26 carry mutations while 117 SCD patient were normal for HL variant and 40 were carry mutation. P-value was not statistically significant. Details of sub groups of sicklers and controls frequency is illustrated in TABLE 1. Lipoprotein levels are partly determined by genes that code for proteins that regulate lipoprotein synthesis. Mutations in these genes may cause disturbances in one or more of the pathways in lipoprotein metabolism resulting in hyper lipoproteinemia, and some of these disorders lead to premature atherosclerosis. All lipid abnormalities have genetic determinants. A study conducted in Italian population with genetic variables *apolipoprotein E* (*Apo E*), *Apo AI*, *Apo CIII*, *Apo B*, *lipoprotein lipase* (*LPL*) and the *hepatic lipase* (*LIPC*) genes and concluded the variation in *LIPC* (*hepatic lipase*) *gene* associates with clinical outcomes in Italian patients with established CAD[12]. A study and concise revive reported the significant presence of hepatic lipase -514C>T polymorphism in Indians[11]. Another study also reported the S447X Polymorphism and hepatic lipase (*LIPC*) association with lipid variations[13,14]. In our study we had reported the frequency of S447X and -514C>T polymorphism in sickle cell patients, however these variant also present in healthy individuals. Earlier studies in Europeans have identified small dense LDL to be associated with coronary artery disease and diabetes. An Indian study resulted in association of small dense LDL with diabetes and CAD in Asian Indians[15]. HTG is considered as a risk factor for CAD in Asian Indians, there is an urgent need to evaluate the association of *APOC3* SstI polymorphism with the risk of developing coronary artery disease in Asian Indians[16]. Low serum cholesterol and other lipoprotein levels in SCD patients is consistent with other reports both in Nigeria and elsewhere. It is important to mention that the levels in Nigerian adult

TABLE 1 : Comparative frequency of LPL and HL variants in sicklers and controls

Mutation	Genotype	Patients			Control N=170	p-value	OR	95%CI
		SA N=45	SS N=50	Sβ N=67				
LPL	-/-	37(82.22%)	43(86%)		148(87.05%)	0.516	0.78	0.40-1.50
(S447X)	+/-	56(83.58%)			18(10.588%)	0.405	1.40	0.69-2.84
	+/+	8(17.77%)	6(12%)		4(2.35%)	0.948	0.78	0.14-4.21
		9(13.43%)						
		0(0)	1(2%)	2(2.98%)				
HL	-/-	34(75.55%)	34(68.0%)		133(78.23%)	0.509	0.81	0.47-1.40
(-514C>T)	+/-	49(73.13%)			27(15.882%	0.290	1.41	0.77-2.57
	+/+	9(20%)	9(18.0%)		10 (5.882%)	0.741	0.75	0.25-2.20
		15(22.38%)						
		2 (4.444%)	2(4.0%)	3(4.477%)				

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sickle cell disease patients is much more lower compared with the lipid levels reported in both African American and Saudi Arabian patients with SCD. Lipid metabolism in SCD appears to be different from that in sickle cell trait and normal haemoglobin in adult Nigerian SCD patients. The exact cause is not known but appears to be multifactorial[17-22]. In our cases the frequency of LPL and HL variant was similar and statistically not significant. So the study concludes there was no correlation of these lipid variants and cardiac clinical outcomes in Indian sickle cell patients.

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