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Research Article

LECITHIN CHOLESTEROL ACYLTRANSFERASE (LCAT) AS BIOMARKERS OF ANGIOGRAPHICALLY PROVEN ATHEROSCLEROSIS

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ABSTRACT

Background: Various studies have shown lipoproteins to be involved in the pathogenesis of atherosclerosis. Lecithin cholesterol acyltransferase (LCAT) plays significant role in the lipoprotein metabolism but its association with atherosclerosis is still to be known.
Aim: To evaluate the level of serum LCAT and study their association with angiographically proven atherosclerosis.
Materials and methods: Study population consisted of angiographically proven 50 cases with atherosclerosis and 50 controls without atherosclerosis. Serum lipid profile was measured on SYNCHRON CX-9 using standard kits. Serum LCAT level was measured by ELISA method.
Results: No statistically significant difference found in LCAT level and lipid profile of cases and controls.
Conclusion: We conclude that LCAT is not associated independently with angiographically proven atherosclerosis but rather its role is dependent on the availability of other mediators of reverse cholesterol transport pathway like HDL and CETP.

INTRODUCTION

Atherosclerosis is a complex multifactorial disease of medium and large sized vessels resulting from the interactions of various environmental and genetic factors[1-2]. Various risk factors have been shown to play important role in the pathogenesis of atherosclerosis. Among various lipid biomarkers, HDL-C is shown to be one of the significant risk factor[3-5]. Several epidemiological studies have shown an inverse correlation between HDL-C and incidence of CAD[6-7] and have reported HDL as an independent negative risk factor for atherosclerosis. HDL is considered to be atheroprotective because of its ability to remove excess cholesterol from macrophage foam cells in atheromatous blood vessels and other tissues via reverse cholesterol transport pathway[8-11]. Recent studies have shown other newer biomarkers such as Lecithin Cholesterol Acyltransferase (LCAT) to play a role in lipoprotein metabolism.

Lecithin Cholesterol Acyltransferase (LCAT) is an enzyme synthesized mainly in liver. Very few genetic variants of LCAT has been found in the population. LCAT is known to play a key role in initial steps of RCT by esterification of free cholesterol thus maintaining the gradient of free cholesterol between peripheral cells and HDL[12]. This results in net cellular removal of cholesterol and conversion of discoid HDL into spherical HDL. Without ongoing esterification of cholesterol, the capacity of HDL to remove and bind additional cholesterol would eventually be diminished over time[12]. Cholesteryl Ester Transfer Protein (CETP) further has been seen to enhance this process by transferring cholesteryl esters formed by LCAT from HDL onto LDL[13-14]. Though LCAT plays significant role in RCT, its role in CAD is still to be understood as it is reported to depend upon the other genetic and environmental factors[15]. Association of Lecithin Cholesterol Acyltransferase (LCAT) with angiographically proven atherosclerosis is still to be established; also very few studies on this marker are there in Indian population.

Our aim was to study the association of serum LCAT, if any, with angiographically proven atherosclerosis.

MATERIALS AND METHODS

The study was carried out jointly in the Department of Biochemistry, Lady Hardinge Medical College and Smt. Sucheta Kriplani Hospital and Department of Cardiology, G.B. Pant Hospital, Delhi. With informed consent 100 non- diabetic subjects undergoing angiography were selected from Cardiology Department of G.B. Pant Hospital. Study population was selected on the basis of angiography; 50 subjects with atherosclerosis as proven by angiography were included in case and 50 subjects without atherosclerosis as

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proven by angiography were included in control group. Both the groups were age and sex matched. Study groups were subjected to detailed history with special reference to the atherosclerosis followed by clinical examination. Our study was approved by the Ethical Committee of Lady Hardinge Medical College.

The venous blood sample was collected from subjects under sterile conditions after overnight fasting. The blood samples for routine parameters were processed immediately for separation of serum and plasma. Serum sample for LCAT analysis were stored at -20 degree till batch was analyzed. Routine parameters and lipid profile were measured by auto analyzer (SYNCHRON CX-9, Beckman Coulter) using standard reagents. Serum LCAT was measured by using Bio Vendor ELISA kit.

Statistical Analysis

Statistical analysis was performed with the SPSS version 20.0 software program. Continuous variables were expressed as mean ± S.D. The variables were compared with a normal distribution by unpaired 2-tailed Student's t-test. A value of $p \leq 0.05$ was considered statistically significant.

RESULTS

The study groups were matched for age and sex. **Table 1** shows baseline characteristics of our study group. Smoking followed by hypertension were the two most prevalent risk factors in our study population. No statistically significant difference was observed in lipid profile of cases and controls **(Table 2).** We did not find any statistically significant difference was in serum LCAT levels of cases and controls. (**Table 3**).

Table1 Characteristics of study groups

	CASE (Mean ±S.D)	CONTROL (Mean ±S.D)	P value
Age	51.22 ± 7.6	48 ±7.2	0.105
Sex (M)	35 (70%)	33(66%)	0.668
(F)	15(30%)	17(34%)	0.544
BMI	22.9 ± 3.4	22.5 ± 2.4	0.005
HYPERTENSION	22 (44%)	9 (18%)	0.000
SMOKING	30 (60%)	11 (22%)	0.695
F/H/O CAD	4 (8%)	3 (6%)	

p value≤0.05 is considered statistically significant.

Table2 Levels of lipid profile parameters in study groups:

Parameters	CASE (Mean ± S.D)	CONTROLS (Mean ± SD)	P value
T.CHOL (mg/dl)	143.4 ± 42.30	142.14 ± 37.30	0.875
TG (mg/dl)	146.08 ± 67.67	134.36 ± 63.89	0.375
HDL (mg/dl)	41.700 ± 8.83	43.580 ± 12.55	0.389
LDL (mg/dl)	81.580 ± 37.57	77.940 ± 34.64	0.616
VLDL (mg/dl)	29.22 ± 13.51	26.84 ± 12.52	0.375
LDL/HDL	1.97 ± 0.80	1.82 ± 0.67	0.308
T CHOL/ HDL	3.58 ± 1.31	3.38 ± 0.89	0.382

p value≤0.05 is considered statistically significant

Table 3 Distribution of CETP and LCAT levels in study group

Parameters	CASE (Mean ± S.D)	CONTROL (Mean ± S.D)	p VALUE
LACT (ng/ml)	50.34 ± 9.29	49.8 ± 7.91	0.764

p value≤0.05 is considered statistically significant.

DISCUSSION

We studied 100 subjects with coronary artery atherosclerosis and divided them into cases and controls on the basis of angiography. SerumLecithin Cholesterol Acyltransferase (LCAT) levels and lipid profile (Total Cholesterol, TG, HDL-C, LDL-C and VLDL) of both cases and controls were measured. In our study population we did notfind any statistically significant difference in LCAT level and lipid profile of cases and controls.

Lecithin Cholesterol Acyltransferase (LCAT) is an enzyme which participate in reverse cholesterol transport by esterification of free cholesterol into cholesteryl esters. LCAT is mainly synthesized in liver and released in plasma in loose association with HDL. HDL via reverse cholesterol transport pathway promotes the removal of excess cellular cholesterol from peripheral tissues. RCT begins with the transfer of free cholesterol from peripheral tissue to the HDL where it is esterified by LCAT. On binding with lipoprotein, LCAT catalyzes the transfer of an acyl group of fatty acid preferably from 2-sn position of lecithin to the 3-hydroxy group of cholesterol resulting in formation of cholesteryl ester and lysolecithin[12]. Cholesteryl ester, being hydrophobic in nature shifts towards the centre of HDL thus preventing the back exchange of cholesterol from HDL. This results in net cellular removal of cholesterol and conversion of discoid HDL into spherical HDL. Without ongoing esterification of cholesterol, the capacity of HDL to remove and bind additional cholesterol would eventually be diminished over time[13,14,16]. CETP further enhances this process by transferring cholesteryl esters formed by LCAT from HDL onto LDL[13-14].

LCAT has been reported to show its antiatherogenic property by promoting the efflux of cholesterol via the reverse cholesterol transport pathway. In our study we did not find any significant difference in LCAT level of cases and controls. This could be because may depend on with has been reported to depend upon the antiatherogenic role of LCAT may depend on the concentration and quality of lipoproteins (HDL and LDL) and cholesteryl ester transfer protein (CETP)[15]. In our study population we didn't find any significant difference in HDL level of cases and controls probably; because we included study subjects with and without CAD on the basis of angiography and most of them already were on statins. Further anti-atherogenic role of LCAT has been questioned by various reports which have shown that the individuals with either partial or complete LCAT deficiency rarely suffer from premature CAD[17-18]. Also few studies also have shown paradoxical findings of lower HDL levels and higher CAD risk in subjects with high esterification rate[19-20]. Although the role of LCAT in cholesterol efflux from cells has largely been substantiated, its overall role in the pathogenesis of coronary heart disease (CHD) is still remains inconclusive.

We conclude, from our study that LCAT is not associated independently with angiographic ally proven atherosclerosis but rather its role is dependent on the availability of other mediators of reverse cholesterol transport pathway like HDL and CETP. Further studies of LCAT along with other RCT mediators like lipoproteins and cholesteryl ester transfer

proteins is recommended to elucidate itsrole in pathogenesis of atherosclerosis.

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