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Status of Small Dense LDL in Fasting and Nonfasting Lipidemia in Coronary Heart Disease

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ABSTRACT

LDL consists of heterogeneous spectrum of particles with highly variable atherogenic potential i.e. small dense LDL. The atherogenicity of sdLDL is due to its high oxidizability, owing to low cholesterol and high PUFA and Apo B content. Since, small dense LDL whose half life is more than LDL-C in plasma, is coming up as new marker for CHD diagnosis. Hence, we aimed our study to know the status of sdLDL along with other lipid parameters in nonfasting condition.The present study comprised of fifty clinically diagnosed cases of CHD admitted in ICU of J.A.group of hospital and fifty age and sex matched healthy individuals were considered as control subjects. Their fasting and nonfasting samples were analysed for lipid profile. There was a significant change in all the lipid parameters in nonfasting condition but small dense LDL varied minimally.On account of the small variation in the levels of sdLDL in fasting and nonfasting state, compared to the other lipid parameters which show greater variability in both states, this small dense LDL can be a better marker for the diagnosis of coronary heart disease

INTRODUCTION

"Life has its particle of risk--and in the bloodstream, some particles are riskier than others. Researchers reported that the littlest LDLs are the worst of all."

By now, every sentient middle-aged adult has heard about "bad" and "good" cholesterol. But cholesterol is cholesterol; whether it's bad or good depends on how it's packaged. The low-density lipoproteins (LDLs) that transport cholesterol

from the liver, where it's made, to other tissues can gum up artery walls, increasing a person's risk for cardiovascular disease.

Relative risk of all lipoproteins in CHD has been extensively studied and the principle target for cardiovascular preventive strategies has been the low density lipoprotein cholesterol. However LDL consists of heterogeneous spectrum of particles with highly variable atherogenic potential i.e. small dense LDL. The atherogenicity of sdLDL is due to its high oxidizability, owing to low cholesterol and high PUFA and Apo B content. Furthermore this molecule is depleted of vitamin E, which accounts for its susceptibility to oxidation [1]. In addition sdLDL is cleared slowly by receptors as compared to large buoyant LDL and thus has a long residence period in plasma, allowing more time for them to be oxidized and taken up by macrophages in extracellular spaces. Low uptake by receptors has been attributed to decrease binding affinity to receptors due to conformational change brought about in ApoB by increase in TG content or decrease in size of LDL[2]. It is the TG content of LDL particles that is associated with systemic inflammation. Moreover, many individuals with LDL-C levels apparently within the normal range may also suffer from CHD [3]. Atherogenic lipoprotein phenotype is characterized by elevated levels of TG and sdLDL particles and reduced HDL cholesterol (HDL –C) [4]. It has been observed that patients suffering from CHD when investigated in fasting condition which is usually advised by clinician shows increased level of total cholesterol, triglycerides, LDL-C and low HDL but many individuals with LDL-C apparently in normal range, may also suffer from CHD. Sometimes patients are admitted in nonfasting condition. The results of lipid profile particularly TG, invariably changed or were incorrect under such circumstances. Since, small dense LDL whose half life is more than LDL-C in plasma, is coming up as new marker for CHD diagnosis. Hence, we aimed our study to know the status of sdLDL along with other lipid parameters in nonfasting condition.

MATERIAL AND METHODS

The present study was conducted at department of Biochemistry and medicine department of J.A.Group of Hospitals, G.R. Medical College, Gwalior. The study included 50 normal healthy persons of matched age and sex (group I) and 50 diagnosed subjects of coronary heart disease admitted in the ICU of J.A. Hospital (group II).

Inclusion criteria: subjects who were diagnosed with CHD and had symptoms like restlessness, chest pain and high blood pressure

Exclusion criteria: subjects with any other disease except CHD were excluded from the study.

The blood samples were drawn on the first day of admission. 5ml of blood sample was obtained from each subject after overnight fasting and 5ml in non fasting condition under all aseptic precautions for the analysis of lipid profile.

ECG, Hb%, total and differential leucocyte count, height and weight were recorded at the time of admission in study proforma.

Lipid profile was estimated by standard biochemical Kits (Erba) using BS 400 fully automated analyser (Mindray). Small dense LDL was calculated by using the regression equation by Srisawasdi et.al. [5]. This study was approved by institutional ethical committee & written consent was also obtained from the patients prior to study.

Statistical analysis

Paired sample t –test was used to compare biochemical parameters within the groups. All analysis was done using Windows based SPSS statistical package (Version 16.0).

RESULTS

In CHD subjects and the control group subjects, overall status of the physiological parameters including age, height, weight, BMI (kg/m²) and hemoglobin showed no significant difference whereas systolic and diastolic blood pressure was significantly higher ($p < .001$) in CHD group (II) compared to the controls (I) (TABLE 1).

TABLE 1: Characteristics Of The Subjects. (*P <.001)**

GROUPS		AGE	Ht.	Wt.	BMI	Hb%	SBP	DBP
GROUP I (n=50)	Mean ± S.D	49.920 6.794	1.623 .081	58.80 6.178	22.46 1.991	12.79 1.076	120.16 7.749	80.52 7.415
GROUP II (n=50)	Mean ± S.D	53.76 11.032	1.6432 .074	60.34 6.103	22.35 1.879	12.27 1.642	147.20 31.431***	90.0 13.248***

There was a significant increase in lipid and lipoprotein profile in CHD subjects compared to control group except HDL. A significant decrease was observed for total cholesterol ($p <.05$) and LDL cholesterol in nonfasting state compared to fasting condition in both group I and group II. In contrast, there was significant increase in serum triglyceride and VLDL levels ($p <.001$) in nonfasting state in CHD patients as well as in the control group. There was no change in HDL –C levels in fasting and nonfasting state in both the groups. Small dense LDL showed only very little variation in nonfasting condtion compared to fasting condition in both the groups ($p < .05$) (TABLE 2)

TABLE 2: showing the status of fasting and nonfasting lipid profile in group I and group II.(*p<.05, **p<.01, ***p<.001)

Group	Parameter		Fasting	Non fasting	Significance
Group-I (control)	TC	RANGE	155.56-225.40	154.12-224.43	P<.01
		Mean ± SD	183.66 15.32	180.56 14.57**	
	TG	RANGE	66.65-119.09	87.18-139.65	P<.001
		Mean ± SD	89.94 12.869	113.18 13.112***	
	VLDL	RANGE	13.33-23.81	17.43-27.93	P<.001
		Mean ± SD	17.98 2.573	22.63 2.622***	
	HDL	RANGE	44.04-55.76	44.13-55.23	NS
		Mean ± SD	50.46 2.615	50.40 2.525***	
	LDL	RANGE	89.21-140.73	83.16-132.32	P<.001
		Mean ± SD	118.38 10.445	110.68 11.821	
	Sd LDL	RANGE	17.78-39.45	17.06-39.99	p<.05
		Mean ± SD	30.55 4.530	31.18 4.934*	
Group-II (CHD)	TC	RANGE	195.32-308.72	192.28-303.12	P<.01
		Mean ± SD	279.34 26.205	275.73 26.874**	
	TG	RANGE	133.32-298.21	155.28-326.41	P<.001
		Mean ± SD	249.33 40.886	274.27 42.499***	
	VLDL	RANGE	25.19-54.19	26.06- 54.02	P<.001
		Mean ± SD	49.86 8.177	54.85 8.499***	
	HDL	RANGE	25.2-54.19	26.06-54.02	NS
		Mean ± SD	39.41 7.966	39.31 7.679(NS)	
	LDL	RANGE	96.48-271.32	90.28-268.44	P<.001
		Mean ± SD	197.03 47.445	189.66 48.197***	
	Sd LDL	RANGE	28.93-104.26	26.73-106.43	P<.05
		Mean ± SD	70.64 19.046	71.72 19.721*	

DISCUSSION

Elevated triglyceride levels have a substantial effect on lipoprotein metabolism, which explains much of the controversy about the role of serum triglycerides as a risk factor for CHD Atherosclerosis is described in some research studies as a postprandial phenomenon. Nonfasting lipoproteins are generally triglyceride rich, and if an individual has a predisposition to producing remnant particles or small, dense LDL-C and HDL-C particles, then clearance of these lipoprotein particles can be delayed as long as 12

hours or more [6]. In present study, the nonfasting triglyceride levels were significantly high compared to the fasting levels. This finding was similar to the findings of[7,8,9]. Levels of fasting and nonfasting triglycerides are highly variable depending in part on the content of the last meal and on the duration from the last meal taken. Nonfasting hypertriglyceridemia, reflecting an elevated concentration of lipoprotein remnant particles, might change atherosclerotic lesion content and might show procoagulant, anti-fibrinolytic and pro-inflammatory effects. The nonfasting VLDL levels showed a similar pattern to TG. In contrast to TG levels, serum LDL-c levels were significantly low in nonfasting state compared to fasting state. This result was supported by the findings of Shankar et al [8]. In fed state, with the influx of TG rich lipoproteins from the intestines and subsequent lipolysis of triglycerides, there is transfer of cholesterol esters from HDL and LDL to these particles through the action of CETP (Cholesterol ester transfer protein). This result in a decrease in LDL-C in nonfasting state compared to fasting state. High levels of VLDL participate in formation of sdLDL [10]. Nonfasting state modulates both metabolism and composition of apo B-100 containing lipoprotein particles and it is probable that the intravascular cholesterol redistribution due to hyperlipidaemia modifies plasma lipoproteins such that there is an increased generation of potentially atherogenic TG rich lipoproteins and small dense LDL. Delayed lipid clearance from body might reveal a state of fat intolerance linked to an elevated risk of CHD that is under genetic control and cannot be detected by simple measurement of fasting lipids. Thus, an increase of fasting and nonfasting TG levels might contribute to the high prevalence of small dense LDL particles in patients with CHD [11].In our study the levels of small dense LDL were highly elevated in CHD subjects but there was a minimal variation in sdLDL levels in nonfasting and fasting state. This result was supported by the frinding of Sabaka et al [12]. On account of the small variation in the levels of sdLDL in fasting and nonfasting state, compared to the other lipid parameters which show greater variability in both states, this small dense LDL can be a better marker for the diagnosis of coronary heart disease.

CONCLUSION

Therefore it is concluded that another reason for considering small dense LDL as a better predictor may be that, they are subfraction of LDL, formed largely in response to high levels of TGs and are the products of intravascular remodeling of TG rich VLDL particle, so they can reflect the combined effect of hypertriglyceridemia in this disease.

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