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Original Research Article

Role of small dense LDL-cholesterol in detecting the risk of cardiovascular disease among smokers

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ABSTRACT

Background: Coronary heart disease is the leading cause of the death and disability in the developed nations and is increasing rapidly in the developing countries. Study aimed to estimate and compare the small dense LDL-cholesterol (sdLDL-C) in healthy smokers & non-smokers.

Materials and Method: This is analytical observational study, conducted at father Muller medical college Mangalore after approval from the institutional Research & Ethics committee. The subjects were selected from the patients coming for the routine health checkups to the hospital. The participants willing to be part of study between the age group of 25-65yrs of age, with history of cigarette smoking were grouped as group II and healthy non-smokers as group I. A 3ml of fasting blood sample was drawn under all precautionary measures and subjected to analysis at central laboratory biochemistry section after separating the serum.

Result: Total of 760 normal healthy individuals were included in the current study with 480 healthy cigarette smokers and 280 healthy non-smokers. Lipid profile showed a significant difference between the smokers and non-smokers with elevated LDL cholesterol and the sdLDL cholesterol and reduction in level of HDL cholesterol among the smokers compared to non-smokers.

Conclusion: There is a significant higher level of small dense LDL cholesterol among the smokers compared to non-smokers, which can help to predict the risk for future cardiovascular bad events among the smokers.

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1. Introduction

Coronary Heart disease is the leading cause of the death and disability in the developed nations and is increasing rapidly in the developing countries.¹ One of the major advances in the modern medicine is the identification of the risk factors for the CHD. Lipoproteins play a vital role in the atherogenesis in the individuals. The Low-density lipoprotein is the major target in the various guidelines for

prevention of the CHD.

However the serum/plasma LDL levels are just insufficient to identify the incidences of CHD events, as approximately more than 50% events occur with normal or even lower LDL-C levels.² LDL is composed heterogeneous particles differing in the size, density & chemical composition. Small dense low-density lipoprotein (sdLDL) is fraction of the smallest particle of LDL with diameter of <25.5nm. They are related closely with the CVD because they are highly atherogenic, increasing the CHD risk up to 3 times. This sdLDL measurement can be done

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by various techniques, such as the NMR, electrophoresis, Ultracentrifugation, dynamic light scattering, photometry, ion mobility analysis & calculation method. In 2011, Srisawasdi et al³ developed an examination technique by estimating the sdLDL using the formula, this can provide the advantage of the cost cutting and lab doesn't require extra reagent or the instrumentation for the same.

Study aimed to estimate and compare the small dense LDL-cholesterol (sdLDL-C) in healthy smokers & non-smokers.

2. Materials and Methods

This is analytical observational study, conducted at father Muller medical college Mangalore after approval from the institutional Research & Ethics committee. The subjects were selected from the patients coming for the routine health checkups to the hospital. The study conducted for the duration of 6 months, and all the consecutive patients and the healthy individuals were recruited based on the criteria of smokers, non-smokers and with cardiac events. The age groups were selected between 25-65yrs. Inclusion: Cigarette smokers as Group II, age matched healthy individuals as the Group I. Exclusion: the patient who had the Triglyceride more than the 400mg/dl, the patients with other diseases, familial hypertriglyceridemias, on medication which alters the lipid parameters. A 3ml of fasting blood sample was drawn under all precautionary measures and subjected to analysis at central laboratory biochemistry section after separating the serum.

The Lipid profile tests include; Total cholesterol (Cholesterol oxidase/peroxidase),⁴⁻⁶ HDL-C (Direct method polymers/detergent),⁷ LDL-C (direct enzymatic, PEG modified),^{8,9} Triglycerides (glycerol phosphate),¹⁰ VLDL (TG/5)¹¹ was analysed on the Roche Cobas 6000 analyser at the clinical biochemistry laboratory. sdLDL-Cholesterol will be calculate using equation set by Srisawasdi et al³ is as follow; $\text{sdLDL-C (mg/dL)} = 0.580 (\text{non-HDL-C}) + 0.407 (\text{dLDL-C}) - 0.719 (\text{cLDL-C}) - 12.05$ non-HDL = TC- HDL-C and cLDL-Cholesterol calculated using the Friedewald formula;¹¹ $\text{cLDL-C} = \text{TC} - \text{HDL-C} - (\text{TG}/5)$.

2.1. Statistical analysis

The sample size was calculated using the online sample size calculator for the study with power of >80% with significance p value <.05. The descriptive data is given as Mean, Standard Deviation, confidence interval, comparison of mean by student t-test. The data was entered on Microsoft excel & analysis done on sophisticated statistical software SPSS version 23 (institutional licensed). The references are managed using the Mendeley software (version 1.17.11).

3. Result

Total of 760 normal healthy individuals were included in the current study with 480 healthy cigarette smokers and 280 healthy non-smokers. The mean age of the smokers was 46yrs and of non-smokers was 45 years with no significant difference statistically. Further analysis of the parameter of interest, the lipid profile showed a significant difference between the smokers and non-smokers with elevated LDL cholesterol and the sdLDL cholesterol and reduction in level of HDL cholesterol among the smokers compared to non-smokers. ($p < 0.05$)

The data is represented as the mean and SD of parameters in healthy males smokers and non-smokers. p-value <.05 is considered as significant, <.001 is Highly significant (HS), >.05 is considered as Non-significant (NS).

4. Discussion

Low-density lipoprotein is a spherical particle with an esterified cholesterol and triglyceride core and an unesterified cholesterol, phospholipid, and apolipoprotein B surface lipid coat (ApoB). One ApoB molecule is found in each LDL particle. The size of the LDL particle is determined by the amount of lipid in the core, and the density is determined by the lipid content.

LDL size is a significant predictor of atherosclerosis and cardiovascular disease, and tiny, dense LDL has been identified as a new risk factor for cardiovascular disease. The LDL subclass pattern characterised by a preponderance of small, dense LDL particles was significantly associated with a threefold increased risk of myocardial infarction, and Koba et al found that small, dense LDL was present in more than 70% of Japanese men with coronary artery disease.¹² Other cardiovascular risk factors such as decreased serum HDL-cholesterol level, increased triglyceride concentration, diabetes mellitus, hypertension, and obesity have been linked to LDL size.¹³ Tobacco use is a substantial risk factor for cardiovascular disease¹⁴ although no clear causal association between tobacco use and tiny, dense LDL has been discovered.

Present study also documented the higher level of small dense LDL Cholesterol among the cigarette smokers compared to the non-smokers, which strengthen the finding that the small dense LDL can be a good marker for detecting the risk for future cardiovascular events. Various other studies documented a higher level of the small dense LDL cholesterol among the smokers, also among the patients with established cardiovascular diseases and atherosclerotic activity.^{3,11,15,16}

5. Conclusion

The study concludes that there is a significant higher level of small dense LDL cholesterol among the smokers compared to non-smokers, which can help to predict

Table 1: Characteristics distribution of the lipid profile among the smokers and non-smokers

	Smokers (n=480) Mean $\pm$ SD	Non-Smokers (n=280) Mean $\pm$ SD	p-value
Age	46 $\pm$ 11	45 $\pm$ 12	NS
Biochemical analysis			
RBS	97.3 $\pm$ 9.9	101.2 $\pm$ 9.8	NS
Total Cholesterol	205.2 $\pm$ 41.2	189.3 $\pm$ 32.8	NS
HDL-C	39.6 $\pm$ 9.5	45.2 $\pm$ 9.3	<.001 HS
dLDL-C	138.1 $\pm$ 29.6	129.3 $\pm$ 31.1	<.001 HS
Triglyceride	179.9 $\pm$ 53.1	153.4 $\pm$ 54.0	<.001 HS
VLDL-C	35.9 $\pm$ 10.1	30.6 $\pm$ 10.8	<.001 HS
sdLDL-C using Srisawasdi	47.0 $\pm$ 11.4	42.6 $\pm$ 13.8	<.001 HS
lbLDL-C	91.0 $\pm$ 20.1	86.7 $\pm$ 19.9	<.001 HS
Ratios			
Cholesterol:HDL-C	5.4 $\pm$ 1.6	4.4 $\pm$ 1.3	<.001 HS
TG:HDL-C	4.9 $\pm$ 1.2	3.6 $\pm$ 1.9	<.001 HS
Non-HDL	165.6 $\pm$ 40.8	144.1 $\pm$ 35.9	<.05 S

the risk for future cardiovascular bad events among the smokers. Other than routine lipid parameters, the sdLDL cholesterol can be used as a risk biomarker for the CVD and atherosclerotic events. Further studies are required with longitudinal duration follow-up to strengthen the finding of the study to harmonize across general population.

6. Conflict of Interest

There is no conflict of interest between the authors, the study is conducted and published with all due permission.

7. Source of Funding

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