



## **Status of Small Dense LDL in Cardiovascular Disease Subjects Taking Drug Therapy**

Pranshi Mishra<sup>1</sup>, Neelima Singh<sup>1</sup>, Puneet Rastogi<sup>2</sup>, Sanjeev Singh<sup>1</sup>, Vikas K. Gupta<sup>3</sup>

<sup>1</sup>Department of Biochemistry, G.R. Medical College, Gwalior

<sup>2</sup>Department of Medicine G.R. Medical College & J.A. Group of Hospital, Gwalior

<sup>3</sup>Department of Biochemistry, LLAMMC, Raigarh

Corresponding Author: Pranshi Mishra

Received: 20/03/2015

Revised: 09/04/2015

Accepted: 20/04/2015

### **ABSTRACT**

Increased plasma LDL-cholesterol (LDL-C) level is one of the most important risk factors for coronary artery disease. The LDL subfraction i.e. small dense LDL is more atherogenic form of the LDL and is observed as an important risk factor for coronary heart disease. Conventional treatment of atherogenic lipid profile aims at reducing total cholesterol, LDL cholesterol or increasing HDL cholesterol by using different treatment modalities available. In this study we aimed to compare the status of lipid profile and small dense LDL in cardiovascular disease subjects who were not taking any drug therapy before admission in hospital and those who were under the treatment. The study comprised of total 70 diagnosed subjects of coronary heart disease admitted in the ICU of J.A. Hospital out of which 30 subjects were included in group I who were not taking any drug therapy before admission in ICU and group II included 40 subjects who were under drug treatment. sdLDL-C levels did not show any significant difference between the two groups in spite of the drugs being given to the group II subjects. This result suggests that drugs therapy may be associated with a decrease in total LDL-particle concentration and other lipid parameters but not the proportion of small dense LDL-C.

**Key Words:** sdLDL-c, LDL, Cardiovascular disease

### **INTRODUCTION**

Increased plasma LDL-cholesterol (LDL-C) level is one of the most important risk factors for coronary artery disease (CAD).<sup>(1,2)</sup> The increase in cholesterol and triglycerides is due to an increase in apolipoprotein B-containing lipoproteins, that is, very low density (VLDL) and low density lipoproteins (LDL). Thus, it is logical that LDL cholesterol remains the primary therapeutic target for coronary heart disease (CHD) prevention. It is the main

cholesterol carrying lipoprotein in the circulation. LDL was originally thought to be monodisperse, i.e. composed of a distribution of particles which are heterogeneous and vary according to the size, the density and the composition of the fat they contain. In particular, small dense LDL (sdLDL) has been demonstrated to be a risk factor for the development of CVD. These small dense LDL particles appear in individuals who are hypertriglyceridemic and have a low concentration of HDL

cholesterol. Elevated LDL cholesterol, TGs and reduced HDL may be present in different individuals in varying combinations. The picture is complicated by the presence of small dense LDL. Moreover the patients with different LDL subfractions respond differently to different therapy. <sup>(3)</sup> The small, dense LDL particles cross very easily to the arterial endothelium and form complexes with the proteoglycans of the media, which undergo oxidation in their turn, thus increasing their atherogenic properties. It is believed that the creation of small, dense LDL is facilitated by an increase in triglycerides. <sup>(4)</sup> Conventional treatment of atherogenic lipid profile aims at reducing total cholesterol, LDL cholesterol or increasing HDL cholesterol by using different treatment modalities available. Several drug therapies are used to treat hyperlipidemia. <sup>(5)</sup> Certain class of drugs potentially lower all LDL subclasses (large, medium, and small particles); therefore, the net effect on LDL particle size is often null or, at most, only moderate. <sup>(6)</sup> Although statins clearly decrease total LDL particle concentration, it is a matter of debate whether statins reduce sdLDL predominantly. <sup>(7,8)</sup> Therefore we aimed our study to compare the status of lipid profile and small dense LDL in cardiovascular disease subjects who were not taking any drug therapy before admission in hospital and those who were under the treatment.

## **MATERIALS 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 comprised of total 70 diagnosed subjects of coronary heart disease admitted in the ICU of J.A. Hospital out of which 30 subjects were included in group I who were not taking any drug therapy before admission in

ICU and group II included 40 subjects who were under drug treatment.

**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.

5ml of blood sample was obtained from each subject after overnight fasting in all aseptic precautions for the analysis of biochemical parameters. ECG, Hb%, total and differential leucocyte count, height and weight were recorded at the time of admission.

Blood sugar and 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. <sup>(9)</sup> This study was approved by institutional ethical committee & written consent was also obtained from the patients prior to study.

## **Statistical Analysis**

Student's t-test was used to compare biochemical parameters between the groups. Pearson's correlation was done to determine the relation of small dense LDL and other risk variables. All analysis was done using Windows based SPSS statistical package (Version 16.0).

## **RESULTS**

In CVD subjects who were under drug treatment and the subjects who were not taking any drugs before admission to the hospital, overall status of the physiological parameters including age, height, weight, BMI (kg/m<sup>2</sup>) and hemoglobin showed no significant difference whereas systolic and diastolic blood pressure was significantly higher ( $p < .001$ ) in group (I) compared to the controls (II) (TABLE 1).

**TABLE 1: Characteristics of the subjects. (\*\*p < .001)**

GROUPS		AGE	Ht.	Wt.	BMI	Hb%	SBP	DBP
GROUP I (without treatment) (n=30)	Mean	54.45	1.695	63.85	22.237	13.397	165.5	100
	±	±	±	±	±	±	±	±
	S.D	9.467	.0312	5.132	1.874	1.111	24.083	21.878
GROUP II (on drug therapy) (n=40)	Mean	52.850	1.693	62.55	21.850	13.265	119.5	78.5
	±	±	±	±	±	±	±	±
	S.D	7.679	.0371	4.395	1.797	1.127	8.256***	7.451***

There is significant decrease in total cholesterol (p<.001), triglycerides (p<.01), LDL-C (p<.05) in subjects of group II as compared to group I subjects except HDL

which increased significantly (p <.05) whereas small dense LDL showed no significant change in group II subjects who were on drug therapy (p=NS) (TABLE -2).

**TABLE 2: \*\*\*significant (p<.001) \*\*significant (p<.01)\*significant (p<.05) <sup>NS</sup> Non significant**

GROUPS		BS	TC	TG	VLDL-C	HDL-C	LDL-C	sdLDL-C
GROUP I Without Treatment (n=30)	Mean	82.44	291.23	186.33	37.27	40.80	190.16	57.33
	±	±	±	±	±	±	±	±
	S.D	7.90	23.41	31.07	6.21	6.97	45.89	18.24
GROUP II With Treatment (n=40)	Mean	83.91	218.93	205.49	41.10	41.96	160.33	57.16
	±	±	±	±	±	±	±	±
	S.D	10.50 <sup>NS</sup>	16.51***	46.13**	9.22**	7.23*	51.86*	21.47 <sup>NS</sup>

## DISCUSSION

Predominance of sd-LDL-C is a major component of an atherogenic lipoprotein phenotype, and a source of increased risk for coronary heart disease. Relative risk of all lipoproteins in CVD has been extensively studied and the principle target for cardiovascular preventive strategies has been the low density lipoprotein cholesterol. (10,11) In our study on comparing the lipid parameters between the two groups, we found that the lipid levels were close to normal range in the subjects who were under the treatment except small dense LDL. sdLDL- C levels did not show any significant difference between the two groups in spite of the drugs being given to the group II subjects. These results were similar to the findings of. (12,13) Conventional treatment of the atherogenic lipid profile aims at reducing the total cholesterol levels, LDL -C levels or increasing HDL-C by using different treatment modalities available and some lifestyle modifications. Drug therapy decreases intracellular cholesterol, increase LDL receptors and accelerate removal of

LDL-C and triglyceride rich lipoprotein. (14)

The most important and widely used drugs for the treatment of hypercholesterolemia are statins. They reduce the cholesterol level by inhibiting HMG-CoA reductase enzymatic activity, the rate limiting enzyme in biosynthetic pathway of cholesterol. These drugs decrease intracellular cholesterol, increase LDL receptors and accelerate removal of LDL-C and TGs-rich lipoprotein and constitute the first line of treatment for reducing LDL-C. Though statins are superior to all other medications for reducing LDL-C concentration but their effect on sd LDL-C is variable. (15,16)

One possible mechanism for lowering of LDL-C by drug therapy but not sdLDL-C is that upregulation of LDL receptor activity by statins decreases large, buoyant LDL more than small, dense LDL, because statins increase LDL receptor activity and large, buoyant LDL is a better ligand for the LDL receptor than is small, dense LDL. This result suggests that drugs therapy may be associated with a decrease in total LDL-particle concentration and other

lipid parameters but not the proportion of small dense LDL-C. <sup>(17)</sup>

## CONCLUSION

It is therefore concluded that sd-LDL-C is a major component of an atherogenic lipoprotein phenotype, and a source of increased risk for cardiovascular disease. Drug therapy may decrease the concentration of total LDL but may not show effect on LDL subfractions i.e. small and dense LDL. It is suggested that the therapeutic inflection of sd- LDL often require the combination of different treatment of drugs, lifestyle modification and dietary intake, which may constitute both primary and secondary prevention of CVD. In addition, individualized treatment is required for proper assessment of various risk factors that promotes CVD, particularly sd-LDL.

## ACKNOWLEDGEMENT

We wish to thank the staffs of biochemistry department, G.R. Medical College, Gwalior for their valuable help in this study.

## REFERENCES

1. Grundy S, Cleeman J, Merz c, Brewer Jr. H, Clark L, Hunnigake D, Pasternak R, Smith Jr. S, Stone N. 2004. Coordinating Committee of the National Cholesterol Education Program, Implications of Recent Clinical Trials for the National Cholesterol Education Program Adult Treatment Panel III Guide-lines. Journal of the American College of Cardiology.44(3):720-32.
2. Yoshino G, Nakano S, Matsumoto T, Murakami E, Morita T, Kuboki K. 2012. Rosuvastatin Reduces Plasma Small Dense LDL-Cholesterol Predominantly in Non-Diabetic Hypercholesterolemic Patient. Pharmacology & Pharmacy.3:72-78
3. Hokanson JE, Austin MA, Zambon A, Brunzell JD. 1993.Plasma triglyceride and LDL heterogeneity in familial combined hyperlipidemia. Arterioscler Thromb.13:427-434
4. C.J. Packard. 2003.Triacylglycerol-rich lipoproteins and the generation of small, dense low densityLipoprotein. Biochemical Society Transactions.31:1-4
5. National Cholesterol Education Program (NCEP). 2001. Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Executive Summary of the third report. JAMA. 285:2486-97.
6. Berneis K, Rizzo M. 2004. LDL size: does it matter? Swiss Med Wkly.134:720-4.
7. Franceschini G, Cassinotti M, Vecchio G, Gianfranceschi G, Pazzucconi F, Murakami T. 1994. Pravastatin effectively lowers LDL cholesterol in familial combined hyperlipidemia without changing LDL subclass pattern. Arterioscler Thromb.14:1569-75.
8. Superko HR, Krauss RM, DiRicco C.1997. Effect of fluvastatin on low-density lipoprotein peak particle diameter. Am J Cardiol. 80:78-81.
9. Srisawasdi P, Chaloeysup S, Teerajetgul Y, Pocathikorn A, Sukasem C. 2011.Estimation of Plasma Small Dense LDL Cholesterol From Classic Lipid Measures. Am J Clin Pathol. 136: 20-29
10. Hirano T, Ito Y, Koba S, Toyoda M, Ikejiri A, et al. (2004) Clinical significance of small dense low-density lipoprotein cholesterol levels determined by the simple precipitation method. Arterioscler Thromb Vasc Biol 24: 558-563.
11. Salman Khan M, Akhtar S, Al-Sagair OA, Arif JM (2011) Protective effect of dietary tocotrienols against infection and inflammation-induced hyperlipidemia: an in vivo and in silico study. Phytother Res 25: 1586-1595.
12. Koba S., Yokota Y., Hirano T., It Y., Ban Y., Tsunoda F., Sato T., Shoji M., Suzuki H., Geshi E., Kobayashi Y, Katagiri T. 2008. 'Small LDL

- cholesterol is superior to LDL cholesterol for determining severe coronary atherosclerosis'. *Journal of Atheroscler and Thromb.* 15: 250-260.
13. Choi CU, Seo HS, Lee EM, Shin SY, Choi UJ, Na JO, Lim HE, Kim JW, Kim EJ, Rha SW, Park CG, Oh DJ. 2010. Statins Do Not Decrease Small, Dense Low-Density Lipoprotein. *Texas Heart Institute Journal.* 37:421-428.
  14. Sharma SB, Garg S. 2012. Small dense LDL: Risk factor for coronary artery disease (CAD) and its Therapeutic Modulation. *Indian Journal of Biochemistry and Biophysics.* 49: 77-85.
  15. McKenney JM, McCormick LS, Schaefer EJ. 2001. Effect of niacin and atorvastatin on lipoprotein subclasses in patients with atherogenic dyslipidemia. *Am J Cardiol.* 88:270-274.
  16. Forster LF, Stewart G, Bedford D, Stewart JP, Rogers E, Shepherd J, Packard CJ, and Caslake MJ. 2002. Influence of atorvastatin and simvastatin on apolipoprotein B metabolism in moderate combined hyperlipidemic subjects with low VLDL and LDL fractional clearance rates. *Atherosclerosis.* 164: 129-145.
  17. Nigon F, Lesnik P, Rouis M, Chapman MJ. 1991. Discrete subspecies of human low density lipoproteins are heterogeneous in their interaction with the cellular LDL receptor. *J Lipid Res.* 32:1741-53.

How to cite this article: Mishra P, Singh N, Rastogi P et. al. Status of small dense LDL in cardiovascular disease subjects taking drug therapy. *Int J Health Sci Res.* 2015; 5(5):173-177.

\*\*\*\*\*

#### **International Journal of Health Sciences & Research (IJHSR)**

##### **Publish your work in this journal**

The International Journal of Health Sciences & Research is a multidisciplinary indexed open access double-blind peer-reviewed international journal that publishes original research articles from all areas of health sciences and allied branches. This monthly journal is characterised by rapid publication of reviews, original research and case reports across all the fields of health sciences. The details of journal are available on its official website ([www.ijhsr.org](http://www.ijhsr.org)).

Submit your manuscript by email: [editor.ijhsr@gmail.com](mailto:editor.ijhsr@gmail.com) OR [editor.ijhsr@yahoo.com](mailto:editor.ijhsr@yahoo.com)