

## PREDICTIVE VALUES OF Lp-PLA<sub>2</sub>, hs-CRP AND LIPIDOGRAM IN CORONARY HEART DISEASE

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### ABSTRACT

**Introduction:** Diabetes is a chronic, metabolic disease characterized by elevated levels of blood glucose, which leads over time to serious damage to the heart, blood vessels, eyes, kidneys, and nerves. At present India has reported the highest number of patients suffering from CHD and it is projected to be 40 million by the year 2020. Research study revealed that conventional risk factors are not sufficient to predict the CHD. Therefore novel markers are invented to predict CHD. In present study Lp-PLA<sub>2</sub> as novel inflammatory cardiac marker in diabetic, diabetic with hyper tension & MI is evaluated extensively. **Material and methods:** In present study total 141

subjects were selected as per inclusive criteria, 41 Type II Diabetic, 40 Type II Diabetic with hypertension, 20 patients of Myocardial Infarction and 40 healthy controls. Biochemical parameters i.e. total cholesterol, triglyceride, HDL & LDL was measured by photometric kits (Dade, Siemens), Lp-PLA<sub>2</sub> & hs-CRP was measured by ELISA kit (The Cayman Chemical).

**Results and Discussion:** Significant co-relation observed between Lp-PLA<sub>2</sub> activity, hs-CRP & lipid parameters, in all study groups. **Conclusion:** Present study concluded that Lp-PLA<sub>2</sub> and hs-CRP increased significantly though Cholesterol, TG, HDL, & LDL values are within normal range. Therefore Lp-PLA<sub>2</sub> and hs-CRP, either one or both, may be considered as an independent inflammatory cardiac marker for early prediction of CHD.

**KEYWORDS:** Lp-PLA<sub>2</sub>, hs-CRP, DM, HT, MI, Lipids.

### INTRODUCTION

In 2012, it was reported that diabetes was the cause of 1.5 million deaths. More than 80% of diabetes deaths occur in low- and middle-income countries.<sup>[1]</sup> In 2014, 9% of adults 18 years

and older had diabetes and the global prevalence of diabetes was estimated to be 9% among adults aged 18+ years.<sup>[2]</sup> WHO projects that diabetes will be the 7<sup>th</sup> leading cause of death in 2030.<sup>[3]</sup> Healthy balanced diet, regular exercise, maintaining BMI and avoiding tobacco use can prevent or delay the onset of type 2 DM.<sup>[4]</sup>

Diabetes increases the risk of heart disease and stroke. In a multi-centric study, 50% of people die with diabetes associated cardiovascular disease.<sup>[5]</sup> Cardiovascular disease is disease of blood vessels and includes coronary heart disease (CHD), stroke, hypertension and heart failure. Of an estimated 58 million deaths globally from all causes in 2005, CVD accounted for 30%.<sup>[6]</sup> The substantial proportion of these deaths (46%) in people under 70 years of age and 79% have been attributed to cardiovascular disease is in this age group.<sup>[7]</sup>

Earlier the diagnosis of CHD depends on conventional risk factors. Conventional risk factors like smoking, hypertension, diabetes are reported to 50% of prevalence and severity of the disease.<sup>[8]</sup> It indicates that those 50% cardiac patients were misdiagnosed by conventional risk factors. Lacuna in diagnosis gives an opportunity for researchers to evaluate novel cardiac markers to predict the risk of CHD. In present study conventional biochemical markers are compared with novel biomarker Lp-PLA<sub>2</sub> and hs-CRP.

Lipoprotein-associated phospholipase A<sub>2</sub> (Lp-PLA<sub>2</sub>) was proved as an inflammatory marker of cardiovascular disease. The enzyme Lp-PLA<sub>2</sub> circulates in the blood bound to LDL cholesterol. The pro-inflammatory property of this enzyme hydrolyzes oxidized phospholipids produces lysophosphatidylcholine and oxidized free fatty acids.<sup>[9]</sup>

## MATERIAL AND METHODS

In this study total 141 subjects were selected as per inclusive criteria, 41 Type II Diabetic, 40 Type II Diabetic with hyper tension, 20 patients of Myocardial Infarction and 40 healthy controls aged between 30 to 75 years. Patient attending diabetic clinic at D Y Patil University, School of Medicine, Navi Mumbai were recruited in this study. Pregnant females, chronic liver failure, kidney disease and previously diagnosed CHD/CVD were excluded from the study. Blood glucose level, Glycosylated haemoglobin & ECG examination performed on suspected patient after written consent. Fasting blood samples were collected in plain bulbs and serum was separated and used for biochemical and enzymatic assay. Cholesterol, Triglycerides, HDL, LDL were measured by Automated-Dimension-Clinical Chemistry Photometric analyser. The Cayman Chemical, LpPLA<sub>2</sub> Assay

Kit and hs-CRP Assay Kit are used for quantitative measurement of Lp-PLA<sub>2</sub> activity & hs CRP.

## RESULTS

The comparison was tested within the groups and between the groups. Early prediction of CHD in all the variables was compared with lipid profile. We have excluded myocardial infarction subjects on medication.

**Table: P-value of study groups**

Parameters	Lipids Parameters measured in mg /dl	Type II D M	Type II DM with HT	Myocardial Infraction
LpPLA <sub>2</sub> (0.0-0.005 $\mu$ mole / min / ml )	Cholesterol (125- 200 mg /dl)	0.002	0.002	0.002
	Triglyceride (25-200 mg/ dl)	0.002	0.001	0.001
	HDL (30-65 mg / dl)	0.001	0.000	0.000
	LDL (80- 130 mg /dl)	0.002	0.01	0.01
hs-CRP (up to 3 mg /L)	Cholesterol	0.00	0.001	0.00
	Triglyceride	0.001	0.001	0.001
	HDL	0.000	0.003	0.002
	LDL	0.001	0.001	0.002

## DISCUSSION

P-value calculated within group for Cholesterol- Lp-PLA<sub>2</sub>, TG- Lp-PLA<sub>2</sub>, HDL- Lp-PLA<sub>2</sub>, LDL- Lp-PLA<sub>2</sub> activity was highly significant at  $p < 0.05$  for early prediction of CHD risk. P-value calculated within group for Cholesterol- hs-CRP, TG- hs-CRP, HDL- hs-CRP, LDL- hs-CRP was highly significant at  $p < 0.05$  for early prediction of CHD risk. (Table1) So in both novel biomarker degree of risk prediction is high.

It is observed that Lp-PLA<sub>2</sub> was not only an independent biomarker but statistically significant predictor of coronary heart disease in subjects with normal Lipidogram. Two fold concentration of Lp-PLA<sub>2</sub> was found in all study groups as compared to control group.

In the MONICA Augsburg survey, Lp-PLA<sub>2</sub> was an independent predictor of coronary heart disease among 934 middle-aged men.<sup>[10]</sup> A prospective population-based study showed that association between Lp-PLA<sub>2</sub> and risk of ischemic stroke.<sup>[11]</sup> In a cross-sectional study, Lp-PLA<sub>2</sub> activity was found to be higher in cardiac stroke patients than in healthy control subjects.<sup>[12]</sup>

CRP is an acute-phase surface protein and nonspecific marker of inflammation, produced in hepatocytes in response to several cytokines.<sup>[13]</sup> Interleukin (IL)-6, is most potent factor for

CRP production. It is released from leukocytes in infection or trauma and from vascular smooth muscle cells in response to atherosclerosis.

The original follow-up study conducted on population of 1,059 patients with IDDM (age 45-64 years). CRP values were measured in 1,045 subjects, 878 were free of myocardial infarction (MI) at baseline. Nonfatal myocardial infarction incidence and CHD mortality were assessed for 7-year follow-up. The output of this large cohort study showed that hs-CRP is an independent risk factor for CHD deaths.<sup>[14]</sup>

Researcher conducted study on type 2 DM with HT, MI and alone diabetic patients. Concentration of hs-CRP measured in all study groups and it was found that that hs-CRP and conventional lipid parameters can be used to predict the risk of CHD.<sup>[15]</sup>

A study published by researchers in patients with established coronary disease, CRP has been shown to predict adverse clinical events. C-reactive protein (CRP) has been shown to increase in acute coronary syndromes even in the absence of myocardial necrosis.<sup>[16]</sup> So hs-CRP is a very promising novel biochemical marker for the prediction or recurrent coronary events.<sup>[17]</sup> The Emerging Risk Factor Collaboration (ERFC) reviewed the association among hs-CRP levels, CV risk factors, and vascular risk in 160,309 individuals from 54 prospective studies.<sup>[18]</sup>

## CONCLUSION

In conclusion, Lp-PLA2 activity & hs-CRP both serve as independent predictor for CHD in the general population. The outcomes of this study provide further evidence for an independent role of Lp-PLA2 and hs-CRP in the prediction of coronary heart disease even in normal lipid levels. Both markers have their own potential & merits in prediction of CHD. Extended research on larger population is recommended to evaluate efficacy of both novel markers.

**Conflict:** Nil

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