

D – DIMER – A PREDICTIVE MARKER FOR MYOCARDIAL INFARCTIONSherin Stephen¹, Sreedha R Krishnan²¹Professor & HOD, Department of Biochemistry, Academy of Medical Sciences, Pariyaram, Kerala.²Post Graduate, Department of Biochemistry, Academy of Medical Sciences, Pariyaram, Kerala.**ABSTRACT****INTRODUCTION**

Coronary artery disease occurs most commonly due to obstruction of the coronary artery by atheromatous plaques. Any intravascular or tissue injury leads to activation of intrinsic or extrinsic pathway which activate coagulation factors and leads to formation of stable fibrin clot. When the balance between clot formation and dissolution is disrupted, thrombosis results. Elevated levels of D-Dimer indicate hyper coagulant activity of thrombin due to activation of coagulation pathways as well as an ongoing thrombotic complication. The present study group consists of 150 patients with coronary artery disease confirmed by angiogram studies and 50 controls without any cardiovascular manifestations. Determination of serum D-Dimer (Latex agglutination method), CK-MB (Immuno inhibition assay), total cholesterol (Modified Roeschlau's method), triglyceride (Glycerol kinase method), HDL (Precipitation method) were done and LDL levels were calculated. D-Dimer level were found to be highly elevated in the study group with a mean value of 623.19 ± 49.76 ng/ml and was statistically significant. So also CK-MB levels showed a mean value of 75.55 ± 53.75 IU/L with good statistical significance. The risk factors like hypertension, diabetes, smoking, alcoholism and family history of CAD also had a positive correlation with D-dimer levels. Further, the decrease in HDL levels had more significance than the elevation of LDL levels in the present study. Hence, estimation of D-Dimer levels can be used as an early independent hemostatic marker in predicting the future risk for developing myocardial infarction, especially in the high risk patients after angioplasty.

KEYWORDS

D-Dimer, CK-MB, Coronary artery disease, LDL, HDL, TG.

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INTRODUCTION: D-dimer is the smallest cross-linked fibrin degradation product formed by action of plasmin during the process of fibrinolysis.¹ Atherosclerosis is the main reason for development of coronary artery disease, which can result in development of fatty streak, fibrous plaque or complicated plaque with thrombosis, calcification and cell necrosis; ultimately leading to significant luminal narrowing of blood vessels.² Elevated D-Dimer present in circulation indicates that blood clot is being formed and subsequently dissolved, thereby showing the presence of an underlying thrombotic condition.³ Thrombosis which indicates the activation of fibrinolytic system precedes vascular occlusion. Rather than being a cause of thrombosis, activation of endogenous fibrinolytic system occur as a response to the presence of pre-existing atherosclerotic disease. Altered platelet function as well as altered coagulation and fibrinolysis associated with the traditional risk factors for CAD contribute to the increased susceptibility to thrombosis in atherosclerosis.⁴ Serum TG levels are strongly related to concentration of fibrinogen and factor VII. The gene controlling the synthesis of apo A-I has the greatest effect on HDL levels.

When LDL is exposed to oxygen free radicals that alter apo B-100 and fatty acid esters, even minimally oxidized LDL will have very high atherogenic properties.⁵

The primary objective of the present study was to evaluate the utility of D-Dimer as an early marker, predict the long term risk and the prognosis of high risk patients after angioplasty in coronary artery disease, along with its correlation with CK-MB levels and lipid profile.

MATERIALS AND METHODS: The present study group consists of 150 male patients with coronary artery disease confirmed by angiographic studies and 50 males without any cardiovascular manifestation taken as controls in the age group 25-60 years. Blood samples were collected from the patients admitted in Academy of Medical Sciences, Pariyaram from June 2015 to December 2015, after obtaining ethical committee clearance. Detailed baseline clinical data of each patient including age, sex, present and past clinical complaints, family history and associated complaints were noted.

The following biochemical tests were done in patients and controls included in the study like estimation of D-dimer, CK-MB, total cholesterol, triglyceride, HDL and LDL. Serum D-dimer was estimated by Latex agglutination method, CK-MB by Immunoinhibition assay, total cholesterol by Modified Roeschlau's method, HDL by Precipitation method, and triglyceride by Glycerol kinase method. VLDL and LDL concentrations were calculated by Fried Wald's equation. Statistical analysis was done using SPSS 17.0.

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RESULTS: In the study group, among the 150 male patients, 11 were in the age group 25-35, (Cumulative percentage 7.4), 33 in the age group 35-45 (Cumulative percentage 29.5), 63 in the age group 45-55 (Cumulative percentage 71.8) and 43 in the age group 55-65 (Cumulative percentage 100). Hypertension was found in 139 patients ($p<0.05$), diabetes. In 109 patients ($p<0.05$), smoking in 77($p<0.05$), alcoholism in 38($p<0.05$) and family history of CAD in 45 patients ($p<0.05$).

The mean D-dimer level in patients was 623.19 ± 49.76 ng/ml when compared to 184.28 ± 28.78 ng/ml in controls with a 'p' value of <0.05 . CK-MB values in patients had a mean value of 75.55 ± 53.75 IU/L while in controls, the mean value was only 13.88 ± 4.07 IU/L ($p<0.05$). When the serum cholesterol levels were estimated, the mean level in patients was 196.09 ± 33.73 mg% and in controls 165.37 ± 14.06 mg% ($p<0.05$). The mean serum triglyceride value in patients was 144.56 ± 71.10 mg% whereas in controls 111.82 ± 27.63 mg% ($p<0.05$). As regards HDL concentration, the mean level in patients was less, 35 ± 8.15 mg% when compared to controls which was 47.9 ± 5.51 mg% and was statistically significant ($p<0.05$). The mean level of LDL in the patients under study was 142.01 ± 34.52 mg% which was higher than that in controls 100.33 ± 11.14 mg% ($p<0.05$).

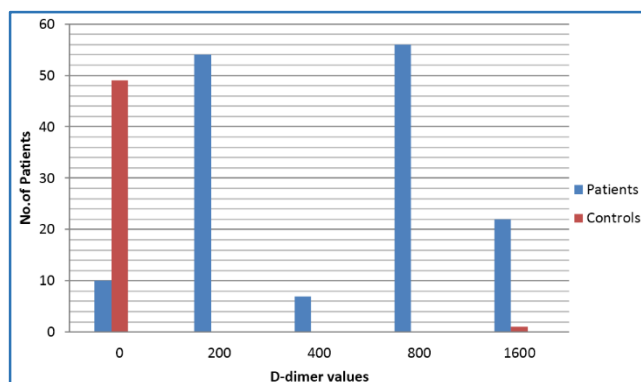


Fig. 1

Parameter	Group	N	Mean	Std Deviation	P value	R value
D-dimer (ng/ml)	Patients	150	623.19	49.46	0.00	0.972
	Control	50	184.28	28.78		
CK-MB (IU/L)	Patients	150	75.55	53.75	0.00	0.883
	Control	50	13.88	4.07		
Total cholesterol (mg%)	Patients	150	196.09	33.73	0.02	0.416
	Control	50	165.37	14.06		
Triglyceride (mg%)	Patients	150	144.56	71.10	0.00	0.894
	Control	50	111.82	27.63		
HDL (mg%)	Patients	150	35.00	8.15	0.02	0.437
	Control	50	47.9	5.51		
LDL (mg%)	Patients	150	142.01	34.52	0.00	0.926
	Control	50	100.33	11.1		

Table 1: Variation between patients and controls with different parameters

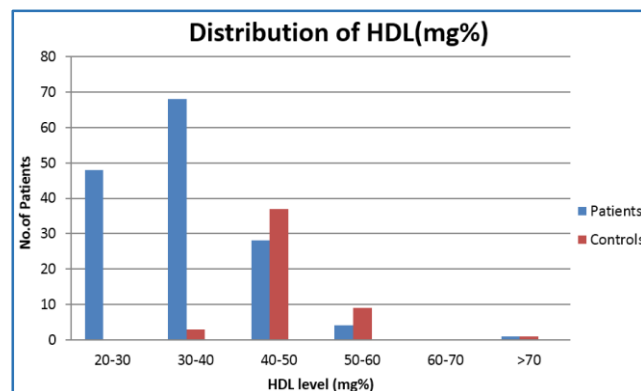


Fig. 2

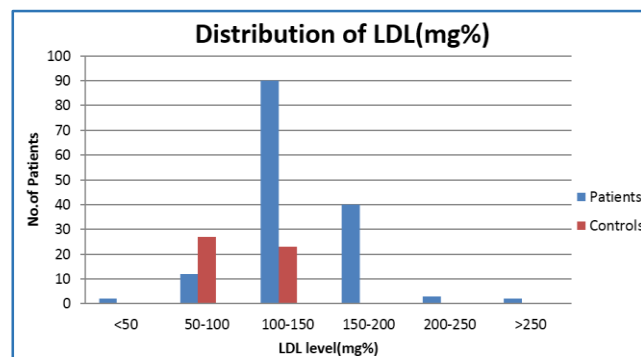


Fig. 3

DISCUSSION: Thrombus formation at the site of atherosclerotic lesion especially on a ruptured plaque plays a central role in atherothrombosis hypothesis. Fibrinolytic system is markedly altered in patients with coronary heart disease.⁶ Arthur. L. Bloom, Charles D Forbes, Duncan P Thomas et al showed that D-dimer assay identifies patients at increased risk for mortality and is a sensitive test to determine the presence of underlying microvascular pathology in critically ill patients. An elevated D-dimer level is associated with an increased risk of later development of venous thromboembolism.⁷ In the present study, the serum D-dimer level were greatly higher in patients than controls and was statistically significant.

Acute myocardial infarction produces CK-MB elevation, which when released into the circulation is acted on by carboxypeptidase that cleaves a lysine residue from the carboxyl terminus to produce an isoform, with a different electrophoretic mobility.⁸ In the patients under study, CK-MB levels (mean 75.55 ± 53.75 IU/L) were highly elevated when compared to controls and was significant statistically. According to the expert panel on detection, evaluation and treatment of high blood cholesterol in adults, a linear relationship exists with a 20% increase in risk of CAD, for each 10% increase in serum cholesterol.⁹ In the patients under study, the mean level of serum total cholesterol in patients was 196.09 ± 33.73 mg% which was also statistically significant. As per the studies conducted by Thomas W Smith, serum triglyceride levels of 200mg/dl or greater was found in 93% of subjects who had MI or died of CAD.¹⁰ In the present study too, the triglyceride levels in patients showed a mean value of 144.56 ± 71.10 mg% with a 'p' value

of <0.05 . The studies of R Wayne Alexander, Rober C Shlant and Valentia Fuster revealed an inverse relationship between HDL cholesterol levels and risk of CAD.¹¹ The mean level of HDL cholesterol was very low in the patients under study than controls. Oxidative modification of LDL has been hypothesized to play a major role in the initiation and progression of atherosclerosis.¹¹ In the present study, LDL cholesterol had an elevated mean value of $142.01 \pm 34.52 \text{ mg\%}$ showing good statistical significance.

CONCLUSION: D-Dimer level was highly elevated in the patients under study. As D-Dimer level directly indicate a hypercoagulable state, it is a very useful early haemostatic marker in predicting the risk of developing coronary events in future as well as in detecting high risk patients after surgeries for CAD. Further, estimation of D-Dimer level can be done by a simple, easy and inexpensive method, when compared to the other markers of CAD and can be adopted as a routine investigation in patients with CAD, to increase their quality of life.

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