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Original Research Article

Role of Lipoprotein (a) in Coronary Artery Disease

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ABSTRACT

Objective: This study was a prospective case-control study to know lipoprotein (a) [Lp(a)] levels and its role as an independent risk factor in coronary artery disease in Jammu population of northern India. Study was done on a consecutive 100 subjects who underwent coronary angiography in Government Medical College, Jammu for a period of one year.
Method: Lp(a) was measured in serum samples by immunoturbidimetric assay by using commercial kit from Diasys Diagnostic Systems GmbH D-65558 Holzheim Germany. The data so obtained was statistically analyzed.
Result: The present study confirmed the evidence that Lp(a) > 30 mg/dl is an independent risk factor for IHD .In present study also, 88.3% of patients with IHD had Lp(a) levels between 26-75 mg/dl. For Lp(a) levels between 26-79 mg/dl, the risk of IHD increased by 15 times among IHD group. In this study, patients with myocardial infarction had higher levels of Lp(a) as compared to patients who had presented with angina. All the same, the study does give an important clue regarding the relationship between lipoprotein (a) and the risk of IHD.

Key words: lipoprotein (a), coronary artery disease, IHD

INTRODUCTION

Coronary artery disease (CAD) means narrowing of the small blood vessels that supply blood and oxygen to the heart. Chronic coronary artery disease is most commonly due to obstruction of coronary arteries by atheromatous plaque. [(1)]
Atherosclerosis is a complex inflammatory-fibroproliferative response to retention of plasma derived atherogenic lipoproteins in the arterial intima. [(2)] Coronary artery disease can manifest as asymptomatic (silent ischemia) and symptomatic – acute myocardial infarction, ischemic cardiomyopathy, angina pectoris and sudden death.

Several studies have led to consider Lipoprotein(a) as an independent and most prevalent inherited risk factor for atherosclerosis and coronary heart disease. [(3-5)] Lipoprotein(a) has been found to be associated with atherosclerosis and thrombosis. [(6-8)]

Lipoprotein(a) provides a better marker of predicting the angiographically defined coronary artery disease as compared to traditional measures. [(9)]

MATERIAL AND METHODS

A prospective case-control study was conducted in the Postgraduate Department of Medicine, Government Medical College, Jammu for a period of one year starting from January 2014 to January 2015. Study group comprised of 60 cases and 40 controls. Cases were selected from the patients admitted to the Indoor Wards of Medicine and Cardiology Department of the Government Medical College and Hospital, Jammu for diagnostic coronary angiography.

Inclusion criterion

(a) Patients with history of typical angina pectoris.
(b) Patients of MI

Exclusion criterion

a) Patients with symptoms suggestive of ischemic heart disease but ECG and enzymatic tests were normal,
b) Malignant disease, hepatic and renal disease
c) Valvular heart disease, Myocarditis, Cardiomyopathy
d) Allergic reaction to intravascular contrast.
e) Patients on drugs known to effect Lp(a) levels *i.e.* neomycin and niacin.

Informed consent was obtained from all the subjects. Subjects were worked-up as per the predesigned proforma.

All the study participants provided a complete medical history, including previous history of myocardial infarction; conventional risk factors for CAD such as smoking, hypertension, diabetes mellitus, hyperlipidemia, family history of premature CAD; drug therapy. All were subjected to a thorough clinical examination and. A 12 lead electrocardiogram was recorded on all subjects.

Routine laboratory investigations other than Lp (a) included complete hemogram, blood sugar, complete urine routine examination, renal function tests, serum electrolytes (Na^+/K^+), lipid profile. Coronary angiography was done to know the type and extent of disease.

Coronary angiography was done on all the subjects. Accordingly in patients with significant coronary artery disease it was classified as one, two and three vessel disease depending upon the number of vessels involved by the disease process.

Specific laboratory tests: plasma triglycerides, cholesterol and high density lipoprotein cholesterol concentrations, low density lipoprotein concentrations and lipoprotein(a) were measured.

Venous blood (10 ml) was withdrawn from all study participants after overnight fast (12 hours).

Quantitative determination of lipoprotein(a) in human serum was done by turbidimetric immunoassay .

Statistical analysis

Data analyzed with the help of computer software SPSS 10.0 for Windows and Epi-info version 6.0.2. Qualitative variables analyzed and reported as percentages. Chi-square test used to assess relationship among the variables. 't' test used to assess significant differences in the mean values.

All statistical tests used were two-tailed and a p-value of < .05 was considered as statistically significant.

RESULTS

Table 1: Lipid profile and risk of IHD

Parameter (mg/dl)	*IHD (Cases)*	*Non-IHD (Controls)*	*'t'-value*	*'p'-value*
Serum cholesterol	221.01 ± 20.04	190.10 ± 10.04	$t_{(98)}$ 9.017	0.0001
HDL	33.71 ± 4.76	43.05 ± 3.66	$t_{(98)}$ –10.47	0.0001
LDL	147.61 ± 14.49	130.77 ± 4.76	$t_{(98)}$ 7.086	0.0001
Triglyceride	187.68 ± 14.28	141.37 ± 3.13	$t_{(98)}$ 20.15	0.0001

The above table shows that mean serum cholesterol levels, mean LDL levels and mean triglyceride levels were higher among the IHD group as compared to non-IHD group whereas mean HDL levels was lower in the IHD as compared to non-IHD group and was also found to be statistically significant (p = 0.0001). This shows that high serum cholesterol, LDL and triglyceride levels predisposes to IHD whereas high HDL levels serves as a protective parameter for IHD.

Table 2 : Lp(a) and risk of IHD

Parameter (mg/dl)	*IHD (Cases)*	*Non-IHD (Controls)*	*'t'-value*	*'p'-value*
Lp(a)	35.39 ± 11.84	24.40 ± 5.57	$t_{(98)}$ 5.471	0.0001

Mean Lp(a) levels in the IHD group was higher as compared to those in the non-IHD group (35.39 ± 11.89 versus 24.40 ± 5.57) respectively and was found to be statistically significant. Thus, lipoprotein(a) is a risk factor for IHD.

Table 3 : Plasma Lp(a) levels in IHD and non-IHD group

Plasma Lp(a) levels (mg/dl)	*IHD* (Cases)*		*Non-IHD** (Controls)*		*Total*	*Crude OR (95% CI)*
	(No.)	(%)	(No.)	(%)		
< 5	–	–	1	2.5	1	Undefined
5-25	5	8.3	23	57.5	28	1.00 (reference)
26-75	53	88.3	16	40.0	69	15.90 (4.71-57.30)
≥ 76	2	3.4	–	–	2	Undefined
Total	60	100	40	100	100	

Raised Lp(a) levels (*i.e.*> 26) was found in 55 (91.6%) patients with IHD.

Distribution of Lp(a) levels in the IHD and non-IHD groups showed that 53/60 (88.3%) patients with IHD had Lp(a) levels between 26-75 mg/dl whereas 23/40 (57.5%) subjects with non-IHD had lower Lp(a) levels between (5-25 mg/dl

It is also seen that the risk for IHD was maximum for Lp(a) levels between 26-75 mg/dl (crude odds ratio 15.90, 95% CI, 4.71-57.30). Thus, high Lp(a) levels > 26 mg/dl can be considered to be a positive predictor for IHD.

Table 4 : Mode of presentation among the IHD group and mean Lp(a) levels

Presentation	*Number (No.)*	*Percentage (%)*	*Mean Lp(a) Levels ± SD (mg/dl)*
Angina	36	60.0	32.38 ± 11.87
Myocardial Infarction	24	40.0	39.89 ± 10.48

Out of 60 patients with IHD, 36 had angina and 24 had myocardial infarction. Mean Lp(a) levels ± SD (mg/dl) was more in patients who had presented with myocardial infarction as compared to those with angina (see Table).

Table 5: Plasma Lp(a) levels and number of diseased vessels

Severity of Disease	*Number (No.)*	*Percentage (%)*	*Mean Plasma Lp(a) Levels ± SD (mg/dl)*
One Vessel Disease	20	33.0	22.70 ± 5.88
Two Vessel Disease	23	40.0	35.96 ± 7.15
Three Vessel Disease	17	27.0	43.64 ± 16.08

Table 6 : **Results of logistic regression**

Variable	*Lipoprotein(a)*
Constant	–5.68
β	0.2087
SE	0.0450
R	0.3805
Significance	0.0000
Adjusted OR	1.23

DISCUSSION

In this study, all the subjects were worked-up according to the predesigned proforma. Statistical analysis of the data was done.

Out of 60 patients with IHD there were higher proportions of males as compared to females (81.7% versus 18.3%, respectively).

Lipid profile and risk of IHD

Several studies have shown that an 88 mg/dl increase in triglycerides levels significantly increase the relative risk of CAD by 30% in men and 75% in women. [(10,11)] In present study, results were alike, mean triglyceride levels were significantly higher in IHD group as compared to non-IHD group (Table-1), thus, further supporting the hypothesis that high triglyceride levels are a risk factor for IHD.

Also, there were significantly low HDL-cholesterol levels in the IHD group compared to non-IHD group. Low HDL is associated with increased risk of CAD even if triglycerides and total cholesterol are not elevated. [(12,13)]

Lipoprotein(a) and risk of IHD

In numerous studies mainly in white population, elevation of plasma Lp(a) have been significantly correlated with CAD. [(14-16)]

an Indian study showed that elevated Lp(a) levels was associated with increased CAD. [17]

The present study also demonstrated that the mean Lp(a) levels ± SD in the IHD group was more as compared to the non-IHD group (35.39 ± 11.84 versus 24.40 ± 5.57, respectively) and the differences in values were statistically significant further supporting the hypothesis that elevated Lp(a) levels is an independent risk factor for IHD (Table 2).

Plasma Lp(a) levels and risk of IHD

Lp(a) values > 30 mg/dl are generally accepted as an independent risk factor for CHD. [18-20]

In this study too, mean Lp(a) levels in the IHD group was 35.39 ± 11.84 mg/dl as compared to 24.40 ± 5.57 mg/dl in the non-IHD and the difference in levels were statistically significant (p <0.0001) confirming the evidence that Lp(a) >30 mg/dl is an independent risk factor for IHD (Table 2 and 3).

Mean Lp(a) levels in myocardial infarction and angina

In this study, patients with myocardial infarction had higher levels of Lp(a) as compared to patients who had presented with angina (39.89 ± 10.48 versus 32.38 ± 11.87 mg/dl, respectively) (Table 4).

Mean Lp(a) levels and number of diseased vessels on coronary angiography

Lipoprotein(a) is considered to be an independent risk factor for multivessel CAD. Some earlier studies have addressed themselves to the association between lipoprotein(a) and coronary atherosclerosis. [21-23]

The present data also expand our earlier experience. In this study, there were significant increase in the mean Lp(a) levels as the severity of CAD increases *i.e.* number of vessels involved assessed by coronary angiography and mean Lp(a) levels were 27.70 ± 5.86; 35.96 ± 7.15 and 43.64 ± 16.08 for one vessel disease, two vessel disease and three vessel disease, respectively (Table 5)

CONCLUSION

In conclusion, logistic regression was employed to assess the independent effect of all the variables. Only lipoprotein levels were found to be significantly associated with the risk of IHD (adjusted OR 1.23). This means with every 1 mg/dl increase in the Lp(a) levels, the risk of acquiring IHD increases by 23% in an individual. However, other variables found to be associated on crude analysis lost their significance on multivariate analysis (Table 6).

In the present study, on a consecutive 100 subjects undergoing coronary angiography, following results were obtained:-

1. Lp(a) was found to be an independent risk factor for IHD.
2. Lp(a) levels > 26 mg/dl increased the risk for IHD.
3. For every 1 mg rise in serum Lp(a) levels the risk for IHD rose by 23%.

However, determination of Lp(a) levels may provide an important contribution to the clinical assessment of individuals at high risk for CAD. Lp(a) levels should be measured :-

1. In patients with premature CHD.
2. Those with a strong family history of cardiovascular disease (CVD).
3. Who have undergone angioplasty or coronary artery bypass grafting.
4. Those with documented cardiovascular disease in the absence of traditional risk factors.

In patients with elevated Lp(a), the preventive and therapeutic goals consist of diligently searching and drastically reducing all concurrent modifiable risk factors.

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