Original Article

Plasma Lipoprotein (a) Levels In Acute Coronary Syndrome At A Tertiary Care Hospital In South India

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ABSTRACT

Background: Increasing prevalence of coronary heart disease (CHD) occurs in Indian population due to rapid changes in demography and life style, consequent to economic development. Prevalence of coronary artery disease (CAD) in south Indians is high compared to north Indians. Investigation in the recent past have suggested that lipoprotein (a) (Lp(a)) concentrations in serum could be a risk factor for occurrence of acute coronary syndrome (ACS).

Aims and objectives: (1) To observe whether Lp(a) is significantly elevated in patients with ACS in comparison to healthy controls (2) To assess association of Lp(a) in ACS.

Materials and methods: 45 cases who were admitted in intensive coronary care unit with clinical findings suggestive of ST segment elevation myocardial infarction (STEMI) (n=35), Non ST segment elevation myocardial infarction (NSTEMI) (n=2) and unstable angina (n=8) were included in the study group. 45 sex and age matched healthy individuals were taken as control group.

Results: Mean plasma Lp(a) levels of study group is higher than that of control group [23.87±7.56mg/dl versus 10.40mg/dl±3.11mg/dl] (p =·000) which is statistically significant. Total cholesterol (TC), triglycerides (TGL), low density lipoprotein (LDL),TC/HDL ratio were statistically high and high density lipoprotein(HDL) was statistically low in study group compared to controls. There is no difference in mean plasma Lp(a) values in males and females in both study and controls.

Conclusion: Increased Lp(a) levels are seen in ACS and is associated with the occurrence of ACS in present study.

Key words: Acute coronary syndrome, Coronary artery disease, Lipoprotein (a), TC/HDL ratio

INTRODUCTION :

The Acute Coronary Syndrome is the clinical manifestation of the critical phase of coronary artery disease (CAD). The clinical features depend upon extent and severity of myocardial ischemia. CAD evolves often unnoticed over decades culminating in myocardial infarction. Myocardial infarction and its complications are the principal causes of death in patients with CAD. ACS refers to a range of myocardial ischemic states which includes patient with ST segment elevation myocardial infarction (STEMI), non ST segment elevation (NON STEMI) and unstable angina.

It has been predicted that CAD might become the most prevalent disease in India by the year 2020.[1] Rapid change in demography and life style consequent to economic development attribute to increase in the incidence of CAD in Indians.[2] Only 50% of occurrence of CAD is caused by traditional risk factors,[3] hence search is for the emerging risk factors like Lp(a), fibrinogen, homocysteine, apo-B,etc.[1,4] Lp(a) is composed of low density

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lipoprotein (LDL) particle bound to plasminogen like glycoprotein named apolipoprotein (a)[5] by a disulphide bridge. Lp(a) is synthesized in the liver, the metabolism of Lp(a) is independent of other lipoproteins. Lp(a) turn over studies have shown approximately 70% of the apo[a] component of Lp(a) may be released in the circulation and rest is degraded via LDL –R.[6] Lp(a) concentrations are genetically determined with more than 90% of the variation being determined within the gene for apo(a), difference is primarily due to production rather than catabolism of Lp(a).[7] The prevalence of CAD is two times higher (10%) in urban than in rural India. South Indians have higher prevalence 7% in rural and 14% in urban areas.[8] Lp(a) is an independent risk factor in occurrence of CAD. Studies conducted in south India have shown increased levels of Lp(a) levels in CAD.[3,9] Lp(a) may constitute a link between the process of atherosclerosis and thrombosis.[10]

Hence the aim of the present study is to observe whether high concentration of Lp(a) is seen in ACS and its association with the occurrence of ACS.

MATERIALS AND METHODS:

This study was conducted at Thanjavur medical college hospital, Thanjavur, after getting approval from ethical committee. In the present study, the age group of both study and control group ranged from 30 to 65 years, males and females were included and informed consent was obtained.

Forty five (27 males and 18 females) newly diagnosed cases of ACS who were admitted in ICCU with clinical findings suggestive of STEMI (n=35), NSTEMI (n=2), unstable angina (n=8) were included in the study group. 45 sex and age matched, healthy individuals were taken as control group.

EXCLUSION CRITERIA

Patients with nephrotic syndrome, chronic renal failure, hypothyroidism, diabetes mellitus, previous history of acute coronary syndrome and on drugs like steroids, lipid lowering drugs (statins, fibrates) and hormone replacement therapy were excluded from the study.

BLOOD COLLECTION

Fasting venous blood samples (day after the admission with ACS) were collected under aseptic conditions. 5ml of blood was drawn by intravenous route. 2ml of blood was transferred to EDTA tubes for Lp(a) estimation and 3ml was transferred to plain vacutainers for estimation of total cholesterol, TGL, HDL, fasting blood glucose, urea, creatinine. The samples in the EDTA tube were centrifuged, plasma diluted (1:8000) and stored at -20 C in deep freezer for Lp(a) estimation. Human lipoprotein(a) assay was done using ELISA kit (assay max human Lp(a) kit-Assaypro). The estimation of total cholesterol, TGL, HDL was done using enzymatic kits in XL 300 auto analyser. Friedewald's formula was used to calculate LDL values.

STATISTICAL ANALYSIS

Data were entered in IBM SPSS version 20 software and descriptive statistics like percentage were used. Analysis was done using student's t-test.

RESULTS

Table 1 shows mean plasma Lp(a) levels and lipid parameters in the study and control group. Table 2 shows mean plasma Lp(a) and TC/HDL ratio in males and females. Table 3 shows plasma Lp(a) levels in different age groups. The significance of various parameters are expressed by means of P values as per $P < 0.05$ – significant, $P < 0.001$– highly significant and NS – Not significant.

DISCUSSION

CAD in Indians has been rising steadily over past 40 years affecting mainly younger age group in the absence of traditional risk factors. Lp(a) concentration are related to atherothrombogenesis and may be a key link between lipids and CAD occurrence. Rising affluence, sedentary and stressful life styles are additional risk factors for CAD occurrence at younger age group. In the present study, mean plasma Lp(a) levels of study group is higher than control group (23.87mg/dl±7.56mg/dl versus 10.40±3.11mg/dl) which is statistically significant.

Table 1: Statistical analysis of general, Lp(a) and Lipid Parameters

S. No	Variables	Study (n=45) Mean ± SD	Control (n=45) Mean ± SD	P value
1.	Age (Years)	52.8±9.30	50.2±9.07	P=0.194^{NS}
2.	BMI	25.40±3.48	25.49±1.84	P=0.874^{NS}
3.	Lp (a) mg/dl	23.87±7.56	10.4±3.11	P=0.000**
4.	TC mg/dl	217 .02±34.34	182 .33±14.52	P=0.000**
5.	TGL mg/dl	208±38.09	132.67±17.79	P=0.000**
6.	HDL mg/dl	37.60±3.70	42.71±3.48	P=0.000**
7.	VLDL mg/dl	42.06±7.52	27.51±0.28	P=0.000**
8.	LDL mg/dl	135.98±32.43	131±14.91	P=0.000**
9.	TC/HDL ratio	5.86±1.33	4.30±.54	P=0.000**

Index, Lp(a): Lipoprotein (a), TC: Total Cholesterol, TGL: Triglycerides, HDL: High Density Lipoprotein, VLDL: Very Low Density Lipoprotein, LDL: Low Density Lipoprotein.

Table 2: Mean Plasma Lp (a) and TC / HDL ratio in Males and Females

S. No	Variables	Study			Control		
		Male n = 27	Female n = 18	P value	Male n=27	Female n = 18	P value
1	Lp (a) mg/dl	24.52±7.33	22.89±7.99	P=0.491^{NS}	10.49±3.17	10.41±3.10	P=0.988^{NS}
2	TC/HDL ratio	5.70±1.16	6.09±1.55	P=0.372^{NS}	4.30±.56	4.30±.51	P=0.937^{NS}

*P<0.05, ** P<0.001, S – Significant, NS – Not Significant, Lp(a): Lipoprotein (a), TC: Total Cholesterol, HDL: High Density Lipoprotein

Table 3: Plasma Lp (a) levels in different age groups

S. No	Age Group In years	Study		Control		P value
		No.	Mean±SD mg/dl	No.	Mean ±SD Mg/dl	
1.	< 40	4	27.43±4.75	7	10.11±2.14	P=0.003*
2.	41 to 50	13	25.01±6.61	16	11.78±4.50	P=0.000**
3.	51 to 60	18	21.07±7.6	18	9.66±1.61	P=0.000**
4.	> 60	10	26.00±8.70	4	9.31±0.76	P=0.000**

P<0.05, P<0.001, S – Significant, NS – Not Significant

Optimum time for assessment of serum lipid profile in patients with myocardial infarction is within 24 hours of acute episode of ACS.[11] Hence the samples were collected within 24 hours of onset in present study.

Lifelong levels of Lp(a) are attained by age of two and it is heritable.[10] Enas et al suggested Lp(a) of 20 mg/dl as upper limit of normal Lp (a) in Indian population.[10,12] Higher mean plasma Lp (a) levels in study group correlated with mean Lp(a) levels in CAD group observed by D. Rajasekar et al.[3] and Isser et al. (9.28 mg± 2.5 mg/dl versus 22.54 ± 5.4 mg/dl) in controls and study group respectively.[13]

These mean levels are seen in 30 to 40 % Asian Indians which is considered as threshold for high risk of CAD. Lp(a) is categorised as an emerging risk factor by Adult treatment panel III of National Cholesterol Education Programme. CAD occurrence rate is higher in individual with elevated Lp(a). The higher levels of Lp(a) correlate with prematurity, severity, extent and progression of coronary atherosclerosis as well as occurrence and recurrence of myocardial infarction among Asian Indian. Asian Indians have high ratio of TC/HDL, TG/HDL and apo B /apo A1.These ratios highly correlated with premature incidence and severity of CAD as well as myocardial infarction among Asian Indians.[14]

In present study, TC/HDL ratio in study group is

higher than control group (5.86±1.33versus 4.30±.54). This matched with the study done in south India by D. Rajasekar et al. and Angeline et al. [3,9] Major reason for increasing TC/HDL ratio seen in present study may be due to the dietary changes in the form of increase intake of foods of animal origin, increase in intake of saturated hydrogenated fat and there is also decrease intake of dietary fibres.

Among patients with Lp(a) excess, the CAD risk increased to 3 fold in the absence of other risk factors and increased to 8 fold with low HDL and to 25 fold with high TC/HDL ratio.[14] Most of the study reports emphasis that elevated serum Lp(a) concentration is independent risk factor for CAD occurrence.[8,9] In the present study, the occurrence of ACS in study group suggest that the disease risk is high due to increased concentration of Lp(a).

Lp(a) excess may promote initiation and early development of atheromatous plaques. Lp(a) is involved in atherothrombogensis via LDL particles that may promote atherosclerosis and plasminogen like apolipoprotein (a) interfering with fibrinolysis and causing thrombosis. Lp(a) can enter into human atherosclerotic plaques and implicated in foam cell formation, smooth muscle cells proliferation, plaque inflammation and instabilization. Lp(a) binds with proinflammatory oxidized phospholipids, accumulates more at sites of arterial injury than LDL.[5]

Prevalence of CAD is higher in South Indians compared to other states[8,15] Indians are at increased risk of developing myocardial infarction almost 10 years earlier than counterparts in developed countries as well as in other developing countries.[10,16] This scenario is also seen in lower income group in spite of difference in life styles, culture etc., indicating the urgency of addressing the associated risk factors. [16]

The appropriate management for high levels Lp(a) is limited. By modifying diet or using standard lipid lowering agents do not lower Lp(a) levels and therapeutic option available to lower Lp(a) is niacin. Lowering low density cholesterol is the one therapeutic option available which may attenuate the pathological action of Lp(a).[17,18] Identifying interaction between Lp(a) and other risk factors would enable identifying the individual at increased risk for Lp(a) mediated disease and treat appropriately.

LIMITATION:

Study with large sample size is to be conducted to confirm the findings of present study.

CONCLUSION:

High level of Lp(a) has significant association with acute coronary syndrome in present study.

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