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A Study of Lipoprotein (A) in Coronary Artery Disease Patients

KEYWORDS: lipoprotein (a), coronary artery disease, lipid tetrad index

Dr B.Srinivas	Dr.S.Prem Sagar	Dr D.Anil Kumar
Assistant Professor Assistant Professor of Medicine,Gandhi Medical college,Secunderabad, Telangana (Auto) Kumbakonam.	Assistant Professor of Medicine, Gandhi Medical College, Secunderabad, Telangana	Assistant Professor of Medicine, Gandhi Medical College, Secunderabad Telangana

ABSTRACT *OBJECTIVES: To study lipoprotein (a) levels and lipid tetrad index in patients with premature coronary artery disease.*

METHODS: A hospital based observational study of lipoprotein (a) and lipid tetrad index in patients with premature coronary artery disease.

RESULTS: A total of 90 patients diagnosed with coronary artery disease were subjected to measurement of serum lipoprotein (a) mean value 65.8, total cholesterol mean value 210.66, triglycerides mean value 207.9 mg.LDL cholesterol mean value 130.5, HDL cholesterol mean value 43.4 and lipid tetrad index mean value 54286.4.

CONCLUSIONS: A positive correlation was observed with elevated lipoprotein (a) and lipid tetrad index with incidence of premature coronary artery disease.

INTRODUCTION

Coronary artery disease (CAD) accounts for 12million death annually in and is commonest cause of death globally.CAD has rapidly emerged as the major contributor to mortality and morbidity in India. What is even unfortunate is that CAD is increasing in younger age groups and running malignant course in certain groups like south Asians, the risk factor profile, age of onset and the course of disease appears to be different in Indians

Considering the burden of CAD especially in young age, in India this study is under taken to understand the newer risk factor like lipoprotein (a) (Lp(a)) in this part of world.

The alarming rise in incidence of CAD in younger age group has prompted for search of additional risk factors in this group. The Asian Indian paradox is that the incidence of CAD is high(6% when compared to 2%to4% in west) despite the lower prevalence of conventional risk factors like hypertension, obesity, hyperlipidemia, smoking except diabetes approximately 30-5O% of patients in India do not have conventional risk factors. Newer risk factors like hyperhomocystinemia, hypertriglyceridemia, low HDL, high lipo protein(a) may explain the paradox.

Lp (a) is a genetically determined plasminogen like lipoprotein that has been demonstrated as a powerful, independent risk factor for premature atherosclerosis among whites and south Asians and Hispanics in several studies. Hence this study was undertaken to evaluate the incidence of Lp(a) in premature CAD in this region. Also the correlation of Lp(a) to lipid profile is studied ""the lipid tetrad" (a comprehensive index of newer risk factors) is calculated . The ""lipid tetrad "" seems to explain the high incidence of CAD in the absence of conventional risk factors especially in certain groups of genetically predisposed populations like … south Asian group.

Comprehensive lipid terad index is calculated by the formula

TCXTGXLp(a)/HDL

The values are taken as mg/dl. An index less than 10,000 is desirable, 10,000-20,000 as borderline, and more than 20,000 is high.

TC=total cholesterol
TG=triglyceride
Lp(a)=lipoprotein (a)
HDL-C=HDL cholesterol

AIMS

1) To study the lipoprotein (a) and lipid profile levels in patients with premature coronary artery disease(CAD) below 45 years of age
2) To calculate lipid tetrad index
3) To compare the lipoprotein (a) and lipid profile between cases with CAD and controls.

MATERIAL AND METHODS

90 Patients who were admitted to Gandhi hospital with clinical and ECG evidence of CAD, in the form of unstable angina and acute MI were studied.

45 cases with age and sex matched people, selected from hospital staff, who were asymptomatic with normal ECG were taken as controls.

A detailed history regarding presenting complaints like chest pain shortness of breath, palpitation, sweating, syncope, nausea, vomiting were taken in all cases

History of premature CAD, hypertension, diabetes smoking, and alcoholism were noted. Thorough clinical examination was done to detect markers of hypertension.

Routine blood tests like complete blood picture blood sugar,blood urea,serum creatinine,xray chest serial ecgs were taken.

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Venous blood sample with 12 hours of overnight fasting were collected from patients within 24 hours of admission and analysed for total cholesterol HDL triglycerides and lipoprotein (a)

Lipoprotein (a) was analysed by nephelometry. Nephelometry is a technique for estimation of number and size of particles in a technique for estimation of number and size of particles in a suspension by measurement of light scattered from a beam of light passed through the solution by a nephlometer. Lipid tetrad index was calculated

STATISTICAL ANALYSIS

Arithmetic mean standard deviation and standard error of means was calculated. The result is considered significant if P values more than 0.05

RESULTS AND OBSERVATION

In the present study the plasma lipid profile and Lp(a) are measured in 90 patients in patients with premature coronary artery disease and 45 patients taken as controls.

TABLE 1 AGE AND SEX DISTRIBUTION

AGE	MALES	FEMALES	TOTAL
0-10	nil	nil	nil
11-20	nil	nil	nil
21-30	12	nil	12
31-40	36	6	42
41-45	27	9	36
TOTAL	75	15	90

Out of 90 patients, 83.3% were males and16.6% females.

Peak incidence was in 31-40 years age group.

Youngest patient was 21 years old with acute anteroseptal myocardial infarction with elevated total cholesterol, elevated triglycerides, decreased HDL and elevated lipoprotein (a).

TABLE 2 AGE AND SEX DISTRIBUTION CONTROLS

AGE	MALES	FEMALES	TOTAL
0-10	NIL	NIL	NIL
11-20	NIL	NIL	NIL
21-30	12	6	18
31-40	12	6	18
41-45	6	3	9
TOTAL	30	15	45

Out of the control population, 66.6% were males and33.4% were females. Control population was selected from hospital and nursing staff with no symptoms and normal resting ECG.

TABLE 3 CONVENTIONAL RISK FACTOR IN PATIENTS

Risk factor	dyslipidemia	Lipoprotein (a)males	Lipoprotein (a)females
Family history Of premature MI	24	15	3
smoking	36	15	nil
diabetes	21	12	nil
hypertension	12	6	3
obesity	18	6	3

As dyslipidemia and Lp(a) are parameters studied,they are estimated and compared for their association with conventional risk factors.

26% of the patients had family history out of whom 75% had dyslipidemia and 75% had elevated Lp(a).

40%of the patients were smokers, out of whom 58%had dyslipidemia and 41% had elevated Lp(a).

23% had diabetes, out of whom 100% had dyslipidemia and57% had elevated Lp(a).

13% had hypertension out of whom 75%had dyslipidemia and 75% had elevated Lp(a).

20% had obesity out of whom 83%had dyslipidemia and 50% had elevated Lp(a).

TABLE 4 CONVENTIONAL RISK FACTORS IN CONTROLS

Risk factor	dyslipidemia	Lipoprotein(a) males	Lipoprotein(a) females
Family history Of premature MI	6	3	NIL
smoking	3	NIL	nil
diabetes	3	NIL	nil
hypertension	NIL	NIL	NIL
obesity	NIL	NIL	NIL

Out of the control group, 13% had family history and 6% had elevated Lp(a).

NORMAL VALUES CONSIDERED AS PER NATIONAL CHOLESTEROL EDUCATION PROGRAMME The mean normal values above which it was noted abnormal were

Total cholesterol >200mg%

LDL>130mg%

Triglycerides>200MG% although 150-200 mg% is considered high normal value by NCEP

HDL<45mg% in females

HDL<35mg% in males

Comprehensive lipid tetrad index

The mean lipid tetrad index in present study group is 54286.4 where as in the control group it is 10966. It is elevated in 73% of the patients in study group whereas it is elevated in 26% of control group.The **lipid tetrad index is considered** normal when the value is <10000

Table 5. AGE AND SEX DISTRIBUTION OF INDIVIDUAL ABNORMALITIES HYPERCHOLESTEROLEMIA

	AGE GROUP	AGE GROUP	AGE GROUP	AGE GROUP	AGE GROUP	AGE GROUP	TOTAL
	21-30 YRS (MALE)	21-30 YRS (FEMALE)	31-40 YRS (MALE)	31-40 YRS (FEMALE)	41-45 YRS (MALE)	41-45YRS(FEMALE)	
STUDY GROUP	6	nil	18	6	12	12	41
CONTROL GROUP	3	NIL	NIL	NIL	3	NIL	6

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Out of 90 patients in the present study group 56% (41) had hyper cholesterolemia, when compared to 13% (6) in control population.
Out of 90 patients 71% were females and 29% were females.
70% of patients with hypercholesterolemia had elevated lipoprotein(a).The mean value of cholesterol in present study group was 210.6mg compared to 168 mg in control population.

Table 6. HYPERTRIGYCERDEMIA

	AGE GROUP	AGE GROUP	AGE GROUP	AGE GROUP	AGE GROUP	AGE GROUP	TOTAL
	21-30YRSMALE	21-30YRSFEMALE	31-40YRSMALE	31-40YRSFEMALE	41-45YRSMALE	41-45YRSFEMALE	
Study group	6	nil	9	6	9	9	39
Control group	nil	nil	3	nil	6	3	12

Out of 90 patients in present study group 53% (39) had hypertriglycerdemia when compared to 26% in control population.

61% were men and 38% were women.

Peak incidence was noticed in 41-45 age group 46%

76% of patients with elevated triglycerides also had elevated lipoprotein (a).

The mean value of triglyceride obtained in the present study is 207.9mg compared to 144 mg in controls.

Table 7. ELEVATED LDL

	21-30 males	21-30 females	31-40 males	31-40 females	41-45 males	41-45females	total
Study group	3	3	12	3	12	6	36
Control group	3	nil	nil	nil	3	nil	6

Out of 90 patients in present study group 36% had elevated LDL when compared to 13% in controls.

36% were females and 64% were malesPeak incidence was observed third and fourth decade.

DECREASED HDL

	21-30 males	21-30 females	31-40 males	31-40 females	41-45 males	41-45females	total
Study group	2	NIL	15	6	6	9	42
Control group	nil	nil	3	nil	3	nil	6

Out of 90 patients 46% had decreased HDL, when compared to 13 in controls.

65% were men and 35% were women Peak incidence was noted in the age group of 31-40 years, i.e-50%.

The mean value HDL in present study group was 43.4 mg compared to 54.4 in control population.

CLINICAL PROFILE AND COMPLICATION

CLINICAL DIAGNOSIS	NUMBER	PERCENTAGE	MEAN Lp(a)
Stable effort angina	nil	nil	nil
Unstable angina	3	3.3	47
STEMI	84	93	42.8
NSTEMI	nil	nil	45.4
Silent MI	3	3.3	41.4
COMPLICATIONS			
Arrhyhthmias(multiple ventricular ectopics Ventricular tachycardia	15		
LVF			
Cardiogenic shock	3	3%	62%

Out of 90 patients in the present study, 93% (84) were STEMI and 3.3% were unstable angina. Complications were present in 23% of patients. The mean level of Lp (a) in patients with ventricular arrhythmias was 65.5 and with cardiogenic shock was 62mg.This shows elevated levels of Lp (a) were associated with increased complications.

DISCUSSION

In the present study, plasma lipid profile and Lp(a) were measured in 90 patients(< 45years) admitted to Gandhi hospital,secunderabad with acute myocardial infarction and 45 controls from hospital staff who do not have any evidence of CAD and an attempt is made to compare and analyze the incidence of dyslipidemia and Lp(a) in the study group and control group.

AGE DISTRIBUTION

The peak incidence in the 3rd and 4th decades infer that genetically inherited and acquired dyslipidemia are the most common cause for coronary artery disease in the 3rd and 4th decades

SEX DISTRIBUTION

In this present study group 83.3% were males and 16.6% were females. This is in conformity with the well proven fact that male sex is a major unmodifiable risk factor.

CONVENTIONAL RISK FACTORS FAMILY HISTORY OF PREMATURE CAD

Out of 90 patients in present study 26% patients have positive family history of premature MI, when compared to 6% in controls. Among them, 75% had dyslipidemia in the form of hypercholesterolemia and hypertriglyceridemia. 75 % of the patients with positive family history had elevated Lp(a).these observations are in conformity with oter studies like govindrajulu etal,R.K.Dalai et al K.V.J.Tilak et al and CADI study.This infers That genetically inherited dyslipidemia are common causes of premature CAD.In the present study group along with hypercholesterolemia, hypertriglyceridemia was found to be significant risk factor in this part of world.

HYPERTENSION

13% of patients in present study had hypertension,out of

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whom,75% had dyslipidemia and 75% had elevated Lp(a). This observations infer that hypertension alone may not be a significant risk factor in younger age group but it may multiply the risk of premature CAD when dyslipidemia and elevated Lp(a) are present.

DIABETES MELLITUS

In the present study group 23% had diabetes mellitus compared to 6% in control population. 100% in study group had dylipidemia in the form of hypercholesterolemia ,hypertriglycerdemia and elevated Lp(a).57% of diabetics had elevated Lp(a) denoting that elevated Lp(a) is significantly associated with diabetic dyslipidemia and metabolic syndrome. This is in conformity with other studies like Govind Rajulu et al,R.K.Dalai et al , CADI study.

HYPERCHOLESTEROLEMIA

Hypercholesterolemia was observed in 56% of patients compared to 13% in control group.The mean value in study group was 210.66mg%whereas the mean value in control group was 210.66mg%.From these observations it can be concluded that hypercholesterolemia is major risk factor for premature CAD.This was also observed in Framingham heart study.

DECREASED HDL.

The mean HDL in the study group was 43.4mg% and the mean HDL in control group was 54.4mg%.From these facts it can be inferred that decreased HDL is a risk factor for coronary artery disease. The mean HDL in present study is higher (43.4mg %) when compared to other studies.

Table 10. TABLE SHOWING COMPARSION OF STUDIES

	Total cholesterol mg	LDL mg	HDL mg	TGL mg	Lp(a) mg	Lipid tetrad
Chicago church study 1992	211	143.9	32.9	178.55	36	42371.4
RKDalai study 2001	236.643	169.6	32.6	279.4	41.2	52262.9
KVGK Tilak study2001	213.21	132.6	38.21	211.01	58.48	68597.2
Govind rajulu study 2002	214.38	146.81	33	190.09	33.55	40751.4
Present study	210.66	130.5	43.4	207.9	42.8	54286.4

HYPERTRIGLYCERDEMIA

The mean value in the study group was 207.9 and the mean value in control group was 144 mg.Hypertriglyceridemia

is an emerging risk factor for premature CAD.Hypertrigycerdemia noted in present study with mean value of 209mg compared to mean value of 179mg in Chicago church study,inferring that this specific dyslidimeia is more common in Indians.

INCREASED LDL

Increased LDL was seen in 36% of the study group compared to 13% in control group. From these observation it can be conferred that LDL is an important risk factor for premature CAD. This is in conformity with other Indian studies.

ELEVATED LIPOPROTEIN (a)

Elevated lipoprotein (a) was oserved in 66% of patients in present study group with a mean level of 42.8 mg% when compared to 6% of controls.Out of them 75% were males and 25% were females.the mean level of Lp(a) in CADI study was 38.11mg%.The Indian studies like Govind Rajulu etal,R.K.Dalal etal and K.V.J Tilak et al showed 34mg,43mg and 60mg respectively.These observations infer that mean Lp(a) levels are high in premature CAD.

ASSOCIATION OF ELEVATED Lp(a) WITH OTHER RISK FACTORS

70% of patients with hypercholesterolemia had elevated Lp(a) 76% of patients with hypertriglyceridemia had elevated Lp(a) 57% of diabetic patients had elevated Lp(a) Conversely 40% of the patients with elevated Lp(a) did not have hypercholesterolemia and 50% did not have hypertriglyceridemia.these observations infer that elevated Lp(a)confers both independent and multiplicative risk when combined with other factors.

COMPLICATIONS

In the present study, the incidence of complications was 23%(21/90)with a mean Lp(a) value of 65.8mg.This shows that elevated Lp(a) is not only associated with premature CAD, but also confers more risk for complications.

LIPID TETRAD INDEX

73% of the patients in the present study had elevated lipid tetrad index (more than 20,000) compared to26% in control group. This in concordance with the other Indian studies and the CADI study. These observations infer that lipid tetrad index is a very sensitive and comprehensive index for assessing the overall risk for premature CAD.tThe Govind Rajulu et al study showed near normal Lp(a) values but high lipid tetrad index.

CONCLUSIONS

Elevated Lp(a) is significant risk factor for premature CAD Lipid tetrad index is a very sensitive and comprehensive index for assessing the overall risk for premature CAD.

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