RELATION BETWEEN LIPOPROTEIN(a) AND EXTENSION OF CORONARY ATHEROSCLEROTIC LESIONS

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SUMMARY: Lipoprotein(a) [Lp(a)], together with other serum lipoproteins have an important role in coronary heart disease and peripheral atherosclerosis. In the present study, the relation between serum levels of Lp(a), lipids and other lipoproteins are compared with the severity of coronary lesions and the number of involved vessels.

In this study, 212 patients with suspected coronary artery disease undergoing coronary angiography and 200 apparently healthy individuals were used as the control group for comparative studies. Serum total cholesterol, high-density lipoprotein-cholesterol (HDL-C) and triglycerides were measured by standard colorimetric methods. Low-density lipoprotein-cholesterol (LDL-C) values were estimated immuno-turbidimetrically using Cobas autoanalyzer.

In the patient group, the increased serum level of Lp(a) was correlated with the number of involved vessels and the severity of coronary lesions. However, no significant correlation was found between serum levels of lipids and other lipoproteins with the number of involved vessels or with the severity of coronary lesions. Apart from the hypertension and history of myocardial infarction, no correlation was observed between serum levels of Lp(a) and other risk factors of cardiovascular disease.

It may be concluded that in spite of increase in serum levels of lipids and lipoproteins in atherosclerosis, Lp(a) is an independent risk factor. In this study, the relation observed between the serum levels of Lp(a) and the extension of atherosclerotic lesions can be regarded as an index for the relation of Lp(a) to the early, still clinically asymptomatic steps of the pathogenesis of coronary disease.

Key Words: Lipoprotein(a), Coronary artery disease.

INTRODUCTION

Lp(a) is a cholesterol-rich lipoprotein of unknown function that differs from low-density lipoprotein (LDL or Beta-lipoprotein) by virtue of a covalently bound glycosylated protein; apolipoprotein(a) [apo(a)] (1,2). The amino acid sequence of apo(a) resembles that of plasminogen (3,4), enabling Lp(a) to bind fibrin, to compete with plasminogen for receptor binding sites and to exhibit other antifibrinolytic actions consistent with an atherogenic role (5,6). Elevated serum Lp(a) levels are associated with an increased risk of cardiovascular dis-

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Table 1: Comparison of mean serum levels of Lp(a) in C.H.D patients and control groups, according to the sex.

Mean levels of serum Lp(a) (mg/dl)				
	Male	Female	M and F (sum)	p value
Patient	41.9 ± 13.4	39.2 ± 11.8	40.5 ± 12	< 0.05
Control	18.7 ± 12.2	20 ± 5.1	19.3 ± 8.3	
p value	p > 0.05			

ease, but only if LDL levels are also high (7,8). Whereas the role of plasma Lp(a) levels as a risk factor for coronary artery disease (CAD) particularly in men <55 years is certain (9,10), the relation between Lp(a) and extension of CAD is not clear (11). To investigate the possible relationship of serum levels of Lp(a), lipids and other lipoproteins, with severity of coronary lesions and number of vessel diseased, these parameters were examined in 212 angiographically defined CAD patients and in a group of control subjects with no angiographic or clinical evidence of CAD.

MATERIALS AND METHODS

We studied 212 patients (158 males and 54 females) with suspected coronary artery disease undergoing coronary angiography and 200 apparently healthy individuals (139 males and 64 females) as control. Both patients and control subjects were asked the same questions about history of diabetes or hypertension, current use of antihypertensive medications, smoking history and previous myocardial infarction or stroke. According to the results of angiography, the patients were divided into four subgroups; patients with minimal, single, two and three vessels involved.

Venous blood samples were obtained from all subjects after 12 hours fast. Total cholesterol and triglycerides in plasma were measured by enzymatic methods (12,13). The high-density lipoprotein fraction was separated from plasma by precipitation with polyethylene glycol and the cholesterol content was measured using a colorimetric method according to Warnick *et. al.* (14). The concentration of low-density lipoprotein cholesterol was calculated by formula of Friedewald *et. al.* (15,16). Lp(a) levels were measured using an automated immunoprecipitin analysis kit on a Cobas Bio-centrifugal analyzer (17).

RESULTS

In this study, comparing with control group, a two-fold elevation of serum levels of Lp(a) was noticed in

Table 2: Comparison of mean serum levels of Lp(a), Triglyceride, Cholesterol, LDL-C, HDL-C, VLDL-C and LDL-C/HDL-C ratio, with number of involved coronary artery vessels.

Degree of stenosis	Number	Lp (a)	Triglyceride	Cholesterol	HDL-C	LDL-C	VLDL-C	LDL-C / HDL-C
minimal	22	26 ± 12	170 ± 97	201 ± 58	42 ± 18	125 ± 64	34 ± 19	3.3 ± 1.5
SVD	50	38 ± 20	250 ± 116	235 ± 112	43 ± 18	142 ± 107	50 ± 23	3.5 ± 2.1
2VD	60	42 ± 21	245 ± 123	205 ± 43	36 ± 16	120 ± 38	49 ± 24	3.6 ± 1.5
3VD	80	55 ± 23	213 ± 126	188 ± 42	39 ± 13	108 ± 38	42 ± 25	3 ± 1.2
Control	200	19.3 ± 8.3	123 ± 28	184 ± 18	41 ± 8	117 ± 19	25 ± 5	2.9 ± 0.9

SVD : Single vessel disease
2VD : Two vessel disease
3VD : Three vessel disease

Table 3: Relationship between the mean levels of Lp(a), Triglyceride, Cholesterol, LDL-C, HDL-C, VLDL-C, LDL-C/HDL-C ratio and the severity of coronary atherosclerosis.

Degree of stenosis		Number	Lp (a)	Triglyceride	Cholesterol	HDL-C	LDL-C	VLDL-C	LDL-C / HDL-C
LAD	Without stenosis	18	31.6 ± 13.6	216 ± 84	246 ± 161	52 ± 23	156 ± 64	43 ± 16	3.3 ± 3
	Non significant	25	38.8 ± 9.8	218 ± 119	213 ± 83	35 ± 9	135 ± 76	43 ± 24	3.9 ± 1.7
	Significant	27	44 ± 20..5	229 ± 120	200 ± 45	38 ± 13	115 ± 38	45 ± 25	3.2 ± 1.4
LCX	Without stenosis	16	38.5 ± 20	230 ± 123	208 ± 50	39 ± 13	122 ± 38	46 ± 24	3.3 ± 1.3
	Non significant	26	45.4 ± 21	204 ± 94	220 ± 70	45 ± 19	133 ± 71	40 ± 19	3.3 ± 1.8
	Significant	41	49 ± 21	231 ± 128	199 ± 76	37 ± 12	115 ± 73	46 ± 25	3.2 ± 1.7
RCA	Without stenosis	22	32.2 ± 10	223 ± 111	231 ± 113	41 ± 15	145 ± 68	44 ± 22	3.6 ± 1.9
	Non significant	23	33 ± 18	237 ± 121	198 ± 41	39 ± 14	111 ± 37	47 ± 28	3.2 ± 1.7
	Significant	32	47.5 ± 20	223 ± 118	199 ± 52	38 ± 14	115 ± 47	44 ± 23	3.2 ± 1.4
Control group		200	19.3 ± 8.3	123 ± 28	184 ± 18	41 ± 8	117 ± 19	25 ± 5	2.9 ± 0.9

LAD: Left anterior descending
LCX: Left circumflex
RCA: Right coronary artery

C.H.D patients. As shown in Table 1, the mean levels of serum Lp(a) in patients and controls were 40.5 mg/dl and 19.3 mg/dl respectively ($p<0.05$). The results were not sex dependent in both patients and control groups, and were almost similar in both sexes ($p<0.05$).

As shown in Table 2, a marked increase in serum concentration of Lp(a), with number of involved coronary vessels, was noticed ($p<0.05$). The highest levels were found in patients with 3 involved coronary vessels (55 mg/dl), those of patients with two vessels and single vessel involved, being 42 mg/dl and 38 mg/dl respectively.

The relationship between the serum levels of Lp(a) and the severity of coronary artery lesions was studied. As shown in Table 3, the patients were divided in three groups according to the severity of coronary artery lesions. The statistical analysis (ANOVA) of the data, showed a significant correlation between the severity of lesions and the mean serum levels of Lp(a) ($p<0.05$).

In this study, 75% of patients were male and the rest were female. About 64% of them were at age between 50-60 years. The relation between serum levels of Lp(a) and age, or other risk factors of cardiovascular diseases, were evaluated and no marked correlation were noticed except with hypertension ($p<0.05$) and history of myocardial infarction ($p<0.05$).

No significant differences were observed between serum levels of lipids or routinely measured lipoproteins (VLDL-C, LDL-C and HDL-C) and number of involved coronary artery vessels (Table 2) or the severity of coronary lesions (Table 3).

DISCUSSION

An association between Lp(a) and C.H.D was firstly described by Dahlen in 1974 (18). Kostner estimated from case control data that normolipidemic patients with Lp(a) plasma concentration higher than 30 mg/dl have a 1.75 fold elevated risk of myocardial infarction (19). In this study, comparing with control group, significantly high levels of Lp(a) were observed in patients with angiographically diagnosed C.H.D. Similar results have been reported by others, during the last decade. Like other reports, the results of this study were not sex dependent (20,21).

In this study, we also showed a meaningful correlation between the serum levels of Lp(a) and extent of atherosclerotic lesions. By increased number of involved coronary artery vessels, increased levels of Lp(a) in the serum were observed. In the case of serum levels of lipids and routinely measured lipoproteins (VLDL-C, LDL-C and HDL-C), no correlation between the measured parameters and extent of coronary artery stenosis was noticed.

A large number of epidemiological studies have established a strong link between Lp(a) levels and atherosclerosis. Many theories have been advanced to explain the association between elevated levels of Lp(a) and premature or accelerated atherosclerosis. Among these, two mechanisms remain popular (22). The plasminogen inhibitor mechanism (23-25) and cholesterol targeting theory (26-28). The findings of our study emphasize atherogenic potential of Lp(a) and lead us to conclude that Lp(a) is an independent factor for atherosclerosis. This may have a great importance, because Lp(a) can be used as a valuable marker in early diagnosis of atherogenesis.

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