ORIGINAL ARTICLE

Lipoprotein (A) in Patients with Type 2 Diabetes Compared with Non-Diabetic Patients

Amir Ziaee[1*], Majid Sarreshtedari[2], Nejhla Abrishamchian[3], Toktam Karimzadeh[1], Sonia Oveisi[2], Azam Ghorbani[2]

1. Metabolic Disease Research Center, Qazvin, Iran
2. Qazvin University of Medical Sciences, Qazvin, Iran
3. Zahedan University of Medical Sciences, Zahedan, Iran

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ABSTRACT

OBJECTIVE: To determine the level of Lipoprotein (a) in diabetic patients comparing to control group.

MATERIALS AND METHODS: This cross-sectional study was conducted on the patients referred to Endocrinology Clinic of Bu Ali-Sina Hospital in 2009. 180 subjects including 90 diabetic and 90 healthy subjects as control group enrolled in this study. All diabetic patients had glycemic control. We measured serum FBS, TG, cholesterol, LDL, HDL and serum Lp (a) in both groups. Data were analyzed by T-test and chi-square.

RESULTS: BMI, sex and age were similar in two groups. Lp (a) level was significantly higher in diabetic ones compared with control group (35.27 ± 28.6 vs. 20.22 ± 10.3 mg/dl, $P < 0.001$). Serum TG, Cholesterol, LDL were also significantly higher in diabetics ($P < 0.001$) while HDL was lower. HDL-Cholesterol level was significantly higher in diabetic men than women [OR = 0.18 CI 95% (0.06- 0.56)**],** and there was positive correlation between FBS level and lipid profile**.**

CONCLUSION: Lp (a) as an independent risk factor for atherosclerosis has elevated level in diabetic patients. So lowering its concentration would help prevention of CAD, a known cause of death in diabetic patients.

KEYWORDS: Lipoprotein (a), Lipid profile, Type 2 diabetes mellitus.

INTRODUCTION

Type 2 diabetes mellitus is defined as a disorder in insulin secretion, insulin resistance or increased gluconeogenesis. Chronic complications of diabetes are divided into two groups; vascular or non-vascular (1). They cause damage to several organs and thus it is determined as patients mortality rate (1,2). The most common cause of death (75 to 85%) in diabetic patients is coronary disease. Some known risk factors for heart diseases are declined serum HDL, increased serum LDL and Apo B, insulin resistance, truncal obesity, cigarette smoking and family history of atherosclerosis (2).

The most common forms of dyslipidemia seen in diabetic patients are hypertriglyceridemia and decrease in serum HDL cholesterol level. Diabetes does not cause increase in serum LDL level itself; but LDL particles in these patients have more risk of athrogenic than

***Correspondence:** Amir Ziaee, Metabolic Disease Research Center, Bu Ali-Sina Hospital, Qazvin, Iran.
Tel: (+98) 2813360084. **Email:** aziaee1963@yahoo.com

usual. LDL particles are more sensitive to oxidation and glycosilation in patients with type 2 diabetes (2).

Lipoprotein (a) [Lp (a)] is a modified form of LDL with similar plasminogen aminoacide arrange. So it can play a role in fibrinolysis and thrombosis mechanism (1).

The correlation of increased Lp (a) level and coronary heart disease (CHD) has been investigated in retrospective epidemiologic and cross-sectional studies. These are also controversy in findings of studies regarding relation between serum Lp (a) level and diabetes. Some reported the increased level of serum Lp (a) in uncontrolled diabetic patients, while some others did not (3).

However, it is shown that cholesterol [LDL, IDL, VLDL, Lp (a)] is a predictive factor for CHD in diabetic men and women (1,2). Therefore, this study was designed to compare the serum Lp (a) level in patients with type 2 diabetes and non-diabetic individuals.

MATERIALS AND METHODS

In this case-control study, 180 patients who referred to the clinic of endocrinology in a university hospital in Qazvin were recruited and divided into two groups. The case group consisted of patients with type 2 diabetes. Individuals in control group (n = 90) were patients' relatives who volunteered to participate in the study and had FBS level less than 100 mg/dl.

Diagnosis of diabetes confirmed by patient symptoms was accompanied by one of these two laboratory tests: fasting blood sugar (FBS) ≥126 mg/dl or random blood glucose concentration ≥200 mg/dl.

All the patients were aged 30 to 70. Patients with renal failure (creatinine >2 or albominuria >2+ in urine analysis), collagen–vascular or hepatocellular diseases, myocardial infarction or cerebrovascular attack history were not included. The subjects who were prescribed corticosteroids, immunosuppressive agents, estrogen, beta-blockers or statins, and who drank alcohol more than 80 gram per day were excluded from the study.

Study protocol was proved in the Ethics Committee of Qazvin University of Medical Sciences. After the informed written consent was obtained from the subjects, they referred to reference laboratory for checking their serum Lp (a), triglyceride (TG), total cholesterol (TC), LDL and HDL cholesterol levels. FBS was also measured for all subject. Their body mass index (BMI) was calculated by dividing weight (in Kg) by squared height (in meters).

Lp (a) level was measured by using Pars Azman kit (Made in Germany, Diasys. Diagnostic. Exp date: 2010, 101 No 87001-3) by immunoturbidometeric Assay (ITMA) and with Hitachi autoanalysor. Lp (a) less than 3 mg/dl consider as normal .

Data were processed by SPSS software and analyzed by t- test and Chi- square test. Probable – value less than 0.05 considered statistically significant.

RESULTS

These groups were similar in demographic variables (Table 1). The FBS differences between groups were inevitable. The mean value of TG, TC, HDL, LDL, Lp (a) were statistically significant between two groups (Table 2).

Table 1- Demographic characteristics in diabetics compared with non-diabetics

Variables (mg/dl)	Diabetic (mean±SD)	Non-diabetic (Mean±SD)	*p* value
Male.Female	20.70	30.60	0.134
Age (year)	53.6 ± 4.6	53.0 ± 4.5	0.339
BMI (kg/m^2)	26.6 ± 2.4	26.4 ± 1.4	0.553

Table 2- Lipid profile in diabetics compared with non-diabetics

Variables (mg/dl)	Diabetic (Mean±SD)	Non diabetic (Mean±SD)	*p* value
LDL	110.9 ± 18.5	106.1 ± 12	<0.03
TC	189.8 ± 28.1	162.9 ± 21.1	<0.001
TG	187.4 ± 42.6	145.5 ± 26.1	<0.001
HDL	29.2 ± 15.2	41.4 ± 22.6	<0.001
Lp (a)	35.3 ± 28.7	20.2 ± 10.3	<0.001

Lipid Profile and BMI in diabetic patients compared to non-diabetics indicated that diabetic patients had dyslipidemia in their lipid profile (Table 3). That is, the more BMI increased, the more the level of component of lipid profile raised; but there was not such correlation between BMI and FBS.

There was a linear and positive correlation between FBS level and lipid profile, however, there was no correlation between BMI and FBS (Table 4). Just serum HDL-Cholesterol level was significantly higher in men compared to women OR = 0.18 CI 95% (0.06-0.56). This can be protective against CAD in men compared with women (Table 5).

Table 3- Lipid profile and BMI in diabetic patients compared to non-diabetics

Depended variable	In depended variables	X2	*P* value	OR	CI%95
Diabetes	LDL	5.7	0.02	2.2	1.14-4.2
	Cholesterol	20.4	0.01	15.13	3.43-66.6
	TG	50.4	0.001	16.17	6.71-38.96
	HDL	8.4	0.006	3.67	1.46-9.18
	Lp (a)	34.5	0.001	9.78	4.22-22.6
	BMI	0.58	0.5	1.4	0.59-3.35
	Gender	2.34	0.169	1.71	0.86-3.38

Table 4- Correlation between FBS level and lipid profile, BMI

	Variable	Pearson Correlation(r)	*P* Value
FBS	LDL	0.34	0.001
	Cholesterol	0.6	0.001
	TG	0.59	0.001
	Lp (a)	0.37	0.001
	HDL	0.35	0.001
	BMI	0.136	0.07

Table 5- Lipid profile and BMI in male diabetics compared to female diabetics

Variables	Male N(%)	Female N(%)	X_2	P-value	OR	CI%95
LDL ≤100	4(4.8)	16(19.0)	0.1	1	0.8	0.2-2.82
LDL >100	15(17.9)	49(58.3)				
Cholesterol ≤200	12 (14.3)	50(59.5)	1.44	0.25	0.5	0.17-1.5
Cholesterol >200	7(8.3)	15(17.9)				
TG≤150	0	6(7.1)	1.89	0.33	1.32	1.16-1.49
TG>150	19(22.6)	59(70.2)				
HDL*	9(14.3)	54(85.7)	9.99	0.005	0.18	0.06- 0.56
HDL**	10(11.9)	11(13.1)				
Lp (a) ≤30	11(13.1)	33(39.3)	0.3	0.6	1.33	0.48-3.74
Lp (a) >30	8(9.5)	32(38.1)				
BMI ≤25	3(3.6)	7(8.3)	0.35	0.69	1.55	0.36-6.69
BMI >25	16(19.0)	58(69.0)				

*HDL <40 in men and HDL <50 in women

** HDL ≥40 in men and HDL ≥50 in women

DISCUSSION

In this case-control study our findings showed that serum Lp (a) level was significantly higher in diabetic patients compared to non-diabetic ones. Although women had higher serum Lp (a) levels, this difference was not statistically significant.

There are controversial reports on the effect of diabetes on serum Lp (a) levels (2,4). In agreement with our findings, some studies have shown increased levels of serum Lp (a) in patients with diabetes. Insulin therapy also decreases serum Lp (a) concentration in non-obese diabetic patients. (5)

Nakhjavani also showed that patients with diabetes had higher serum Lp (a) levels than subjects in control group. There was no gender difference in serum Lp (a) levels in control group (4). In this study, serum Lp (a) levels was significantly higher in women with diabetes than men with diabetes. Serum Lp (a) level >30 mg/dl was more in premenopausal women than in postmenopausal women OR = 5.08, 2.41 in diabetic men and 1.9 in women in control group compared to men in control group after adjusting age and BMI between groups (4).

In the present study, diabetic patients compared to control group had abnormal Lp (a) with OR = 9.78 CI 95% (4.22-22.6), but there was no significant deference between men and women. Habib reported a significant difference in Lp (a) level between the diabetics and control group (6). Smaoui also compared 200 diabetic patients (case group) with 100 non-diabetic ones (control group) and showed higher level of serum Lp (a) concentration in case group (P = 0.007), but they did not report any significant correlation between serum Lp (a) level and indexes of blood glucose control (FBS and HbA_1c) (7).

Singla also reported increased level of serum Lp (a) in type 2 diabetic patients. they compared 60 diabetic patients with 50 age and sex matched non-diabetic subjects and showed that Lp (a) level does not reflect glycemic status and is also independent of increase in LDL:HDL ratio suggesting different metabolic pathways and the genetic connection for LDL and Lp (a) (8).

Arauz (9) found a higher mean level of Lp (a) in both type 1 and type 2 diabetic subjects, but found no association of glycated hemoglobin with Lp (a) in type 2 subjects. It is also shown that well controlled type 2 diabetics have lower serum Lp (a) level (10).

Some studies found no difference in serum Lp (a) level between patients with diabetes and controls (11-14). Unluhixarcil studied diabetic patients in two groups, with or without diabetic foot and did not report any significant difference in serum Lp (a) level between the groups (38.3 ± 5.8 vs. 0.05 ± 4.2 mg/dl), but level of serum Lp (a) was higher in patients with gangrene foot sore (83.8 ± 8.3 mg/dl) (15). Chopre also showed that serum Lp (a) level is related to intensity of retinopathy in diabetic patients (16).

Rani–water (17) and Albaharani (18) demonstrated lower serum Lp (a) levels in patients with type 2 diabetes. However, the relation between Lp (a) level and ischemic heart disease (IHD) has been reported in patients with diabetes in Albaharani findings. They have reported that Lp (a) more than 0/3 g/lit has detected more frequently in diabetic patients who had experienced IHD, comparing to diabetic ones without IHD (18).

Smaoui considered that diabetes cannot directly increase the level of serum Lp (a), but serum Lp (a) level can be predisposing factor for coronary heart disease (CHD) in diabetic men. They had not reported any correlation between diabetes and heart disease. Lp (a) level was not also different between diabetic patients with CHD and control group, but it was significantly higher in diabetic patients with CHD compared with control group (P = 0.001). This confirmed the role of Lp (a) in atherosclerosis mechanism in synergy with LDL cholesterol (7).

Boroumand also showed that patients with atherosclerosis in coronary arteries have higher level of serum Lp (a) significantly. This confirms the atherosclerotic role of Lp (a) as an independent variable in Iranian patients (19).

The correlation between Lp (a) and aortic sclerosis, CHD, peripheral artery disease, stroke and aortic aneurism was also seen in patients with type 2 diabetes (20-23).

Meca also investigated 700 patients with mean age of 73 years and reported the higher occurrence of peripheral artery disorder in patients with type 2 diabetes who are dependent to insulin therapy and have Lp (a) >360 mg/dl compared with others (non-diabetic patients, diabetic patients with independency to insulin therapy, diabetic patients with Lp (a) less than 36 mg/dl) (24).

Diabetes mellitus comprises of a group of disorders that share the phenotype of hyperglycemia. One of the important causes of mortality and morbidity in diabetic patients are complications like atherosclerosis and CHD (25). As traditional risk factors for CDH (hypertension, elevated serum cholesterol, smoking habit and dyslipidemia) (26) could not explain the increased prevalence of CHD in diabetic patients, researchers investigated for other predisposing factors (4,27). Abnormal lipoprotein metabolism may cause atherosclerotic lesion in such patients (8).

Diabetic subjects have increased triglyceride levels and decreased HDL compared with non-diabetics, but diabetes has a small effect on LDL concentration (2). In the present study, mean total cholesterol, TG and LDL were significantly higher in diabetic group compared with non-diabetics (P = 0.001, P = 0.001 and P = 0.02, respectively); however, HDL level was significantly higher in control group (P = 0.006). These are according to dyslipidemic profile expected in diabetic patients.

Albaharanialso showed increased level of TG in diabetic patients. There was also a reverse correlation between Lp (a) and TG in patients with diabetes type 2 (P = 0.002). Reversely, there was positive correlation between LDL, Lp (a) and Apo B among non-diabetic patients (18). Smaoui et al. also reported the higher level of TG, cholesterol and LDL and lower level of HDL in diabetics compared with non-diabetics. However, they reported no significant correlation regarding Apo A1, Apo B between the groups (7).

Korsad also showed that total cholesterol, TG, LDL and HDL were lower in diabetic patients with or without gangrene foot sore compared with control group, despite BMI and glucose control were similar among groups (15).

It is suggested that the later studies focus on assessment of Lp (a) in diabetic patients with ischemic heart disease (IHD) or microalbuminuria. It is also recommended that clinicians evaluate the serum Lp (a) and lipid profile in diabetic patients simultaneously.

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