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Original Research Article

Evaluation of serum lipoprotein(a) level in type 2 diabetic patients and non-diabetic people

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ABSTRACT

Background: Type 2 diabetes mellitus has high morbidity and results in increased risk of mortality mainly due to cardiovascular diseases. Different factors have been found to be responsible for the increased prevalence of coronary artery disease in T2DM. One of these factors includes raised serum level of lipoprotein(a) (Lp(a)). The purpose of the present study is to assess the serum level of Lp(a) in type 2 diabetes mellitus patients and non-diabetic people with find the difference of serum Lp(a) between good and poor glycaemic control.
Methods: This cross-sectional study was carried out in the department of Biochemistry and Endocrinology, Chittagong Medical College Hospital, Chattogram from July 2017 to June 2018. We assess a total of 100 type 2 diabetic patients and a group of 50 non-diabetic people with the age range 31-60 years. Blood samples were collected in fasting state and analysed for FPG, HbA1c%, serum lipid profile (TC, TG, LDL & HDL) and Lp(a). Data were analysed by T-test and chi-square test.
Results: The serum Lp(a) levels were significantly elevated in type 2 diabetic patients compared to non-diabetic people (44.32±2.6 vs. 13.02±0.81). There were also significant difference of serum Lp(a) between good and poor glycaemic control.
Conclusions: Lp(a) is an independent risk factor for atherosclerosis and has elevated level in diabetic patients. So, selective screening with lowering its concentration would help prevention of coronary artery disease, a known cause of death in diabetic patients.

Keywords: Serum Lp(a), Type 2 DM, HbA1c%, Fasting lipid profile

INTRODUCTION

Diabetes mellitus is a major public health problem that is approaching epidemic proportions worldwide. It is now one of the most challenging health problems in the 21st century.[1] Globally, an estimated 383 million people are living with diabetes mellitus and is expected to rise 593 million by 2035.[2] Type 2 diabetes mellitus is most common form of diabetes comprising 90-95% of all diabetic cases.[3] It is characterized by chronic hyperglycaemia due to insulin resistance and relative insulin deficiency. Type 2 diabetes results from interaction between genetic, environmental and behavioural risk factors.[4] Diabetes mellitus is the major cause of secondary dyslipidaemia which is characterized by a triad of high serum triglyceride concentration, low serum HDL concentration and increased serum LDL concentration.[5-6] Current research recommends that a small dense LDL particle which is known as Lp(a) also elevated in type 2 diabetes mellitus.[7] Lp(a) is said to be 2-3 times more dangerous than normal size LDL particle.[8] Many prospective epidemiological studies have reported

positive associations of Lp(a) concentration with atherosclerosis, coronary artery disease and stroke.[9-11] Lp(a) was discovered in human serum in 1963 by Kare Berg during a study of variation in LDL antigenicity.[12] Lp(a) is LDL like particle that consist of one molecule of apolipoprotein(a) and another molecule of apolipoprotein B-100. Apo(a) covalently bound to apo B-100 by disulphide bond.[13] Lp(a) is a plasma lipoprotein synthesized by the liver and circulated in blood. Lp(a) plasma concentrations mainly controlled by the apolipoprotein(a) gene (LPA gene) located on chromosome 6q26-27.[14] The half-life of Lp(a) in the circulation is about 3-4 days. The serum level of Lp(a) is said to be increased when it is >14 mg/dl but the atherogenic properties of Lp(a) levels are expressed over 30 mg/dl.[15] Several studies have reported high serum concentration of Lp(a) in diabetic patients compared to nondiabetic people.[7,16] Serum Lp(a) is now considered as a new risk factor for cardiovascular disease and showed a genetic link to accelerate atherogenesis in diabetes mellitus.[17] Many epidemiological studies suggested that, Lp(a) level was consistently elevated in South Asians compared to other ethnic groups.[17-18]

Therefore the present study was designed to compare the serum Lp(a) level between the patients with type 2 diabetes mellitus and non-diabetic people.

METHODS

This cross-sectional study was carried out in the department of biochemistry and endocrinology, Chittagong medical college hospital, Chittagong from July 2017 to June 2018. 100 diagnosed type 2 diabetic cases and 50 non-diabetic people with the age range of 31 to 60 years were selected by non-probability consecutive sampling. Permission for the study was taken from the ERC of CMC. Informed consent from each subject were taken before the collection of samples. Patients with GDM, stroke, IHD, renal failure, liver failure, malignant diseases and acute infection were excluded from the study.

All the data were processed and analysed using Microsoft excel and IBM-SPSSv22.0 for Windows. Statistical inference was based on 95% confidence interval and p value <0.05 was considered statistically significant. Variables were expressed as mean±standard error of means (SEM). Statistical difference was studied using Student t-test (two tailed, independent). Chi square ($\chi 2$) test was used to see the association. The summarized data were presented in the form of tables and figures.

RESULTS

The distribution of sex in diabetic cases, N=100 (male/female-43/57) and in non-diabetic people, N=50 (male/female-22/28) is depicted in (Figure 1). There were significant differences of FPG and HbA1c% in diabetics and non-diabetics is shown in (Table 1). Serum Lp(a), total cholesterol, TG and LDL were significantly higher in diabetics than that of nondiabetics and serum HDL was significantly lower in diabetics than nondiabetics is depicted in (Table 2).

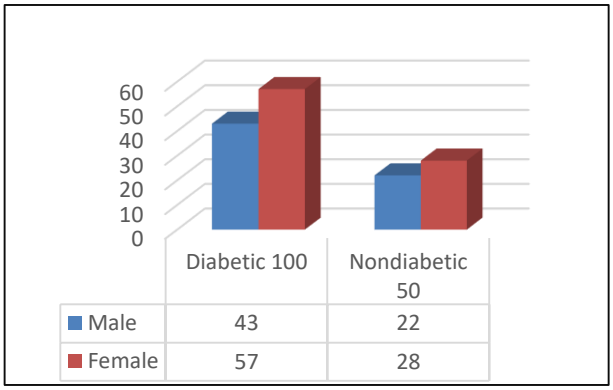

Figure 1: Distribution of sex in diabetic cases and nondiabetic people.

Subjects with normal Lp(a) level were 14 in diabetics and 39 in nondiabetics and 21 patients had Lp(a) level in borderline risk group and in nondiabetics it was 11, again in cases 65 patients were found in high-risk group is shown in (Table 3).

Total cholesterol, LDL-cholesterol were significantly higher in >30 mg/dl group compared to that of <30 mg/dl group in diabetic cases as depicted in (Table 4). There was significant differences of serum Lp(a) level between good and poor glycaemic control in diabetics cases as shown in (Table 5). The comparison of type 2 diabetes mellitus patients with non-diabetic people with an $\chi 2$ value=59.7 and odds ratio=21.77 for increased Lp(a). These were statistically significant i.e., there was association of increased Lp(a) with type 2 diabetes mellitus as shown in (Table 6).

Table 1: Comparison of fasting plasma glucose and HbA1c% amongst diabetics and nondiabetics by t-test significance.

Variables	Diabetics (N=80)	Nondiabetics (N=70)	P value	Significance
Fasting plasma glucose (mmol/l)	8.66±0.30 (3.5-19.1)	5.19±0.06 (3.6-6.0)	<0.05	Significant
HbA1c%	7.94±0.14 (5.1-11.5)	5.24±0.03 (4.9-5.6)	<0.05	Significant

Table 2: Comparison of Lipid parameters amongst diabetics (N=100) and nondiabetics (N=50) by t-test significance.

Variables	Diabetics	Nondiabetics	P value	Significance
Serum Lp (a) (mg/dl)	44.32±2.6 (09-115)	13.02±0.81 (08-30)	<0.05	Significant
T. Cholesterol (mg/dl) (Mean±SEM)	218.1±4.4 (120-316)	176.78±2.96 (106-199)	<0.05	Significant
Serum TG (mg/dl) (Mean±SEM)	191.4±7.03 (67-510)	122.4±2.36 (90-147)	<0.05	Significant
S. LDL (mg/dl) (Mean±SEM)	132.4±3.61 (61-235)	88.36±0.93 (79-98)	<0.05	Significant
S. HDL (mg/dl) (Mean±SEM)	37.2±0.6 (24-55)	49.68±0.81 (40-66)	<0.05	Significant

Table 3: Frequency distribution of serum Lp(a) level in diabetics (N=100) and nondiabetics (N=50).

Variables	Diabetics	Non-diabetics
Normal Lp(a) (<14 mg/dl)	14	39
≥14-≤30 mg/dl (Borderline high)	21	11
>30 mg/dl (High risk)	65	00

Table 4: Comparison of fasting serum lipid profile between Lp(a)≤30 mg/dl group and >30 mg/dl group in diabetics cases (n=100) by t-test significance.

Variables	Lp(a)≤30 mg/dl (N=35)	Lp(a)>30 mg/dl (N=65)	P value	Significance
Total cholesterol (mg/dl) (Mean±SEM)	197.57±5.03 (120-253)	229.21±5.94 (135-316)	<0.05	Significant
Serum TG (mg/dl) (Mean±SEM)	192.28±14.68 (90-510)	190.98±7.59 (67-420)	>0.05	Not significant
Serum LDL (mg/dl) (Mean±SEM)	113.94±4.99 (61-200)	142.4±4.43 (80-235)	<0.05	Significant
Serum HDL (mg/dl) (Mean±SEM)	38.34±1.12 (27-55)	36.6±0.71 (24-54)	>0.05	Not significant

Table 5: Distribution of serum Lp(a) level according to glycaemic status in diabetics cases.

Glycemic status	HbA1c>7% (N=69)	HbA1c≤7% (N=31)	P value	Significance
HbA1c%	51.92±3.08 (10-115)	45.61±3.52 (09-115)	<0.05	Significant

Table 6: Association between type 2 diabetes mellitus and serum Lp(a) levels.

Groups	Category of Lp(a)		Total	χ2 value and Odds ratio	P value (significance)
	Lp(a)≥14 mg/dl	Lp(a)<14 mg/dl			
Type 2 diabetic cases	86	14	100	$\chi 2=59.7$	<0.05 (significant)
Nondiabetic People	11	39	50	Odds ratio=21.77	<0.05 (significant)

DISCUSSION

In this cross-sectional study, out of 100 diabetic patients 43 were male and 57 were female. On the other hand out of 50 non-diabetic people 22 were male and 28 were female. This study showed the significant difference of FBS, HbA1c% and serum cholesterol, LDL, HDL and TG between diabetic cases and non-diabetic people. It has been established that patients with type 2 DM have increased morbidity and mortality due to coronary risk events. This increased risk has been shown to be independent from conventional risk factors.[19] Different factors have been found to be responsible for an increased prevalence of CAD in DM. One of these are the elevated levels of serum Lp(a).[20] Our study has revealed that Lp(a) levels were significantly elevated in diabetic

patients than non-diabetic people. In this study, increased serum Lp(a) was also significantly associated with type 2 diabetes mellitus patients as seen in table VI ($\chi 2=59.7$, $p<0.05$). The current data of increased serum Lp(a) level in type 2 diabetes mellitus patient was similar to the studies done by other authors like Singla, Ogbera, Joseph, Ziaee.[21-24]

In another studies the researchers failed to demonstrate the association of serum Lp(a) with type 2 diabetes mellitus.[25-26] The possible reason could be the large size of apo(a) isoforms leading to lower Lp(a) levels.[27] This study showed that 86% type 2 diabetic patients had increased serum Lp(a) level. Again, in diabetic cases 21 patients had serum Lp(a) level in borderline risk group (>14 to 30 mg/dl) and in nondiabetics 11 subjects were found to be in this group. On the other hand, 65 patients had Lp(a) level in high-risk group (>30 mg/dl). Total cholesterol, LDL-cholesterol were significantly higher in Lp(a)>30 mg/dl group compared to that of Lp(a) <30 mg/dl group in diabetic cases. Lp(a) value more than 30 mg/dl (>30mg/dl) has been considered as an important predictor of vascular disease in type 2 diabetes mellitus patients.[28-30]

In type 2 diabetic cases serum Lp(a) level was compared with their degree of glycaemic control. In cases having HbA1c more than 7%, serum Lp(a) level was significantly higher than that of HbA1c less or equal 7% (51.92±3.08 verses 27.38±3.74%). This finding was in accordance with the finding from another study.[31]

The author also suggested that gaining metabolic control have a positive effect on serum Lp(a) level. The mechanism of elevated Lp(a) in diabetes mellitus is glycation of its apolipoproteins, which causes decreased metabolism of Lp(a). Glycation also prolongs the half-life of Lp(a), which may leads the higher plasma concentration of Lp(a) in diabetes mellitus.[31] It is an established fact that type 2 diabetes mellitus is a strong risk factor for coronary artery disease.[6,32] Moreover many prospective epidemiological studies have reported the positive associations of serum Lp(a) with atherosclerosis, coronary artery disease and stroke.[33-34] The observations of the designed study is an adjunct to the finding of other studies where researchers raised the possibility of serum Lp(a) as an additional finding for cardiovascular and cerebrovascular risk assessment in type 2 diabetes mellitus patients.

CONCLUSION

From the present study we can conclude that type 2 diabetes mellitus is strongly associated with increased Lp(a) levels. Elevated Lp(a) levels promote atherosclerosis and thrombosis. So, Lp(a) may be a new metabolic syndrome risk factor and it may be useful as a cardiovascular risk biomarker in future clinical practice.

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