ORIGINAL ARTICLE

Association of Serum Lipoprotein (a) with BMI and Waist Circumference in Type 2 Diabetic Patients

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Abstract:

Background: Type 2 diabetes is a widespread chronic condition that originates from a complex interaction between genetic and environmental factors, along with contributing risks such as obesity and physical inactivity. Its associated complications present a significant public health concern worldwide. Dyslipidemia is the most common complication of type 2 diabetes mellitus. Elevated serum lipoprotein(a) is now considered a new lipid-related complication of type 2 diabetes mellitus. Obesity is also considered an essential factor of elevated lipoprotein(a) in type 2 diabetes mellitus. The present study aims to find out the association of serum lipoprotein(a) with BMI and waist circumference in type 2 diabetic patients. Methodology: The study was conducted by a hospital-based cross-sectional study of hundred (100) diagnosed type 2 diabetic patients aged between 31 and 60 years. This study was conducted in the Department of Biochemistry, Chittagong Medical College, and the inpatient & outpatient Department of Endocrinology, Chittagong Medical College Hospital. Samples were taken by non-probability consecutive sampling. Essential variables in this study were FPG, serum lipoprotein(a), BMI, and waist circumference. Results: The mean value of serum level of Lp(a) was raised in type 2 diabetic patients (44.32 ± 2.6 mg/dl). Serum Lp(a) levels were positively and significantly correlated with BMI and waist circumference and not associated with fasting plasma glucose. There were also significant differences in BMI and waist circumference in Lp(a) ≤30 mg/dl group and Lp(a) >30 mg/dl group. Conclusions: The results of the present study pointed to the significance of diabetic management in the control of lipid abnormalities, where the control of obesity is of importance.

Key words: Serum Lp(a), Type 2 DM, BMI, Waist Circumference.

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Introduction:

Diabetes mellitus is characterized by metabolic imbalances in carbohydrates, proteins, and fats due to decreased insulin secretion, impaired insulin function, or a combination of both[1]. The global prevalence of diabetes mellitus is sharply increasing due to population aging, urbanization, and lifestyle modification[2]. There are two primary forms of diabetes, and type 2 diabetes is the most common form. It accounts for 90-95% of all diabetic patients1 and is expected to increase to 439 million by 2030[3].

It is already established that diabetes mellitus is the primary cause of secondary dyslipidemia[4]. This pattern of dyslipidemia in diabetes mellitus leads to vascular complications[5]. Recent evidence suggests that a small, dense LDL-like particle, Lp(a), is elevated in type 2 diabetes mellitus. This elevated

Lp(a) level is associated with the increased risk of cardiovascular diseases even more than any other lipids[6-7]. According to numerous prospective epidemiological studies, atherosclerosis, coronary artery disease, and stroke are all positively correlated with increased Lp(a) concentration[8-9].

In human serum, Lp(a) was first identified by Kare Berg in 1963 as an LDL variant during a study of LDL antigenicity[10]. Lp(a) is a lipoprotein similar to LDL, composed of one apolipoprotein(a) molecule and one apolipoprotein B-100 molecule, linked by a disulfide bond[11]. It is produced by the liver and transported in the bloodstream. The levels of Lp(a) in plasma are primarily regulated by the apolipoprotein(a) (LPA) gene, located on chromosome 6q26-27[12].The size of apo(a) proteins varies due to polymorphism in the LPA gene, which results from a differing number of kringle IV repeats. These genetic variations lead to differences in apo(a) protein size, known as "apo(a) isoforms." Generally, there is an inverse relationship between apo(a) isoform size and Lp(a) plasma concentration[13].

Lp(a) has a half-life of 3-4 days in the bloodstream. Lp(a) levels in the serum are considered elevated when they exceed 14 mg/dL, but their atherogenic effects become significant above 30 mg/dL. It is now recognized as an emerging risk factor for cardiovascular disease and has been genetically linked to accelerated atherogenesis in diabetes mellitus[15]. Increased Lp(a) levels have also been linked to intermediary indicators of cardiovascular disease risk, such as obesity, abdominal obesity, and high blood pressure[16,17]. Obesity is characterized by an excess buildup of body fat, which, in severe cases, poses a significant health risk. It is a complex situation influenced by various factors, including genetic, metabolic, cultural, environmental, socioeconomic, and behavioral aspects[19]. Different methods are used for the measurement of obesity, including the determination of (a) body mass index, (b) skin fold thickness or waist circumference or waist-hip ratio, (c) fat cell size & number, and (d) body density. Body mass index has gained favor as a better measure for adiposity[20].

Traditional lipid-lowering medications like statins or fibrates typically do not affect serum Lp(a) levels. Besides that, niacin (vitamin B3) is the most effective agent that lowers the Lp(a) level by 30-40%21. Many studies showed that Lp(a) levels were also elevated in certain disease conditions such as renal failure and autoimmune disease but decreased in liver disease[22-24]. The present study was designed to find out the relationship between Lp(a) and BMI and waist circumference in type 2 diabetic patients in this part of our country.

Materials and method:

This study was conducted in the Department of Biochemistry, Chittagong Medical College, and Endocrinology's inpatient & outpatient department, Chittagong Medical College Hospital. The study was one year, from July 2017 to June 2018. Data were collected by a pre-formed questionnaire containing all the variables of interest and fulfilling the exclusion & inclusion criteria for the study population. 100 diagnosed type 2 diabetes patients, aged between 31 and 60 years, were selected using non-probability consecutive sampling. Ethical approval for this study was obtained from the Ethical Review Committee of CMC. Informed consent was taken from each subject before the physical examination and collection of samples. Height was measured with a freestanding stadiometer without footwear and headgear. Weight was measured by using a digital LED weight machine. Weight (kg) is divided by height (m) squared to find BMI. Waist circumference was assessed using a plastic measuring tape positioned horizontally at the midpoint between the lower rib margin and the upper iliac crest along the mid-axillary line while maintaining participant privacy.

A female attendance measure was the waist circumferences of female participants. With aseptic precautions, 5 ml of fasting venous blood was obtained from each participant via a sterile syringe after a physical exam. While 2 ml venous blood samples were collected in a sodium fluoride tube for measuring fasting plasma glucose, another 3 ml blood samples were taken in a red top tube and allowed to clot for the collection of serum. To measure Lp(a), serum was separated by centrifugation for 5 minutes at 4000 RPM.

Plasma glucose was sampled using the glucose oxidase-peroxidase method and the multichannel autoanalyzer. Serum Lp(a) level was calculated by nephelometry using a Siemens BN proSpec analyzer. The study analyzed data using Microsoft Excel and IBM SPSS v22.0, determining the associations between Lp(a) and FPG, BMI, and waist circumference through Pearson's correlation. Student's t-tests were used for group comparisons. Statistical significance was stated as $p \leq 0.05$ (95% confidence interval), and results are expressed as mean ± SEM. Results are shown in tables and figures.

Results:

This cross-sectional study included 100 individuals with diagnosed type 2 diabetes, comprising 43 males and 57 females. The average age of the participants was 46.2 ± 0.9 years. Participants had a mean age of 46.2 ± 0.9 years. Data are stated as mean ± SEM, and statistical significance was indicated as $p \leq 0.05$ (95% CI).

Table 1: Baseline characteristics of the study subjects (n=100)

Characteristics	Mean ± SEM	Range
Age (years)	46.2 ± 0.90	31 – 60
FPG (mmol/L)	8.66 ± 0.30	3.5 – 19.1
Serum Lp(a) (mg/dl)	44.32 ± 2.6	09 - 115
BMI (kg/m2)	26.38 ± 0.35	17.39 – 36.11
WC(cm)- Male WC(cm)- Female	93.72 ± 0.77 83.75 ± 0.92	78 – 102 68 - 96

Table 2 presents procedural parameters such as type, duration, and recovery time for both groups. Lower GI tract procedures were more common in both groups (Propofol: 61.7%; Conventional: 56.7%; p=0.8). The Propofol group had a significantly shorter mean procedure duration (38.5 ± 10.2 minutes) compared to the Conventional group (43.6 ± 11.5 minutes; p=0.01), indicating greater efficiency with propofol sedation. Recovery time was also significantly faster in the Propofol group (15.5 ± 5.4 minutes) than in the Conventional group (35 ± 15.5 minutes; p<0.001).

Table 2: Association of serum Lp(a) with BMI and central obesity incases (n=100)

Variables	Lp(a) <14	Lp(a) ≥14	χ^2 value	p value	Significance
Normal BMI Increased BMI	8 6	19 67	7.50	p <0.05	Significant
Without central obesity With central obesity	9 5	22 64	8.43	p <0.05	Significant

Table II shows that BMI and central obesity were significantly associated with increased serum Lp(a) levels in cases.

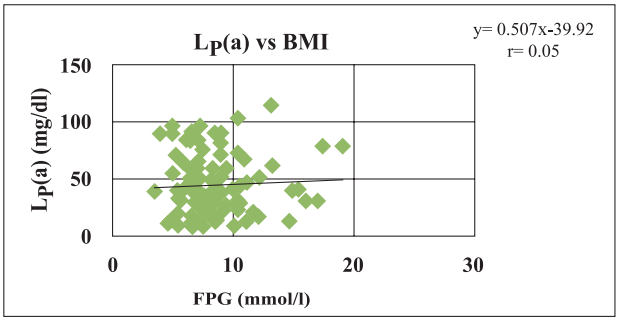

Figure 1: Correlation between serum Lp(a) and FPG (r = 0.05)

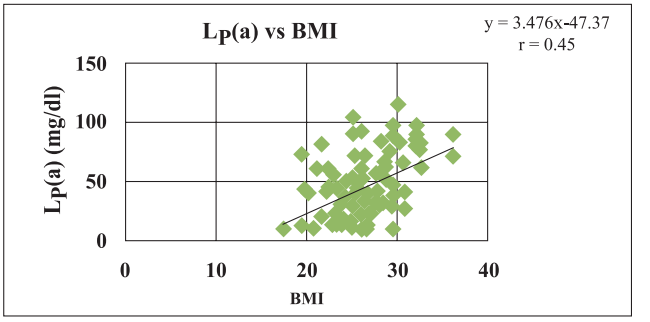

Figure 2: The positive correlation between serum Lp(a) and BMI (r = +0.45)

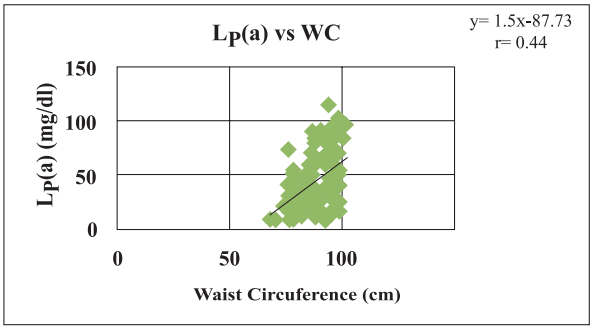

Figure 3: The positive correlation between serum Lp(a) and waist circumference (r = +0.44)

Table 3: Comparison of BMI and waist circumference between Lp(a) ≤30 mg/dl group and >30 mg/dl group in cases (n=100)

Variables	Lp(a) ≤30 mg/dl (n=35)	Lp(a) >30 mg/dl (n=65)	p value	Significance
BMI (kg/m^2) (Mean ± SEM)	25.08 ± 0.48 (17.39 - 30.76)	27.07 ± 0.45 (19.53 – 36.11)	p <0.05	Significant
Waist Circumference(cm) (Mean ± SEM)	84.54 ± 1.41 (68 - 98)	89.92 ± 0.88 (76 – 102)	p <0.05	Significant

Table III reveals that there were significant differences in BMI and waist circumference in Lp(a) ≤30 mg/dl group and Lp(a) >30 mg/dl group in cases.

Discussion:

Accelerated coronary and peripheral vascular atherosclerosis is one of the most common and serious complications of long-term diabetes mellitus[25]. Along with other risk factors, including hypertension, smoking, and obesity, increasing importance has been given to secondary dyslipidemia in the causation of accelerated atherosclerosis[26]. In the present study, the mean values of FPG, serum Lp(a), BMI, and waist circumferences were higher than the desired values. So, in this study, patients with type 2 diabetes mellitus had obesity, central obesity, and poor glycemic controls. Hence, there was a tendency for increased serum Lp(a) in type 2 diabetic patients to be associated with raised BMI and increased waist circumference. Thus, there may be a trend to develop vascular disease as per metabolic syndrome[27].

In the current study, serum Lp(a) levels were significantly associated with BMI and waist circumference. There were also positive correlations among Lp(a) with BMI and waist

circumference. These observations were supported in another study[28]. In that study, BMI and waist circumference are independent determinants of Lp(a) concentrations in type 2 diabetes mellitus[28]. However, there was no correlation between Lp(a) and fasting plasma glucose. A similar finding was observed by Premkumar *et al*.[29] and Candido *et al*.[30] Although BMI is a strong predictor of lipids and lipoprotein levels among adults, some authors found no correlation between BMI and Lp(a)[31].

The present study showed that there were increased serum Lp(a) levels (>14mg/dl) in type 2 diabetic patients (44.32 ± 2.6 mg/dl). Similar findings were observed by other authors like Joseph *et al*.[32] and Ziaee *et al*.[33] In diabetes mellitus, elevated serum Lp(a) is caused by glycation of its apolipoproteins. Glycation also extends the half-life of Lp(a), which may lead to a higher plasma concentration of Lp(a) in diabetes mellitus[34]. As Lp(a) parameters are different in different ethnic group populations, most of the research showed that South Asians have higher levels of Lp(a) concentrations[35].

The atherogenic properties of serum Lp(a) levels are expressed over 30 mg/dl14. In this study, BMI and waist circumference were compared between Lp(a) ≤30 mg/dl group and Lp(a) >30 mg/dl group. There were marked differences in BMI and waist circumference in the two groups. So, this difference suggested that BMI and waist circumference are confounding factors of elevated Lp(a). These findings are in accordance with the study by Stephan *et al*.[36] However, in another study, researchers failed to demonstrate a significant difference[37].

Diabetes mellitus and obesity have an intricate relationship, with type 2 diabetes strongly associated with obesity[38]. Obesity is common among the study subjects. Subjects with high BMI and waist circumference tend to have abnormal lipoprotein(a) levels. However, further studies are required to define the biological connection between obesity and Lp(a) in type 2 diabetes mellitus.

Conclusion:

The present study suggests that serum Lp(a) concentration was associated with obesity and acts as an important determinant of raised serum Lp(a) in type 2 diabetic patients. This has important implications for the increased susceptibility to vascular disease associated with Lp(a) in diabetic patients.

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