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DIAGNOSTIC ROLE OF LIPOPROTEIN (A) IN TYPE-2 DIABETES MELLITUS

SANJEEDA TABASUM. M*

Shri JJT University Vidyanagari, Churu Jhunjhunu Road,
Chudela District-Jhunjhunu, Rajasthan-333001

ABSTRACT

Aim & Objective: To evaluate lipoprotein (a) in Diabetic population for the diagnostic role as a cardiac risk biomarker.Materials & Methods: A total of 302 subjects included in a case control study, of 198 diabetic and 104 controls, who were sex and age matched and non-alcoholic. Serum total cholesterol and triglyceride, HDL Cholesterol were measured using Siemens kits and Lp(a) measured using Agappe kit analysed on Chem 200 automated analyser. Results & Discussions: Patients were gender matched with p-value=0.273. Sugar parameters with significant results of p-value 0.001** and mean value of FBS being 169.09±82.44 mg/dL and PPBS mean being 267.17±102.75 mg/dL compared to control group. Lipid parameters have shown total cholesterol mean of diabetic group being 294.94±110.48 mg/dL and 202.36±50.48 mg/dL with the p being 0.001** and triglyceride mean being 273.77±148.27 mg/dL, control being 112.05±39.16 mg/dL with the p value 0.001**. HDL: LDL has also shown significant value of p being 0.001**. SGOT (AST) mean of diabetic group127.22 ±10.26 U/L and normal control 25.23±U/L and SGPT (ALT) mean of diabetics 30.29±11.22U/L, control mean 26.65±7.5U/L the p-value 0.003**.Lipoprotein (a) has shown significant levels in diabetic population of mean being 36.89±11.18U/L showing significance of p=<0.001**.Hence can be called in short as cardiac risk biomarker.

KEY WORDS: DM-diabetes Mellitus, Lp(a)-Lipoprotein a,

SANJEEDA TABASUM. M
Shri JJT University Vidyanagari, Churu Jhunjhunu Road,
Chudela District-Jhunjhunu, Rajasthan-333001

Corresponding author

INTRODUCTION

Diabetes is one of the main threats in this 21st century. Diabetes mellitus induces hypercholesterolemia and a markedly increased predisposition to atherosclerosis, the incidence of myocardial infarction is twice as high in diabetes as in non-diabetics. There is also increased risk of stroke and atherosclerosis induced gangrene of the lower extremities [1]. An abnormality of lipoprotein metabolism causes various hypo or hyper lipoproteinemias. The most common cause of this is Diabetes Mellitus where insulin deficiency causes excessive mobilization of free fatty acids and underutilization of Chylomicrons and very low density lipoproteins (VLDL) leading to hypertriacylglycerolemia. Plasma lipids consists of triacylglycerols (16%), phospholipids (30%), Cholesterol(14%) and cholesteryl esters (36%) and much small fraction of long chain fatty acids (free fatty acid)(4%). Free fatty acid is most active component of the plasma lipids[2]. The association of abnormalities of plasma lipids with atherosclerosis and ischemic heart disease has stimulated much research on the subject. The lipoproteins which circulate in the blood differ in size and composition. In addition to the acute severe complication of insulin deficiency there are chronic complications which may occur more frequently in patients who have been inadequately treated. Poor control of the disease is thought to predispose to the development of degenerative arterial disease (atherosclerosis) in the coronary, cerebral and peripheral arteries. This has been attributed to the hyperlipemia and hypercholesterolaemia of the chronic diabeticstate[3]. Lipoprotein (a) also called Lp(a) is a lipoprotein subclass. Studies have identified Lipoprotein (a) as a putative risk factor for atherosclerotic diseases such as coronary heart diseases and stroke [4,5,6]. Lipoprotein (a) was discovered in 1963 by Kare Berg [7] and the human gene encoding this protein was cloned in 1987 [8]. Lipoprotein (a) indicates a coagulant risk of plaque thrombosis. Lipoprotein (a) accumulates in the vessel wall and inhibits binding of PLG to the cell surface, reducing plasmin generation which increases clotting. These unique features of Lp(a) suggest the generation of clots and atherosclerosis[9]. Higher lipoprotein (a) concentrations are associated with premature coronary heart diseases; persons with diabetes and high lipoprotein (a) level appear to be at increased risk of asymptomatic coronary disease.C-Reactive protein (CRP) is produced by the liver and released into the blood stream as part of the body's response to tissue injury, infection or irritation. CRP levels as low as 0.3 milligrams per litre can still signal inflammation that involves the cardiovascular system (the heart and blood vessels). Currently, CRP levels are used to help determine the risk of developing heart disease in individuals who already have other risk factors. Thus hs-CRP test can not only help identify who is particularly at risk for heart disease. Of importance, elevated CRP levels can predict first heart attacks in individuals with no known coronary artery disease.

METHODOLOGY

Comparative case-control study was conducted in the Biochemistry laboratory, National Institute of Unani Medicine Hospital, Bangalore. A total of three hundred and two subjects, comprising of 198 diagnosed patients of diabetes type 2 and 104 controls who were age and sex matched healthy subjects were included after informed consent. The patients suffering from other serious illness or diseases. hypothyroidism, hepatitis, taking hormonal replacement therapy (HRT), anti-inflammatory drugs or statin and pregnant patients alcoholics and smokers were excluded. Blood samples were drawn following overnight fast and the assays were performed at adhering to the standard protocols and quality control procedures. Glucose was estimated by GOD/POD method (Siemens). Serum Cholesterol and Triglyceride by enzymatic colorimetric method (Siemens).Estimation of HDL-Cholesterol by phosphotungstate Method (Siemens). Estimation of SGOT(AST) and SGPT(ALT) by UV kinetic (IFCC). Estimation of alkaline phosphotase by PNPP Method (Siemens).Lipoprotein (a) was measure by Agappe kit. All the analysis was done in Chem 200 fully Automated Random Access

Biochemistry Analyser. Diabetes was defined as a serum fasting glucose concentration of more than 126mg/dL or the use of diabetes medication.

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RESULTS

The study was conducted among 198 diabetic cases and 104 normal subjects.Patients were gender matched with 115 males and 83 femaleswih the p-value of 0.273.

Table 1
Gender distribution of patients studied

Gender	Group I		Group II	
	No	%	No	%
Male	115	58.0	53	50.9
Female	83	41.9	51	49.0
Total	198	100.0	104	100.0

Samples are gender matched with P = 0.273

Table 2
Comparison of sugar parameters of patients studied

Sugar parameters	Group I	Group II	P value
FBS mg/dl	169.09±82.44	92.35±15.84	<0.001**
PPBS mg/dl	267.19±102.75	119.07±16.11	<0.001**

Table 3
Comparison of lipid parameters of patients studied

Lipid parameters	Group I	Group II	P value
Total cholesterol mg/dl	294.94±110.48	202.36±50.48	<0.001**
Triglycerides mg/dl	273.77±148.27	112.05±39.16	<0.001**
HDL mg/dl	38.87±7.14	52.82±11.06	<0.001**
LDL mg/dl	201.51±96.68	127.13±45.69	<0.001**
HDL:LDL mg/dl	0.24±0.15	0.55±0.71	<0.001**

Table 4
Comparison of Biochemical parameters of patients studied

Biochemical parameters	Group I	Group II	P value
SGOT U/L	27.22±10.26	25.23±8.77	0.094+
SGPT U/L	30.29±11.22	26.65±7.5	0.003**
Alkaline phosphatase U/L	113.68±28.63	111.73±25.34	0.560

Comparison of the sugar parameters of the patients for FBS and PPBS studied has shown significant results of p-value 0.001** (significance being < 0.05) and the mean value of FBS being 169.09±82.44 mg/dL and PPBS mean value being 267.17±102.75 mg/dL compared to control group 2 having FBS mean 92.35 ±15.84 mg/dL and 119.07±16.11 mg/dL for FBS and PPBS. Hence the significance value of p being 0.001** as in table 2.These two groups were further analyzed for lipid parameters and have shown total cholesterol mean value of diabetic group and control group being 294.94±110.48 mg/dL and 202.36±50.48 mg/dL respectively with the p value being 0.001** (significance being < 0.05) and triglyceride mean 273.77±148.27 mg/dL compared to control 112.05±39.16 mg/dL with the p value of 0.001(significance being < 0.05). HDL mean

of test group 38.87±7.14 and control group 52.82±11.06 and LDL mean 201.51±96.68,control group being 127.13±45.69.HDL:LDL has also shown significant value of p- 0.001** (significance being < 0.05) with mean of 0.24±0.15 and control mean of 0.55.71± 0.71 as in table 3.Comparison of the other Biochemical parameters have also shown very significant results with SGOT (AST) mean of diabetic group127.22 ±10.26 U/L and normal group being 25.23±U/L with p-0.094*. SGPT (ALT) mean of diabetic group being 30.29±11.22U/L and control group mean being 26.65±7.5U/L and p- 0.003** and hence very significant in diabetic population as in table 4. Comparative study between hs-CRP for the diabetic and non-diabetic have also given a significant results that high sensitive CRP (hs CRP) is higher in group 1 diabetic patients mean=2.46±0.77 and control mean being 0.9±1.02 with the significance of P=<0.001** as in table 5.

Table 5
: Comparison of hs CRP in two groups of patients studied

hs CRP	Group I		Group II	
	No	%	No	%
<3.0	164	82.8	103	99.0
>3.0	34	17.1	1	1.0
Total	198	100.0	104	100.0
Mean ± SD	2.46±0.77		0.9±1.02	

Mean hs-CRP is significantly higher in group I compared to Group II with P=<0.001*

Table 6
Comparison of Lp(a) in two groups of patients studied

LP(a)	Group I		Group II	
	No	%	No	%
<20	6	3.0	43	41.3
20-40	125	63.1	54	51.9
>40	67	33.8	7	6.7
Total	198	100.0	104	100.0
Mean ± SD	36.89±11.18		24.06±9.78	

Mean LP(a) is significantly higher in cases with P=<0.001*

Lipoprotein (a) whose diagnostic role is under study has been very significant with Mean of diabetic group=36.89±11.18 and control group mean 24.06±9.78 and the P=<0.001**(significance being < 0.05) as in table 6.

DISCUSSION

A comparative case control study was being carried out for the urban population of Bangalore where there is a lot of stress among the age groups of 20-60 years. Hence our study may help in understanding the importance of the testing of this lipoprotein (a) in assessing the level of atherogenisis among the diabetic population and to advise the patients in preventing the further deterioration of health conditions. Higher mean of Lp(a) were observed in patients than controls and the the difference was statistically significant(p<0.01). Our study is in agreement with earlier studies [10,11,12.] Among Asian Indians higher prevalence of coronary heart disease is reported in South India[13.] Earlier studies have have also proved the evidence that lipoprotein (a) plays a significant role in atherosclerosis and is one of the top five or six factors for cardiovascular disease[14.]C-Reactive protein, a sensitive indicator of inflammation, is an independent risk factor for CAD, and has been shown to be higher in Asian Indians than in Europian whites. Which is accounted for by greater central obesity and insulin resistance in Indians[15,16.] Hence our study is in agreement with the previous

studies. The increased prevalence of high risk in type 2-diabetic patients may be due to increased prevalence of low molecular weight isoform of apoprotein (a).Diabetes is recognized as an important risk factor for CAD, and diabetic patients are at 2-fold increased risk of cardiovascular mortality compared to other non-diabetics[17]

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