

Serum Levels of Lipoprotein A in Patients with Diabetic Retinopathy



Medical Science

KEYWORDS : Diabetes Mellitus, Diabetic Retinopathy, Lipoprotein a, Coronary Heart Disease, Microvascular diseases.

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ABSTRACT

Diabetic patients are prone to develop microangiopathy clinically manifested as diabetic nephropathy, neuropathy and retinopathy. In developed countries, diabetic retinopathy (DR) is the leading cause of vision loss in adults of working age. Lipoprotein(a) [Lp(a)] is a low density lipoprotein like particle containing Apo-lipoprotein B100 disulphide, linked to one large glycoprotein called Apo-Lp(a), a particle comprised of low density lipoprotein and covalently bound Apo-Lp(a), and is considered a pro-atherogenic, pro-thrombotic risk factor for coronary heart disease (CHD). The present study is focused to know association between Lp(a) and diabetic retinopathy in local population. The present study enrolled total 36 subjects in which, 18 subjects having diabetes without retinopathy as controls and 18 subjects having diabetic retinopathy (DR) as cases. Assessment of DR was performed by ophthalmoscopy and/or biomicroscopy through dilated pupils. Anthropometric measurements including weight and height were obtained using standardized techniques. Venous blood samples were collected, and all examinations were performed at 8.00 h after an overnight fast. Measurement of HbA1c was done by Turbidimetric inhibition immune assay (Dimension xpand plus). Creatinine was estimated by modified Zafé's method (Dimension xpand plus). TSH was estimated by Electrochemiluminescence (ECLIA) (Advia centur cp instrument). Lipoprotein(a) was assayed by Immunoturbidimetric assay for the quantitative determination of lipoprotein (a) in human serum on Dimension xpand plus instrument. We observed higher Lp(a) levels in patients with diabetic retinopathy compared to patients having diabetes without retinopathy. In conclusion, Lp(a) levels may be increased in patients with retinopathy. Lp(a) is involved in the development of atherothrombosis and activation of acute inflammation exerting a proatherogenic and hypofibrinolytic effect.

Introduction:

Atherosclerotic vascular diseases such as coronary heart disease, cerebrovascular disease, and peripheral vascular disease are a major cause of morbidity and mortality in patients with diabetes mellitus (DM)¹. Diabetic patients are also prone to develop microangiopathy clinically manifested as diabetic nephropathy, neuropathy and retinopathy.² In developed countries, diabetic retinopathy (DR) is the leading cause of vision loss in adults of working age.³ Early identification and treatment are key priorities for reducing the morbidity of diabetic retinopathy (DR). Population and family studies have shown the pathogenesis of DR due to the interaction of several environmental, nutritional, and genetic risk factors.⁴ Risk factors for DR include hyperglycemia, hypertension, and dyslipidemia. It has been demonstrated that atherogenic lipoproteins, such as total cholesterol, LDL cholesterol, oxidized low density lipoprotein, and triglycerides, are associated with progression of retinopathy, proliferative retinopathy, and the development of macular oedema.⁵⁻⁷ Lipoprotein(a) [Lp(a)] is a low density lipoprotein like particle containing Apo-lipoprotein B100 disulphide, linked to one large glycoprotein called Apo-Lp(a), a particle comprised of low density lipoprotein and covalently bound Apo-Lp(a), and is considered a pro-atherogenic, pro-thrombotic risk factor for coronary heart disease (CHD)⁸. Many prospective epidemiological studies have reported positive associations of baseline Lp(a) concentration with CHD risk⁹⁻¹³. The present study is focused to know association between Lp(a) and diabetic retinopathy in local population.

Materials & Methods:

Study Design. The present study was carried out on patients with DM regularly attending our outpatients department at Heritage institute of medical sciences, Varanasi. We enrolled total 36 subjects in the study, 18 subjects having diabetes without retinopathy as controls and 18 subjects having diabetic retinopathy (DR) as cases. The exclusion criteria were (1) patients who were already on lipid lowering drugs or glitazones; (2) Females taking oral contraceptive pills or hormone replacement therapy; (3) Familial hypercholesterolemia; (4) Hypothyroidism; (5) Patients with chronic liver disease; (6) Patients with kidney disease. Assessment of DR was performed by ophthalmoscopy and/or biomicroscopy through dilated pupils by a retinal specialist. Informed consent was obtained from all patients.

Anthropometric measurements including weight and height were obtained using standardized techniques. Height was measured with a tape to the nearest centimetre. Subjects were requested to stand upright without shoes with their back against the wall, heels together, and eyes directed forward. Weight was measured with a traditional spring balance that was kept on a firm horizontal surface. Subjects were asked to wear light clothing. Body mass index (BMI) was calculated by using the formula: weight (Kg)/height (m²).

Venous blood samples were drawn from patients, and all examinations were performed at 8.00 h after an overnight fast. Fasting sample was collected in gray vacutainer for FBS estimation, Lavender color EDTA vacutainer for HbA1c estimation, Plain vacutainer for TSH and creatinine estimation. The fasting plasma glucose concentrations were assayed using the glucose-oxidase peroxidase method. (Dimension xpand plus). Measurement of HbA1c was done by Turbidimetric inhibition immune assay (Dimension xpand plus). Creatinine was estimated by modified Zafé's method (Dimension xpand plus). TSH was estimated by ECLIA (Advia centur cp instrument)

Lipoprotein(a) was assayed by Immunoturbidimetric assay for

the quantitative determination of lipoprotein (a) in human serum on Dimension xpand plus instrument.

Test Principle: Immunospectrophotometric assay

- Sample and addition of R1 (Phosphate buffer)
- Addition of R2 (anti-lipoprotein (a) antibody) and start of reaction:

Anti-lipoprotein (a) antibodies react with antigen in the sample to form an antigen/antibody complex which is determined turbidimetrically after agglutination.

Statistical analysis:

Statistical analysis was done using SPSS V16.0. Student's t test was performed, to compare the mean between different groups.

Results:

The patients with DR had a longer duration of diabetes (8 versus 4.5 years; $P < 0.5$) and higher glycosylated haemoglobin levels (9.4% versus 8.8%; < 0.5) compared to subjects without DR. As regards diabetic management, Out of 18 controls, total 14 were on oral antidiabetic drugs, for example, metformin and/or sulfonylurea; 4 were on metformin + insulin. Out of 18 cases, total 13 were on oral antidiabetic drugs, for example, metformin and/or sulfonylurea; 5 were on metformin + insulin. Lp(a) levels were measured in all subjects. We observed higher Lp(a) levels in patients with diabetic retinopathy compared to patients having diabetes without retinopathy (Table 1).

Table 1: Mean & SD of various parameters

Parameter	Controls(n=18) (Mean ± SD)	Cases(n=18) (Mean ± SD)	P value
Age	52.9±8.42	60.2±6.9	0.07*
Duration of diabetes(years)	4.5±4.1	8±5.8	0.48*
BMI(wt in kg/ht m ²)	24.4±4.2	24.8±4.1	0.7
HbA1c(%)	8.8±2.3	9.4±3.2	0.48*
FBS(mg/dL)	182.6±61.7	132±55.9	0.01*
Creatinine(mg/dL)	1.05±0.61	1.62±1.34	0.1*
TSH(μIU/L)	3.1±2.2	2.2±0.9	0.1*
Lipoprotein a(mg/dL)	33.5±1.7	51.5±3.3	0.000*

*p value <0.5 significant

Discussion & conclusion:

Diabetes mellitus confers a two-fold higher risk for a wide range of vascular diseases, independent of other conventional risk factors¹⁵. Any additional risk factor along with diabetes would increase the vascular risk that might prove to be catastrophic to the sufferer. High Lp(a) level has been proven to be a risk factor for atherosclerosis and related morbidity and mortality in many studies⁹⁻¹³.

DR represents a common and severe complication of diabetes, thus there is a need to implement effective strategies being able to prevent DR and to identify specific and early predictors¹⁶.

The majority of studies in type 2 diabetes found increased levels of Lp(a) in plasma with a few exception¹⁷⁻²⁰. On the other hand, Rainwater et al have reported that Lp(a) concentrations were significantly lower in type 2 diabetes population compared to matched nondiabetic subjects²¹.

Jenkins et al showed an increase of Lp(a) in type 2 diabetes with retinopathy. The potential causal relationship between Lp(a) and retinopathy is still not clear. Elevated Lp(a) levels may play a causative role in DR by damaging the microcirculation²².

It has been hypothesized based on the potential for Lp(a) to cause vessel damage through lipoprotein oxidation and on the potential antifibrinolytic and prothrombotic effects of Lp(a)²².

In the present study we observed that Lp(a) levels increased in a significant percentage of patients with retinopathy compared to diabetic patients without retinopathy.

In conclusion, Lp (a) levels may be increased in patients with retinopathy. Lp (a) is involved in the development of atherosclerosis and activation of acute inflammation exerting a proatherogenic and hypofibrinolytic effect. Limitations of our study are the modest size of the patients and the absence of separate models for men and women, due to the small numbers. Larger studies using more defined populations are required to better understand the relationship between Lp(a) concentrations and retinopathy in patients with diabetes mellitus.

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