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CORRELATION BETWEEN DIABETIC RETINOPATHY AND LIPOPROTEIN(A)IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT

Background: Retinopathy is a significant complication among patients of diabetes mellitus. Raised serum Lipoprotein(a) [Lp(a)] levels have found to be an independent risk factor for thromboembolic events and atherogenesis. Also, the capillary occlusion is a frequent observation in diabetic retinopathy, Lp(a) is postulated to play a critical role in the initiation and progression of diabetic retinopathy. **Material & Methods:**200 patients with type 2 diabetes mellitus of five years or more duration were enrolled for study by simple random sampling. Patients enrolled in this study have been diagnosed to have type 2 diabetes mellitus as per the American Diabetes Association criteria. Among these 200 patients, 100 patients who had no retinopathy served as the control group, and 100 who had retinopathy enrolled in the study group. **Results:** The average Lp(a) levels in patients who had retinopathy were 69.38 mg/dl and in the control group 28.11 mg/dl. This difference was obtained to be statistically significant.TheLp(a) levels in patients who had NPDR were 66.49 mg / dl and in patients with PDR Lp(a) levels were 105.10 mg/dl. This difference was also reported to be statistically significant. On applying logistic regression analysis, diabetic retinopathy was reported to be statistically related to serum Lp(a) levels (P<0.001, odds ratio 1.068).**Conclusion:** Lipoprotein (a) levels were found significantly greater in patients with diabetic retinopathy in comparison to patients who had no retinopathy. Hence Lipoprotein (a) may act as an independent risk factor for developing diabetic retinopathy.

Keywords: Diabetic retinopathy, lipoprotein(a), diabetes mellitus.

INTRODUCTION

Retinopathy is a significant complication among patients of diabetes mellitus**(1)**. Numerous epidemiological risk factors had been researched and studied for the development of diabetic retinopathy such as the age of the patient at the time of diagnosis, duration of diabetes, glycemic control, serum lipids, blood pressure and nephropathy**(2)**.

Plasma lipoprotein patterns and lipids profile also had been observed to be abnormal in cases of type 1 and type 2 diabetes mellitus. Although, the leading cause for the initiation and progression of retinopathy could not be described by the previous known studies**(3)**.

India is becoming the diabetic capital of the world. Hence, diabetes is a growing epidemic in our society, with an increasing incidence worldwide. To combat this, though diabetes can be easily diagnosed and detected overall, its actual effect seen over the several systems in the form of vascular complications are

rarely fully recognized. It is a fact that the various difficulties and manifestations of diabetes mellitus are still very hard to detect, and the majority of the patients usually end up in the critical stages or a disability form **(4)**.

Raised serum Lipoprotein(a) [Lp(a)] levels have found to be an independent risk factor for thromboembolic events and atherogenesis in both diabetics and nondiabetics**(5)**. Also, the capillary occlusion is a frequent observation in diabetic retinopathy, Lp(a) is postulated to play a critical role in the initiation and progression of diabetic retinopathy**(6)**.

We conducted the present study to evaluate serum Lp(a) levels in the patients with type 2 diabetes Mellitus among Indian population with and without diabetic retinopathy and to estimate the correlation, if any, between the severity of diabetic retinopathy and serum Lp(a) levels.

MATERIALS & METHODS

The present prospective study was conductedat Department of Ophthalmology, SMS Medical College, Jaipur on 200 patients with type 2 diabetes mellitus of five years or more duration was enrolled for study by simple random sampling. Patients enrolled in this study have been diagnosed to have type 2 diabetes mellitus as per the American Diabetes Association criteria. **(3)**

Institutional Ethics Committee Clearance was taken before the start of the study and written informed consent for the study purpose was obtained from all the patients. Among these 200 patients, 100 patients who had no retinopathy served as the control group, and 100 who had retinopathy enrolled in the study group**.** Patients whom dilatation of pupils was contraindicated, like angle-closure glaucoma, patients with hazy media which impaired the visualization of the fundus, patients with diabetes of fewer than five years of duration, patients on hyperlipidemic or hypolipidemic drugs were excluded from the study.

1% tropicamide eye drops were used to achieve maximum dilatation of both eyes pupils. Direct ophthalmoscopy was done for fundus examination in both eyes with +20 D lens and +90D Volk's lens used for Indirect ophthalmoscopy in the investigation of the macula. Fundus findings were graded as No signs of retinopathy, Nonproliferative diabetic retinopathy (NPDR), Proliferative diabetic retinopathy (PDR).

Fasting blood samples (5 to 7 ml) were drawn for estimation of the Lp(a)and total lipid profile. Other routine investigations including glycated hemoglobin, blood urea, and urine analysis were also carried out. All the patients were subjected to a detailed clinical examination in accordance with pretested proforma. The data were analyzed using MS Excel 2010, Epi Info v7 and SPSS v22.

RESULTS

In the present study out of a total of 200 patients, the 100 patients forming the study group 90 patients had NPDR, and ten patients had PDR. The average age of the study group patients was 58.1years and in the control group 58.1years. The study group included 55 females and 45 males whereas the control group comprised 44 men and On the contrary, several studies in Caucasians mostly done 56 women.

Both the study and control group were age and sex-matched. Table 1 shows the clinical and laboratory characteristics of the subjects. Patients with diabetic retinopathy were found to have a longer duration of the disease. Age, fasting glucose levels, triglycerides, total cholesterol, high-density lipoprotein (HDL) cholesterol, and low-density lipoprotein (LDL) cholesterol concentrations were comparable in the three groups. The average Lp(a) levels in patients with retinopathy were 69.38mg / dl and in the control group 28.11 mg/dl. This difference was reported to be statistically significant [Fig. 1]. The Lp(a) levels in patients who had NPDR were 66.49 mg/dl, and in patients who had PDR, the levels were 105.10 mg/dl. This difference was also reported to be statistically significant [Fig. 2]. When logistic regression analysis was applied, diabetic retinopathy was said to be

statistically related to serum Lp(a) levels (P<0.001, odds ratio 1.068).

Table 1: Clinical and laboratory findings of the subjects

	Controls	Non-proliferative diabetic retinopathy	Proliferative diabetic retinopathy
Number	100	90	**10**
Age (years)	58.1	58.1	**56.4 (NS)**
Diabetes duration (years)	6.84 ± 5.82	8.64 ± 6.24	**13.46 ± 6.83 (S)**
Fasting serum glucose (mg/dl)	170.32	180.67	**183.81 (NS)**
HbA1C (%)	7.91	8.09	**8.56 (NS)**
Cholesterol (mg/dl)	185.4	194.7	**212.1 (NS)**
Triglycerides (mg/dl)	201.16	186.62	**188.50 (NS)**
High density lipoprotein cholesterol (mg/dl)	34.80	33.79	**38.29 (NS)**
Low density lipoprotein cholesterol (mg/dl)	116.76	119.05	**108.71 (NS)**
Lipoprotein(a) mg/dl	**28.11 ± 2.61**	**66.49 ± 8.06**	**105.10 ± 21.17 (S)**

Fig 1: Lp (a) levels in patients with diabetic retinopathy and with no diabetic retinopathy

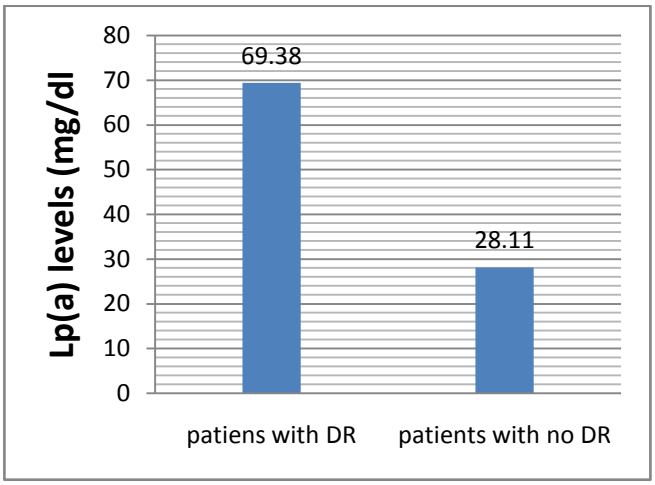
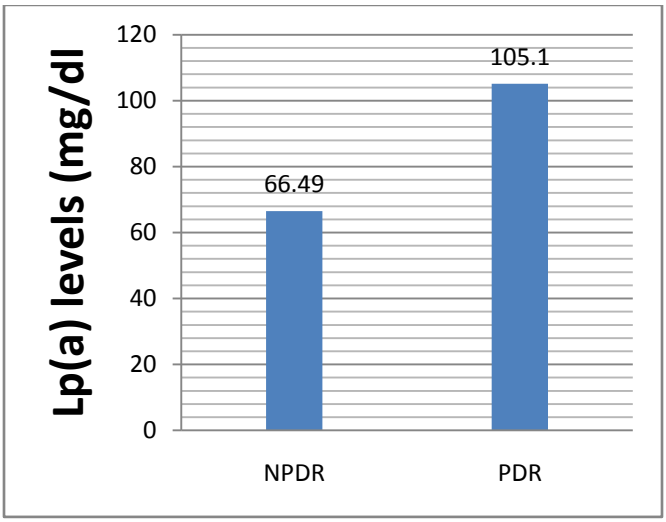


Fig 2: Lp (a) levels in patients in NPDR vs. PDR



DISCUSSION

The present study was conducted to find out the risk factors for retinopathy in diabetic patients and the association of presenting complaints with lipoprotein a. Total study subjects were 100 cases and 100 controls, which were enrolled based on inclusion and exclusion criteria. Presenting symptoms among diabetic patients distribution showed that retinopathy was one of the most critical consequences in both type 1 and type 2 diabetes.

Along with that the duration of diabetes and the poor glycemic control were the two most important risk factors in the progression of retinopathy**(7)**. Although, these risk factors solely do not describe the development of retinopathy. It can be not present in some patients with poor glycemic control during an extended period, whereas some patients may develop retinopathic pathology in the comparatively short period in spite of good metabolic control**(8)**. This describes the probability of other risk factors responsible in the occurrence of diabetic retinopathy.

Hence the present study was conducted to find out the association of Lp(a), a subfraction of LDL cholesterol in the etiopathogenesis of diabetic retinopathy. The present study found that the average serum Lp(a) levels in cases of diabetic retinopathy was observed significantly higher than in cases without retinopathy which complied with the previously done studies conducted in Japan which stated high serum Lp(a) levels in patients with diabetic retinopathy **(9)**.

On the other hand, some studies conducted among patients with type 1 diabetes reported that Lp(a) levels werenotcorrelatedwith retinopathy **(10)**. Likewise, the correlation of serum Lp(a) levels and diabetic retinopathy and its severity present study reported that Lp(a) levels increase proportionally with the severity of retinopathy. The means Lp(a) levels in diabetic patients with PDR were statistically significant and higher than patients had NPDR.

This complies with the study done by Kim et al. which reported that type 2diabetic patients with PDR had raised serum Lp(a) levels**(11)**. A study conducted by Maiolietalshowedthatincreased serum apolipoprotein (a) levels in the diabetic retinopathy group (NPDR and PDR) compared with the non-retinopathy group. **(12)** A study conducted by Heesenet al also found a higher incidence of proliferative retinopathy in type 2 diabetic patients with raised Lp(a) levels. **(13)**

A study conducted by Verrottiet al observed that the serum lipoprotein and lipids concentrations in patients who had type 1 diabetes mellitus and different severity of retinopathy. **(14)** They also found that statistically significant higher Lp(a) values in patients who had proliferative and NPDRincomparision to patients who had diabetic retinopathy.

On the contrary, the two studies conducted byMorisakiet al**(9)**, and Onuma et al **(15)** reported no significant association between the Lp (a) levels and patients with NPDR and PDR. The reason behind these contrary findings are not apparent at present, but differences in sample size and study population, type of diabetes and classification of diabetic retinopathy may be factors. Lp(a) is a genetically determined and regulated by apolipoprotein(a) gene located on the long arm of a chromosome **(6)**.

Plasma Lp(a) levels in are also variable and depend ontheethnicity, i.e. Indians, have high serum levels of Lp(a) **(16)**.

CONCLUSION

We concluded from the present study thatLipoprotein (a) levels were found significantly greater in patients with diabetic retinopathy in comparison to patients who had no retinopathy. Hence Lipoprotein (a) may be act as an independent risk factor for developing diabetic retinopathy.

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