A Prospective Cross-Sectional Study of Exudative Diabetic Retinopathy and Its Association with Serum Lipid Levels

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Abstract:Purpose: *This prospective cross sectional study awsa done to study the association of serum lipids and exudative diabetic retinopathy.**Methods:** This was across sectional study conducted in patients visiting the outdoorunit of Department of Ophthalmology ,Maharani Lakshmi Bai Medical College Jhansi out during the period of 19 months from March 2015 to September 2016. This study included patients with age above 40 years, with diabetes, which is defined as a fasting plasma glucose of more than or equal to 126 mg/dl or a 2-hour post glucose load plasma glucose of more than or equal to 200 mg/dl or a random plasma glucose of more than or equal to 200 mg/dl in the presence of symptoms of hyperglycemia ,and duration > 5 years.Patients were divided in two groups GroupA included patients .**Results:** Among 150 patients in our study, 70 (46.7%) patients were having exudative diabetic retinopathy with or without CSME. Rest 80(53.3%) patients were having diabetic retinopathy without hard exudates or had no diabetic retinopathy Comparision between mean cholesterol in study group Group A 223.31 ± 51.20 and Group B 185.21 ± 30.02 showed p value <0.05 which was stastically significant. There was significant difference between mean triglyceride value in study group Group A (163.62 ±26.21) and in Group B w(135.29 ± 22.12),mean LDL cholesterol in group A (151.23 ± 27.12 mg/dl)and in group B, (125.20 ± 22.22 mg/dl) and mean HDL cholesterol in group A (38.21 ± 5.20 mg/dl) and in group B (46.25 ± 6.75 mg/dl). No statistically significant difference was found on comparison of mean values of VLDL cholesterol in two groups**Conclusions:** The present study suggests that serum cholesterol, LDL, Triglycerides and low HDL levels have a significant and independent effect on retinal hard exudates.*

Keywords: *cholesterol, diabetes mellitus, diabetic retinopathy, high density lipoprotein, low density lipoprotein, macular edema, triglyceride.*

I. Introduction

Diabetic retinopathy is a common complication of DM characterized by macular edema and frequently accompanied by lipid exudation. The pathogenesis of diabetic retinopathy [1]is not completely understood, but established risk factors include poor glycemic control, hypertension, increasing age, and duration of diabetes. A relationship between lipid levels and macular edema appears to be biologically plausible. High lipid levels are known to cause endothelial dysfunction via a local inflammatory response, with consequent release of cytokines and growth factors, activation of oxygen-sensitive biological changes in vessel walls, increases in LDL oxidation, and quenching of nitric oxide.[2] In turn, endothelial dysfunction in the diabetic vasculature results in blood retinal barrier breakdown in animal models of diabetic retinopathy though data are lacking in humans.[3]Moreover, elevated levels of LDL and triglycerides in diabetes have been linked with higher levels of fluorescent advanced glycation end products, which are hypothesized to play an important role in the pathogenesis of diabetes complications.[4] Hard exudates are waxy yellow material with relatively indistinct borders seen in the outer plexiform and inner nuclear layers.[5] They result from abnormal vascular leakage with breakdown lipid products from degenerating neural retinal elements. They may be discrete, confluent or may form a circinate pattern around a cluster of leaking microaneurysms or microvascular abnormalities.[6] If present in the foveal region, they may impair vision. Various systems of classification were developed to help us study the natural course of disease and assist us in taking decisions regarding treatment for the patient.Some of the important ones are Duke-Elder's classification[7], Kanski's classification[8], Airlee-House classification and modified Airlee-House classification or modern ETDRS classification[9]
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II. Method and material

This prospective cross-sectional study was carried out in Department of Ophthalmology, MLB Medical College over a period of 19 months. Patients were included in the study under the following inclusion and exclusion criteria:

Inclusion Criteria:
1) Age above 40 years.
2) All patients with diabetes, which is defined as a fasting plasma glucose of more than or equal to 126 mg/dl or a 2-hour post glucose load plasma glucose of more than or equal to 200 mg/dl glucose in the presence of symptoms of hyperglycemia ,and duration > 5 years.
3) Those who were physically fit to undergo a dilated fundus examination and fundus photographic evaluation.

Exclusion Criteria:
1) Pregnancy
2) Chronic alcoholic
3) Malignant hypertension
4) Chronic blood loss
5) Primary renal disorder
6) Glaucomatous patient
7) Active systemic infection
8) Co-existing ocular disorders like uveitis, opaque/hazy media, high myopia, vitreoretinal degeneration and dystrophy, retinitis, pigmentosa and ocular surgeries < 6 month duration.

Consent:
Proper informed written consent were taken from each individual explaining the procedures and their complications.

Pre-Treatment Work Up:

After selecting the patient, a detailed clinical record was prepared including age, sex, address, occupation, family history, duration of the diabetes and history of previous treatments. Detailed ocular examination was carried out by using Snellen's chart for BCVA, S/L biomicroscopy by 90D for fundus examination, tonometry by Schiotz tonometer for IOP assessment . Ophthalmoscopic examination(direct/indirect) and fundus photography was done under full mydriasis and FFA if clinically required.

Dyslipidemia was defined using NCEP ATP III guidelines as: Total cholesterol ≥ 200 mg/dl and or HDL cholesterol < 40 mg/dl or LDL cholesterol ≥ 100 mg/dl and/or triglycerides ≥ 150 mg/dl will be considered abnormal. Various parameters of the lipid profile were estimated by commercially available enzymatic in vitro assay kits using Flex reagent cartridge on the dimension clinical chemistry system and were expressed as mg/dl.

III.   Method :

All patients were selected under inclusion and exclusion criteria and divided into two groups as follows :-
A. GROUP A : Patients with history of diabetes mellitus >5 years with signs of exudative diabetic retinopathy
B. GROUP B : Patients with history of diabetes mellitus >5 years with no signs of exudative diabetic retinopathy

Statistical analysis:

Data was analyzed by Mean Standard Deviation and T-tests assuming unequal variance in MS Excel 2007 version

IV.   Results

Table No. 1 -SEX WISE DISTRIBUTION OF PATIENTS

SEX	GROUP A		GROUP B		TOTAL	
	No.	%	No.	%	No.	%
MALE	49	70	58	72.5	107	71.3
FEMALE	21	30	22	27.5	43	28.7
TOTAL	70	100	80	100	150	100
Chi –square test	χ^2 =0.114, p> 0.05					

* Table no. 1 shows that out of 150 patients, 107(71.3%) were male and 43(27.5%) were female.
* In Group A , there were 49(70%) male and 21(30%) female and in group B , there were 58(72.5%) male and 22(27.5%) female

Table No. 2 : AGE WISE DISTRIBUTION OF PATIENTS

AGE (YRS)	GROUP A	GROUP B	TOTAL PATIENTS	
	No	No	No	%
41-50	7	10	17	11.3
51-60	25	28	53	35.3
61-70	28	37	65	43.4

>70	10	5	15	10
TOTAL	70	80	150	100
MEAN ± SD	63.21 ± 7.25	62.24 ± 7.73	62.81 ± 8.48	
t=0.789, p>0.05				

- Table no. 2 shows that the mean age of patients in group 1 is 63.21±7.25 years and the mean age of group 2 is 62.24 ± 7.73 years.
- The mean age of total patients in the study was 62.81 ± 8.48 years

Table No 3 – DURATION OF DISEASE OF TOTAL PATIENTS

DURATION OF DISEASE (in years)	GROUP A No.	GROUP B No.	TOTAL No.	%
5-10	8	21	29	19.33
10-15	29	35	64	42.67
>15	33	24	57	38.00
TOTAL	70	80	150	100
MEAN ± SD	16.08 ± 4.11	12.78 ± 4.30	15.91 ± 5.22	
t=4.789, p<0.05				

- Table no 3 shows that the mean duration of disease in group A was 16.08 ± 4.11 years and in group B it was 12.78 ± 4.30 years.
- The mean duration of disease of total patients in **the** study was 15.91 ± 5.22 years.

Table No. 4 – TOTAL CHOLESTEROL OF PATIENTS-

TOTAL CHOLESTEROL (mg/dl)	GROUP A	GROUP B	TOTAL PATIENTS
< 200	22	44	66
200 - 239	23	35	58
≥ 240	25	1	26
MEAN ± SD	223.31 ± 51.20	185.21 ± 30.02	199.96 ± 37.22
t=5.082, p<0.05			

- The mean total cholesterol in group A was 223.31 ± 51.20 mg/ dl and in group B, it was 185.21 ± 30.02 mg/dl.
- There is statistically significant difference between Group A and group B.

Table No. 5 – LDL CHOLESTEROL OF PATIENTS

LDL CHOLESTEROL (mg/dl)	**GROUP A**	**GROUP B**	**TOTAL PATIENTS**
<130	15	42	57
130 – 159	35	37	72
≥ 160	20	2	22
MEAN ± SD	151.23 ± 27.12	125.20 ± 22.22	135.65 ± 26.24
t=6.457, p<0.05			

- The mean LDL cholesterol in group A was 151.23 ± 27.12 mg/dl and in group B, it was 125.20 ± 22.22 mg/dl.
- There is statistically significant difference between Group A and group B.

Table No. 6 – VLDL CHOLESTEROL OF PATIENTS

VLDL CHOLESTEROL (mg/dl)	GROUP A	GROUP B	TOTAL PATIENTS
< 30	37	48	85
≥ 30	33	32	65
MEAN ± SD	29.96 ± 6.22	28.46 ± 5.73	30.80 ± 6.52
t=1.537, p>0.05			

- The mean VLDL cholesterol in group A was 29.96 ± 6.22 mg/dl and in group B, it was 28.46 ± 5.73 mg/dl.
- There is statistically insignificant difference between Group A and group B.

Table No. 7 – TRIGLYCERIDE LEVEL OF PATIENTS

TRIGLYCERIDES (mg/dl)	GROUP A	GROUP B	TOTAL PATIENTS
< 150	25	65	90
≥ 150	45	15	60
MEAN ± SD	163.62 ± 26.21	135.29 ± 22.12	148.56 ± 25.42
t=7.195, p<0.05			

- The mean triglyceride level in group A was 141.62 ± 26.21 mg/dl and in group B, it was 135.29 ± 22.12 mg/dl.
- There is statistically significant difference between Group A and group B.

Table No. 8- HDL CHOLESTEROL OF PATIENTS

HDL CHOLESTEROL (mg/dl)	GROUP A	GROUP B	TOTAL PATIENTS
> 60	2	5	7
36-60	56	68	124
≤ 35	12	7	19
MEAN ± SD	38.21 ± 5.20	46.25 ± 6.75	42.98 ± 5.80
t=8.084, p<0.05			

- The mean HDL cholesterol in group A was 38.21 ± 5.20 mg/dl and in group B , it was 46.25 ± 6.75 mg/dl.
- There is statistically significant difference between Group A and group B.

Table No 9 – LDL/HDL RATIO OF THE PATIENTS

LDL/HDL RATIO	GROUP A	GROUP B	TOTAL PATIENTS
< 2.5	12	32	44
2.5-5	39	42	81
> 5	19	6	25
MEAN ± SD	4.01 ± 0.76	3.2 ± 0.66	3.57 ± 0.70
t=3.689, p<0.05			

- The LDL/HDL ratio in group A was 4.01 ± 0.76 and in group B, it was 3.2 ± 0.66.
- There is statistically significant difference between Group A and group B.

V.   Discussion

Diabetic retinopathy (DR), a major microvascular complication of diabetes,has a significant impact on the world's health systems.[10] It is projected that number of people with DR worldwide will grow from 126.6 million in 2010 to 191.0 million by 2030, and the number with vision-threatening diabetic retinopathy (VTDR) is expected to increase from 37.3 million to 56.3million.[11]According to the latest World Health Organization (WHO) report, India has 31.7 million diabetic subjects, and the number is expected to increase to 79.4 million by 2030.[12]

Our study was conducted at MLB Medical College in the year 2014-2015 which included 150 patients who fulfilled the inclusion criteria The present cross sectional prospective study was done to study relation of serum lipid levels and microalbuminuria with exudative diabetic retinopathy .The study was carried out during the period of 19 months from March 2015 to September 2016 on patients coming to the outpatient of Department of Ophthalmology M.L.B. Medical College, Jhansi.

A total no. of 150 patients were enrolled for the study. The results of this study are summarized as –

- The study included 107 males (71.3%) and 43 females (28.7%%).ie male preponderance.
- Majority of the patients were > 60 years of age.
- The total duration of diabetes in months of group A mean 16.08 ± 4.11 and in group B mean 12.78 ± 4.30 . The p value is <0.005 which is statistically significant which mean increase in duration was assosciated with exudative diabetic retinopathy.
- Exudative retinopathy was more with raised total cholesterol . Comparision between mean cholesterol in study group Group A 223.31 ± 51.20 and Group B 185.21 ± 30.02 showed p value <0.05 which was stastically significant.

- There was a significant increase of LDL cholesterol levels between study group and cholesterol groups. Comparison of mean of LDL cholesterol between two groups were statistically significant.
- No statistically significant difference was found on comparison of mean values of VLDL cholesterol in two groups
- Increase triglyceride was observed in exudative diabetic retinopathy patients . Mean triglyceride value in study group Group A was 163.62 ±26.21 and in Group B was 135.29 ± 22.12. On comparison of mean between two groups p value was <0.05 which is statistically significant.
- Low HDL cholesterol was associated with exudative retinopathy. There was statistically significant difference between mean HDL cholesterol in two groups.

VI.   Conclusion

The present study suggests that the treating ophthalmologists should get a complete blood lipid profile test done if the patient has retinal hard exudates on fundus examination. This study also highlights the need for routine prescription of lipid-lowering drugs in addition to dietary restrictions and regular physical exercise in north Indian diabetic patients with documented retinal hard exudates due to the widespread occurrence of dyslipidemia in these patients. These drugs have already proven beneficial effect in reducing the risk of adverse cardiovascular events like myocardial infarction and stroke. The presence of microalbuminuria should warn the treating physician of the need to monitor the retina along with kidney function. This, in turn, may reduce the occurrence of irreversible visual loss due to DR.

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