



Original Research Article

Association of serum lipid levels and social factors with diabetic retinopathy in patients with type 2 diabetes mellitus: Study from tertiary care center of Western Maharashtra

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ABSTRACT

Purpose: To study the prevalence of dyslipidemia and to find out the correlation between serum lipid levels and social factors like occupation, locality(urban/rural) and education status with diabetic retinopathy in patients with type 2 diabetes mellitus.

Materials and Methods: 200 patients with type 2 diabetes mellitus were segregated into 2 categories:- First category of patients with diabetic retinopathy and second category of patients without diabetic retinopathy. Serum lipid levels of subjects were measured and social history like occupation, locality (urban/rural) and education status was taken. Observations were compared to check association between above factors and diabetic retinopathy.

Results: The prevalence of dyslipidemia was found to be 75.50%. Mean \pm SD of LDL(mg/dL) in patients with diabetic retinopathy was 118.86 ± 40.58 which was significantly higher as compared to patients without diabetic retinopathy (p value=0.006). No significant association was seen in the distribution of total cholesterol(mg/dL), HDL(mg/dL), Triglyceride(mg/dL) with diabetic retinopathy (p value>.05). 10% of patients with DR worked as clerks while 52% were homemakers, thus, significant association was seen in the relationship of occupation with the presence of diabetic retinopathy (p value<.05). Diabetic retinopathy was more prevalent among type 2 diabetics living in urban areas (p<0.0001). 16% of patients with DR had studied up to primary school while 28% of patients with DR had studied up to high school, thus significant association was seen between the education status of the patients and the occurrence of diabetic retinopathy (p value<.05).

Conclusion: Elevated serum LDL levels were found to be a significant risk factor for diabetic retinopathy. Clerks and homemakers were more predisposed to diabetic retinopathy. Subjects who received education up to primary school and high school and subjects living in urban areas had significantly increased rates of diabetic retinopathy.

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1. Introduction

Diabetes mellitus (DM) is a widespread multifactorial disease that imposes a serious burden to our healthcare system. India alone is estimated to have about 69.2 million diabetics and these numbers are predicted to soar as high as 123.5 million by the year 2040.^{1,2}

Type 2 diabetics include those individuals who are seen to have insulin resistance (IR) and usually relative deficiency of insulin. Diabetes mellitus leads to microvascular and macrovascular complications. Macrovascular abnormalities include coronary vascular disease, stroke and peripheral vascular disease. The microvascular complications include diabetic retinopathy, diabetic nephropathy and diabetic neuropathy. Chronically elevated blood sugar levels, increase in the reactive oxygen

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species, decrease in the nitric oxides and increase in fatty acids contribute to the chronic vascular complications by changing the vascular response.³

A multitude of risk factors have been studied to understand how DR develops and progresses. These include the type of diabetes mellitus and the duration of the disease, gender, age, body-mass index (BMI), glycemic control, hypertension, nephropathy, smoking, pregnancy and serum lipid levels.^{4,5} The importance of serum lipid levels in the development and progression of DR has been assessed worldwide with a lot of variable results. Dyslipidemia, characterized by raised levels of serum total cholesterol (TC), triglycerides (TG), low density lipoprotein cholesterol (LDL-C) and reduced levels of high density lipoprotein cholesterol (HDL-C) have been hypothesized as probable risk factors for DR. Hyperlipidemia is known to cause dysfunction in the endothelium due to reduced nitric oxide and also the breakdown of BRB which leads to lipid exudation and lipoprotein exudation that leads to various changes in DR and leads to diabetic macular edema (DME) formation.⁶ Diabetic macular edema is a common cause of severe vision loss in diabetic patients.^{7,8}

Various social factors like occupation, whether the individual lives in a rural or urban locality and education may be associated with diabetic retinopathy. This could be due to changes in lifestyle and diet in these individuals and also due to differences in awareness about the disease and the need for screening. There are also discrepancies in availability of resources and affordability among various social groups.

There have been variations in results and observations from various international studies and there is a scarcity of data from available local literature. Hence, we conducted this study in our tertiary care hospital to explore this interesting relationship between serum lipid levels and other social factors and DR in our local population.

2. Materials and Methods

A hospital based observational, cross sectional study was conducted in a tertiary hospital and research centre in Western Maharashtra, from September 2018 to August 2020. 200 patients with type 2 diabetes mellitus, aged 30-70 years were included in the study. Participants were segregated into 2 categories:- (i) category-I of patients with diabetic retinopathy and (ii) category-II of patients without diabetic retinopathy.

Patients with type 1 or indeterminate diabetes mellitus, where OCT was not possible due to hazy media or refusals, any prior ocular treatment, concomitant fundus pathology potentially affecting the macula (e.g arterial/venous occlusions), patients having corneal diseases, inflammatory eye diseases, optic neuropathy and age related macular degeneration, any other ocular pathology that could influence the progression of retinopathy (high

myopia, glaucoma, retinitis pigmentosa, other causes of optic atrophy, etc.), any history of radiation to the head or neck region, carotid vascular disease detected by carotid doppler and patients on hemo or /peritoneal dialysis were excluded from the study.

Participant information sheet (PIS) regarding details of study were prepared in English and Marathi language. PIS was given to the participants and they were explained in detail about the study in a language best understood by the patient. Participants were enrolled after getting written informed consent.

A Detailed history from each patient was obtained Following data was collected:

1. Age
2. Sex
3. Locality (urban/rural)
4. Occupation
5. Education status

Vision was assessed using illuminated Snellen's Chart. Anterior segment was evaluated in detail by slit lamp examination and fundus examination was done in a dark room with indirect ophthalmoscope. Fundus was also evaluated by means of direct ophthalmoscopy and slit lamp biomicroscopy with +90D lens. Fundus camera was used to obtain a fundus photograph. Participants were segregated into 2 categories. Group-1 included patients with type 2 diabetes mellitus with diabetic retinopathy. Group-2 included patients with type 2 diabetes mellitus without diabetic retinopathy. For grading the severity of diabetic retinopathy, Early Treatment Diabetic Retinopathy Study (ETDRS) protocol was followed. For a detailed analysis, the DR group was further divided into patients with NPDR and those with PDR based on the ETDRS protocol.

To measure serum lipid levels, patient was kept fasting for 12 hours (No food or drink, except water). 2 ml of blood was collected from a resting patient using an optimal venopuncture technique in a red vacutainer and serum lipid levels namely serum total cholesterol, HDL cholesterol, LDL cholesterol and triglycerides were measured. Normal range of serum TC is <200mg/dl, serum HDL-C is 35-80mg/dl in males and 42-88mg/dl in females, serum LDL-C is <130mg/dl, serum TG is 40-160 mg/dl. Fasting plasma glucose was measured after an overnight fast (8 hours fasting with no food, drink except water). 2 ml of blood was then collected in a grey vacutainer tube containing sodium fluoride as a preservative and fasting blood glucose was measured. Normal levels of fasting blood glucose range between 70-100 mg/dl. Fasting blood glucose level of 126 mg/dl or above is indicative of diabetes mellitus. To measure HbA1C, 2 ml of blood was collected in a lavender vacutainer containing EDTA as a preservative. Normal level of HbA1C is 4.8-5.9%. HbA1C of 6.5% or higher is indicative of diabetes mellitus. The above lab tests were

conducted and results were documented.

All details of participants were kept under strict confidentiality. Data was collected, compiled and tabulated in excel sheet. The categorical variables were presented in number and percentage (%) form and the continuous variables were presented as mean \pm SD and median. Normality of the data was tested by Kolmogorov-Smirnov test. If the normality was rejected, then the non-parametric test was used.

Statistical tests were applied as follows:

1. Quantitative variables were compared using Independent t test/Mann-Whitney Test (when the data sets were not normally distributed) between the two groups.
2. Qualitative variables were compared using Chi-Square test/Fisher's Exact test.

A p Value of <0.05 was considered to be statistically significant.

The data was analysed using Statistical Package for Social Sciences (SPSS) version 21.0.

3. Results

Prevalence of dyslipidemia in our study was 75.50 % (151 patients).

Mean \pm SD of LDL(mg/dL) in diabetic retinopathy was 118.86 ± 40.58 mg/dl and 103.97 ± 36.34 mg/dl in patients without diabetic retinopathy. Thus significant association was seen between serum LDL levels and diabetic retinopathy. ($p=0.006$)

Mean \pm SD of HDL (mg/dL) in patients with diabetic retinopathy was 38.02 ± 6.43 mg/dl and in patients without diabetic retinopathy was 38.34 ± 8.5 mg/dl with no significant association between them. ($p=0.764$)

Mean \pm SD of total cholesterol (mg/dL) in diabetic retinopathy was 177.76 ± 56.45 mg/dl and in patients without diabetic retinopathy was 168.48 ± 37.55 mg/dl and no significant association was seen between them. ($p=0.172$)

Median (IQR) of Triglyceride (mg/dL) in patients with diabetic retinopathy was 135.5 (118-208.5) mg/dl and in patients without diabetic retinopathy was 144.5 (124.5-186)mg/dl with no significant association between them. ($p=0.597$)

Patients living in urban areas had more prevalence of diabetic retinopathy in our study. ($p<0.0001$)

Diabetic retinopathy was more prevalent among clerks and homemakers. ($p=0.004$)

Patients with primary school and high school education had significant association with diabetic retinopathy. ($p=0.007$)

4. Discussion

In present study, out of 200 patients, 151 patients had dyslipidemia and 76 patients had diabetic retinopathy with

dyslipidemia. The prevalence of dyslipidemia was found to be as high as 75.50% (Table 1). High prevalence of dyslipidemia has also been reported by Parikh et al.,⁹ who found the prevalence of dyslipidemia (the parameters used were: triglycerides above 150 mg/dl or LDL-C equal to or more than 100 mg/dl or HDL-C less than 40 mg/dl for males and less than 50 mg/dl among females) in diabetics ($n=788$) to be 97.8% in females and 85.5% in males. In another study by Joshi SR et al., 13.9% subjects were found to have raised total cholesterol, 29.5% of subjects had elevated triglyceride levels, 72.3% of subjects had reduced levels of HDL cholesterol, 11.8% of subjects had raised levels of LDL cholesterol and 79% of subjects had one of the lipid abnormalities.¹⁰

In our study, mean \pm SD of LDL(mg/dL) in patients with diabetic retinopathy was 118.86 ± 40.58 which was significantly higher as compared to patients without diabetic retinopathy (Table 2) indicating a significant association of LDL(mg/dL) with diabetic retinopathy. (p value= 0.006). This can be corroborated with the 1996, ETDRS report no. 22, which evaluated the relationship between serum lipid levels and retinal hard exudates in 2709 patients with diabetic retinopathy. At baseline, patients who were found to have elevated serum total cholesterol or elevated serum low-density lipoprotein cholesterol (LDL-C) levels were more likely to have retinal hard exudate.¹¹

In our study, no significant association was seen in the distribution of total cholesterol (mg/dL), HDL(mg/dL), Triglyceride(mg/dL) with diabetic retinopathy (p value $>.05$)(Table 2)

Similar results were seen in a meta-analysis of 7 studies conducted by Yue Zhou et al., where obvious differences in TG, TC and HDL-C levels between patients with diabetic retinopathy and those without diabetic retinopathy were not found. However, slightly higher LDL-C levels were observed in the DR cases and in their study, Fenofibrate was proven to be beneficial in patients with DR and dyslipidemia.¹² In a study by Idiculla J et al.,¹³ retinal hard exudate formation was found to have a positive statistical correlation with the presence of dyslipidemia ($p=0.02$), increased levels of total cholesterol ($p=0.002$) and also LDL levels ($p=0.001$).

In our study, significant association was found in the distribution of locality with diabetic retinopathy (p value $<.05$). 88% of patients with diabetic retinopathy (Table 3) resided in urban areas. This was significantly higher as compared to patients without diabetic retinopathy (52% resided in urban areas). These findings were similar to a study conducted in Chennai, India, where DR prevalence was observed to be 18% in urban areas.¹⁴ compared to 10.8 % in rural areas.¹⁵ This could be due to differences in the diet in urban areas and patients succumbing to diabetes related complications in rural areas due to difficulty in accessing better healthcare facilities. However, in a study

Table 1: Prevalence of dyslipidemia of study subjects

Dyslipidemia	Frequency	Percentage
No	49	24.50%
Yes	151	75.50%
Total	200	100.00%

Table 2: Association of lipid profile with diabetic retinopathy

Lipid profile	Diabetic retinopathy(n=100)	No diabetic retinopathy(n=100)	Total	P value	Test performed
Total cholesterol (mg/dL)					
Normal	69 (69%)	79 (79%)	148 (74%)	0.107	Chi square test,2.599
Deranged	31 (31%)	21 (21%)	52 (26%)		
Mean ± SD	177.76 ± 56.45	168.48 ± 37.55	173.12 ± 48.05	0.172	t test;1.369
Median(IQR)	169(132-210)	166 (134.25-190)	167 (132-201)		
Range	108-372	91-269	91-372		
HDL(mg/dL)					
Normal	46 (46%)	52 (52%)	98 (49%)	0.396	Chi square test,0.72
Deranged	54 (54%)	48 (48%)	102 (51%)		
Mean ± SD	38.02 ± 6.43	38.34 ± 8.5	38.18 ± 7.52	0.764	t test;0.3
Median(IQR)	38(35-42)	38 (34.75-42)	38(35-42)		
Range	22-53	21-64	21-64		
LDL(mg/dL)					
Normal	59 (59%)	78 (78%)	137 (68.50%)	0.004	Chi square test,8.365
Deranged	41 (41%)	22 (22%)	63 (31.50%)		
Mean ± SD	118.86 ± 40.58	103.97 ± 36.34	111.42 ± 39.14	0.006	t test;2.733
Median(IQR)	118.5(82-141)	100 (76-125.25)	102(80.75-138)		
Range	56-240	49-190	49-240		
Triglyceride(mg/dL)					
Normal	71(71%)	60 (60%)	131 (65.50%)	0.102	Chi square test,2.677
Deranged	29 (29%)	40 (40%)	69 (34.50%)		
Mean ± SD	161.02 ± 81.55	152.15 ± 48.6	156.58 ± 67.1	0.597	Mann Whitney test;4784
Median(IQR)	135.5 (118-208.5)	144.5 (124.5-186)	140 (119.5-189)		
Range	42-431	67-260	42-431		

Table 3: Association of locality with diabetic retinopathy

Locality	Diabetic retinopathy(n=100)	No diabetic retinopathy(n=100)	Total	P value	Test performed
Rural	12 (12%)	48 (48%)	60 (30%)	<.0001	Chi square test,30.857
Urban	88 (88%)	52 (52%)	140 (70%)		
Total	100 (100%)	100 (100%)	200 (100%)		

Table 4: Association of occupation with diabetic retinopathy

Occupation	Diabetic retinopathy(n=100)	No diabetic retinopathy(n=100)	Total	P value	Test performed
Astrologer	0 (0%)	1 (1%)	1 (0.50%)	0.004	Fisher Exact test
Clerk	10 (10%)	4 (4%)	14 (7%)		
Electrician	1 (1%)	0 (0%)	1 (0.50%)		
Farmer	13 (13%)	32 (32%)	45 (22.50%)		
Homemaker	52 (52%)	34 (34%)	86 (43%)		
Plumber	1 (1%)	4 (4%)	5 (2.50%)		
Retired clerk	3 (3%)	0 (0%)	3 (1.50%)		
Retired mechanic	1 (1%)	0 (0%)	1 (0.50%)		
Retired welder	2 (2%)	6 (6%)	8 (4%)		
Shop owner	8 (8%)	9 (9%)	17 (8.50%)		
Teacher	6 (6%)	7 (7%)	13 (6.50%)		
Vendor	3 (3%)	3 (3%)	6 (3%)		
Total	100 (100%)	100 (100%)	200 (100%)		

Table 5: Association of education status with diabetic retinopathy

Education status	Diabetic retinopathy(n=100)	No diabetic retinopathy(n=100)	Total	P value	Test performed
No formal education	20 (20%)	43 (43%)	63 (31.50%)	0.007	Chi square test,14.201
Primary school	16 (16%)	9 (9%)	25 (12.50%)		
Middle school	20 (20%)	20 (20%)	40 (20%)		
High school	28 (28%)	16 (16%)	44 (22%)		
College	16 (16%)	12 (12%)	28 (14%)		
Total	100 (100%)	100 (100%)	200 (100%)		

conducted in China, DR prevalence in urban areas (18.1%) was much lower than in rural areas (29.1–43.1%).^{16,17}

Significant association was seen in the relationship of occupation with the presence of diabetic retinopathy in our study (p value<.05). 10% of patients with DR worked as clerks while 52% were homemakers (Table 4). This was significantly higher as compared to patients without diabetic retinopathy (4%, 34% respectively). 32% of patients without diabetic retinopathy were farmers compared to 13% of patients with diabetic retinopathy.

One prior study found that people working in sales, people engaged in manual work and unemployed individuals or housewives were screened less frequently for DR. However, the frequency of screening for DN was not affected by the occupation of the patient.¹⁸

In our study, significant association was seen between the education status of the patients and the occurrence of diabetic retinopathy (p value<.05). 16% of patients with DR had studied up to primary school while 28% of patients with DR had studied up/to high school(Table 5). This was significantly higher as compared to patients without diabetic retinopathy (9%, 16% respectively). On the other hand, 43% of patients without DR had no formal education which was significantly higher than patients with diabetic retinopathy (20%). Many previous studies^{18–21} have confirmed that lower educational levels reduce frequency of DN and DR screening which could be due to lack of awareness and inability to understand the seriousness and the consequences of the complications of diabetes and due to lack of support and resources.

5. Conclusion

Various systemic risk factors have been studied and linked to diabetic retinopathy. Serum lipid levels seem to play a salient role in the progression of diabetic retinopathy. Significant association was seen in the distribution of LDL cholesterol in patients with diabetic retinopathy.

Clerks and homemakers were more predisposed to diabetic retinopathy. Subjects who were educated up to primary school and high school and subjects living in urban areas had significantly increased rates of diabetic retinopathy.

6. Source of Funding

None.

7. Conflict of Interest

The authors declare that there is no conflict of interest

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