Original Research Article

Correlation between lipid profile and other risk factors with severity of diabetic retinopathy

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Abstract

Context: Diabetic Retinopathy is a major cause of irreversible blindness throughout the world, affecting 21.7% of Indians with Type 2 diabetes and aged more than 40. Whether lipid profile is associated with the development and severity of diabetic retinopathy (DR) is not very clear. There are some studies that have been able to show such an association, while some have not been able to do so. **Aims:** 1. To study the association between serum lipid levels and severity of diabetic retinopathy 2. To study the association between selected socio-demographic, clinical and comorbid parameters and diabetic retinopathy **Settings and design:** Descriptive hospital based case series **Materials and Methods:** 100 consecutive diabetic retinopathy patients attending ophthalmology OPD during this period were included in the study after taking informed consent. Patient details such as age, sex, body mass index (BMI), waist: hip ratio (WHR), blood pressure, addictions, duration of diabetes, details of diabetes medication, and other comorbid conditions were entered in a pre-tested proforma. The diabetic retinopathy was assessed classified according to the Early Treatment Diabetic Retinopathy Study grading system. All the study participants were tested for Fasting Blood Sugar levels (FBSL), Post Prandial Blood Sugar Levels (PPBSL), HBA1C, Lipid profile comprising Serum Total Cholesterol (TC), Triglycerides (TG), High Density (HDL) and Low Density Lipoprotein (LDL). **Statistical Analysis:** using SPSS software version 22. Descriptive analysis using frequencies and percentages. Chi-square test, Unpaired t test and One way ANOVA test. **Results:** Serum cholesterol (P = 0.000), serum triglycerides (P = 0.001) and LDL cholesterol (P = 0.000) had positive correlation with severity of DR, HDL had a negative correlation with DR (P=0.000). BMI (P =0.014), WHR (P=0.025), FBSL (P=0.009) and PPBSL (P=0.000) had a statistically significant correlation with DR. HBA1C, Blood Pressure were not significantly associated with severity of DR. Increasing age (P=0.45), hypertension (P=0.10), and smoking (P=0.83) was not significantly associated with DR severity. **Conclusion:** There is a significant association between higher serum lipid levels and severity of Diabetic Retinopathy; and a lower level of serum lipids may be protective against diabetic retinopathy, maculopathy and loss of vision.

Key Words: Lipid profile, risk factors, diabetic retinopathy.

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INTRODUCTION

Diabetic Retinopathy is a major cause of irreversible blindness throughout the world. It affects an estimated 21.7% of Indians with Type 2 diabetes and aged more than 40.[1] The determinants of development and severity of diabetic retinopathy include age of presentation, glycaemic control, pregnancy, associated comorbidities such as chronic kidney dysfunction, hypertension and smoking. Whether lipid profile is associated with the development and severity of diabetic retinopathy is not very clear. There are many studies done in the past in India, and some of these studies have been able to establish an association between the two,[2,3] while some have not been able to do so.[4,5] The main mechanism

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behind the association between the two is that high serum lipids give rise to endothelial dysfunction and decreased bioavailability of Nitric oxide, which leads to endothelial cell damage and leaky blood vessels resulting in exudation and thus diabetic retinopathy.[6,7]The present study was conducted to study the association between lipid profile and severity of diabetic retinopathy.

AIMS AND OBJECTIVE

1. To study the association between serum lipid levels and severity of diabetic retinopathy
2. To study the association between selected socio-demographic, clinical and comorbid parameters and diabetic retinopathy

MATERIALS AND METHODS

This descriptive hospital based case series was conducted in the outpatient Department of Ophthalmology at Goa Medical College, Bambolim, during July to August 2018 after obtaining approval from the Institutional Ethics Committee of the Goa Medical College. 100 consecutive diabetic retinopathy patients attending ophthalmology OPD during this period were included in the study after taking informed consent. Patients with severe chronic kidney disease, severe anaemia, glaucoma or prior retinal surgery were excluded from the study. Patient details such as age, sex, body mass index (BMI), waist:hip ratio(WHR),blood pressure, addictions, duration of diabetes, details of diabetes medication, and other comorbid conditions wereduly obtained and entered in a pre-tested proforma. The Diabetic Retinopathy status was assessed using direct and indirect ophthalmoscopy and slit-lamp biomicroscopy and classified according to the Early Treatment Diabetic Retinopathy Study (ETDRS) grading system as Non Proliferative Diabetic Retinopathy(NPDR), Proliferative Diabetic Retinopathy(PDR) and Advanced Diabetic Eye Disease (ADED). NPDR was further graded as mild NPDR, moderate NPDR, severe and very severe NPDR. Patients were also examined for presence of Diabetic Macular Edema (DME), which was confirmed using Optical Coherence Tomography (OCT). All the study participants were tested for Fasting Blood Sugar levels (FBSL), Post Prandial Blood Sugar Levels (PPBSL), HBA1C, Lipid profile comprising Serum Total Cholesterol (TC), Triglycerides (TG), High Density (HDL) and Low Density Lipoprotein(LDL).

Data was entered in Microsoft excel and analysed using Statistical Package for Social Sciences software packages (SPSS) software version 22. Descriptive analysis used to express the results as frequencies and percentages. Chi-square test, Unpaired t test and One way ANOVA test were utilised for determining statistical significance and P value <0.05 was considered statistically significant.

RESULTS

Table 1: Socio-demographic profile of DR patients

Variables	Patients with DR Number (%)
Age (years)	
≤20	1(1)
21-40	18(18)
41-60	57(57)
61-80	24(24)
Sex	
Males	61(61)
Females	39(39)
Residence	
Rural	33(33)
Urban	67(67)
Occupation	
Unskilled	10(10)
Semi-skilled	14(14)
Skilled	4(4)
Clerical, shop owner, etc	12(12)
Semi-professional	4(4)
Professional	14(14)
Others*	42(42)
Education	
Illiterate	44(44)
Primary	10(10)
Upper primary	5(5)

Secondary	6(6)
Senior secondary	5(5)
Graduate	30(30)
Socioeconomic status(Modified B.G Prasad classification 2018)	
I	33(33)
II	30(30)
III	21(21)
IV	11(11)
V	5(5)

*Others – Retired, unemployed, housewife, student

Table 2: Association of lipid profile with severity of diabetic retinopathy

Lipid parameter	Mild NPDR	Moderate NPDR	Severe NPDR	Very severe NPDR	PDR	ADED	F value	P value*
	(Mean ± SD)							
Total cholesterol	194.46 ± 27.97	210.15 ± 25.40	225.25 ± 30.72	240.88 ± 16.30	256.50 ± 37.68	244.75 ± 20.29	11.908	0.000
Triglycerides	173.85 ± 62.05	188.30 ± 44.96	237.75 ± 97.78	272.75 ± 90.02	220.00 ± 69.28	227.58 ± 70.69	4.522	0.001
LDL	131.76 ± 20.47	143.44 ± 20.72	160.25 ± 27.45	172.13 ± 23.22	145.00 ± 33.16	168.55 ± 32.42	7.726	0.000
HDL	44.05 ± 6.08	40.81 ± 6.36	37.50 ± 4.38	38.88 ± 3.44	39.25 ± 2.217	35.83 ± 5.44	5.163	0.000

*one way ANOVA test is used to study the difference in means (P value <0.05 is considered significant)

Table 3: Association of lipid profile of diabetic retinopathy patients with and without maculopathy

Lipid parameters	DR patients without maculopathy (n = 71)	DR patients with maculopathy (n = 29)	t value	P value*
Total cholesterol	206.58 ± 31.73	230.07 ± 29.78	3.418	0.001
Triglycerides	181.76 ± 56.47	241.45 ± 84.32	4.126	0.000
LDL	138.59 ± 25.25	160.93 ± 25.12	4.013	0.000
HDL	42.18 ± 6.51	38.31 ± 4.83	-2.888	0.005

*Unpaired t test is used to study difference in means (p value < 0.05 is considered significant)

Table 4: Association of selectedclinico-biochemical parameters with severity of diabetic retinopathy

Study Variable	Mild NPDR	Moderate NPDR	Severe NPDR	Very severe NPDR	PDR	ADED	F value	P value*
	(Mean ± SD)							
HbA1c (%)	8.30 ±1.79	11 ± 11.28	8.76 ± 1.23	8.46 ± 1.06	10.05 ± 1.11	10.13 ± 9.46	1.576	0.174
BMI (kg/m$^{2)}$	21.50 ± 3.36	22.70 ± 3.37	24.07 ± 4.72	24.51 ± 4.83	25.32 ± 4.69	25.26 ± 3.39	3.022	0.014
WHR (cm)	0.803 ± 0.073	0.834 ± 0.082	0.871 ± 0.075	0.84 ± 0.07	0.847 ± 0.125	0.886 ± 0.074	2.704	0.025
SBP (mmHg)	124.8 ± 13.89	126.81 ± 14.7	124 ± 12.32	129 ± 8.88	140 ± 2.82	137.67 ± 14.03	2.505	0.326
DBP (mmHg)	79.76 ± 4.29	81.33 ± 4.67	81.5 ± 4.62	79.75 ± 4.2	83 ± 4.76	83.33 ± 4.37	1.628	0.160
FBSL (mg/dL)	135.05 ± 30.87	143.78 ± 26.54	152 ± 28.10	143.5 ± 25.46	166.5 ± 37	176 ± 54.38	3.254	0.009
PPBSL (mg/dL)	169.8 ± 45.54	187.7 ± 40.97	224.88 ± 86.62	187.38 ± 24.55	259.25 ± 95.35	259.17 ± 75.22	6.957	0.000

*One way ANOVA test is used to study difference in means (P value <0.05 is considered significant)

Table 5: Association of selected socio-demographic, clinical and comorbid conditions with severity of diabetic retinopathy

Variables	Mild NPDR	Moderate NPDR	Severe NPDR	Very severe NPDR	PDR	ADED	Chi square value	P value
			Number (%)					
			Age (years)					
≤20	1(2.4)	0(0)	0(0)	0(0)	0(0)	0(0)	15.01	0.45
21-40	9(22)	2(7.4)	3(37.5)	1(12.5)	0(0)	3(25)		
41-60	19(46.3)	21(77.8)	2(25)	4(50)	3(75)	8(66.7)		
61-80	12(29.3)	4(14.8)	3(37.5)	3(37.5)	1(25)	1(8.3)		
			Sex					
Males	26(63.4)	14(51.9)	4(50)	7(87.5)	3(75)	7(58.3)	4.18	0.52
Females	15(36.6)	13(48.1)	4(50)	1(12.5)	1(25)	5(41.7)		
			Duration of DM (years)					
≤10	26(63.4)	21(77.8)	7(87.5)	4(50)	2(50)	8(60.7)	7.39	0.68
11-20	14(34.1)	5(18.5)	1(12.5)	4(50)	2(50)	3(25)		
>20	1(2.4)	1(3.7)	0(0)	0(0)	0(0)	1(8.3)		
			Hypertension					
Yes	13(31.7)	10(37)	3(37.5)	3(37.5)	4(100)	7(58.3)	8.99	0.10
			Current Cigarette smoking					
Yes	9(22)	3(11.1)	1(12.5)	2(25)	1(25)	3(25)	2.10	0.83

*Chi square test is used to study the difference in proportion (P value <0.05 is considered significant)

Out of 100 diabetic retinopathy patients enrolled in our study 41% were detected to have mild NPDR, 27% had moderate NPDR whereas 8% had severe and very severe NPDR respectively. PDR and ADED was seen in 4% and 12% respectively. Maculopathy was seen in 29% of the participants. Table 1 presents the socio-demographic profile of the study participants. The mean age of the study participants was 51.9± 12 years. The mean duration of Diabetes was 9.92±. 5.23 years. It was seen that mean BMI and WHR were 22.88± 3.85 and 0.83±0.083 respectively. It was noted that 27% participants were known case of dyslipidaemia and43% of the DR patients had associated comorbid conditions like Hypertension (40%), Ischaemic Heart Disease (2%) and Chronic Obstructive Pulmonary Disease (1%). In the present study it was observed that Serum cholesterol (P = 0.000), serum triglycerides (P = 0.001) and LDL cholesterol (P = 0.000) had positive correlation with severity of DR, however HDL was associated with reduced likelihood of having severe diabetic retinopathy levels (P=0.000), as shown in the table 2. The association of the lipid sub-fractions in DR subjects with and without diabetic macular edema (DME) was also studied and it was observed that Serum total cholesterol (P = 0.001), serum triglycerides (P=0.000) and serum LDL cholesterol (P = 0.000) concentrations were significantly higher in the retinopathy subjects with DME compared with those without DME. However it was seen that Serum HDL (P=0.005) had negative correlation with DR severity. (Table 3) Table 4 showed statistically significant association of BMI (P =0.014), WHR (P=0.025), FBSL (P=0.009) and PPBSL (P=0.000) with severity of DR. However, HBA1C, Systolic and Diastolic Blood Pressure (SBP, DPB) were not significantly associated with the severity of DR. Table 5 revealed that increasing age (P=0.45), coexisting hypertension (P=0.10), and current cigarette smoking (P=0.83) was not significantly associated with DR severity.

DISCUSSION

The association between severity of diabetic retinopathy or Maculopathy with altered lipid profile has been debated for a long time. There have been many reports from previous literature, some of which suggest and some contradict such an association. In our study we have found a positive correlation between the severity of diabetic retinopathy and Serum cholesterol (P = 0.000), serum triglycerides (P = 0.001) and LDL cholesterol (P = 0.000). However Serum HDL was found to have a negative correlation with the severity of diabetic retinopathy (P=0.000). The association of the lipid sub-fractions in DR subjects with and without Diabetic

Macular Edema (DME) was also studied and it was observed that Serum total cholesterol (P = 0.001), serum triglycerides (P=0.000), serum LDL- cholesterol (P = 0.000) concentrations were significantly higher in the retinopathy subjects with DME compared with those without DME. However it was seen that Serum HDL (P=0.005) had negative correlation with DR severity. Similar studies done independently by Rema M *et al*[2] in Chennai and by Idiculla J *et al*[3] showed that an altered lipid profile was associated with the development and severity of diabetic retinopathy and maculopathy. However a study by Ozer PA *et al*[4] and another by Ebru NC *et al*[5] showed no such association. There were several other studies done outside India e.g. in the United States by Wong TY *et al*,[8] among the Australian Population by Tapp RJ *et al*,[9] and in Denmark by Hove MN *et al*,[10] which showed no association between lipid profile and severity of diabetic retinopathy and maculopathy. It was striking to note that in a study done by Wong TY *et al*[11] in the population of Singapore, it was reported that high Cholesterol levels prevented the development of Diabetic Retinopathy. A report was published by ETDRS (Early Treatment of Diabetes Retinopathy Study) in the year 1996,[12] according to which patients who had a higher level of total Cholesterol and LDL at presentation, were more prone to develop diabeticretinopathy. The main mechanism behind the association between raised serum lipids and the development of diabetic retinopathy is that; hyperglycaemia causes diabetic retinopathy and Maculopathy by giving rise to endothelial dysfunction and causes the blood vessels to become leaky, leading to exudation of serum lipids.[13] Lipid lowering agents are important in the management of diabetic retinopathy and also decrease theneed for laser therapy in the patients.[14] In our study we found a statistically significant association between FBSL (P=0.009) and PPBSL (P=0.000) with severity of DR. However, HBA1C, SBP, DBP were not significantly associated with the severity of DR. A similar study conducted by Pradeepa R, Anitha B *et al*[15] in South Indian population with Type 2 Diabetes showed similar findings. The Diabetes Control and Complication trial group (DCCT)[16] in 1993 reported a reduction in the severity of diabetic retinopathy with control of HbA1C. A statistically significant association was noted between BMI (P =0.014) and WHR (P=0.025) with severity of diabetic retinopathy. BMI is a very commonly used parameter to assess the fitness of an individual; and is estimated by taking a ratio of weight (in Kilograms) and height (in centimetres).[17] It has been reported that individuals with high BMI have a higher level of C-peptide levels,[16] which increases the risk of diabetic retinopathy.[19] It is also observed that individuals with a higher BMI often have co-existing hypertension and dyslipidaemia, both of which are risk factors for Diabetic Retinopathy.[20]Higher BMI is also associated with a higher level of vascular endothelial growth factors, which are involved in the development of diabetic retinopathy.[21] The positive correlation between higher WHR and severity of diabetic retinopathy is explained by the fact that there is a higher level of inflammatory mediators and insulin resistance in those individuals with high waist hip ratio and abdominal obesity.[22,23] In our study we did not find a statistically significant correlation between increasing age, coexisting hypertension, and current cigarette smoking with the severity of diabetic retinopathy and maculopathy.

CONCLUSION

From our study findings we conclude that there is a significant association between higher serum lipid levels and severity of diabetic retinopathy; and a lower level of serum lipids may be protective against diabetic retinopathy, maculopathy and loss of vision.

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