# Correlation of Diabetic Retinopathy with Serum Lipids

Smita Dileep Javadekar[1*], Sindal Deokrishna[2], Karambelkar V. H.[3], Pooja Agrawal[4]

{[1]Associate Professor, [2]Professor and H.O.D., [3]Professor, [4]Resident}

Dept of Ophthalmology, KIMSDU, Malkapur, Karad, Maharashtra, INDIA.

[*]Corresponding Address:

smita10157@yahoo.co.in

***Research Article***

***Abstract:*** **Aim:** To find out the Correlation of Diabetic retinopathy with serum lipids in Type 2 diabetic subjects. **Settings and Design:** Cross sectional nonrandomized study. **Materials and Methods:** 311 patients with more than 5 years of Type 2 diabetes were assessed for presence and severity of retinopathy and were co related with age, sex, duration of DM and serum lipids. Diabetic Retinopathy was diagnosed by fundus examination and classified according to the Early Treatment Diabetic Retinopathy Study (ETDRS) grading system. **Results:** Overall 76.5% (238) had DR and 23.5% (73) had no Diabetic Retinopathy. The mean serum cholesterol ($P$<0.05), serum triglycerides ($P$ <0.05) and non-high-density lipoprotein (HDL)-cholesterol ($P$ <0.05) concentrations were higher in subjects with Diabetic Retinopathy compared with those without Diabetic Retinopathy. Significant association of triglycerides ($P$< 0.05) and LDL-cholesterol with clinically significant macular edema (CSME) ($P$< 0.05). **Conclusion:** Significant association is found of dyslipidaemia with Diabetic Retinopathy and CSME.

***Key words:*** Diabetic retinopathy, CSME, serum lipids, dyslipidaemia.

## Introduction

Diabetic retinopathy is a leading cause of irreversible blindbess. Diabetes is known to be very high in Indian subcontinent with distinct features like early onset, genetic predisposition (1, 2, 3, 4). The risk factors for DR are degree of glycaemic and blood pressure control, duration of diabetes, presence of nephropathy and raised serum lipids. Elevated lipid concentrations may be an additional risk factor for diabetic macular oedema, particularly the deposition of hard exudates in the retina.(5,6) Data from the Early Treatment Diabetic Retinopathy Study (ETDRS) demonstrate that elevated levels of serum lipids are associated with both the development and the severity of retinal hard exudates in patients with diabetic retinopathy. These waxy yellow deposits, frequently seen at the border of edematous retina, develop when the endothelial cells in the retinal capillaries lose their tight junctions and "leak" lipoprotein, crystalloid, and water into the extracellular space of the retina. When hard exudates accumulate in the center of the macula, they can lead to a decrease in visual acuity(7)

### Need for study

Diabetic retinopathy remains a major cause of visual impairment among working population & is a leading cause of visual loss in older patients (8) thus it has tremendous social & economic impact. There is economical burden on family as well as health care systems. We can control lipid profile and prevent visual impairment or visual loss if there is significant correlation of Diabetic retinopathy & dyslipidaemia.

### Aims

To study the association of serum lipids with diabetic retinopathy (DR) in Type 2 diabetic subjects

To evaluate relationship of various components of serum lipids with severity of DR & formation of clinically significant macular edema (CSME)

## Materials & methods

### Source of data

Patients with more than five years of diagnosed Diabetes Type 2 attending Ophthalmology OPD at Krishna Hospital, Malkapur, Karad Maharashtra.

### Study design

Cross sectional nonrandomized study.

### Duration

One & half year (Oct.2010 to Feb. 2012)

### Sample size

311 patients with more than five years of diagnosed Diabetes Type 2.

### Inclusion Criteria

Patients with more than five years of diagnosed Diabetes Type 2.

### Exclusion criteria

Patients giving H/O less than 5 years of diagnosed Diabetes

Patients giving H/O ocular surgery < 6months

Pregnancy

Hypertension

Active infection

Co existing ocular diseases like uveitis, opaque hazy media

Retinal vascular diseases due to other causes than due to Diabetic Retinopathy
Vitreoretinal degenerations & dystrophies
High Myopia
Non compliant patients

## Methodology

Patients having more than five years of diagnosed Diabetes Type 2 were enrolled into study after taking informed & written consent.
All preliminary Ophthalmological examination along with slit lamp examination was carried according to proforma.
Detailed fundoscopy was done with indirect ophthalmoscope with 20D lens and slit lamp biomicroscopy with 78D lens.
Fundus photographs were taken in patients with any grade of Diabetic Retinopathy by Topcon fundus camera
Patients were grouped as Group A without retinopathy & Group B with retinopathy.
Group B was further grouped according to modified Early Treatment of Diabetic Retinopathy Study (ETDRS) protocol as follows
Group 1 patient with mild nonproliferative diabetic retinopathy (NPDR)
Group 2 moderate non proliferative diabetic retinopathy (NPDR)
Group 3 patients with severe NPDR
Group 4 Patients with proliferative diabetic retinopathy(PDR)
Presence of hard exudates was noted
Clinically significant macular edema (CSME)using slitlamp biomicroscopy with 78D lens was noted & severity was recorded as
1 Mild CSME –Retinal thickening at or near macula
2 Moderate CSME – Hard exudates with retinal thickening at or near macula
3 Severe CSME - Zone or zones of retinal thickening 1 disc area in size, at least part of which is within one disc diameter of center of macula
Preliminary investigations (CBC, BSL fasting & post prandial, Routine urine, Glycosylated Hb, ECG) were done in each & every patient
Serum lipid measurements using fasting samples were done. Analysis of serum cholesterol, serum triglycerides and cholesterol components like high-density lipoprotein (HDL)-cholesterol
LDL-cholesterol were calculated
Serum cholesterol > 200mg/dl, HDL< 40mg/dl, LDL > 100mg/dl, Triglycerides > 150mg/dl were considered as dyslipidaemia (Harrison's Principles of Internal Medicine 17th edition)

**Statistical Analysis**

P value less than 0.05 was considered statistically significant.
Various univariate analysis were done to evaluate effect of factors such as age, sex, duration of diabetes on degree of retinopathy & CSME

## Results

From Oct.2010 to Feb. 2012 total 311patients with more than five years of diagnosed Diabetes Type 2 attending Ophthalmology OPD at Krishna Hospital, Malkapur, Karad, Maharashtra. were analysed and data obtained is as follows
Total 311 patients were evaluated out of which 238 (76.52%) had diabetic retinopathy & 73 (23.48%) were not having Diabetic retinopathy
129 patients had various grades of CSME
Age – 20 to 80 yrs
Males – 207, Females – 104
Duration of diabetes – 5 to 25 years

**Table 1:** Relationship between Age & Diabetic Retinopathy

| Age | Group A | Group B | | | | Total |
|---|---|---|---|---|---|---|
| | | Group1 | Group 2 | Group 3 | Group4 | |
| **20 - 40** | 1(1%) | 6(8%) | 4(4%) | 1(2%) | 1(4%) | **13** |
| **41 - 60** | 22(44%) | 33(42%) | 45(46%) | 18(46%) | 6(26%) | **134** |
| **>60** | 40(55%) | 39(50%) | 49(50%) | 20(52%) | 16(70%) | **164** |
| **Total** | **73** | **78** | **98** | **39** | **23** | **311** |

With increasing age there is significantly increased prevalence of Diabetic Retinopathy $P < 0.05$

**Table 2:** Relationship between age & CSME

| Age | Absent | Mild | Moderate | Severe | Total |
|---|---|---|---|---|---|
| **20 - 40** | 9(5%) | 2(3%) | 2(4%) | 0(0%) | **13** |
| **41 - 60** | 82(45%) | 20(31%) | 25(54%) | 7(39%) | **134** |
| **>60** | 91(50%) | 42(66%) | 20(42%) | 11(61%) | **164** |
| **Total** | **182** | **64** | **47** | **18** | **311** |

Prevalence of CSME significantly increases with age $P < 0.05$

**Table 3**: Relationship between sex & Diabetic Retinopathy

| Sex | Group A | Group B | | | | Total |
|---|---|---|---|---|---|---|
| | | Group1 | Group 2 | Group 3 | Group4 | |
| **Male** | 51(70%) | 49(63%) | 65(67%) | 28(72%) | 14(74%) | **207** |
| **Female** | 22(30%) | 29(37%) | 33(33%) | 11(28%) | 9(26%) | **104** |
| **Total** | **73** | **78** | **98** | **39** | **23** | **311** |

There was no significant relationship between sex & various stages of Diabetic Retinopathy ( P > 0.05)

**Table 4:** Relationship between sex & CSME

| Sex | Absent | Mild | Moderate | Severe | Total |
|---|---|---|---|---|---|
| **Male** | 117(64%) | 48(75%) | 30(64%) | 12(67%) | **207** |
| **Female** | 65(36%) | 16(25%) | 17(36%) | 6(33%) | **104** |
| **Total** | **182** | **64** | **47** | **18** | **311** |

There was no significant relationship between sex & various stages of CSME ( P > 0.05)

**Table 5**: Relationship between duration of Diabetes Mellitus(DM) & Diabetic Retinopathy

| Duration of DM | Group A | Group B | | | | Total |
|---|---|---|---|---|---|---|
| | | Group1 | Group 2 | Group 3 | Group4 | |
| **5 - 10 yrs** | 49(47%) | 36(3%) | 24(22%) | 7(5%) | 8(6%) | **104** |
| **11 - 25 yrs** | 24(12%) | 42(20%) | 74(35%) | 32(15%) | 15(7%) | **207** |
| **Total** | **73** | **78** | **98** | **39** | **23** | **311** |

As duration of Diabetes increases prevalence of Retinopathy also significantly increases (P < 0.05)

**Table 6**: Relationship between duration of Diabetes Mellitus(DM) & CSME

| Duration of DM | Absent | Mild | Moderate | Severe | Total |
|---|---|---|---|---|---|
| **5 - 10 yrs** | 74(71%) | 14(15%) | 12(11%) | 4(3%) | **104** |
| **11 - 25 yrs** | 108(52%) | 50(24% | 35(17%) | 14(7%) | **207** |
| **Total** | **182** | **64** | **47** | **18** | **311** |

As duration of Diabetes increases prevalence of CSME also significantly increases (P < 0.05)

**Table 7**: Relationship between Diabetic retinopathy & Dyslipidaemia

| Dyslipidaemia | Group A | Group B | | | | Total |
|---|---|---|---|---|---|---|
| | | Group1 | Group 2 | Group 3 | Group4 | |
| **Present** | 24(33%) | 38(49%) | 45(46%) | 23(59%) | 15(65%) | **145** |
| **Absent** | 49(67%) | 40(51%) | 53(54%) | 16(41%) | 8(35%) | **166** |
| **Total** | **73** | **78** | **98** | **39** | **23** | **311** |

145 (49.51%) patients had dyslipidaemia out of which 121(83.44%) had Diabetic retinopathy & 83(57.24%) had CSME independent of levels of Hb1Ac. 96 (66.20%) had reduced Best corrected visual acuity (BCVA)

**Table 8**: Relationship between CSME & Dyslipidaemia

| Dyslipidaemia | Absent | Mild | Moderate | Severe | Total |
|---|---|---|---|---|---|
| **Present** | 59(32%) | 45(70%) | 30(64%) | 11(61%) | **145** |
| **Absent** | 123(68%) | 19(30%) | 17(36%) | 7(39%) | **166** |
| **Total** | **182** | **64** | **47** | **18** | **311** |

Prevalence of Diabetic Retinopathy & CSME was significantly higher in Dyslipidaemia patients (P < 0.05)

**Table 9**: Relationship between Diabetic retinopathy, CSME & Dyslipidaemia

| Control of DM | No. of pts with Retinopathy | No. of pts with CSME |
|---|---|---|
| Hb1Ac>6% | 65 | 48 |
| Hb1Ac</=6% | 56 | 35 |
| Total | 121 | 83 |
| P Value | >0.05 | >0.05 |

Dyslipidaemia was independent of levels of Hb1Ac

**Table 10:** Distribution of various lipid components among Diabetic retinopathy patients

| Deranged Lipid component | No. of patients |
|---|---|
| Total cholesterol | 96 |
| HDL | 88 |
| LDL | 64 |
| VLDL | 74 |
| Triglycerides | 134 |

**Table 11:** Distribution of various lipid components among CSME patients

| Deranged Lipid component | No. of patients |
|---|---|
| Total cholesterol | 47 |
| HDL | 42 |
| LDL | 56 |
| VLDL | 34 |
| Triglycerides | 68 |

Triglycerides & HDL were more deranged in Diabetic Retinopathy, while Triglycerides & LDL were more deranged in CSME patients.

## Discussion

Various studies have shown an association of Dyslipidimia with macrovascular complications of diabetes (e.g. coronary artery disease), but few have studied the association of serum lipids with microvascular complications such as DR and the available results are conflicting (9–21). Association of LDL-cholesterol in subjects with DR was first shown by Dornan *et al*. (9). Severity of hard exudates in macula with unadjusted serum cholesterol was observed in Wisconsin Epidemiology Study of Diabetic Retinopathy (WESDR), Klein *et al*. (10)/ In our study we have found significant association of dyslipidaemia & Diabetic retinopathy (83.44%) as well as CSME(57.24%). Similar results were seen in ETDRS and WESDR studies ( 10,12). In comparison to other components Triglycerides & HDL were more deranged in Diabetic Retinopathy, while Triglycerides & LDL were more deranged in CSME patients This also correlates with ETDRS and WESDR studies (10,12). Elevated total cholesterol also showed significant reduced BCVA (66.20%) ( $P < 0.05$). According to above observations it is seen that Diabetic retinopathy & CSME both have higher prevalence in productive age group. At this age children & parents are dependent on him economically. If he is visually handicapped at this age there is economical as well as social burden on family, society & healthcare systems. It is also observed that as duration of Diabetes increases chances to have Diabetic retinopathy & CSME also increase. So we have time in our hands to convince these patients regarding control of serum Lipids. All clinicians should be aware of Retinal complications of Diabetes.

## Conclusion

Deranged values of total cholesterol are an independent risk factor for the Diabetic retinopathy & CSME. Triglycerides & HDL are deranged in Diabetic Retinopathy, while Triglycerides & LDL are more deranged in CSME patients. Along with regular blood sugar check up all Diabetics should get their serum lipids checked up regularly & control them if deranged. Preservation of good vision may be a motivating factor for lowering serum lipids.

## References


1. Ramchandran A, Jali MV, Mohan V, Snehlata C, Vishvanathan M. Higher prevalence of diabetes in an urban population in south India BMJ 297, 587- 90, 1988.
2. Mohan V, Ramchandran A, Snehlata C, Mohan R, Bharni G, Vishvanathan M. High prevalence of maturity onset diabetes of young(MODY) among Indians Diabetes care 8, 371-4, 1985.
3. Mohan V, Sharp PS, Aber V, Mather HM, Kohner E M. Family histories of Asian Indianad European NIDDM patients Pract Diabetes(U.K.)3, 254- 6, 1986.
4. Vishvanathan M. Mohan V, Snehlata C, Ramchandran A High prevalence of Type 2 diabetes (NIDDM) among offspring of conjugal type 2 diabetic patients in south India. Diabetologica 28, 907-10, 1985.
5. Porta M, Bandello F. Diabetic retinopathy—a clinical update. Diabetologia, 45: 1617–1634, 2002.
6. Aiello LP, Cahill MT, Wong JS. Systemic considerations in the management of diabetic retinopathy. Am J Ophthalmol., 132:760–776, 2001.
7. Ferris FL 111, Patz A: Macular edema: a complication of diabetic retinopathy. Surv Ophthalmol 28:452-461,1984.
8. Marshall, S.M., & Flyvbjerg, A. Prevention & early detection of vascular complications of diabetes BMJ 333, 475- 480, 2006.
9. Dornan TL, Carter RD, Bron AJ, Turner RC, Mann JI. Low densitylipoprotein cholesterol: an association with the severity of diabeticretinopathy. Diabetologia., 22: 167–170, 1982.
10. Klein BE, Klein R, Moss SE. Is serum cholesterol associated with progression of diabetic retinopathy or macular edema in persons with younger-onset diabetes of long duration? Am J Ophthalmol; 128: 652–654, 1999.
11. Ferris FL 3rd, Chew EY, Hoogwerf BJ. Serum lipids and diabetic retinopathy. Diabetes Care; 19: 1291–1293, 1996.
12. Chew EY, Klein ML, Ferris FL 3rd, Remaley NA, Murphy RP, Chantry K et al. Association of elevated serum lipid levels with retinal hard exudate in diabetic retinopathy. Early Treatment Diabetic Retinopathy Study (ETDRS) Report 22. Arch Ophthalmol; 114: 1079–1084, 1996.
13. Rema M, Mohan V, Susheela L, Ramachandran A, Viswanathan M. Increased LDL cholesterol in non insulin dependent diabetes with maculopathy. Acta Diabetologica Latina; 21: 85–89, 1984.
14. el Haddad OA, Saad MK. Prevalence and risk factors for diabetic retinopathy among Omani diabetics. Br J Ophthalmol; 82:901–906, 1998.
15. Mouton DP, Gill AJ. Prevalence of diabetic retinopathy and evaluation of risk factors. A review of 1005 diabetic clinic patients. S Afr Med J.; 74: 399–402, 1998.

16. Marshall G, Garg SK, Jackson WE, Holmes DL, Chase HP. Factor influencing the onset and progression of diabetic retinopathy in subjects with insulin dependent diabetes mellitus. Ophthalmolog; 100: 1133–1139, 1993.
17. Sinav S, Onelge MA, Onelge S, Sinav B. Plasma lipids and lipoproteins in retinopathy of type I (insulin-dependent) diabetic patients. Ann Ophthalmol; 25: 64–66, 1993.
18. Kordonouri O, Danne T, Hopfenmuller W, Enders I, Hovener G, Weber B. Lipid profiles and blood pressure: are they risk factors for the development of early background retinopathy and incipient nephropathy in children with insulin-dependent diabetes mellitus? Acta Paediatr; 85: 43–48, 1996.
19. Weber B, Burger W, Hartmann R, Hovener G, Malchus R, Oberdisse U. Risk factors for the development of retinopathy in children and adolescents with Type 1 (insulin dependent) diabetes mellitus. Diabetologia; 29: 23–29, 1986.
20. Sjolie AK, Stephenson J, Aldington S, Kohner E, Janka H, Stevens L et al. Retinopathy and vision loss in insulin dependent diabetes in Europe. The EURODIAB IDDM complication Study. Ophthalmology; 104:252–260, 1997.
21. Larsson LI, Alm A, Lithner F, Dahlen G, Bergstrom R. The association of hyperlipidemia with retinopathy in diabetic patients aged 15–50 years in the county of Umea. Acta Ophthalmol Scand; 77: 585–591, 1999.