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A Cross-Sectional Study of Association between Severity Of Diabetic Retinopathy With Hyperlipidemia

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Abstract
Purpose of the study*-The current study is undertaken to determine the association of serum lipid profile with diabetic retinopathy and its severity. The conflicting reports in the literature regarding the association between serum lipid levels and diabetic retinopathy and the paucity of studies relative to the existing case load warrants this study.****Methods****- The study comprised a total of 200 patients with type II diabetes mellitus (100 With diabetic retinopathy and 100 without diabetic retinopathy) and 100 age and sex matched control, examined at the Department of Ophthalmology, government medical college , Kota,over a period of one year.Ophthalmoscopic and biomicroscopic examination of ocular fundus wasdone.GradingoftheseverityofretinopathywasdoneaccordingtotheETDRSclassification.SerumlipidprofileandBloodsugarestimationwereestimatedbyenzymaticmethod.*
Results*- The mean value of total cholesterol was higher in both group 1 and group 2 with value being higher in group1 (237.33mg/dl) as compared to group 2 (215.30mg/dl). Triglyceride levels also followed the similar trend with group 1 having mean value of 220.34mg/dl and group 2 having 179.94 mg/dl. Differences of both total cholesterol and Triglycerides values had statistical significance (p <0.0001) between all groups.* ***Conclusion****- The present study demonstrated significant correlation between diabetic retinopathy and hpercholesterolemia. Increased cholesterol level was significantly associated with the occurrence of all grades of retinopathy especially severe NPDR, very severe NPDR and PDR.*
Keywords*- diabetic retinopathy, serum cholesterol and triglycerides*

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I. Introduction

Diabetic retinopathy (DR) is a major complication of diabetes mellitus (DM), which remains a leading cause of visual loss in working-age populations. The diagnosis of DR is made by clinical manifestations of vascular abnormalities in the retina. Clinically, DR is divided into two stages: non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR). Diabetic retinopathy is frequently accompanied by lipid exudation[1]. Elevated serum lipid levels are associated with an increased risk of retinal hard exudate in persons with diabetic retinopathy. Although retinal hard exudate usually accompanies diabetic macular edema, increasing amounts of exudate appear to be independently associated with an increased risk of visual impairment[2].

The association between serum lipid levels and diabetic retinopathy has been investigated in few studies. Some studies show a positive relationship between serum cholesterol and low-density lipoprotein levels and retinal hard exudation. Other studies show serum triglyceride levels as being important in the progression of retinopathy. Certain other studies show no relationship between serum lipid levels and diabetic retinopathy.The current study is undertaken to determine the association of serum lipid profile with diabetic retinopathy and its severity.

II. Material and Methods

Study Subjects were established cases with age of more than 40years, having diabetes more than 5years, Physically & mentally fit giving informed consent. They were divided into

1. **Group I** - Diabetic patients with different stages of retinopathy includes 100 patients
2. **Group II** - Diabetic patients without retinopathy includes 100 patients
3. **Group 3 -** Non diabetic 100 Control subjects were selected by age and sex matching for group 3.

Criteria for exclusion –

1. Patients with significant hazy media which impairs visualization of the fundus.
2. Patients with pupillary abnormalities which prevent adequate dilatation for fundus visualisation.
3. Patients on hypolipidemic drugs.

4. Patients who have been treated earlier with either LASER or Intravitreal anti- VEGF injections
5. History of severe ocular trauma, intraocular/ refractive surgery or any ocular or neurological disease.
6. Any pathologic ocular condition that could cause a visual disturbances were excluded.

All the study subjects went thorough ophthalmic evaluation which included slit-lamp biomicroscopic examination of anterior segment, best corrected visual acuity (BCVA) of each eye was recorded using Snellen chart, detailed fundus examination after mydriasis with 1% tropicamide and 5% phenylephrine eye drops using direct ophthalmoscopy, indirect ophthalmoscopy with +20D lens and stereoscopic slit lamp biomicroscopy of the disc and macula using + 78D Volk lens.

All cases were examined for the presence or absence of diabetic retinopathy. Those cases with fundus showing features of diabetic retinopathy were graded into five classes on the basis of ETDRS classification[3]. Thus, a total of six categories made based on the fundus picture of the patients –

1. No diabetic retinopathy
2. Mild NPDR
3. Moderate NPDR
4. Severe NPDR
5. Very severe NPDR and
6. PDR.

The Serum fasting total cholesterol, triglyceride, low density lipoprotein, high density lipoprotein, blood Sugar and Post prandial blood Sugar tests were carried out by enzymatic method using auto analyser in the Central Laboratory

Dyslipidemia defined using NCEP ATP III guidelines as: Total cholesterol ≥ 200 mg/dl, HDL cholesterol < 40 mg/dl, LDL cholesterol ≥ 100 mg/dl , Triglycerides ≥ 150 mg/dl .

Data compared with each grade of diabetic retinopathy and its association with three groups was determined statistically**.** Data was analysed using SPSS (Statistical Presentation System Software) for Windows software (version16.0). The minimal level of significance was set at $p<0.05$.

III. Observation And Results

Mean age in each group was 61.52 ± 7.03, 58.32 ± 6.00 and 61.33 ± 7.59 years. Male to female ratio was 1.86, 2.22 and 1.32 in group 1, 2 and 3 respectively. In the study patients, the duration since diagnosis of diabetes mellitus (diabetic age) ranged from 5-25 years. The mean duration in group 1 and group 2 was 9.04 ±4.67 and 6.26 ± 1.58 years respectively. 70% of the patients in group 1 and 76% in group 2 were on oral hypoglycemic (OH) only and remaining 30% in group 1 and 24 % in group 2 were on both insulin and OH.

Most of the patients had cataract of different grades and types. The percentage of subjects with cataract in anterior segment in group 1, 2 and 3 were 54.0%, 58.0% and 56.0% respectively while 26%, 12% and 20% were pseudophakic respectively. There was no significant difference in anterior segment features in different groups.

Table – 1: Mean values of lipid sub fraction and blood sugar in each group

Mean	Group -1	Group-2	Group -3	P value
Total Cholesterol	237.33± 36.54	215.30± 49.15	152.39±26.52	0.0001
Triglycerides	220.34± 55.65	179.94± 20.80	129.05±15.53	0.0001
HDL	47.44±7.64	51.41±13.78	53.15±8.19	0.0004
LDL	118.35± 27.04	128.47± 12.28	101.04±18.50	0.0001
FBS	132.42±55.77	103.96±34.32	83.56±12.20	0.0001
PPBS	217.27±96.28	180.71±76.43	124.91±11.97	0.0001

The mean value of total cholesterol was higher in both group 1 and group 2 with value being higher in group1 (237.33mg/dl) as compared to group 2 (215.30mg/dl). Triglyceride levels also followed the similar trend with group 1 having mean value of 220.34mg/dl and group 2 having 179.94 mg/dl. Differences of both total cholesterol and Triglycerides values had statistical significance ($p <0.0001$) between all groups. Most of the subjects in group 1 had uncontrolled diabetes suggested by elevated FBS and PPBS levels. Mean FBS level and PPBS levels were higher in group 1 as compared to group 2 and difference was statistically significant.

Table – 11: Mean values of the lipid sub fractions blood sugar in subjects categorized according to severity of diabetic retinopathy

Mean	Group 1					Group 2	P value
	Mild NPDR	Moderate NPDR	Severe NPDR	Very Severe NPDR	PDR		
Total Cholesterol	231.53 ±35.53	233.21 ±24.37	235.75 ±42.80	248 ±52.38	269.66 ±44.64	215.32 ±49.15	0.0081
Triglycerides	203.71 ±40.37	225.50 ±72.74	232.75 ±57.78	236.62 ±82.83	243 ±47.33	179.94 ±20.80	0.0142
HDL	50.07 ±7.79	47.90 ±7.0	44.75 ±5.13	42.25 ±8.0	42.33 ±7.29	51.41 ±13.78	0.0093
LDL	99.10 ±15.48	113.71 ±19.32	136.41 ±9.37	153.62 ±12.35	162.77 ±19.10	128.47 ±12.28	0.0001
FBS	133 ± 64.58	123.2 ± 53.04	139.8 ± 50.81	139.0 ± 40.36	164.7 ± 32.11	103.96 ±34.32	.001
PPBS	194 ± 81.38	228 ± 101.8	248 ± 144.1	249 ±56	258.2 ± 69	180.7 1±76.43	.001

Serum levels of total cholesterol and all other lipid levels increases with severity of diabetic retinopathy. Serum total cholesterol concentrations were higher in subjects with PDR compared with subjects with mild NPDR (p =0.0081). Similar pattern is observed for fating and post prandial; blood sugar.

IV. Discussion

The present studyhad malepredominance with themaletofemaleratio[M: F]was67: 33.Similar malepreponderancewasalsoseenintheCURES Eye study[4], UKPDS study[5] and the AndhraPradesh EyeDiseasestudy (APEDS) [6]. Less reporting of female patient in OPD in India, could be the reason. However, study conducted by Guptaet al[61]the difference with respect to the sex distributionwas statistically not significant and nearly equal male to female ratio.TheMeanageineachgroupwas61.52± 7.03,58.32±6.0and61.33±7.59 years. The relationship of retinopathy with age was in concordance to that found inmany other studies. Like several other epidemiologicstudies,this study alsoshowedan increased prevalence of DR withincreasing age. APED Study[6] and CURESEyeStudy[4] alsohavefoundsignificantcorrelationbetweenthepatient ageanddiabeticretinopathy. Although prevalence of DR increases significantly in geriatric patient above 80 years, the number of patient recorded in this age group in our study and indeed most of the studies in this subject remains on lower side probably because of these patients are more dependent on others and that makes it difficult for them to visit out patient.

Inthepresentstudy,thedurationsincediagnosisofdiabetes(diabeticage) ranged from 5 – 25 years. As the discovery of diabetes could have been delayed due todelayed laboratory test or lack of symptomsand the insidiousonset of type 2 diabetes, there may be some bias in estimating the real duration ofdiabetes in these patients. The mean duration ofdiabetes was 9.04±4.67 and 6.26±1.58 years respectively in group 1 and group 2. Theassociationoflongerdurationwithahighertheriskof DR (p=0.000)was reported in DCCT[7]; WESDR/Kleinetal[8];UKPDS[5]; Larsson et al[9]. Similarly in India, Gupta et al[10]APEDS study[6] Agarwal et al[11]studieshaveshownanincreasedprevalenceofDRasthedurationofdiabetesincreased. The CURES Eye study hasfoundthatforevery fiveyearincreasein duration of diabetes, theriskforDRincreasedby1.89times[4].

A statistically significant association between diabetic retinopathy and high total cholesterol level was observed in the present study (p = <0.01)). An elevated cholesterol level was significantly associated with the occurrence of all grades of retinopathy. Themeanvalueoftotalcholesterolingroup1,group2,andgroup3were237.33±36.54mg/dl, 215.30±49.15 mg/dl and 152.39± 26.52 mg/dl respectively. Themeantriglyceridelevel, HDL, LDL werealsohigheringroup1ascomparedto other two groups andthiscorrelationwere alsostatistically significant (p=<0.01).Researchers found that patients with elevated total serum cholesterol levels or serum low-density lipoprotein cholesterol levels at baseline were twice as likely to develop diabetic retinopathy as those with normal levels. (EarlyTreatmentDiabetic RetinopathyStudy(ETDRS) [3].During their study of the risk factors associated with diabetic retinopathy among diabetic patients, Al-Bdour et al[12] found a positive correlation between diabetic retinopathy and hypercholesterolemia (p=0.04). This finding is in accordance with thefindingsofthepresentstudy.Larssonetal[9] alsofoundsignificantcorrelationbetweenhigherlevelsofserumtotal cholesterolandretinopathy.

The CURES eye study assessed the association of serum lipids with diabetic retinopathy in urban South Indians. The serum level of triglyceride (P= 0.001) and total cholesterol (P= 0.014) was higher in patients with diabetic retinopathy than in those without it. Thisassociationwasmaintainedevenafter adjusting for age, as age by itself is a significant risk factor for hyperlipidemia.Agarwal et al[11] and Sachdev et al[13] alsoobserved raised level of total and LDL cholesterol and reduced level of HDL/LDLcholesterol ratioin patients with diabetic retinopathy.These resultsare inconcordancewiththepresentstudyashypercholesterolemiaandhypertriglyceridemiawasfoundtobeariskfactorforretinopathyinthecurrentstudy.

Kleinetal[8],whileassessingtheserumlipidlevelsinthesubjectswhoparticipatedinWisconsinEpidemiologicStudy of Diabetic Retinopathyfoundsignificanttrend forincreasingseverityofdiabeticretinopathyandofretinalhardexudatewithincreasingcholesterol. In the present study similarly there was an overallassociation of DR withtotalcholesterol and itcorrelates wellwiththeseverityofDR also. With increasing severity of DR (from mild NPDR to moderate NPDR to severe NPDR to PDR), serum level of cholesterol, triglyceride and LDL also increases with significant association (p value <0.05).

Similar topresentstudy,the EURODIABComplications Studyfound thattriglyceridelevel wasrelatedtoalllevels of retinopathy[14].Lyons et al[7] studiedserumlipoprotein subclass profiles intheDiabetesControlandComplicationsTrial/Epidemiology of Diabetes Interventions and ComplicationsStudy(DCCT/EDIC)cohortandfoundthatseverityofretinopathywas negativelyassociatedwithHDLcholesterol and positivelyassociatedwithtriglyceride. Gupta et al[10] made similar observation and demonstratedthatdiabetics with raised LDL levelsshowed higherprevalenceof Diabeticretinopathy(38%)comparedto others(28.3%)(p=0.05). After adjusting for age, duration of diabetes, HbA1c, and albumin excretion rate, elevated triglyceride was found to be a significant risk factor for moderate and severe non proliferative retinopathy in the EURODIAB study[14]. There was an increased level of serum cholesterol levels in CURES eye study participants with moderate NPDR compared with those without DR (p<.01). Triglyceride concentrations were higher in those with mild NPDR with those with those without DR (p<.01) [4].

The present study showed a trend of increase in the severity of diabeticretinopathywiththeincreasinglevelsofdifferentserumlipidsub fractions.Larssonet al[9] also showed a linear relationship of serum cholesterol levels with severity of diabeticretinopathy.WESDRstudyalsofoundthattherewasasignificanttrendforincreasingseverityofdiabeticretinopathywithincreasingcholesterol[4].

There is strong evidence to suggest that the long term glycemiccontrol playsanimportantroleindelayingtheonsetandslowingdown theprogressionofDR[4].In the present studymost of the subjectinthegroup1hadpoorglycemic controlsuggested raised FBS and PPBS levels. The mean values of FBS and PPBS werehigher in group 1 than in group 2, reinforcing the fact that the development andprogression of DR is influenced by the level of hyperglycemia. TheUKPDS (UK Prospective Diabetes Study) also showed that intensive glucose controlreduced the risk of a two-step change in retinopathy by 21% at 12 years follow up[5].Wisconsin Epidemiological Study of Diabetic Retinopathy (WESDR) also found thatrisk of retinopathy is related to the control of blood glucose levels[11]. The CURES EyeStudy observed a linear trend between prevelance of DR and poor glycemic control[4].

Thedrawbacks of thestudy are that the fundusphotographs for recordingoffunduschanges,whichis thestandardpattern, werenottakenforallpatients.In such conditionsitismore common tounderestimate than to overestimatefunduschanges related to diabetic retinopathy. Other risk factors for thedevelopmentofretinopathylikeanemia were not evaluated in this study. Hyperglycemiamay beanimportantconfoundingfactor in the study with respect to both hypercholesterolemia and diabetic retinopathy.ThepotentialforconfoundingdemandsadjustingforHbA1ctoassurethatanyobserved association between lipids and retinopathy is not a spurious finding. But thistestwasnotdone. Furthermore, referring uncontrolled diabetics to the tertiary centre would have allowed selection bias to creep into the study.

V. Conclusion

Numerous studies have shown an association of lipid fractions with macrovascular complications of diabetes (e.g. coronary artery disease), while relatively few have looked at the association of serum lipids with microvascular complications such diabetic retinopathy and the available results are conflicting. The present study demonstrated statistically significant correlation between Diabetic retinopathy and hypercholesterolemia. Increased cholesterol level was significantly associated with the occurrence of all grades of retinopathy especially severe NPDR, very severe NPDR and PDR. Further studies are required to establish the causal relationship between Dyslipidemia and diabetic retinopathy.

Bibliography

[1]. Chowdhury TA, Hopkins D, Dodson PM, Vafidis DF. The role of serum lipids in exudative diabetic maculopathy: is there a place for lipid lowering therapy? Eye 2002 (16): 689–693.

[2]. Reanita, Bardosono S, Victor AA. Relationship between plasma lipid profile and the severity of diabetic retinopathy in type 2 diabetes patients. Med J Indones 2008; 17: 221-225.

[3]. ChewEY,Klein ML,FerrisFL3rd,RemaleyNA,MurphyRP and ChantryKetal. Association of elevated serum lipid levels with retinal hard exudate in diabeticretinopathy. Early Treatment Diabetic Retinopathy Study (ETDRS) Report 22.ArchOphthalmol.1996Sep; 114:1079-84.

[4]. Rema M, Srivastava BK, Anitha B, Deepa R, Mohan V. Association of serumlipids with diabeticretinopathy inurban South Indians—theChennai UrbanRural Epidemiology Study (CURES)EyeStudy—2.DiabeticMedicine2006;23:1029–1036.

[5]. ParomitaK,PeacockI,DonnellyR.TheUKProspective DiabetesStud y (UKPDS): clinical and therapeutic implications for type 2 diabetes. Br J ClinPharmacol.1999November;48(5):643–648.

[6]. KrishnaiahS,DasT,NirmalanPK,ShamannaBR,NuthetiR,RaoGNetal. Riskfactorsfordiabeticretinopathy:FindingsfromTheAndhraPradeshEyeDiseaseStudy.ClinOphthalmol.2007December;1(4):475–482.

[7]. Lyons TJ, Jenkins AJ, Zheng D, Lackland DT, McGee D, Garvey WT et al. andTheDCCT/EDICResearchGroup.DiabeticRetinopathyand SerumLipoprotein Subclasses in the DCCT/EDIC Cohort Investigative Ophthalmology & VisualScience,March2004;45:910-918.

[8]. Klein BEK, Moss SE, Klein R, Surawicz TS. The WisconsinEpidemiologicStudyofDiabeticRetinopathy (WESDR),XIII:relationshipbetweenserumcholesteroltoretinopathyandhardexudate.Ophthalmology1991;98:1261-5.

[9]. Lill- IngerLarsson,AlbertAlm,FolkeLithner,GostaDahlen and ReinholdBergstromTheassociationofhyperlipidemiawithretinopathyindiabeticpatients aged 15-50 yearsin the county of Umea. Acta Ophthalmol. Scand.1999;77:585–591.

[10]. Sunil Gupta, Ajay Ambade. Prevalence of Diabetic Retinopathy and InfluencingFactors amongst type 2 Diabetics from Central India. International Journal of DiabetesinDevelopingCountries,2004;24:75-78.

[11]. Agarwal RP,MeetaSingla,Vyas SP,Sabir Hussain,Jain GC,Kochar DR.Prevalence of retinopathy and its relation with various risk factors in type 1diabetes mellitus-hospital based study India. International Journal of DiabetesinDevelopingCountries2001;21:184-190.

[12]. Muawyah D Al-Bdour, Maha I Al- Till, Khawla M Abu Samra. Risk factors for diabetic retinopathy among Jordanian diabetics. Middle East African Journal of Ophthalmology2008;15:77-80.

[13]. Sachdev N, Sahni A. Association of systemic risk factors with the severity ofretinalhardexudatesinanorthIndianpopulationwithtype2diabetes.JPostgradMed2010Sep;56:3-6.

[14]. Sjolie AK, Stephenson J, Aldington S, et al. Retinopathy and vision loss ininsulin-dependent diabetes in Europe. The EURODIAB IDDM ComplicationsStudy.Ophthalmology1997Feb;104(2):252-60.

Dr. Harlalsingh, et. al. "A Cross-Sectional Study of Association between Severity Of Diabetic Retinopathy With Hyperlipidemia." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 21(11), 2022, pp. 49-53.