

# Study of Association of Serum Lipids with Diabetic Retinopathy in Type 2 Diabetes Mellitus

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## Abstract:

The present study was conducted to find out the role of serum lipids in the development of diabetic retinopathy in type II Diabetes Mellitus. One hundred fifty subjects aged 30-70 years attending OPD at Old Civil hospital, Surat, participated in the study and were divided into three groups. Group I included 50 healthy non-diabetic subjects who served as control. Group II included 50 diabetic subjects with no signs of diabetic retinopathy and Group III included 50 diabetics with diabetic retinopathy. Funduscopy under homatropine was done in all the subjects. Serum triglycerides and total cholesterol were estimated by enzymatic methods and High Density Lipoprotein by precipitation method. Serum Low density lipoprotein was calculated using Friedewald's formula. It was found that triglyceride levels were significantly raised ( $p < 0.05$ ) in subjects with diabetic retinopathy as compared to those without diabetic retinopathy showing a positive association of Triglycerides with the incidence of diabetic retinopathy. Whereas no such association was found between low density lipoprotein and total cholesterol levels with the prevalence of diabetic retinopathy.

**Key Words:** Triglycerides (TG), Total Cholesterol (TC), Low Density Lipoproteins(LDL), Diabetic Retinopathy(DR).

## Introduction:

In 2009-10 out of 285 million people suffering from Type II Diabetes Mellitus (DM) worldwide, 51 millions were Indians as per International Diabetic Federation. Diabetes along with its fatal complications, is one of the leading cause of mortality and morbidity. Chronic complications of DM includes macro vascular complications like coronary artery disease, cerebrovascular disease and peripheral vascular disease along with microvascular complications like retinopathy, nephropathy and neuropathy. Risk factors like duration of diabetes, glycemic control (HbA1c), systolic blood pressure, dyslipidemias, smoking and microalbuminurias have been linked with complications of DM. Various studies have shown a positive correlation between elevated serum lipids (TG, LDL, TC) and macrovascular complications like ischemic heart disease. However, studies of association of elevated serum lipids with microvascular complications like diabetic retinopathy (DR) have shown varying results. In this study attempt has been made to quantify and specify the role of various components of serum lipids with the prevalence of DR.

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## Material and Methods:

The present study was carried out on 150 subjects aged between 30-70 years attending the outpatient department at Old Civil Hospital, Surat. A written consent was taken from all subjects and details of procedure were explained to them in the local language. A detailed medical history and findings of clinical examination were recorded in a proforma. Subjects with type-I DM, type-II DM of less than 5 years duration, severe hypertension, acute infections, known cardiovascular and renal diseases, liver dysfunction, severe anemia and thyroid disorders were excluded on the basis of history, examination and routine investigations like blood test, chest X-ray, electrocardiogram (ECG) and urine analysis. After overnight fasting and 2 hours after meals, fasting and postprandial blood samples were obtained from all the subjects. Fasting Blood Sugar (FBS) and Postprandial Blood Sugar (PPBS) were estimated by Glucose oxidase-peroxidase method. Funduscopy was done after dilatation using homatropine. Subjects with signs of micro-aneurysm, retinal dot blot hemorrhages, cotton wool spots, hard exudates is Non progressive Diabetic Retinopathy and neovascularisation progressive Diabetic Retinopathy were labeled as diabetic retinopathy. The 150 subjects were divided into three groups as follows:

Group I: 50 subjects with FBS  $\leq$  110mg% and

PPBS  $\leq$  140mg% without any drug or insulin, were taken as control group. Group II: 50 subjects with history of DM for more than 5 years but no signs of DR. Group III: 50 subjects with DM for more than 5 years and signs of DR.

Serum lipids were measured in the fasting blood sample. Serum triglycerides (TG) and cholesterol were measured by enzymatic methods, Glycerol 3 phosphate oxidase N-ethyl sulphopropyl anisidine and cholesterol oxidase-peroxidase end point methods respectively. Serum high density lipoprotein (HDL) was estimated by precipitation method Polyethylene glycol precipitation method. Serum low density lipoprotein (LDL) was calculated using Friedwald's formula ( $LDL = TC - HDL - TG/5$ ). The data obtained was compared statistically by applying oneway anova test.

**Results:**

Seventy eight percent subjects in Group II and 92% in Group III were more than 45 years of age as compared to 66% in the control group. Retinopathy is a rare finding (8%) in subjects of less than 45 years of age (Table I). This suggests that Type II DM is common after 4<sup>th</sup> decade of life and the risk of DR also increases with the increase in age; it may be due to increased duration of the disease.

Table I: Age wise distribution of the subjects participating in the study.

Age in years	Group I	Group II	Group III
30-44	34%	22%	8%
45-59	48%	62%	46%
60-75	18%	16%	46%

Seventy two percent in Group II and 68% in Group III were males as compared to 64% males in the control group. Results show that with increase in the duration of disease there was an increase incidence of DR ( $p < 0.0001$ ). Fasting blood sugar and HbA1c were significantly raised in those with DR as compared to those without DR ( $p < 0.05$ ), both of which are significantly raised as compared to the control group ( $p < 0.0001$ ). This suggests the role of poor glycemic control (raised HbA1c) in the prevalence of diabetic retinopathy (Table II).

A raised levels of TG, LDL and Cholesterol was observed in the Diabetic subjects (Group II and III) as compared to the control Group which was highly significant ( $p < 0.0001$ ). On comparing Group II and III, it was observed that TG levels were significantly

Table II: Comparison of sex, duration, FBS and HbA1c levels in the three groups.

Variables	Mean+SD			f-value
	Group I	Group II	Group III	p-value
Sex	32males & 18 females	36 males & 14 females	34 males & 16 females	-
Duration of DM (in years)	-	7.6 $\pm$ 2.2	10.2 $\pm$ 3.4	-
FBS (mg %)	78.08 $\pm$ 12.12	128.64 $\pm$ 19.5	136 $\pm$ 22.8	142.43 <0.0001**
HbA1c (%)	5.67 $\pm$ 0.35	7.88 $\pm$ 0.77	9.92 $\pm$ 1.5	227.43 <0.0001**

Table III: Comparison of serum lipids in the three groups.

Variables	Mean+SD			f-value
	GROUP I	GROUP II	GROUP III	p-value
Cholesterol (mg%)	165.9 $\pm$ 23.19	200.74 $\pm$ 38.74	212.35 $\pm$ 54.05	17.67 <0.0001**
HDL (mg %)	48 $\pm$ 12.69	43.15 $\pm$ 7.69	42.54 $\pm$ 11.6	3.78 <0.025*
LDL (mg %)	106.39 $\pm$ 30.16	127.61 $\pm$ 34.8	136.21 $\pm$ 34.8	10.60 <0.0001**
TG (mg %)	133.74 $\pm$ 38.74	150.57 $\pm$ 44.74	168.28 $\pm$ 40.26	8.73 <0.0001**

\*Significant ( $p < 0.05$ ), \*\* Highly Significant ( $p < 0.0001$ )

raised ( $p < 0.05$ ) in those with DR as compared to those without DR, where as LDL and cholesterol were not found to be significantly raised ( $p = 0.22$ ) in Group III as compared to Group II. This suggest that TG is associated with the increased incidence of diabetic retinopathy in DM subjects and not LDL or cholesterol.

**Discussion:**

Various studies have proven the role of elevated serum lipids with macro vascular complications of DM like coronary artery disease but, studies of association of lipids with specific micro vascular complications of DM like retinopathy have shown varying results. Dornan et al (1982) first showed the an association of LDL cholesterol with diabetic retinopathy. In Wisconsin epidemiological study of diabetic retinopathy, Klein et al (1999) correlated raised cholesterol levels with macular hard exudates. Early treatment diabetic retinopathy study associated TC and LDL with the onset and severity of retinal hard exudates (Chew et al, 1966). Severity of retionphaty was positively associated with TG in type I DM and negatively associated with HDL choestrol in DCCT/EDIC cohort (Lysons et al, 2004). Mohan et al (1984) reported an association between raised LDL and macular edema in the Indian population. Later Rema

et al (2006) showed association of TG with DR and LDL with diabetic macular oedema in Chennai Urban Rural Epidemiology Study Eye study (CURES) 2. However, Larsson et al (1999) and Hove et al (2004) found no association between TG, TC and HDL with diabetic retinopathy. Kulshreshtha et al (1979) observed raised levels of cholesterol and NEFA (non esterified fatty acids) in patients of DR. Benarous et al (2011) reported that phospholipids are not associated with DR but with Clinically significant macular oedema. Sasongko et al (2011) showed that apolipoprotein AI is inversely related and apolipoprotein B is directly related to DR and are strong biomarkers of DR than lipid profile in Australian population. Ozer et al (2009) found no correlation between serum lipids and macular edema in diabetic patients. Sachdev & Sahni (2010) proved that cholesterol and LDL are risk factors for retinal hard exudates in Type II DM in North Indian population. Keech et al (2007) showed that lipid lowering agent like fenofibrate, decreases the progression of DR. Uçgun et al (2007) showed that TC and LDL are elevated in patients with macular edema and hard exudates.

In the present study, it was found that TC, LDL and TG levels were significantly higher ( $p < 0.0001$ ) in diabetic subjects (Group II and III) as compared to the control group. This is due to the increased flow of glucose and fatty acids to liver due to lack of insulin. Decreased clearance of LDL and TG is due to over production of apolipoprotein B and low lipoprotein lipase activity. On comparing Group II and III it was found that TG levels were significantly raised ( $p < 0.05$ ) in patients of DR. The raised TG levels leads to increased blood viscosity and altered fibrinolytic activity which leads to formation of hard exudates. Also, TG incorporates into the cell membrane, altering its fluidity and permeability which leads to hemorrhage and oedema. This also leads to endothelial cell dysfunction and local inflammatory response releasing cytokines and growth factors which are responsible for neovascularisation in retina (Joussen et al, 2001). In the present study TC and LDL levels were not found to be significantly raised ( $p > 0.05$ ) in those with DR as compared to those without DR. The study suggest the role of raised TG and not LDL and TC in the incidence of retinopathy in Type II DM.

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