

# A Study of Correlation of Serum Lipids and Glycosylated Haemoglobin in Diabetic Retinopathy and Relation of Hyperhomocysteinemia in Diabetic Retinopathy

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**Abstract:** *The study of correlation of serum lipids and glycosylated haemoglobin and hyperhomocysteinemia in diabetic retinopathy in diabetic retinopathy. Aim: To estimate serum lipids and glycosylated haemoglobin levels in patients with and without diabetic retinopathy and to determine correlation between serum lipids and glycosylated haemoglobin levels with the severity of diabetic retinopathy. Setting and design: Two year prospective study done in 200 eyes. Material and methods: The study included 100 patients with varying grades of diabetic retinopathy and 100 patients without diabetic retinopathy. A detailed history was taken and clinical examination was done and specific investigation were done to estimate HbA1c, blood glucose (fasting and post prandial), Triglycerides, S.HDL, S.LDL, Fundus examination was carried out in all of them. Statistical analysis: the data was analysed using student's T test and 'z' test. Result: Increasing glycosylated haemoglobin levels were associated with increased incidence of diabetic retinopathy and levels were associated with increased progression of diabetic retinopathy from moderate NPDR to severe NPDR. Diabetic patients with retinopathy had a higher mean HbA1c levels as compared to diabetic patients without retinopathy. Increasing serum lipid levels were associated with development but not the severity of diabetic retinopathy. Serum LDL levels in the study group and control group were statistically significant and the results suggest a possible association between hyperhomocysteinemia in diabetic in retinopathy. Conclusion: Serum lipid levels are significantly raised in patients with diabetic retinopathy and higher levels are associated with an increased incidence of diabetic retinopathy. Higher serum lipid levels are not associated with more severe retinopathy. Glycosylated haemoglobin is significantly raised in patients with diabetic retinopathy and higher levels are associated with progression from moderate NPDR and severe NPDR and data indicate that hyperhomocysteinemia could be an independent risk factor for DR.*

**Keywords:** HbA1c (Glycosylated haemoglobin), HDL(High density lipoproteins), LDL(Low density lipoproteins),NPDR(Non proliferative diabetic retinopathy), Hyperhomocysteinemia

## 1. Introduction

Diabetes Mellitus is a heterogeneous group of metabolic disorder characterized by chronic hyperglycaemia with disturbance of carbohydrate, fat and protein metabolism resulting from defect in insulin secretion, insulin action or both.

Diabetic eye is the fourth major cause of blindness worldwide after cataract, glaucoma and trachoma.

Diabetes has emerged as a major healthcare problem in India. According to Diabetes Atlas published by the International Diabetes Federation (IDF), there were an estimated 40 million persons with diabetes in India in 2007 and this number is predicted to rise to almost 70 million people by 2025. Type 2 diabetes is the most common form of diabetes. Patients with type 2 diabetes usually have insulin resistance and relative rather than absolute insulin deficiency. Type 2 diabetes frequently goes undiagnosed for many years and such patients are at increased risk of developing macro-vascular and micro-vascular complications (1). In this study Retinopathy was taken in to account as a specific micro-vascular complication of diabetes. It is estimated that diabetes affects 4 % of world's population, almost half of them have some degree of diabetic retinopathy at any given time(2). In India with epidemic increase in type 2 diabetes as reported by WHO(3), diabetic retinopathy is fast becoming an important cause of visual disability. However, this morbidity is largely

preventable and treatable if managed with timely interventions.

## 2. Objectives

- 1) To estimate serum lipids and glycosylated haemoglobin levels in patients with diabetes mellitus with and without diabetic retinopathy.
- 2) To determine correlation between serum lipids and HbA1c levels with the severity of diabetic retinopathy.

## 3. Material and Methods

The study was done from November 2015 to June 2017, on 200 patients who were diagnosed to have diabetes mellitus and attended the outpatient clinic of Department of Ophthalmology, or Department of Medicine, or was admitted in wards of S.N. Medical College, Agra. The study included 100 patients with diabetic retinopathy and 100 patients without diabetic retinopathy.

A detailed history was elicited from the patients as per protocol. A comprehensive ophthalmological examination including visual acuity using Snellen's chart and a thorough anterior segment examination with oblique illumination using torch light and slit lamp biomicroscope was carried out. Intraocular pressure was recorded using Schiotz tonometer. The pupils were dilated with 1% tropicamide or /and 5-10 % phenylephrine and / or 1% cyclopentolate eye

drops to achieve maximum pupillary dilatation. Phenylephrine was avoided in patients with history of systemic hypertension. A detailed fundus examination of both types was done using direct ophthalmoscopy and indirect ophthalmoscopy. Examination of the macula was done +90D Volk's lens wherever indicated.

5-7 ml of fasting venous samples were drawn from patients for estimation of total lipid profile and glycosylated haemoglobin. Other routine investigations included serum creatinine, urine microalbuminuria and fasting blood sugar were also done:

#### 4. Observations and Analysis

The present study was done on patients diagnosed to have Diabetes Mellitus, varying grades of diabetic retinopathy attending outpatient department. This was compared with a control group which included 100 individuals with Diabetic mellitus but no evidence of Diabetic Retinopathy. Controls were age matched and sex matched with the study groups.

There were 53 males and 47 females in the study group, whereas the control group is included 54 males and 46 females. Age of the patients in the study group ranged between 30 and 80 years, the mean age being  $56.12 \pm 9.08$  years. In the control group, the mean age was  $53.33 \pm 12.75$  years.

Sex	Control group	Study group
Male	54	53
Female	46	47
Total	100	100

In study group, mild NPDR was seen in 49 subjects (49%), moderate NPDR in 26 subjects (26%), severe NPDR IN 10 subjects (10%) and PDR was seen in 15 (15%) subjects.

Diabetic grade of retinopathy	Study group(n)	%
Mild NPDR	49	49
Moderate NPDR	26	26
Severe NPDR	10	10
PDR	15	15

The average glycosylated haemoglobin (HbA1c) level in the study group was  $8.73 \pm 2.45$ , whereas in the control group the level was  $7.07 \pm 1.93$ . This was statistically significant (P value < 0.01).

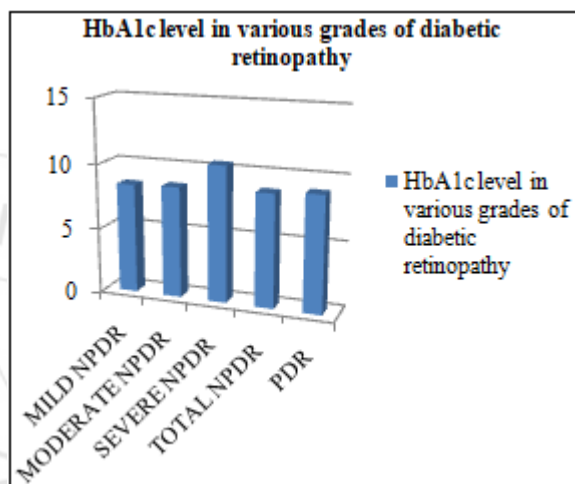
Group	N	HbA1c (%) (Mean +SD)
Control	100	$7.07 \pm 1.93$
Study	100	$8.73 \pm 2.45$

Non proliferative diabetic retinopathy was found in 85 of the 100 cases and the mean HbA1c level was  $8.70 \pm 2.31$ . Mild NPDR was found in 49 patients and the mean HbA1c level in this group was  $8.43 \pm 2.31$ , while moderate NPDR was

found in 26 patients and mean HbA1c was  $8.53 \pm 2.16$ , while severe NPDR was found among 10 patients in whom the mean HbA1c was  $10.45 \pm 2.97$ .

Proliferative diabetic retinopathy (PDR) was found in 15 of the 100 cases and the mean HbA1c level in this group was  $8.93 \pm 3.20$ .

Grade of diabetic retinopathy	N	HbA1c (Mean ±SD)
Mild NPDR	49	$8.43 \pm 2.13$
Moderate NPDR	26	$8.53 \pm 2.16$
Severe NPDR	10	$10.45 \pm 2.97$
Total NPDR	85	$8.70 \pm 2.31$
PDR	15	$8.93 \pm 3.20$



The average cholesterol level in the control groups was  $179.20 \pm 57.13$  mg/dl. The average cholesterol level in the study group was  $201.56 \pm 65.54$  mg/dl and the difference is statistically significant (p < 0.01).

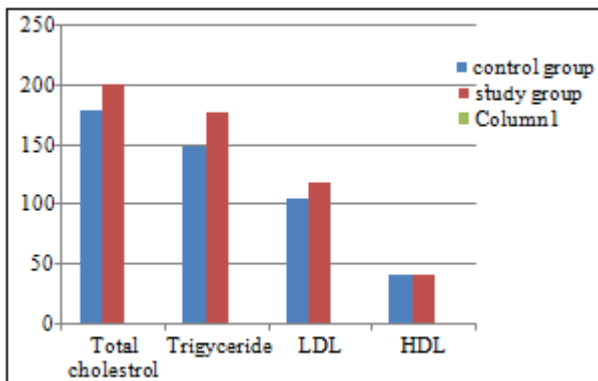
The average triglyceride level in the control group was  $149.40 \pm 81.59$  mg/dl and in study group is  $177.64 \pm 89.65$  mg/dl and the difference is statistically significant (P < 0.01).

On comparing the LDL levels in the study and control groups, the difference between the average LDL levels in the two groups, i.e.  $18.98 \pm 45.31$  mg/dl and  $104.28 \pm 34.76$  mg/dl respectively, was found statistically significant (P < 0.05).

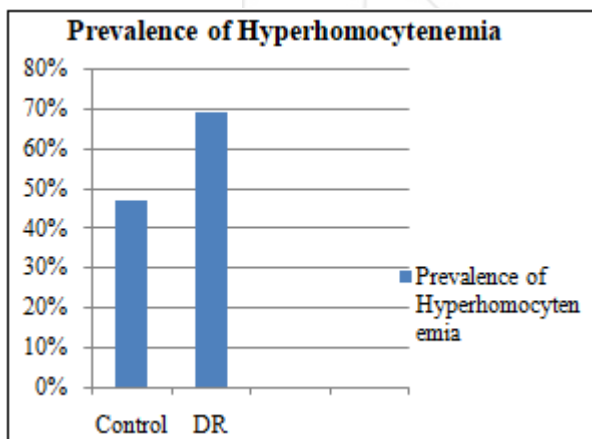
The average HDL level in the control group was  $41.11 \pm 11.95$  mg/dl and study group was  $41.29 \pm 13.90$  mg/dl. The difference between the two groups is statistically not significant (p > 0.10).

The average HDL/LDL ratio in the control group was  $0.46 \pm 0.27$  and study group was  $0.40 \pm 0.23$  and difference between the two groups was statistically significant (p < 0.01).

Group of DR	n	Total cholesterol(mg/dl) (mean ±SD)	Triglyceride (mg/dl)(mean±SD)	LDL (mg/dl) (mean±SD)	HDL(mg/dl) (Mean ±SD)
Control groups	100	179.20±57.13	149.40±81.59	104.28±34.76	41.23±11.95
NPDR	85	201.27±65.34	182.40±94.51	119.46±46.38	40.15±13.34
Mild NPDR	49	196.24±62.13	181.12±100.63	113.08±44.16	40.37±12.66
Moderate NPDR	26	198.85±65.53	179.65±73.34	123.15±46.67	38.15±14.86
Severe NPDR	10	232.20±78.20	195.80±119.13	141.10±53.33	44.30±12.72
PDR	15	203.20±61.91	150.63±48.11	116.27±40.02	47.73±15.68
Study group(total)	100	201.56±64.54	177.64±89.65	118.98±45.31	41.29±13.90



The mean plasma homocysteine levels were significantly higher in the diabetic retinopathy group compare to control group ( $p < 0.05$ ). The prevalence of hyperhomocystenemia ( $> 12 \mu\text{mol/l}$ ), which was significantly different ( $p < 0.01$ ) between the groups: 69% in DR, 47% in control group. DR patients had significantly higher levels of homocysteine than control group. These results suggest an association between hyperhomocystenemia and diabetic retinopathy.



## 5. Discussions

This study included 200 patients of diabetes mellitus which were divided into two groups – group I study group (100 patient with DR) and group II control group (100 patient without DR). these patients underwent a detailed anterior segment and fundus examination under full mydriasis. fasting blood samples were collected and serum lipid and glycosylated haemoglobin levels were analysed.

There was no statistically difference as far as the age and sex of the patients were concerned in the study and control groups. The association between serum lipid levels and diabetic retinopathy has been investigated in many studies (Dorman et al(4),1982; Dhir et al(5), 1984; Chew et al(6), 1996).

The average total cholesterol levels in our study group was  $201.56 \pm 64.54$  md/dl, which was statistically higher than that in the control group ( $179.20 \pm 57.13$  mg/dl), and this is similar to studies reported by Dhir et al (1996) and Chew et al (1996).

The average serum triglyceride levels in our study group were  $177.64 \pm 89.59$  mg/dl, which was again significantly higher than the average level of  $140.40 \pm 81.59$  mg/dl in the control group.

A similar result was derived after assessing the average serum LDL levels in the study group and control group, which were  $118.98 \pm 45.32$  mg/dl and  $104.28 \pm 34.76$  mg/dl respectively. However, there was no statistically significant difference is found in the serum levels of HDL in the study groups and control groups, the level being  $41.29 \pm 90$  mg/dl and  $41.23 \pm 11.94$  mg/dl respectively.

These data are in the agreement with some of the other authors mentioned below:

Dorman et al(4) (1982) evaluated the profiles of total and lipoprotein cholesterol and triglyceride in 11 IDDM subjects without retinopathy, 10 with background retinopathy and 10 with proliferative retinopathy. They reported higher levels of total cholesterol and LDL cholesterol in patients with PDR than in the patients with background of no retinopathy, as was also in the case of our study.

Dhir et al(5) (1984) studied the association of the diabetic retinopathy with serum lipid levels in 51 diabetic patients and 31 control subjects. Their results showed a significant increase in triglycerides, total cholesterol LDL and VLDL and decrease in HDL in diabetic patients as compared to controls.

Chew et al(6)(1996) evaluated the relationship between serum lipid levels, retinal hard exudates and visual acuity in the patients with diabetic retinopathy. Results of this study also showed that the patients with the elevated serum cholesterol levels and serum LDL cholesterol at were twice as likely to have hard exudates as patients with normal levels.

Moreover, in the present study is also in agreement with the Larsson et al (1999) and supports the assumption that the higher levels of serum total cholesterol and higher levels of serum lipoproteins are associated with more severe retinopathy. However, in contrast to this study, there are the studies reported by Agardh et al(7) (1986) and Klein et al(8) (1999) which show no relationship between serum lipid levels and developmental and progression of diabetic retinopathy.



Glycosylated haemoglobin and diabetic retinopathy: the average glycosylated haemoglobin level in our study was  $8.73 \pm 2.45\%$  which was significantly higher than in control group  $7.07 \pm 1.93$ . The patients with diabetic retinopathy were to have significantly higher levels of glycosylated haemoglobin than those with no evidence of diabetic retinopathy. The data in this study is in the agreement with the studies done by:

Klein et al(9)(1996) studied the relation of glycaemic control to the microvascular complications in diabetes mellitus. They found that the glycosylated haemoglobin level at the baseline was strongly related to the incidence, progression, or both of diabetic retinopathy in the persons with either IDDM or NIDDM.

In the present study is also an agreement with Morisaki et al (10)(1994) and supports the results that the HbA1c is an independent risk factors for diabetic retinopathy in all the cases.

Thus, the present study observed serum lipids and glycosylated haemoglobin levels are elevated in patients with diabetic retinopathy. The levels of glycosylated haemoglobin correlate to a certain extent with the severity of diabetic retinopathy, whereas, serum lipid levels do not correlate with the increasing severity of diabetic retinopathy.

## 6. Conclusions

The study was undertaken to evaluate the role of serum lipids and glycosylated haemoglobin as the risk factors in the development and progression of diabetic retinopathy. There was statistically significant difference is found in serum triglyceride, serum LDL, glycosylated haemoglobin levels but no difference in HDL levels.

Increasing glycosylated haemoglobin levels were associated with increased incidence of diabetic retinopathy and increased progression of diabetic retinopathy from the stage of moderate to severe NPDR.

Serum lipid levels are significantly raised in patients with diabetic retinopathy and higher levels are associated with an increased incidence of diabetic retinopathy.

Study suggested that hyperhomocysteinemia could be an independent risk factor for DR.

## 7. Source of Financial Support

Nil

## 8. Conflict of Interest

None

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