Co-Relation Of Serum Lipids And Glycosylated Haemoglobin With Changes In Retina In Type -2 Diabetes

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Abstract: Background:This study was done to study the correlation between serum lipids and glycosylated haemoglobin with changes in retina in type 2 diabetes mellitus. Method: 80 subjects were taken for this study from diabetic clinic of civil hospital Ahmedabad and 40 controls were taken from community. They were divided into 3 groups. A detailed history was taken and clinical examination was done and specific investigations were done to estimate HbA1c, blood glucose levels (fasting and post prandial), S.triglyceride, S.HDL, S. cholesterol, S.LDL. Fundus examination was carried out in all of them. Result: The incidence of diabetic retinopathy was high with increase in age & duration of diabetes. Mean glycosylated haemoglobin levels in diabetic subjects were more as compared to mean HbA1c levels in healthy non-diabetic control subjects. Diabetic patients with retinopathy had a higher mean HbA1c levels as compared to diabetic patients without retinopathy. Conclusion: High HbA1c and dyslipidaemia indicate chronicity of type-2 D.M. with poor glycaemic control these patients are more prone for diabetic retinopathy.
With age and duration of typr-2 D.M. risk increases for retinopathy.

Key Words: DM, Diabetic Retinopathy (DR), glycosylated haemoglobin (HbA1c).

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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.[1] 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.

Objectives:

1) To study HBA1C and the serum lipid profile in type 2 diabetes mellitus.
2) To study the changes in the retina associated with type 2 diabetes mellitus and grade it according to non-proliferative and proliferative DR.
3) To study if there is any correlation between serum lipids and HbA1c with changes in retina in type 2 diabetes.

Material and Method: The current study was done from June 2009 to June 2010. Total 80 subjects were taken from diabetic clinic at civil hospital Ahmedabad and 40 healthy volunteers were taken from community as control. All the patients who had duration of diabetes of 5 years or more were selected for this study and selected age was 40 years or more than 40 years. For the purpose of study they were divided into three groups as follows:

- Group-1 : 40 participants without diabetes
- Group-2 : 40 patients with diabetes but no clinically evident DR

- Group-3 : 40 patients with diabetes and associated DR

A detailed history, examination and significant investigations were done after taking consent from all the participants of the study.

Investigations were done using following Method

- Glycosylated Haemoglobin was estimated by Cation exchange resin method.
- Fasting blood sugar (FBS) and post prandial blood sugar (PPBS) was estimated by Glucose Oxidase-Peroxidase(GOD-POD) method, using Enzopak kit in fully auto-chemistry-analyser.
- S. Triglyceride was estimated by Glycerol 3 phosphate Oxidase N ethyl N sulfopropyl N anisidine method.
- S. HDL was estimated by PTA method using fully auto-chemistry-analyser.
- S. Cholesterol was estimated by Cholesterol Oxidase-Peroxidase end point method.
- S. LDL was calculated using Friedewald formula.
  LDL = Total cholesterol – HDL – TG/5.
- Fundoscopywas done after dilating the pupil using 1 % Homatropine by direct ophthalmoscope.

Results: In our study, 77.5% of patients in group-III i.e. those with retinopathy were ≥ 50 years of age, while those in group- II i.e. those without retinopathy,70% of patients were <50 year of age. In our study it is found that incidence of retinopathy was found increasing with increased age.

Fig 1: Age wise distribution of the patients who participated in the study.

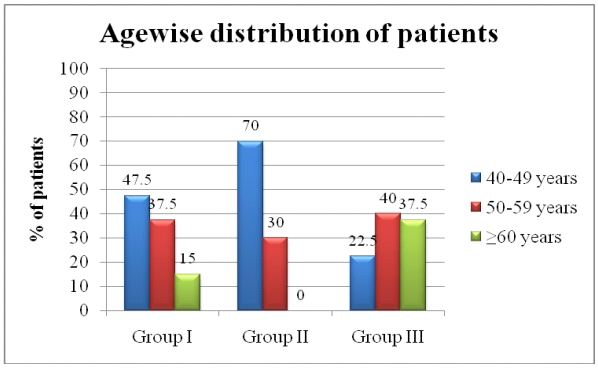
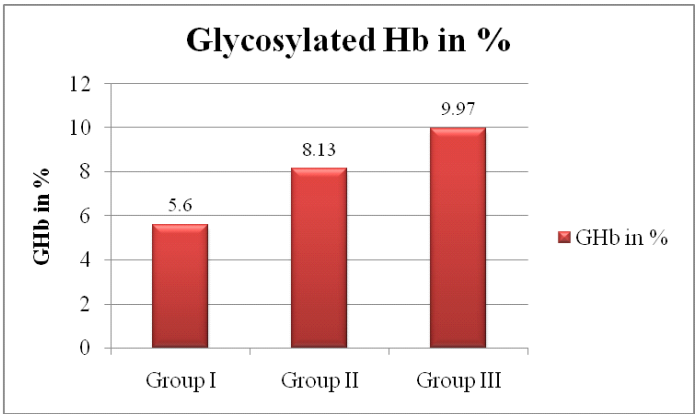


Table 2: Distribution of diabetic patients in group-II and III according to duration of diabetes.

Years of H/O DM	Group II		Group III	
	No.	%	No.	%
5-9	22	55	3	7.5
10-14	16	40	11	27.5
≥15	2	5	26	65
Total	40	100	40	100.0

Fig 2: Comparison of glycosylated haemoglobin among the three groups.(gm %)



In our study, we observed that HbA1c level in diabetes patients (group-II and group- III) was significantly higher as compared to control group.(p<0.0001).Also it was observed that patients with diabetic retinopathy (group-III) had significantly higher HbA1c level as compared to patients without diabetic retinopathy (group-II).

Table 2: Lipid profile of 120 participants of this study. (n = 40 in each group)

LIPID (mg %) (Mean ± SD)	Group I	Group II	Group III
S. Triglyceride	107.3 ± 18.16	165.8 ± 15.4	198 ± 21.5
S. HDL	41.92 ± 6.07	39.52 ± 3.78	34.4 ± 3.75
S. Cholesterol	168 ± 24.75	197.95 ± 17.86	240.1 ± 21.02
S. LDL	104.42 ± 20.96	126.52± 18.22	168 ± 19.9

S.Triglyceride , S.LDL and S.Cholesterol were elevated and S.HDL was decreased in diabetic subjects as compared to control, whereas on

comparing group-II and group-III, S.TG, S.Cholesterol and S.LDL were more elevated in group- III i.e. those with retinopathy than that of group-II i.e. those without retinopathy.

Discussion: The current study was conducted to assess the S.lipid level & HbA_1c level & its correlation with retinopathy in diabetic subjects.

In our study, 77.5% of patients with retinopathy were ≥50 years of age, while only 22.5% patients were of<50 years of age which suggested that increasing age was contributing factor for development of diabetic retinopathy. Manariat et al[4] have also shown similar findings.

Our study also showed that incidence of diabetic retinopathy was increasing significantly with duration of DM ≥ 10 years & it wasmaximum after 15 years. Tapp et al in 2003 concluded that duration of diabetes was the risk factor of DR[5]. It was also proved by UK Prospective Diabetes Study Group[6].In the CURES Eye study 41.8 % had diabetic retinopathy after 15 years of diabetes and severity of diabetic retinopathy proportionally increased with longer duration of diabetes. In addition it has been demonstrated that for every five years increase in duration of diabetes, the risk of diabetic retinopathy increases by 1.89 times[7].Mitchel et al reported that about 8 % patients developed diabetic retinopathy for each year that duration of diabetes increased[8]. , a population based cohort study of diabetes had shown that in person with type 2 diabetes the prevalence of diabetic retinopathy ranged from 29 % in those with duration of diabetes < 5 years to 78 % in those with diabetes duration over 15 years[9].As the duration of diabetes is a total reflection of blood glucose control and exposure to other risk factors, duration of diabetes is an important risk factor for incidence and development of retinopathy.The Wisconsin Epidemiological Study of Diabetic Retinopathy, a population based cohort study of diabetes had shown that in person with type 2 diabetes the prevalence of diabetic retinopathy ranged from 29 % in those with duration of diabetes < 5 years to 78 % in those with diabetes duration over 15 years [9].Thus duration of diabetes has probably emerged out as the strongest risk factor toward the development of diabetic retinopathy.

In our study control group was found to have mean HbA1c of 5.6± 0.37 gm%, diabetics without retinopathy had mean HbA1c of 8.13± 0.54 gm%& diabetics with retinopathy had mean HbA1c of 9.97±1.26 gm%. It shows that HbA1c value in group-III was significantly higher than HbA1c in group-II which was again higher as compared to control group. Due to more intracellular glucose in diabetics there is enhanced HbA1c due to non-enzymatic glycosylation of proteins leading to raised HbA1c in diabetics. Raised HbA1c indicates poor glycaemic control many scientists have shown that incidence of retinopathy is more with poor glycaemic control.Maberley DAL et al in 2007 also demonstrated that poor glycaemic control was associated with increased risk of retinopathy in diabetics[10]. Manariatet al[4] and Tapp et al[5] also proved that HbA1c was risk factor of DR.In the CURES Eye Study a linear trend in the prevalence of retinopathy with increase in quartiles of HbA1c (trend Chi square: 51.6, $p < 0.001$) from 8.1 % (HbA1c level < 6.9 %) to 31.7 % (HbA1c > 10.3 %) was observed. For every 2 % elevation of HbA1c, the risk for diabetic retinopathy increased by a factor of 1.7[7]. Thus it was observed that long term glycaemic control plays an important role in delaying the onset and lowering down the progression of DR.

Currently four major biochemical pathways have been hypothesized to explain the mechanism of diabetic eye disease all starting initially from hyperglycaemia induced vascular injury. These mainly include (1) enhanced glucose flux through the polyol pathway. (2) Increased intracellular formation of advanced glycation end products (AGE) that affect the retinal blood flow, permeability and other micro-vascular parameters. (3) Activation of .protein kinase C (PKC) isoforms and (4) stimulation of hexosamine pathway. Studies have suggested that these mechanisms seem to reflect a hyperglycaemia induced process initiated by superoxide overproduction by mitochondrial electron transport chain[11].

It was found in our study that S.triglyceride, S.cholesterol& S.LDL were significantly higher in diabetic patients as compared to control subjects. One of the determinants of diabetic hypertriglyceridemia is overproduction of VLDL

triglycerides, which is most likely due to increased flow of glucose & free fatty acid to the liver & defect in clearance of VLDL triglycerides. In poorly controlled diabetes there is impaired LDL catabolism which leads to elevated S.LDL level. HDL cholesterol level isdecreased in diabetes due to replacement of cholesterol in the core of HDL by triglycerides from hypertriglyceridemia.Ignatius C. madukaet al[12] in 2007 concluded that there was statistically significant increase in value of S.triglyceride, total cholesterol, HDL cholesterol, LDL cholesterol when compared with the non-diabetic subjects.

It was also found in our study that there was significant rise in lipid profile in those with retinopathy as compared to those without retinopathy. Thus, this study suggests association of serum lipids with DR. Many studies supported this result our observations.Hecke MV et al[13]in 2005 &Meleth AD et al[14] in 2005 also proved dyslipidaemia as a risk factor for diabetic retinopathy. According to Hoorn Study which was a population based study including 2484 subjects who were 50 to 74 year old Caucasians, plasma total cholesterol, HDL cholesterol and S. triglyceride level showed association with retinal exudates[15].It has also been shown that in type 2 diabetes subjects there was increase in lipid peroxidation in plasma and probably this process could be accelerated in patients with diabetic complications[16].

Conclusion: Our study concludes:

- The incidence of diabetic retinopathy increases, as the age increases.
- The incidence of diabetic retinopathy increases with increase in duration of diabetes. Diabetic retinopathy is more common after 10 years of diabetes.
- Mean glycosylated haemoglobin levels in diabetic subjects are more.
- Diabetic patients with retinopathy have a higher mean HbA1c levels as compared to diabetic patients without retinopathy. Higher HbA1c levels suggest poor long term glycaemic control.
- Serum cholesterol, serum LDL & serum triglyceride are elevated in diabetic patients. Diabetic patients also have low serum HDL level.
- Both high HbA1c and dyslipidaemia indicate chronicity of type-3 D.M. with poor glycaemic control. Such patients are more prone to develop diabetic retinopathy. So regular fundoscopy is recommended in patients of D.M., especially in those who are having high HbA1c and dyslipidaemia.

References:

1. Peter H Bennett, Williams C. Knowler: Joslin's Diabetes mellitus, 13th edition. Definition, diagnosis and classification of diabetes mellitus and glucose homeostasis, chapter 19, 331-339.
2. Aiello LP, Gardener TW et al. Diabetic Care 1998;21;143-56
3. Wild S, Roglic G et al. Global prevalence of diabetes, estimates for the year 2000 and projections for 2030. Diabetes care 2004; 27: 1047-53
4. Manariat MR, Afkhami M, Shoja MR. Retinopathy and microalbuminuria in Type II diabetic patients. BMJ Ophthalmol 2004;4: 9-12.
5. Tapp RJ, Shaw JE, Harper CA, de Courten MP, Balkau B, McCarty DJ et al. The prevalence of and factors associated with diabetic retinopathy in the Australian population. Diabetes Care 2003; 26: 1731-1737.
6. UK Prospective Diabetes Study Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with Type II diabetes. UKPDS33. Lancet 1998; 352; 837-853.
7. Rema M, Premkumar S et al. Prevalence of diabetic retinopathy in urban India: The Chennai Urban Rural Epidemiology Study (CURES) Eye Study, I. Invest Ophthalmol Vis Sci 2005; 46, 2328-33.
8. Mitchell P, Moffitt P. Update and implications from the Newcastle diabetic retinopathy study. Aust N Z J Ophthalmol 1990; 18: 13-17.
9. Klein R, Klein BE at al. The Wisconsin epidemiologic study of Diabetic retinopathy: XVII. The 14 years incidence and progression of diabetic retinopathy

and associated risk factors in Type II Diabetes. Ophthalmology 1998; 105: 1801-15.

10. Maberley DAL, Hollands H et al. The prevalence of low vision and blindness in a Canadian inner city. Eye. 2007; 21(4): 528-533.
11. Rema M, Shanthirani CS et al. Prevalence of diabetic retinopathy in a selected south Indian Population-The Chennai Urban population Study (CUPS): Diabetes Res ClinPract 2000, 50, S252.
12. Ignatius C. Maduka, Joel O. Onyeanusi et al. Lipid and lipoprotein profile in Nigerian NIDDM patients: Biomed Res (India) 2007; 18(1), 49-53.
13. Hecke MV, Dekker JM et al. Inflammation and endothelial dysfunction are associated with retinopathy: the hoorn study. Diabetologia 2005; 48: 1300-6.
14. Meleth AD, Agron E et al. Serum inflammatory markers in diabetic retinopathy. Invest Ophthalmol Vis Sci 2005; 46: 4295-301
15. Hendrik A, Moll A et al. blood pressure, lipids and obesity are associated with retinopathy: the Hoorn study. Diabetes care, 2002; 25(8): 1320-1325.
16. Sundaram RK, BhaskarA et al. Antioxidant status and lipid peroxidation in Type II Diabetes mellitus with and without complications. Clinical Science 1996, 90: 255-60.

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