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A Prospective Study of Diabetic Retinopathy and its Association with Serum Lipid Levels and Microalbuminuria

Dr. Sanjay Sharma[1], Dr. Preeti Sharma[2], Dr. Manan Kaushik[3], Dr. Rohan Bowry[4]

[1]M.S, Fellow of Vitreoretinal Surgery (FRVS), Assistant Professor - Subharti Medical College, Meerut, India

[2]M.B.B.S, M.S.(Fellow Pediatric Ophthalmology)

[3, 4]M.B.B.S, M.S

Abstract: ***Objective: A prospective study of diabetic retinopathy and its association with serum lipid levels and microalbuminuria. Design: A prospective clinical study of 50 diabetic patients with exudative maculopathy was selected from the retina clinic, LLRM Medical College, Meerut. Methods: A detailed history including age, sex, onset/duration/type/control status of diabetes, complete systemic examination and ocular examination which included BCVA, IOP, ocular movements, anterior chamber examination and complete fundus examination was done and the type of maculopathy was noted and graded. Results: 68% of the patients with exudative maculopathy were associated with abnormal serum lipid profile and 100% were associated with presence of proteinuria. Conclusion: We found in our study that both proteinuria and abnormal lipid profile had a strong correlation with progression of diabetic retinopathy along with other proven risk factors.***

1. Introduction

Diabetes mellitus is defined as a group of diseases characterized by hyperglycaemia with disturbances of carbohydrate, fat andproteinmetabolism resulting from defects in insulin secretion, insulin action or both. It is a chronic hyperglycemia that causes most of the microvascular damage and contributes, together with other associated risk to the premature development of macro vascular diseases[1].

Estimates have held that 5 to 10 years of sustained hyperglycemia are needed to develop clinically significant manifestation of microangiopathy such as non-proliferative retinopathy and early nephropathy.

Diabetes Mellitus type 2 will affect the older patients and with the increasing duration of diabetes the incidence of the retinopathy will also increase. Type 1 diabetes will also have an impact, as these patients live longer and hence are at a risk of becoming blind.

After 20 years 100% of type 1 and 60% of type2 diabetics will develop diabetic retinopathy. Proliferative diabetic retinopathy and its complications are the cause for blindness in type 1. The majorcause for blindness in the type 2 variety is diabetic macular oedema. There is some evidence to implicate serum lipids in exudative maculopathy, cross-sectional studies suggests that higher serum lipid levels are found in patients with macular exudates and prospective studies have shown an increased risk of exudative maculopathy if baseline cholesterol is high[2].

Diabetic maculopathy is a common complication of diabetes mellitus, characterized by macular oedema and frequently accompanied by lipid exudation. It is the major cause for loss of vision in diabetic patients.

Keeping in mind the increasing number of cases and the potential hazard to vision that can occur in diabetic patients with exudative diabetic maculopathy, we undertook this study.

Aims and Objective

- To study the clinical presentation of Retinopathy and its relation to associated albuminuria in patients of Diabetic Mellitus
- To study the relationship between exudative diabetic maculopathy and serum lipid level.

2. Materials and Methods

We conducted a prospective clinical study of 50 patients who had exudative maculopathy and were confirmed cases of diabetes mellitus. Baseline characteristics of the patients included a detailed history, age, sex, age of onset, duration, type of diabetes, controlled status, family history, complete systemic examination(to rule out diabetic changes), ocular examination which included BCVA, IOP and ocular movements were observed. Anterior chamber examination was done with special emphasis on rubeosis iridis, cataract and pupillary reaction. Complete fundus examination was done and diabetic retinopathy was graded according to ETDRS.

Statistical analysis was done using Chi-square test or Fisher Exact test depending upon the adequacy of sample frequency to compare the significant abnormal levels of serum lipids with age, sex, type of DM , duration of DM, exudative maculopathy and urine albumin levels.

The aim of our study was to analyse the relationship between exudative maculopathy and serum lipid levels. We also studied the relationship between diabetic maculopathy and urine protein levels.

Inclusion criteria

- Known cases of diabetes mellitus both IDDM and NIDDM.
- Patients with diabetic maculopathy.
- Patients with post laser non-resolving exudative maculopathy.

Exclusion criteria

- Pregnant women
- Glaucomatous patients
- Patients with vitreous haemorrhage.
- Patients with dense cataracts and post cataract surgery.
- Patients with post vitrectomised eyes.

3. Observations and Results

This is a prospective clinical study of patients with Diabetes mellitus. Fifty patients formed the study group. We studied the relationship of exudative maculopathy with serum lipid profile and also with the presence or absence of proteinuria. 68.0% of patients with exudative maculopathy were associated with abnormal serum lipid profile and 100.0%were associated with the presence of proteinuria.

Of the 34 patients with high lipid profile

- 87.23% had high serum total cholesterol.
- 68.08% had high serum triglycerides.
- All patients had serum HDL levels within normal range
- 53.19% had high serum LDL levels and Lp (a)levels
- 0.51% patients had high serum VLDL levels.
- Even though there were more number of patients with increased cholesterol levels, the triglycerides increased to greater extent.

Retinopathy was present in 64% and 36% patients had no sign of retinopathy. In Age group with Retinopathy group 50% were between 40-49yrs, 68.18% were b/t 50-59yrs and 75% were of more than 60yrs.

Of the 100 eyes 6 had cluster exudates, 28 had ring and 30had waxy type of exudates.

Of the patients with high serum lipid profile BDR was seen in 18Pts. and PPDR in 9Pts and PDR in 5Pts. 40.42% eyes of patients with high lipid levels had VA s 660.44.68 % eyes had VA between 6/18-6/36 and 14.9% had VA between 6/6-6/12.

More than 50.0 % of eyes had severe (grade III) maculopathy inpatients with high serum lipid profile. Total cholesterol was significantly higher in the severe (grade III) maculopathy group. All forms of exudates (cluster, ring and waxy plaques) were higher in the macroalbuminuria group.

Correlation between Severity of Retinopathy and Severity of Nephropathy

Retinopathy	Micro albuminuria		Macro albuminuria		Total	
	Number	%	Number	%	Number	%
Background Diabetic Retinopathy	8	80	10	45.45	18	56.25
Pre- Proliferative D.R.	2	20	7	31.81	9	22.12
Proliferative D.R.	-	-	5	22.72	5	15.62
Total	10	100	22	100	32	100

Abnormal Lipid Profile Vs Diabetic Status

Abnormal Lipid Fractions	Fasting Blood Sugar				p – Value
	<200mg%(n=20)		>200mg%(n=30)		
	N	%	n	%	
Total Cholesterol	18	85	24	80	>0.05
Triglycerides	12	60	20	66.66	0.306
HDL	-	-	-	-	-
LDL	8	40	17	56.66	0.119
VLDL	1	5	3	10	0.629
LP(a)	7	35	18	60	0.031

4. Discussion

Lipid profile and the presence of proteinuria was studied in 50 known diabetic patients. Hard exudates are known to be associated with increased duration of diabetes, proteinuria, high serum cholesterol, phospholipid, total lipid abnormalities, etc. In our study 68% of patients i.e., 34 patients had abnormal lipid profile.

The incidence of maculopathy increases with the duration of diabetes and this was proportional to age of the patient in our study.

It is well known that prevalence of diabetic maculopathy is higher in NIDDM than IDDM.A high incidence of maculopathy was seen in NIDDM patients according to a study by Biswas et al[3] in 2002.Our study showed increased incidence of diabetic maculopathy with increased duration from 55.26% in 5-9yrs duration to 83.33% in 10-14yrsand even 100% in more than15yrsduration.Study by Biswas et al[3], shows that maculopathy starts earlier in NIDDM and increases with duration of diabetes.

In the present study in 40% eyes visual acuity observed less than 6/6046% had less than 6/18 and only 14.0% had visual acuity of 6/6 to 6/12.In the ETDRS study the risk of losing visual acuity was associated with severity of hard exudates even after adjusting for macular oedema. In further analysis, elevated serum cholesterol at base line increased the risk of visual loss by 50.0% compared to lower serum cholesterol levels. These findings have been supported by examination of a subgroup of the WESDR cohort[4].

In our study 68% patients had abnormal lipid profile affecting all the fractions except the HDL. The protective function of HDL was lost and at the same time the cholesterol, triglycerides, LDL and lipo protein played the role in the pathogenesis of exudative maculopathy.

Triglycerides were thought to be more important in the formation of hard exudates in NIDDM patients[2].

Clinical and experimental evidence suggests that good control of metabolic aspect of diabetes delays the onset and decreases the severity of retinopathy[5].Continuous relation exists between glycemic control and incidence and progression of the microvascular complications. Our study showed high levels of all lipid fractions with poor metabolic control of diabetes

Poor diabetic control is associated more with hypertriglyceridaemia andhypercholesterolaemia[6].

In the present study except total cholesterol all other fractions were seen to be more commonly abnormal in PDR than in NPDR.

Study by Dorman et al, found that total cholesterol was higher in patients with PDR than NPDR or no retinopathy due to raised level of LDL cholesterol. HDL levels were similar in patients with or without retinopathy. HDL/LDL ratios were lower with more severe retinopathy. Triglyceride levels were not related to retinopathy[6].

Therefore abnormal serum lipid profile was commonly associated with waxy deposits, grade-III type of maculopathy, PDR, poorer vision and is chaemic heart disease.

In the present study all forms of exudates are more common in patients with serum total cholesterol>200 mgs%.

In the ETDRS[7] study patients with serum cholesterol 240 mgs% were twice more likely to have hard exudates than patients with the total cholesterol <200 mgs% at base line. Patients with serum cholesterol ≥240 mgs% developed hard exudates 50.0% faster.

In microalbuminuria lipoprotein synthesis is increased as a response to increased albumin loss. Microalbuminuria may reflect ageneral vascular damage, which per se could lead to an accumulation of atherogenic lipid particles and promote atherogenesis.

In the present study 50 patients were analysed for the presence of proteinuria both micro and macro albuminuria in equal numbers i.e.25 in each group.

Shukla et al[8], showed that nephropathy was significantly associated with macular ischaemia (p-0.025). From the above discussion we infer that lipid profile is definitely higher in patients with diabetic exudative maculopathy. There is a significant role of proteinuria on Diabetic retinopathy.

5. Limitations of the Study

This study included small No. of patients and no controls were used. Proteinuria was measured using the commercially available lab techniques with different sensitivities which was a major source of bias. Long follow up of patients receiving lipid lowering agents was not done to evaluate its effect on regression of hard exudates and improvement in visual acuity

6. Conclusion

In our study 80% of the subjects havingmicroalbuminuria showed only background diabetic Retinal changes. A major shift from microalbuminuria to macro albuminuria resulted in a similar increase in percentage of proliferative diabetic retinopathy.

A similar increase was also seen in the development of maculopathy with the increasing severity innephropathy from 12% in microalbuminuria to 52% in those having macroalbuminuria.

Our study demonstrated a close relationship between albuminuria and prevalence of diabetic retinopathy. Micro albuminuria was associated with the occurrence of Background diabetic retinopathy. Macro albuminuria was associated with proliferative diabetic retinopathy. Also, Patients with abnormal lipid Profile showed more severe exudative maculopathy. We found in our study that both Proteinuria and Abnormal lipid profile had a strong correlation with progression of Diabetic Retinopathy along with other proven risk factors.

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