



Association of dyslipidemia and Diabetic Retinopathy among patients coming to OPD of Katihar Medical College Hospital and its visual outcome: A prospective observational study

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Introduction

Diabetic retinopathy (DR) is one of the major microvascular complications of diabetes. It is one of the most common cause of preventable blindness in diabetic adults. Dyslipidemia, a major systemic disorder, is one of the most important risk factors for cardiovascular disease. Patients with diabetes have an increased risk of suffering from dyslipidemia concurrently.

Aims and Objective of the study

- To find out the association between Diabetic Retinopathy (DR) and Lipid Profile.
- To find out the possible mechanisms involving lipid metabolism and diabetic retinopathy.
- To find out the effect of lipid-lowering therapies on diabetic retinopathy.

Background

For traditional lipid markers, evidence is available that total cholesterol and low-density lipoprotein cholesterol are associated with the presence of

hard exudates in patients with DR. The study of nontraditional lipid markers is advancing only in recently years. The severity of DR is inversely associated with apolipoprotein A1 (ApoA1), whereas ApoB and the ApoB-to-ApoA1 ratio are positively associated with DR. The role of lipid-lowering medication is to work as adjunctive therapy for better control of diabetes-related complications including DR.

Material and Method

This retrospective study was conducted in the Ophthalmology Department in Katihar Medical College & Hospital, Katihar, Bihar from 1 January 2018 to 31 December 2019. The study was conducted with the approval of the Institutional Ethics committee with proper consent taken from the patients.

Inclusion Criteria

Patients with more than 5 years of diagnosed diabetes Type 2 were included.

Duration of diabetes ranged from 5 to 25 years.

Age group 20 to 80 years of age.

Exclusion Criteria

- Patients with history less than 5 years of diagnosed diabetes.
- Ocular surgery less than 6 months.
- Those with accelerated hypertension.
- Active ocular infection.
- Co-existing ocular disorders such as: -

Uveitis, Opaque or Hazy media, Retinal disorders such as retinal vein or artery occlusions or retinitis pigmentosa, vitreoretinal degenerations, dystrophies, high myopia, glaucoma and cataract were excluded from the study.

Result

A total of 40 patients were included in the study, there were 26 male and 14 females patients.

Of the 40 patients included in the study, 30 (75%) had DR and 10 (25%) did not have DR. Various grades of CSME were detected in 17 patients (42.5%).

Patients were divided into four groups as follows.

Group 1 included patients with no DR (the control group).

Group 2 included patients with mild-to-moderate nonproliferative DR with or without haemorrhages.

Group 3 included patients with severe nonproliferative DR with small haemorrhages

Group 4 included patients with proliferative DR with massive HES.

All patients were subjected to the following

- Full history taking:** Age of the patient, type of diabetes, duration of diabetes, mode of diabetic control, family history of diabetes mellitus and history of known ocular or medical diseases
- Clinical examination included:** Assessment of visual acuity, Refraction, Tonometry using applanation tonometer, Complete ophthalmological examination including slit-lamp biomicroscopy for anterior segment examination and using 78-D lens with or indirect ophthalmoscope with 20-D lens for fundus examinations and best-

corrected visual acuity using illuminated Landolt chart

3. Investigations

- Ocular:** Fundus Fluorescein Angiography and Optical Coherent Tomography
- Systemic:** Lipid profile measurements using Fasting samples, Fasting and Post-Prandial blood sugar and HbA1c.

Serum lipid measurements were carried out using fasting samples.

For the purpose of analysis, dyslipidaemia was defined as follows:

Serum Total cholesterol > 160 mg/dl

Triglyceride levels > 150 mg/dl

Low-density lipoprotein (LDL) levels > 100 mg/dl

High-density lipoprotein (HDL) < 40 mg/dl for men and less than 50 mg/dl for women^[6].

Patients were given antilipidemic therapy according to the type of lipid elevated by medical specialist as follows.

Atorvastatin 20 mg tablet was given daily after dinner for 2 weeks to patients with high total cholesterol or high cholesterol components [LDL and very-low-density lipoprotein (VLDL)].

After 9 months, the investigations were repeated again to see the effect of treatment.

Results

Between 1st January 2018 to 31st December 2019, 40 diabetic patients underwent this study, of whom 26 (65%) were male and 14 (35%) were female, and the mean age was 50.5 years (range = 20-80 years). Duration of diabetes ranged from 5 to 25 years. Thirty (75%) patients had DR and 10 (25%) patients did not have DR. Various grades of CSME were detected in 12 diabetic patients (42.5%).

Prevalence of DR is significantly increased with increasing age ($P < 0.05$). Various stages of CSME were significantly increased with increasing age ($P < 0.05$). Prevalence of DR is significantly increased with increased duration of diabetes. Various stages of CSME were significantly increased with increased duration of diabetes ($P < 0.05$).

Dyslipidaemia was found in 25 (62.5%) diabetic patients. Dyslipidaemia was found in 21 (70%) DR patients.

Twelve patients (48%) out of the 25 dyslipidaemia patients had CSME.

Serum lipid profile, including total cholesterol, LDL, VLDL and triglyceride level were elevated in DR and CSME. The incidence of patients with elevated total cholesterol and triglycerides was 33% of all DR patients. The incidence of patients with elevated LDL and triglycerides was 23.5% of all DR patients. The incidence of patients with elevated LDL and VLDL was 20% of all DR patients. An overall 23.5% of all DR patients had normal lipid profile.

The percentage of patients with elevated total cholesterol and triglycerides was 30% of all CSME patients. The percentage of patients with elevated LDL and triglycerides was 23.5% of all CSME patients. The percentage of patients with elevated LDL and VLDL was 18% of all CSME patients. An overall 29% of all CSME patients had normal lipid profile.

Haemorrhages was present in 21 (70%) DR patients with total cholesterol level above 230 mg/dl. In addition, hemorrhage was present in 80% of DR patients with the ratio of total cholesterol level to HDL above 4.5.

Retinal exudate decreased in patients who had exudative DR and took antilipid therapy regularly by about 60% in all DR patients. Mean visual acuity was 6/12 in group 1 (the control group), 6/18 in group 2, 6/36 in group 3 and below 6/60 in group 4. Mean visual acuity improved one to two lines on Landolt chart to be 6/12 in group 2, 6/18 in group 3 and 6/60 in group 4

Discussion

It is observed that as the duration of diabetes increases, the chances of having DR and CSME also increase. Various studies have shown an association of dyslipidaemia with macrovascular complications of diabetes (e.g. coronary artery disease), but few have studied the association of serum lipids with microvascular complications

such as DR and the available results are conflicting^{[6],[7]}.

Early Treatment Diabetic Retinopathy Study (ETDRS) and Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) showed a stronger evidence for the role of serum lipids in exudative maculopathy. In the ETDRS, it was also reported that higher baseline total and LDL-cholesterol levels increased the risk for retinal exudation by two-fold. Dornan *et al.*^[6] found that there is an association between total serum cholesterol and DR.

In our study, we found that total serum cholesterol level is directly associated with the severity of retinal HEs in patients with DR and dyslipidaemia. These results were nearly similar to the results gained by Rema *et al.*^[8], who found that individuals with elevated total serum cholesterol, LDL-cholesterol, or triglyceride levels are more likely to have or develop retinal HEs, which can be associated with risk for vision loss, independent of the extent of macular edema. Patients with a total cholesterol/HDL-cholesterol ratio of 4.5 or greater were almost twice as likely to have retinal HEs compared with those with a ratio less than 4.5. Patients with a higher quartile of total cholesterol or LDL-cholesterol levels were 5-6 times more likely to have retinal HEs than those with lowest quartiles. Moreover, patients with elevated total cholesterol (240 mg/dl or 6.21 mmol/l) were twice as likely to have retinal HEs at baseline (odds ratio = 2.00; 99% confidence interval = 1.35-2.95).

Similar results were found when comparing the elevated LDL levels (160 mg/dl or 1.14 mmol/l) with the lowest level of LDL (130 mg/dl or 3.37 mmol/l) and the odds ratio was 1.97 (99% confidence interval = 1.3-2.96).

Patients with elevated cholesterol and triglyceride levels were 50% more likely to develop retinal HEs. Elevated serum cholesterol at baseline also increased the risk for visual loss by 50% compared with lower serum cholesterol levels.

Actions to Control Cardiovascular Risk in Diabetes (ACCORD)^[12] is a randomized

controlled clinical trial with three components, determining the effects of lowering blood glucose, lowering blood pressure, and using fibrates to lower serum triglycerides and raise serum HDL-cholesterol levels (on a background of statin treatment) on cardiovascular disease in patients with type 2 diabetes, and a subset of participants with this study will be evaluated with a standardized protocol for comprehensive eye examinations and fundus photography consisting of the seven stereoscopic fields. An important association of DR with total cholesterol and serum triglycerides was showed^[8].

High serum triglycerides have also been shown to be associated with the increased risk of the development and progression of retinopathy by Hadjadj *et al.*^[13].

There has been increasing interest in the link between serum lipids and maculopathy in view of the evolving medical treatment. In type 2 diabetic patients, DME showed an association with increased LDL levels^[12]. Elevated serum cholesterol at baseline also increased the risk for visual loss by 50% compared with lower serum cholesterol levels^[9].

This association was maintained even after adjusting for age, as age by itself is a significant risk factor for hyperlipidaemia. The other significant finding in type 2 diabetes was that DME also showed a strong correlation with high LDL levels in the same study^[8].

We also found that the risk for visual acuity loss was associated with both the presence and increasing severity of HE at baseline, adjusted for the presence and increasing severity of macular oedema.

Conclusion

DR is one of the most important causes of vision loss worldwide. Serum lipid levels have a significant effect on the severity of retinal HEs. As the density of these HEs increases, they tend to migrate towards the foveal centre where their deposition predisposes to subfoveal fibrosis.

Lowering serum lipids has shown benefit on both proliferative DR and maculopathy.

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