Risk Factors Associated with Clinically Significant Macular Edema in Patients with Type 2 Diabetes Mellitus

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Abstract

Introduction: Diabetic macular edema (DME) is the major cause of vision loss in diabetic retinopathy (DR). Apart from diabetes, a number of other systemic factors have an important role in occurrence and progression of DME. Control of these factors along with control of blood sugars can prevent or reverse the maculopathy, thereby restore the vision of diabetic patients.

Methodology: Cross-sectional comparative study. Patients with Type 2 diabetes were screened for DR. After thorough examination including fundus examination, patients were divided into two groups (Group 1 - Retinopathy with clinically significant macular edema [CSME] and Group 2 - Retinopathy without CSME). A detailed history of the duration of diabetes, treatment history, hypertension, and hyperlipidemia were taken. The mean values of three consecutive blood pressure (BP) readings were assessed. Following blood investigation, serum lipid profile, glycosylated hemoglobin (HbA1c), urine albumin, renal function test of the concerned patients were done. The significance of the above risk factors was compared in both the groups involved in the study.

Results: In the present study of 170 patients with DR, there was no significant difference in the age and gender distribution among two groups. The mean value of fasting blood sugar, postprandial blood sugar, and HbA1c were higher in the study group than control group. In this study, the mean value of systolic BP and diastolic BP were significantly higher in the study group compared to control group. Serum lipids, serum cholesterol, triglycerides, low-density lipoprotein (LDL), and very LDL levels were significantly higher in patients with CSME. Microalbuminuria and macroalbuminuria showed a correlation with CSME.

Conclusion: Systemic risk factor shows a significant association with CSME in DR. Thus, early detection of these risk factors and their control has a significant role in preventing the development and progression of maculopathy in DR patients thereby preventing severe visual loss.

Key words: Albuminuria, Clinically significant macular edema, Diabetic retinopathy, Glycosylated hemoglobin, Hypertension, Lipid profile

INTRODUCTION

Diabetic retinopathy (DR) is a chronic progressive, potentially sight-threatening disease of the retinal vasculature associated with the prolonged hyperglycemia and other conditions linked to diabetes mellitus (DM) such as hypertension.¹ It eventually afflicts virtually all patients with diabetes. It is estimated that diabetes affects 4% of the world’s population, almost half of whom have some degree of DR at given time.²,³ DR occurs in all Type 1 and 75% of Type 2 DM after 15 years of duration of diabetes.²,⁴,⁵ Visual disability from DM is a significant public health problem. However, this morbidity is largely preventable and treatable.²

Diabetic macular edema (DME) is the most frequent cause of severe vision impairment in diabetic patients.⁶ Diabetic maculopathy can occur at any level of retinopathy and alter the structure of macula, significantly affecting its function. Although treatment of established retinopathy can reduce
the risk of visual loss by 60%, DR remains the leading cause of blindness among working-aged adults in the world.

The identification of risk factors is important for the evolution of better management strategies for DR. Previous studies have shown possible risk factors for retinopathy included diabetic duration, glycemic control, age of onset diabetic treatment, systemic hypertension, renal function/nephropathy, body mass, sex, human leukocyte antigen status, cigarette smoking, and elevated blood lipids.\(^\text{5,7-17}\) Despite the recognized importance of maculopathy as a cause of visual morbidity in diabetes, risk factors for maculopathy have received considerably less attention in the literature. Diabetic duration, age, sex, age of diagnosis, insulin use, higher glycosylated hemoglobin (HbA1C), diuretic use, systemic hypertension, and proteinuria have been associated with DME.\(^\text{14,18}\) Once diabetic maculopathy occurs, there is no satisfactory treatment and the prognosis of visual outcome is poor, so it is always better to prevent its development. Hence, there is a need for a study to find out the risk factors associated with the development of clinically significant macular edema (CSME) in diabetic patients, to control the same and subsequently reduce the incidence of diabetic maculopathy in future.

**METHODOLOGY**

This is a cross-sectional comparative study conducted in the Department of Ophthalmology from January 2014 to July 2015.

**Inclusion Criteria**

All patients (outpatients and inpatients) of either sex with Type 2 DM who will be screened for DR at ophthalmology outpatient department and found to have DR with or without CSME.

**Exclusion Criteria**

(1) Patients who have undergone any intraocular surgery in the past 3 months, (2) patients undergone any intraocular laser treatment or intraocular injection in the past 3 months, (3) patients with history of intake of drugs (corticosteroids, nephrotoxic) in the past 3 months or any non-diabetic renal disease, (4) patients suffering from non-diabetic maculopathy (age-related macular degeneration/macular dystrophy), (5) patients with chronic liver disease, (6) patients with significant media haziness preventing adequate visualization of the fundus, and (7) patients with insulin dependent DM or gestational DM.

All patients presenting with Type 2 DM were subjected to complete ophthalmologic examination by assessing the visual acuity with Snellen chart, slit lamp examination, intraocular pressure with I care tonometry. Fundus examination was conducted with a direct ophthalmoscope, indirect ophthalmoscope, and slit lamp biomicroscopy using +90D lens.

After fundus examination, only patients having retinopathy in at least one eye were selected for further study and subsequently divided into 2 groups (Group 1 - Retinopathy with CSME and Group 2 - Retinopathy without CSME). Informed consent was taken from the concerned patients. Fundus picture of the patients was taken with DRS and fundus camera. DR was classified according to early treatment DR study criteria. OCT was done in a few patients with CSME to quantify and find out the type of macular edema. FFA was done in a few patients to decide on the treatment plan.

A detailed history of the duration of diabetes, type of treatment, smoking/tobacco use, hyperlipidemia and hypertension were taken from the above-selected patients. The mean value of the three consecutive blood pressure (BP) reading was assessed. Following blood investigations (serum lipid profile, glycosylated Hb, urine albumin, and renal function test) of the concerned patients was done. HbA1c determination is based on the turbidimetric inhibition immunoassay. The significance of the above risk factors was compared in both the groups involved in the study like descriptive.

The data were analyzed using various statistical tests such as descriptive and inferential statistics, mean ± standard deviation (minimum-maximum), Student’s t-test (two-tailed independent), and Chi-square or Fischer exact test.

**RESULTS**

In this comparative study, 85 patients were allotted in each group. The mean age of the patients in the study group (with CSME) was 57.02 ± 9.75 and in the control group (without CSME) mean age was 56.42 ± 9.25. There was no significant difference in age distribution between the two groups \(P = 0.681\) (Table 1). In the study group, 46 (54.1%) were males and 29 (34.1%) were females. In the control group, 56 (65.9%) were males and 29 (34.1%) were females. There was no significant difference in the gender distribution among the two group \(P = 0.117\).

In this study, 20% had duration <5 years, 27.1% in between 5 and 10 years, 25.9% in between 11 and 15 years, 16.5% in between 16 and 20 years, and 10.6% >20 years. In the control group, the majority of patients had duration <5 years (44.7%). This shows that the duration of diabetics is more in a study group with \(P = 0.003\).
Table 2 shows the distribution of the patients in both the groups on the basis of treatment. In the study group, out of 85 patients, 2 (2.4%) have not received any treatment, whereas in the control group, none of the patients were there without treatment. The majority of the patients in both the groups were on treatment with oral hypoglycemic agents (57.7% in the study group and 74.1% in control group). In the study, 40% patients were on treatment with insulin, whereas in control group, 16.4% were on treatment with insulin.

Tables 3 and 4 compare the laboratory investigations between the two groups which are studied such as fasting blood sugars, postprandial blood sugar (PPBS), HbA1c, lipid profile, and urine albumin levels.

Table 5 shows the best corrected visual acuity (BCVA) in patients of both the groups (considering the BCVA of the worst eye). In the study group, out of 85 patients, none had BCVA of 6/6, whereas in the control group, 20 patients had BCVA of 6/6. The majority of patients in the study group had moderate visual impairment (51.76%), whereas in the control group, only 24.71% had moderate visual impairment. In the study group, out of 85 patients, 21 (24.71%) had severe visual impairment, whereas in the control group, only 1 patient (1.18%) had severe visual impairment.

Table 6 shows the severity of DR in both the groups (according to the worst eye). The majority of patients in
Table 6: Comparison of the severity of DR between the study and control group

<table>
<thead>
<tr>
<th>Fundus</th>
<th>Study group (n=85)</th>
<th>Control group (n=85)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild NPDR</td>
<td>10 (11.76)</td>
<td>32 (37.65)</td>
</tr>
<tr>
<td>Moderate NPDR</td>
<td>33 (38.82)</td>
<td>32 (37.65)</td>
</tr>
<tr>
<td>Severe NPDR</td>
<td>23 (27.06)</td>
<td>11 (12.94)</td>
</tr>
<tr>
<td>PDR</td>
<td>19 (22.35)</td>
<td>10 (11.76)</td>
</tr>
</tbody>
</table>

DR: Diabetic retinopathy, NPDR: Non-proliferative diabetic retinopathy, PDR: Proliferative diabetic retinopathy

In this study, the mean systolic and diastolic BP were significantly higher in patients with CSME.

There has been increasing interest in the link between the serum lipids and maculopathy in view of the evolving medical treatment for hyperlipidemia. In this study, serum cholesterol, triglycerides level (TGL), low-density lipoprotein (LDL), and very LDL levels were significantly higher in patients with CSME. The association between serum lipids and CSME is biologically plausible. Several proposed mechanisms discussed in earlier reports include the direct involvement of serum lipids in endothelial dysfunction20 which subsequently results in the breakdown of the blood-retinal barrier.

In our study, the incidence of microalbuminuria and macroalbuminuria is significantly more associated with CSME. 81.2% patients with CSME had macroalbuminuria and 12.9% patients with CSME had microalbuminuria. This shows that both clinical and subclinical nephropathy has an important role in diabetic maculopathy. Hypoalbuminemia, which may be secondary to renal loss of albumin, has been postulated to be one of the factors involved in the formation of macular edema.

CONCLUSION

In this study, duration of DM, uncontrolled glycemic status, systemic hypertension, albuminuria, serum cholesterol, TGL, LDL, and VLDL showed a significant association with CSME. However, serum high-density lipoprotein has not shown a correlation with CSME.

REFERENCES


