INTRODUCTION
Diabetes Mellitus refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Depending on the etiology of the Diabetes Mellitus, factors contributing to hyperglycemia include reduced insulin secretion, inefficient insulin action or decreased glucose utilization and increased glucose production.

Diabetic retinopathy (DR) a major microvascular complication of Diabetes mellitus is a major cause of visual disability and blindness. Diabetic retinopathy (DR) is characterized by retinal microvascular abnormalities that progressively lead to retinal non-perfused areas, edema, neovascularization, and tractional retinal detachment. The severity of diabetic retinopathy is directly correlated with the duration and control of diabetes. Early detection and timely intervention can prevent vision loss associated with diabetic retinopathy.

Other complications associated with diabetes mellitus include increased cardiovascular risk, renal dysfunction, peripheral neuropathy, and peripheral vascular disease. Diabetic retinopathy is a major microvascular complication of diabetes mellitus which can lead to blindness if not treated in time. Therefore, it is essential to identify the risk factors associated with diabetic retinopathy to prevent its complications.

PURPOSE: 1. To study the relationship between the severity of diabetic retinopathy and serum lipid levels. 2. To evaluate the relationship between serum lipid levels, diabetic retinopathy changes including CSME.

METHODS: 100 diabetic patients without retinopathy (group A), 100 diabetic patients with retinopathy (group B), 100 nondiabetic patients with no retinopathy as control (group C) according to ETDRS chart were studied. Total cholesterol(TC), triglycerides(TG), high-density lipoprotein(HDL), low-density lipoprotein (LDL), very-low-density lipoprotein (VLDL) and Fasting plasma glucose (FGP), 2hr Plasma Glucose (2hr PG), HbA1C (glycosylated hemoglobin) levels were compared among the groups.

RESULTS: The groups were age and gender matched (P = 0.474 and P = 0.84 respectively, one-way ANNOVA test). The mean duration of diabetes was higher in Group A than Group B (P = <0.0001; P = >0.0001 respectively). The Body Mass Index is higher in both Group A and Group B than Group C (P = <0.0001; P = <0.0001; P = >0.0001 respectively). The mean FBS, PPBS, and HbA1C were higher for Group A and B than the control group C (P = <0.0001; P = <0.0001; P = >0.0001 respectively). The mean TG and VLDL are higher in Group A and B than Group C (P = 0.043; P = 0.044 respectively). The mean LDL was lower in Group A than the other two (P = 0.674).

Out of 56 cases of CSME among diabetic patients, 44(78.5%) had CSME in both eyes which were significantly higher (Z=6.87; p<0.0001). No CSME was found among Group B and C.

CONCLUSION: Serum Lipid levels were significantly associated with the severity of DR and the existence of CSME in those patients.

KEYWORDS:
- Diabetic Retinopathy
- Serum Lipid levels
- Lipid Profile
- Diabetes Mellitus
- CSME
- Patient Characteristics
- Risk Factors
- Statistical Analysis
Also, One Way Analysis of variance (ANOVA) followed by post hoc Tukey’s test was performed with the help of Critical Difference (CD) or Least Significant Difference (LSD) at 5% and 1% level of significance to compare the mean values. p<0.05 was taken to be statistically significant.

Chi-square ($\chi^2$) test showed that there was no significant difference in gender and the patients of the three groups (p=0.84)

ANOVA-test showed that there was no significant difference in the mean ages of the patients of the three groups (p=0.474).

Thus the patients of the three groups were matched for their ages and gender.

t-test showed the mean duration of diabetes of Group-A was significantly higher than that of Group-B.

ANOVA-test showed that there were significant differences in mean FBS, PPBS, and HbA1c of the patients of the three groups (p<0.0001). As per Tukey’s Critical Difference (CD), the mean FBS, PPBS, and HbA1c of the patients of Group-A and Group-B were significantly higher than that of the control group (p<0.0001).

Also, the mean FBS, PPBS, and HbA1c of the patients of Group-A were significantly higher than that of Group-B (p<0.0001).

Table-2: Comparison of parameters related to the level of blood sugar of the patients of the three groups

ANOVA-test showed that there were significant differences in mean FBS, PPBS, and HbA1c of the patients of the three groups (p=0.0001). As per Tukey’s Critical Difference (CD), the mean FBS, PPBS, and HbA1c of the patients of Group-A and Group-B were significantly higher than that of the control group (p<0.0001).

Also, the mean FBS, PPBS, and HbA1c of the patients of Group-A were significantly higher than that of Group-B (p<0.0001).

Table-3: Comparison of the lipid profile of the patients of the three groups

ANOVA-test showed that there were significant differences in mean TG and VLDL of the patients of the three groups (p=0.0001). As per the Tukey’s Critical Difference (CD), the mean TG and VLDL of the patients of Group-A were significantly higher than that of Group-B and control group (p<0.0001).

ANOVA-test showed that there were no significant differences in mean TCH, LDL, and HDL of the patients of the three groups (p=0.05). But the mean of these parameters except HDL was higher in Group-A. Mean HDL was lower in Group-A.

Table-4: Distribution of fundus finding and status of CSME of the diabetic patients

Corrected Chi-square ($\chi^2$) test showed that there was a significant association between fundus finding and status of CSME of the patients (p=0.0001).

The presence of CSME significantly increased with the severity of NDRP.

<table>
<thead>
<tr>
<th>Fundus finding</th>
<th>CSME Present</th>
<th>CSME Absent</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild NPDR</td>
<td>1</td>
<td>27</td>
<td>28</td>
</tr>
<tr>
<td>Row %</td>
<td>3.6</td>
<td>96.4</td>
<td>100.0</td>
</tr>
<tr>
<td>Col %</td>
<td>1.8</td>
<td>11.1</td>
<td>9.3</td>
</tr>
<tr>
<td>Moderate NPDR</td>
<td>23</td>
<td>14</td>
<td>37</td>
</tr>
<tr>
<td>Row %</td>
<td>62.2</td>
<td>37.8</td>
<td>100.0</td>
</tr>
<tr>
<td>Col %</td>
<td>41.1</td>
<td>5.7</td>
<td>12.3</td>
</tr>
<tr>
<td>Severe NPDR</td>
<td>15</td>
<td>1</td>
<td>16</td>
</tr>
<tr>
<td>Row % Col %</td>
<td>93.8</td>
<td>6.3</td>
<td>100.0</td>
</tr>
<tr>
<td></td>
<td>26.8</td>
<td>0.4</td>
<td>5.3</td>
</tr>
<tr>
<td>Very Severe</td>
<td>4</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>NPDR</td>
<td>100.0</td>
<td>0.0</td>
<td>100.0</td>
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<tr>
<td>Row % Col %</td>
<td>7.1</td>
<td>92.9</td>
<td>1.3</td>
</tr>
<tr>
<td>PDR</td>
<td>13</td>
<td>22</td>
<td>15</td>
</tr>
<tr>
<td>Row %</td>
<td>86.7</td>
<td>13.3</td>
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<td>100.0</td>
</tr>
<tr>
<td>Col %</td>
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<td>82.0</td>
<td>18.0</td>
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<tr>
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<tr>
<td>Row %</td>
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<td>81.3</td>
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</tr>
<tr>
<td>Col %</td>
<td>100.0</td>
<td>0.0</td>
<td>100.0</td>
</tr>
</tbody>
</table>

DISCUSSION

The present study was conducted in a tertiary care teaching institute. This was an observational study done to identify the different stages of diabetic retinopathy in correlation with serum lipid levels.

It is believed that the Indian population generally has an unusually efficient glucose metabolism. Paralleling the high prevalence of diabetes is a concern that the complications of diabetes, mainly diabetic retinopathy are increasing.

Hyperglycemia and dyslipidemia are two major metabolic disorders seen in patients with diabetes mellitus. Diabetes mellitus is justifiably known as ‘devil’ or silent killer affecting almost every tissue and cell in the human body. Ocular complications like retinopathy which are microvascular complications are innocuous in onset progressively destructive in their course and are remediable only to a point. Over the years, voluminous information has accumulated on the pathogenesis of diabetes complications like retinopathy. Many clinical trials and researches have yielded fruitful results.

The role of diabetic dyslipidemia in the development of microvascular complications has received much less attention. This study aimed to determine the relationship between serum lipid profile and the severity of diabetic retinopathy in type 2 diabetes patients.

In the present study, 200 patients having type 2 diabetes mellitus were studied. 100 age and gender matched controls were also studied. The patients were categorized with respect to the presence or absence of diabetic retinopathy. In the group having retinopathy, patients were subcategorized depending on the severity/grade of retinopathy and the presence or absence of CSME.

The present study had a near equal gender distribution. The male to female ratio [M: F] was 53:47. In a clinical cohort in Chennai diabetic retinopathy appeared to be prevalent more in the males compared to the females (sex ratio 2:1). Similar male preponderance was also seen in the CURES Eye study, UKPDS study Gupta et al and the Andhra Pradesh Eye Disease Study (APEDS). However, the difference with respect to gender distribution was not significant statistically in the current study (p=0.84).

The mean age in each group was 57.04±10.27; 56.32±9.89; 56.10±10.89 years. The relationship of retinopathy with age was in concordance to that found in many other studies. Like several other epidemiologic studies, this study also showed an increased prevalence of DR with increasing age. APED Study, CURES Eye Study, Dondana, et al also found a significant correlation between the patient’s age and diabetic retinopathy.
In the present study, the duration since diagnosis of diabetes (diabetic age) ranged from 5 - 22 years. There may be some bias in estimating the real duration of diabetes in these patients, as the discovery of diabetes could have been delayed due to a lack of symptoms and the insidious onset of type 2 diabetes. The mean duration of diabetes in group A and group B were 11.12±6.27 and 9.46±5.51 respectively.

The association of longer duration with a higher risk of diabetic retinopathy was in accordance with previously published reports (DCCT; WESDR; Klein et al; UKPDS; Larsson et al; Wong et al; Varma). It is obvious that patients with retinopathy significantly had a longer mean duration of diabetes. Wisconsin Epidemiological Study of Diabetic Retinopathy (WESDR) also found that the risk of retinopathy is directly related to the duration of diabetes. In India, virtually all studies have shown an increased prevalence of DR as the duration of diabetes.

The Hoorn study, a large population-based study to determine the overall association of DR with total triglyceride, it did not correlate with the severity of DR.

In contrast to the present study, the EURODIAB Complications Study found that the triglyceride level was related to all levels of retinopathy.

Klein et al, while assessing the serum lipid levels in the subjects who participated in the Wisconsin Epidemiologic Study of Diabetic Retinopathy found a significant trend for increasing severity of diabetic retinopathy and of retinal hard exudate with increasing cholesterol. In the present study although there was an overall association of DR with total triglyceride, it did not correlate with the severity of DR.

In the present study, all lipid parameters were higher in subjects with severe NPDR, very severe NPDR and PDR compared with subjects without DR. Elevated triglyceride was found to be a significant risk factor for severe NPDR and PDR even after age adjustment, duration of diabetes, HbA1c, and albumin excretion rate in EURODIAB study.

These findings have been supported by examination of a subgroup of patients included in the group for the study had various types and grades of cataract and correction for the same could not be done during statistical analysis. CURES Eye study serum cholesterol concentrations were higher in subjects with moderate NPDR compared with subjects without DR (p<0.05). Triglyceride concentrations were higher in those with mild NPDR compared with those without DR (p<0.05).

The present study found a significant association with the increasing presence of CSME with increased severity of DR. Out of 56 cases of CSME among the diabetic patients 44 (78.5%) had CSME in both eyes which were significantly higher (Z=6.87; p<0.0001). This was in accordance with the study by Al-Bdour et al who found a significant association between the development of diabetic maculopathy and hypercholesterolemia.

Higher total cholesterol was positively associated with the presence of CSME, in a cross-sectional analysis of participants with diabetes in the WESDR Study. CURES Eye Study also showed an association of Diabetic Macular Edema in type 2 diabetic subjects with increased cholesterol.

The present study showed that there was an increase in the severity of diabetic retinopathy with increasing levels of different serum lipid subfractions. Larsson et al showed a linear relationship of serum cholesterol levels with severity of diabetic retinopathy.

CONCLUSION

The number of adults with diabetes in the world is estimated to increase by 122% (135 million in 1995 to 300% in 2025). This increase is expected to be 42% in the developed world and 170% in the developing countries. India stands first with 195% (18 million in 1995 to 54 million in 2025). Numerous studies have shown an association of lipid fractions with hyperglycemia is also associated with dyslipidemia, specifically increased levels of total cholesterol and triglycerides, a slight elevation of LDL, but generally little if any change in HDL. Consequently, hyperglycemia may be an important confounding factor in the study with respect to both diabetic retinopathy and hypertriglyceridemia. HbA1c levels were increased with increasing severity of diabetic retinopathy.
macrovacular complications of diabetes, while relatively few looked at the association of serum lipids with microvascular complications such as diabetic retinopathy and the available results are conflicting.6

The present study demonstrated a statistically significant correlation between diabetic retinopathy and hypertriglyceridemia. Increased triglyceride level was significantly associated with the occurrence of all grades of retinopathy, especially severe NPDR, very severe NPDR and PDR. It showed a statistically significant correlation between FBS, PPBS and HbA1c with the development of CSME in diabetic retinopathy. It showed no correlation with CSME and visual acuity in diabetic patients with no retinopathy and controls.

Further studies are required to establish a causal relationship between dyslipidemia and diabetic retinopathy. If established, these data can lend additional support to current treatment guidelines recommending the aggressive lowering of elevated lipids among diabetic patients. Rigorous lipid control, in addition to its known health benefits in preventing cardiovascular disease, may also lessen ocular morbidity and associated health care costs, thereby potentially improving the quality of life and vision among people with type 2 diabetes.

REFERENCES

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