Correlation between Severity of Diabetic Retinopathy with HbA1c in Type II Diabetic Patients

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Abstract
Introduction: Type 2 Diabetes is now a global endemic and the prevalence is ever increasing with socio economic changes, more geriatric population, urbanisation, dietary changes, less physical exercise and lifestyle changes. The risk of developing microvascular complications increases with duration and severity of diabetes. So through this study we tried to explore the relationship between severity of diabetes with development of retinopathy.

Material & Methods: A total of 472 patients with known history of type 2 Diabetes mellitus attending the ophthalmology OPD of our hospital were for enrolled for the study. The study is a cross sectional study. The cases were subjected to detailed ocular examination after noting their detailed medical and demographic history. Diabetic retinopathy if noted was graded according to ETDRS classification. All patients were investigated for serum creatinine, serum urea, fasting or postprandial blood sugar levels, HbA1c levels and urine microalbumin levels.

Results: Of the total 472 cases there were 261 males and 211 females, so the female: male ratio was 0.8:1. The majority of the patients lie in age group of 41 to 60 years. Patient who did not had any diabetic retinopathy were classified in group 1. While the rest of patients who had diabetic retinopathy was categorized in group 2, which was further divided in 3 groups -into IIa who suffer from mild to moderate NPDR, group IIb suffering from severe to very severe NPDR and group IIc who suffered from proliferative diabetic retinopathy.

Conclusion: There was a statistical significant correlation between the severity of diabetic retinopathy and diabetes duration. Also statistically significant Association was found between Hb a1c values and severity of diabetic retinopathy.

Keywords: HbA1c, diabetes duration, diabetic retinopathy.

Introduction
Diabetes mellitus (DM) is a group of metabolic disorders that results in hyperglycemia because of defects in insulin secretion or its action or both[1]. It is emerging as a global endemic both in developing and developed countries[2]. It is characterized by recurrent or persistent hyperglycemia, and is diagnosed by demonstrating any one of the following: fasting blood sugar (FBS) level at or above 126 mg/dL, plasma glucose at or above 200 mg/dl two hours after a 75 g oral glucose load as in a glucose tolerance test (GTT), random plasma glucose at or above 200 mg/dl, (WHO report, 2006)[3]. The prevalence of diabetes in India is found to be 2.4% in rural and 4–11.6% in urban population[4].
Glycosylated hemoglobin (HbA1c) is a commonly used marker for determining long-term control of blood sugar. The HbA1c test is done every 3 to 4 months, and unlike blood sugar levels, the test does not change with any recent changes in diet, exercise or medicines. Higher levels, indicating poorer control of blood glucose have been associated with cardiovascular disease, nephropathy & retinopathy. The HbA1c assay is the basis of treatment guidelines and is used universally to adjust therapy.

Microvascular complications are very common in diabetes, diabetic retinopathy being the most common. There is direct correlation between the risk of developing diabetic retinopathy, duration of diabetes and severity of hyperglycemia. Most patients with Type 1 Diabetes develop retinopathy within 20 years of diagnosis, and in type 2 diabetes it may develop as early as 7 years before the diagnosis of diabetes. Through this study we tried to correlate the degree of severity of diabetic retinopathy with its diabetes duration and level of hyperglycemia.

This was an outpatient based cross-sectional study in which 472 consecutive patients with known history of type 2 Diabetes mellitus, who attended the outpatient department of ophthalmology OPD were enrolled. Exclusion criteria included patients with gestational diabetes, acute or chronic Kidney Disease, cancer, coronary artery disease, patients with hazy ocular media which did not allow proper fundus visualisation, other retinal pathologies and coexisting conditions like fever, systemic infections, malignant hypertension or congestive cardiac failure. Blood samples were collected after 10 hours of fasting and Vitros 5,1 FS machine was used for testing Hba1c (estimated by turbidimetric innovation method). Chi square test was used to analyse the data and p value of 0.05 or less was considered to be significant.

After a detailed demographic and medical history recording a detailed ocular examination was performed in a preset proforma which included unaided and best corrected visual acuity, complete anterior segment evaluation with slit lamp which special note of details like neovascularization of iris and cataract. Fundus examination was performed both by direct ophthalmoscopy & + 90 D lens using slit lamp for posterior pole examination while periphery was examined by indirect ophthalmoscope and a detailed note of optic disc, macula and general fundus was made. Amsler grid examination to evaluate 20 degree of Central visual field was done in all patients and any deviations from normal were noted. Intraocular pressure was recorded using goldmann applanation tonometer.

The severity of diabetic retinopathy was graded strictly according to it ETDRS classification. Optical coherence tomography was done in all patients and macular thickness was recorded.

**Results**

Out of the total 472 patients registered in the study, there were 261 males and 211 females. The female to male ratio was 0.8 : 1. Majority of the patients were in the age group of 41 to 60 years (54.87%) followed by 61 to 80 years (25.63%) with mean age being 54.43 ± 7.56 years. (Table 1)

**Table 1** Demographic distribution of study population

<table>
<thead>
<tr>
<th>Age group ( years )</th>
<th>No. of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>261</td>
<td>55.29</td>
</tr>
<tr>
<td>Female</td>
<td>211</td>
<td>44.71</td>
</tr>
<tr>
<td>20-40</td>
<td>62</td>
<td>13.13</td>
</tr>
<tr>
<td>21-40</td>
<td>259</td>
<td>54.87</td>
</tr>
<tr>
<td>61-80</td>
<td>121</td>
<td>25.63</td>
</tr>
<tr>
<td>&gt;80</td>
<td>30</td>
<td>6.35</td>
</tr>
</tbody>
</table>

Out of 472, 253 patients did not had any diabetic retinopathy and they are classified as group I. Rest of the 219 patients who had diabetic retinopathy were divided into three groups based on a ETDRS classification- group Ila included mild to moderate NPDR, group Iib included severe to very severe NPDR, while patients with proliferative diabetic retinopathy (PDR) were classified in Group Iic. A statistically significant association between severity of diabetic retinopathy and the duration of diabetes was seen (table 2)
Severity of hyperglycemia was graded according to HbA1c levels. Values less than 7% were considered to be good control of diabetes. Levels between 7.1 to 8.5% - fair control and levels beyond 8.5% were considered to be in poor control.

Table 3 shows that the prevalence of diabetic retinopathy is less (23.53%) among patients with good control of diabetes as compared to those with fair (79.04%) or poor control (98.6%) of diabetes. There is a higher chance of developing a Proliferative diabetic retinopathy in patients with poor control (36.0%) as compared to fair control (4.4%) and good control (0.3%) of HbA1c values. A statistically significant association between severity of retinopathy and HbA1c values was found (p < 0.001) (Table 3).

### Table 2

<table>
<thead>
<tr>
<th>Duration Of Diabetes (Years)</th>
<th>Group I (No Retinopathy)</th>
<th>Group Mild To Moderate</th>
<th>Group IIb (severe to very Severe NPDR)</th>
<th>Group IIc (Proliferative Diabetic Retinopathy)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>&lt;10 years</td>
<td>218</td>
<td>66.4031621</td>
<td>66</td>
<td>53.60</td>
</tr>
<tr>
<td>10-20 years</td>
<td>141</td>
<td>29.2490119</td>
<td>24</td>
<td>26.27</td>
</tr>
<tr>
<td>21-40 years</td>
<td>84</td>
<td>3.55731225</td>
<td>45</td>
<td>26.27</td>
</tr>
<tr>
<td>&gt;40 years</td>
<td>29</td>
<td>0.79051383</td>
<td>22</td>
<td>7.241935</td>
</tr>
</tbody>
</table>

$\chi^2 = 180.56, p < 0.01$

### Table 3

<table>
<thead>
<tr>
<th>HbA1c</th>
<th>Group I (No Retinopathy) (n = 253)</th>
<th>Group IIa (Very Mild To Moderate) (n = 124)</th>
<th>Group IIb (Severe To Very Severe) (n = 61)</th>
<th>Group IIc (Proliferative Diabetic Retinopathy) (n = 34)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=</td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Good control (&lt; =7.0%)</td>
<td>254</td>
<td>76.5625</td>
<td>54</td>
<td>21.09375</td>
</tr>
<tr>
<td>Fair control (7.1-8.5%)</td>
<td>156</td>
<td>33.5443038</td>
<td>56</td>
<td>35.443018</td>
</tr>
<tr>
<td>Poor control (&gt; 8.5%)</td>
<td>58</td>
<td>6.89655172</td>
<td>14</td>
<td>24.137931</td>
</tr>
</tbody>
</table>

The chi-square = 252.8653. The p-value is < 0.00001.

### Discussion

The prevalence of type 2 DM is estimated to double by 2030 [12]. Diabetes is known to be associated with both microvascular and macrovascular complications, including retinopathy, nephropathy, and neuropathy (microvascular) and ischemic heart disease, peripheral vascular disease, and cerebrovascular disease (macrovascular), resulting in organ and tissue damage in approximately one third to one half of people with diabetes [10]. The higher the degree of diabetes, the more likely are the chances to develop these complications.

In our study, we found that most of patients who have diabetic retinopathy, had very mild to moderate non-proliferative diabetic retinopathy (56.62%) followed by severe to very severe non-proliferative diabetic retinopathy (27.85%). Only 34 (15.52%) cases had proliferative diabetic retinopathy. Other cross-sectional studies, also shows that the prevalence of different grades of retinopathy have been shown to be of similar variety among the different glycemic control levels [13-17].

So it is important to evaluate the role of glycemic control and its index on prevalence of diabetic retinopathy. In our study we found that patients...
having a good glycemic control (HbA1c < 7%) had lower prevalence of diabetic retinopathy (23.4%) as compared to those having poor control (HbA1c > 7%) (76.6%). The percentage increased to as high as 93.1% chances of having a diabetic retinopathy if the HbA1c levels are above 8.5 % indicating a poor control of diabetes and more severe micro vascular complications. It was also seen that only 1 (0.4%) patient having good control with HbA1c levels < 7% developed proliferative diabetic retinopathy as compared to 7/158 (4.4%) of those having fair control HbA1c level between 7.1-8.5% and 26/58 (44.8%) of those having HbA1c level > 8.5%. Similar to our study results, Manaviat et al (2004) also found a significant association between HbA1c, level and diabetic retinopathy. A similar association was also observed in other studies as well.

Our study throws light on the relationship between the control level of type 2 diabetes mellitus and diabetic retinopathy. It was seen that higher grades of HbA1c is associated with higher severity of diabetic retinopathy and so can be used as a successful predictor and warning for such patients. Our study was limited by time, so a better understanding of this relationship could be gathered with the help of more longer longitudinal clinical trials with newly diagnosed type 2 diabetic patients.

**Conclusion**

The results of our study endorses and strengthen the view the that higher levels of HbA1c is associated with greater risk and severity of development of diabetic retinopathy and so should and can be used as a predictor for the development of diabetic retinopathy

**References**

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