Risk Indicators of Diabetic Retinopathy in Patients with type 2 Diabetes Screened by Fundus Photographs: A Study from Rural India

B. Silpa¹, Srikanth Evuru²

¹Fellow in Medical Retina, Sankara hospital, Guntur.
²Consultant physician and Diabetologist, Mamatha hospital, Tenali, Guntur district, AP, India

Abstract: This study aims to evaluate the risk indicators of diabetic retinopathy in patients with type 2 diabetes screened by fundus photographs at a tertiary care diabetes centre in Tenali, AP, INDIA. A cross-sectional study was conducted at the outpatient department of MAMATHA HOSPITAL, TENALI, from October 2015 to March 2016. Patients ≥30 years of age were recruited randomly. Demographic, anthropometric, clinical and biochemical data were collected, and ophthalmic screening was done by two field fundus photography. Fundus photographs of 366 patients were graded according to the modified Early Treatment Diabetic Retinopathy Disease Severity Scale (ETDRS) criteria. Retinopathy was present in 27.3% patients. Fifteen percent of patients had non-sight-threatening retinopathy while 12% had sight-threatening retinopathy. Patients with retinopathy had significantly increased mean duration of diabetes, systolic and diastolic blood pressure and HbA1c (p<0.001). Patients with sight-threatening retinopathy also had increased serum cholesterol (p<0.05) and serum creatinine (p<0.001). Multivariate logistic regression revealed male gender (3.5 times, 95% confidence interval (CI): 1.73-7.12), increased duration of diabetes (≥10 years, 5.46 times, 95% CI: 2.15-13.85), hypertension (≥130/85, 1.96 times, 95% CI: 0.95 - 4.03) and poor glycemic control (HbA1C ≥7%, 1.39 times, CI: 1.23 - 1.56) as significant factors for developing retinopathy. Diabetic retinopathy was present in every fourth subject, while sight-threatening retinopathy was present in every eighth subject with type 2 diabetes. The results of the present study highlight the importance of screening for retinopathy. The identification of risk indicators associated with retinopathy in our population may lead to measures of prevention of sight-threatening complication of diabetes. Fundus photographs revealed increased frequency of retinopathy among patients with type II diabetes. Male gender, increased mean duration of diabetes, hypertension and poor glycemic control related with the presence of retinopathy, while increased serum cholesterol and creatinine related with severity of retinopathy. The present study highlights the importance of screening for retinopathy. The presence and severity of retinopathy in this population was attributed to the factors identified in earlier studies. The present study thus validated the findings of studies conducted on diverse populations across the world.

Keywords: Retinopathy. Fundus photography. Risk indicators. Diabetes.

1. Introduction

Diabetes mellitus is considered as one of the leading causes of kidney failure, non-traumatic lower limb amputations and new cases of blindness in the developed world [1]. This overwhelming morbidity of diabetes in largely attributed to long-term chronic complication [2]. Diabetic retinopathy (DR) is one of the microvascular complications of diabetes and a leading cause of visual disability and acquired blindness [3]. Visual impairment as a result of diabetic retinopathy not only has significant impact on quality of life but it can also compromise the ability of a patient to manage his disease successfully [4]. It is also found to have an impact on the incidence of other diabetic complications and overall life expectancy [5].

With increasing prevalence of diabetes, global data support the assumption that DR will become one of the most important causes of blindness in the future. It is anticipated that 20% of people with diabetes will develop DR [6-9]. This alarming situation prompted the investigators to focus on the tertiary prevention of diabetes. A series of epidemiological studies on DR were initiated and identified several factors related with the development and progression of this complication [10 – 16]. However, due to ethnic disparity, difference in life styles and food habits, distinct environment and diverse genetic susceptibility, their findings need to be validated in our population.

Since exploration of the factors related with DR is necessary for the prevention and management of this diabetes complication, some investigators have attempted to address this issue in Pakistan [17 – 23]. However, as far as the literature search done, this is the first study in which screening for DR was carried out by fundus photography, a more sensitive and specific method for the screening of retinopathy than ophthalmoscope [24]. Thus, based on the findings of fundus photographs, two distinct cohorts of diabetic patients with retinopathy and without retinopathy were assembled with reliability. Hence, the present study was designed to find out the association of various factors with retinopathy.

2. Methods

This cross-sectional study was conducted at MAMATHA HOSPITAL, TENALI, from October 2015 to March 2016. Patients were recruited randomly from the outpatient department of MHT after taking a signed informed consent. Greater than 30 – year – old patients with type 2 diabetes of either sex were considered eligible to participate in the study. Patients with type 1 diabetes and pregnant women were excluded. Data on demographic, anthropometric, clinical and biochemical parameters was collected for each recruited patient.
Anthropometry
Height and weight of participants were measured in light clothes after their consent. A digital scale placed on a flat surface was used for measurement of weight. Weight was recorded to the nearest 0.1 kg. Height was measured in erect posture, touching the occiput, back, hip and heels on the wall. Height was taken to the nearest of 0.1 cm. body mass index (BMI) was calculated as weight in kilograms per height in square metres. Blood pressure was measured by adult-fitted standard cuffs in sitting position after 10 min of rest. Hypertension was defined as a blood pressure of ≥130/85 mmHg [25]. Hypertensive also included subjects with known hypertension who were already on antihypertensive medications prescribed by a doctor.

Ophthalmic examination
Each recruited patient went through ophthalmic examination by fundus camera (Canon CR – 1) for screening of diabetic retinopathy. After checking the best correct visual acuity by internally illuminated Snellen’s chart, one to two drops of phenylephrine was instilled in both eyes of the patients. After 20 – 30 min when the pupils were dilated, two field fundus photographs of each eye were taken, one central to the optic disc and the other central to macula. All retinal photographs were graded by a retinal specialist according to the Diabetic Retinopathy Disease Severity Scale, a modification of the Early Treatment Diabetic Retinopathy Disease Severity Scale (ETDRS) [26].

Based on the findings of fundus photographs, patients with signs of diabetic retinopathy were categorized into the DR group and those without sign of retinopathy were in the NDR group. Patients with retinopathy (DR group) were subsequently sub-grouped on the basis of severity of lesions into non-sight-threatening diabetic retinopathy (NSTDR) and sight-threatening diabetic retinopathy (STDR) groups. Since mild or moderate non-proliferative diabetic retinopathy (NPDR) does not pose immediate threat to vision, they were collectively labelled as NSTDR. Diabetic retinopathy that needs immediate referral and urgent treatment was categorized as STDR, PDR and diabetic macular edema alone or in combination with NPDR or PDR were included in the category of STDR.

It is not necessary that both eyes of a person be affected simultaneously and if affected, to be affected by the same severity. Therefore, the presence of retinopathy signs in any eye was considered as sufficient evidence to categorize a person as having diabetic retinopathy. Similarly, the presence of sign of retinopathy of lower grading scale in one eye while higher grading scale in the other eye renders the patient in the

Laboratory assays
Within an hour of blood collection, the samples were centrifuged and separated. Fasting, 2-h blood glucose and lipid profile (serum cholesterol, triglyceride, serum high density lipo-protein) were analyzed by enzymatic colorimetric methods. All these measurements were done by an automatic analyzer (Hitachi 704, Hitachi Ltd Tokyo, Japan) using reagents of Randox Laboratories Ltd. LDL-c was estimated by using standard formula.

Statistical analysis
To explore the influence of various factors on development of retinopathy, succession of univariate was done initially by applying chi square and independent sample t test for categorical and continuous variable, respectively. A p<0.05 was considered statistically significant.

Variables with significant difference in univariate analysis were then entered in the logistic model and categorized into two levels (R = reference category): sex = female (R), male; duration of diabetes (years) = ≤10 (R), >10; glycemic state = HbA1c ≤7 % (R), ≥7 % and hypertension = ≤130/85 (R), ≥130/85. The outcome of logistic regression analysis was expressed in terms of odds ratios (OR) along with their 95 % confidence intervals (95 % CI). All analysis was performed by using SPSS version 13.0.

3. Results
Out of 366 patients, 137 (37.4 %) were males. Mean (± SD) age of the study patients was 48.08 ± 8.02 years, duration of diabetes was 9.17 ± 6.51 (years) and BMI was 28.6 ±5.16 (kg/m²). Retinopathy was evident in the fundus photographs of 27.3 % (n=100) patients. Fifteen percent had non-sight-threatening (NSTDR) while 12.3 % had sight-threatening diabetic retinopathy (STDR) (Fig. 1).

Patients with retinopathy (both non-sight threatening and sight threatening) had significantly increased mean duration of diabetes, systolic and diastolic blood pressure and HbA1c than patients without retinopathy (NDR) (p<0.001). However, patients with sight-threatening retinopathy also had significantly increased serum cholesterol (p<0.05) and serum creatinine (p<0.001) than the NDR group (Table 1).

Multivariate logistic regression analysis revealed gender as a significant factor; with male carrying 3.5 times (95 % CI; 1.73 – 7. 12) more risk for developing retinopathy. A diabetic patient with ≥ 10 years of disease history is 5.46 times (95 % CI; 2.15 – 13.85) at risk to have retinopathy than those with ≤ 10 years of diabetes. Hypertensive patients develop retinopathy twice as often as normotensive patients (1.96 times, CI; 0.95 – 4.03). While patients with poor glycemic control (HbA1c ≥ 7%), were 1.39 times (95 % CI; 1.23 – 1.56) more likely to have retinopathy than patients with good glycemic control (Table 2).

4. Discussion
Diabetic retinopathy is one of the most common microvascular complications of diabetes with varying reported prevalence [10 – 14]. Even studies originating from Pakistan also corroborate the variable prevalence of retinopathy ranges from 15.7 to 55 % [7, 18, 27, 28]. In the present study, frequency of retinopathy was found to be 27.3 %. These inflections in the reported frequencies of retinopathy could be attributed to inclusion of both patients with type 1 and type 2 diabetes, use of difference definitions of diabetes and diabetic retinopathy as well as use of different screening techniques and grading systems in various studies. Thus, direct comparison of the different frequency of diabetic retinopathy in different populations is difficult. However, the presence of higher frequency of
Predicting male gender as a risk factor for developing diabetic retinopathy in our study is in accordance with a study done in Chennai, India, that showed diabetic retinopathy was more prevalent in males [30]. A similar male preponderance has been reported in some other studies [8, 31, 32]. In contrast,

Table 1: Comparison of demographic, anthropometric, clinical and biochemical characteristics of non-sight-threatening (NSTDR) and sight-threatening diabetic retinopathy (STDR) with no diabetic retinopathy (NDR)

<table>
<thead>
<tr>
<th>Variables</th>
<th>NDR</th>
<th>NSTDR</th>
<th>STDR</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>266</td>
<td>48</td>
<td>46</td>
</tr>
<tr>
<td>Age (years)</td>
<td>48.69±3.23</td>
<td>46.32±1.71</td>
<td>46.32±1.71</td>
</tr>
<tr>
<td>Male</td>
<td>85 (31.9%)</td>
<td>46 (93.5%)</td>
<td>46 (100%)</td>
</tr>
<tr>
<td>Female</td>
<td>181 (68.1%)</td>
<td>11 (2.3%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Duration of diabetes (years)</td>
<td>7.71±5.74</td>
<td>12.53±7.14</td>
<td>12.53±7.14</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>73.28±14.02</td>
<td>166.33±56.37</td>
<td>166.33±56.37</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>159.93±8.75</td>
<td>200.74±7.67</td>
<td>200.74±7.67</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>28.65±5.17</td>
<td>177.8±38.7</td>
<td>177.8±38.7</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>79.29±10.4</td>
<td>125.32±17.71</td>
<td>125.32±17.71</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>125.32±17.71</td>
<td>200.74±7.67</td>
<td>200.74±7.67</td>
</tr>
<tr>
<td>Fasting blood sugar (mg/dl)</td>
<td>166.33±56.37</td>
<td>200.74±7.67</td>
<td>200.74±7.67</td>
</tr>
<tr>
<td>Random blood sugar (mg/dl)</td>
<td>200.74±7.67</td>
<td>177.8±38.7</td>
<td>177.8±38.7</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>8.75±2.11</td>
<td>179.86±64.57</td>
<td>179.86±64.57</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>177.82±38.87</td>
<td>118.29±69.52</td>
<td>118.29±69.52</td>
</tr>
<tr>
<td>Triglyceride (mg/dl)</td>
<td>179.86±64.57</td>
<td>41.85±7.18</td>
<td>41.85±7.18</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>42.20±8.48</td>
<td>19.08±5.76</td>
<td>19.08±5.76</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>108.71±2.76</td>
<td>12.53±10.53</td>
<td>12.53±10.53</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>0.99±0.29</td>
<td>0.99±0.29</td>
<td>0.99±0.29</td>
</tr>
</tbody>
</table>

Serum creatinine (mg/dl) 0.99±0.29 1.05±0.35 1.54±0.74**
Values are expressed as mean ± SD/n (%). Student t test/chi square test was used as a test of significance for comparison between without diabetic retinopathy (NDR) with non-sight-threatening diabetic retinopathy (NSTDR) and sight-threatening diabetic retinopathy (STDR) groups.

*<0.05 p value was considered statistically significant.
**<0.001 p value was considered statistically significant.

Table 2: Risk indicators of diabetic retinopathy explored by logistic regression analysis

<table>
<thead>
<tr>
<th>Variables</th>
<th>NDR</th>
<th>NSTDR</th>
<th>STDR</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR</td>
<td>2.31</td>
<td>3.51</td>
<td>1.73 ± 7.12</td>
</tr>
<tr>
<td>95% CI</td>
<td>1.44 – 3.69</td>
<td>5.46</td>
<td>2.13 – 13.85</td>
</tr>
<tr>
<td>Adjusted OR</td>
<td>2.65</td>
<td>1.96</td>
<td>0.95 ± 4.03</td>
</tr>
<tr>
<td>95% CI</td>
<td>1.59 – 4.44</td>
<td>1.39</td>
<td>1.23 ± 1.56</td>
</tr>
</tbody>
</table>

Other studies have not shown a consistent pattern of gender variation in the prevalence of diabetic retinopathy [12, 15, 16]. Multivariate logistic regression analysis showed that males are 3.5 times more prone to develop DR. Though the exact reason is not known, this gender preponderance may be due to the presence of some confounding factors such as obesity or hypertension. However, further research is needed to elucidate the causes of this variation of diabetic retinopathy frequency in gender. Age is not a risk factor for developing diabetic retinopathy. Like diabetes, DR may develop at any age. However, those

It is suggested that the development and progression of DR is influenced by the level of hyperglycaemia. A higher HbA1c in both retinopathy groups compared to non-retinopathy group indicates that poor glycemic control plays a role not only in the development but also in the progression of retinopathy. Similar findings were observed in the Chennai Urban Rural Epidemiology Study (CURES) and UKPDS [30, 36]. Regression analysis in the present study found that patients with poor glycemic status were 1.39 times more likely to develop diabetic retinopathy.
Increased total cholesterol in univariate analysis indicated the role of cholesterol in the progression of retinopathy from non-sight-threatening to sight-threatening group, a finding consistent with the findings of ETDRS groups [39, 40]. It also conforms to the CURES eye study that found association of retinopathy with total cholesterol [41]. However, multivariate logistic regression analysis in the present study failed to demonstrate any risk-related association of total cholesterol with diabetic retinopathy.

An elevated serum creatinine signifies kidney injury. Increased serum creatinine in patients with sight-threatening retinopathy indicates the coexistence of microvascular complications in both organs. Diabetic retinopathy and nephropathy have been found to be closely related in other epidemiological studies [42, 43].

With limitations of study design and patient selection from a tertiary care diabetes centre that restrict causal relation and external validity, respectively, associations of certain factors with retinopathy in our study, validate the findings of earlier studies. Thus, for decreasing the burden of diabetic retinopathy, it is imperative to control the identified factors, particularly those that are considered avoidable.

5. Conclusions

The study helped to identify factors likely to be related to a serious diabetic complication. Male gender, long duration of diabetes, control of hypertension and glycaemia are the important risk indicators of diabetic retinopathy in this group of patients. Good control of the risk indicators explored in the present study may lead to the prevention of this vision-threatening complication of diabetes. The study also underlines the need for screening of patients with diabetes as they are more likely to develop retinopathy.

References


Volume 5 Issue 6, June 2016

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Paper ID: NOV164663
http://dx.doi.org/10.21275/v5i6.NOV164663
1748


Author Profile

Dr. B. Silpa received MBBS degree from Osmania Medical College, Hyderabad, AP, INDIA, M.S post graduation from Mediciti institute of medical sciences, hyderabad, she worked as senior resident and subsequently working as fellow in medical retina in Sankara Eye Hospital, Chinakakani, Guntur dt.

Dr. Srikanth Evuru received MBBS degree from Rangaraya Medical College, Kakinada, AP, INDIA, M.D post graduation from Rajah Mutthia Medical College, Chidambaram, TN, INDIA, he worked as an assistant professor and subsequently working as associate professor at NRI medical college, chinakakani, AP, INDIA

Volume 5 Issue 6, June 2016
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