A Study to Correlate Diabetic Retinopathy with Diabetic Peripheral Neuropathy in Patients with Type 2 Diabetes Mellitus

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Abstract

Background: Diabetes is a metabolic condition characterised by increased blood sugar levels. It can either be due to an absolute insulin deficiency due to an autoimmune destruction of insulin secreting beta cells of the pancreas as in Type 1 Diabetes or a relative insulin deficiency due to insulin resistance in type 2 Diabetes. Diabetic Retinopathy and Diabetic peripheral neuropathy are two complications of this syndrome secondary to microvascular complications.

Methods: The present study is to correlate the severity of diabetic retinopathy (DR) with severity of diabetic peripheral (DPN) and serum lipid profile in patients with type 2 DM and included 214 patients who satisfied the selection criteria and gave written informed consent. For statistical analysis, the worse eye was considered and ETDRS grades of very mild and mild NPDR were grouped together and severe and very severe NPDR were grouped together.

Results: In the present study, diabetic peripheral neuropathy (DPN) was significantly more common in patients with diabetic retinopathy (DR) than in those without DR. A statistically significant positive correlation was found between severity of DR and severity of DPN. The mean vibration perception threshold (VPT) was significantly higher in patients with more severe grades of DR. No statistically significant association was found between presence of dyslipidaemia and presence of DR, DME or DPN. None of the traditional lipid parameters (TG, TC, HDL-C, LDL-C were found to be associated with DR, DME or DPN.

Conclusion: The study was conducted with the aim of correlating the grade of DR with severity of DPN and assessing their association with serum lipid profile in patients with type 2 DM.

Keywords: Diabetic Retinopathy; Diabetic Peripheral Neuropathy; Diabetic Macular Oedema; Metabolic Syndrome; Insulin Resistance

Abbreviations


Introduction

Diabetes mellitus (DM) is a global epidemic. The number of people with DM worldwide is estimated to rise from 425 million in 2017 to 625 million by the year 2045. India is set to emerge as the diabetic capital of the world with the number of people having DM estimated to rise from 72.9 million in 2017 to 134 million by 2045— the largest number in any nation in the world [1].

Diabetes mellitus is a clinical syndrome characterized by hyperglycaemia due to absolute or relative insulin deficiency. In type 1 DM, there is absolute insulin deficiency due to T cell-mediated autoimmune destruction of the insulin-secreting pancreatic beta cells. In type 2 DM, which belongs to a cluster of conditions called the 'insulin resistance syndrome' or the 'metabolic syndrome there is relative insulin deficiency due to resistance to insulin action [2]. Around 90% to 95% of all diabetic patients have Type 2 DM [3].

Small blood vessels in the retina, the vasa nervorum and the renal glomeruli are particularly vulnerable to damage from chronic hyperglycaemia and undergo pathognomonic changes such as capillary basement thickening that eventually lead to microangiopathy [4]. Progressive vascular dysfunction in the retina leads to diabetic retinopathy, in the nerves leads to diabetic neuropathy and in the kidneys leads to diabetic nephropathy. The majority of morbidity, mortality and health care expenditure associated with DM is due to its chronic complications [5].

Diabetic retinopathy (DR) and diabetic peripheral neuropathy (DPN) are two commonly encountered complications of DM. The worldwide prevalence of reported to be 60% in type 1 DM and 25.2% in type 2 DM [6]. DPN was estimated to affect about one third of patients with type 1 DM and more than half of patients with type 2 DM [7]. While DR is the prototype of microvascular complications and the leading cause of irreversible blindness in the working age population [8], DPN is the most commonly encountered microvascular complication and a major risk factor for lower extremity amputation following foot ulcers [9].

Dyslipidaemia refers to changes in both quantity and quality of serum lipoproteins. Type 2 DM is a common cause of secondary dyslipidaemia. Unlike in type 1 DM, in type 2 DM, altered lipid metabolism usually precedes glucose elevation [10] and dyslipidaemia may further contribute to the development and progression of DR and diabetic neuropathy [11].

Both DR and DPN being microangiopathies, share a common pathophysiology and therefore the presence and severity of one could reflect upon that of the other [12]. However, as they are diagnosed and managed by physicians of different specialties, patients often receive only one mode of care and are not referred to the other. A better understanding of the interrelationship between DR and DPN will emphasize the importance of screening for other complications irrespective of the cause of attendance, helping in the early identification of at-risk individuals and allowing for timely intervention. Furthermore, identifying potential modifiable risk factors associated with DR and DPN such as dyslipidaemia and their subsequent control may help in preventing or slowing disease progression.

Previous Indian studies on the association between DR and DPN in type 2 DM have found a statistically significant positive correlation between the two. However, studies correlating the grade of DR with the severity of DPN are limited [13-17]. Also, the association of serum lipid profile abnormalities with DR and DPN found in various studies has been inconsistent [13-17].

Aim of the Study

This study was conducted with the aim of correlating the grade of DR with severity of DPN and assessing their association with serum lipid profile in patients with type 2 DM.

Materials and Methods

Study design and period

The present study is a duration based cross-sectional study conducted from January 2018 to December 2018.
A Study to Correlate Diabetic Retinopathy with Diabetic Peripheral Neuropathy in Patients with Type 2 Diabetes Mellitus

Source of data

Clinically diagnosed cases of type-2 DM visiting the Ophthalmology out-patient department as well as those admitted under the departments of Ophthalmology, General Medicine, Endocrinology and Neurology at Vydehi Institute of Medical Sciences and Research Centre, Whitefield, Bangalore.

Sampling procedure

Out of the 600 patients with clinically diagnosed type 2 DM who were evaluated, 214 patients who fulfilled the selection criteria and gave written informed consent were included in the study by simple random sampling.

Selection criteria

Inclusion criteria: Patients with type-2 DM (diagnosed as per the American Diabetes Association Criteria) for 5 years or more.

Exclusion criteria

- Comorbidities which may increase severity of DR or DPN or both
- Uncontrolled hypertension
- Chronic kidney disease or diabetic nephropathy
- Severe anaemia (Haemoglobin < 8 g/dL)
- Hypothyroidism
- History of neuropathy prior to diagnosis of diabetes mellitus
- Other conditions that can cause peripheral neuropathy
- Vitamin B12 deficiency
- Peripheral arterial disease
- Alcohol consumption (more than 10 g/day)
- Other conditions such as: hepatic disease, spinal abnormalities, vasculitis, arthritis, malignancies and infections such as HIV, Hepatitis B or C and leprosy
- Patients on treatment for dyslipidaemia
- Other retinal diseases such as retinitis pigmentosa, age related macular degeneration, retinal dystrophies and pathological myopia
- Established cases of glaucoma with glaucomatous optic atrophy
- Conditions causing opaque media such as advanced cataract, corneal degenerations and corneal dystrophies.

Ethical clearance: Prior to commencement of the study, ethical clearance was obtained from the Institutional Ethical Committee- VIEC/2016/APP/152

Methods of data collection

Informed written consent of the participant was taken.

History and baseline data were collected using a pre-structured proforma.

**Ophthalmological examination:** Best-corrected visual acuity was recorded using Snellen’s visual acuity chart for distance and Jaeger’s chart for near vision. Intraocular pressure was measured by Goldmann applanation tonometry. Slit lamp examination of the anterior and posterior segment was done. Pupils of both eyes were dilated with tropicamide eye drops followed by:

- A detailed fundus examination of both eyes under the slit lamp using 78D and 90D lenses,
- Indirect ophthalmoscopy using +20D lens,
- 7 field fundus photography and Spectral Domain Optical Coherence Tomography imaging of the macula,
- Fundus fluorescein angiography and gonioscopy were done when indicated.

Diabetic Retinopathy and diabetic macular oedema were graded as per the Abbreviated Early Treatment Diabetic Retinopathy Study (ETDRS) classification [18].

**Non-proliferative diabetic retinopathy (NPDR)**

- No diabetic Retinopathy.
- Very mild NPDR: Microaneurysms only.
- Mild NPDR: Microaneurysms and retinal haemorrhages up to the level of moderate NPDR.
- Moderate NPDR: Severe retinal haemorrhages (about 20 medium-large per quadrant) in 1 - 3 quadrants or mild IRMA
- Severe NPDR haemorrhages in all 4 quadrants, Significant venous beading in 2 or more quadrants Moderate IRMA in one or more quadrant.
- Very severe NPDR: 2 or more of the criteria for severe NPDR.

**Proliferative diabetic retinopathy (PDR)**

- Mild-moderate PDR: Neovascularization of the disc (NVD) or neovascularization elsewhere (NVE), but extent insufficient to meet the high-risk criteria.
- High-risk PDR: NVD > 1/3-disc area, Any NVD with vitreous haemorrhage NVE > ½ disc area with vitreous haemorrhage

**Clinically significant macular oedema (as defined in the ETDRS) [18]:**

- Retinal thickening within 500 μm of the centre of the macula.
- Hard exudates within 500 μm of the centre of the macula associated with adjacent retinal thickening.
- Retinal thickening of 1-disc area or more, any part of which is within 1-disc diameter of the centre of the macula.

**Assessment of diabetic peripheral neuropathy**

DPN was diagnosed and graded using the validated Toronto Clinical Neuropathy Score (TCNS) [19] derived from the clinical assessment of:

_Citation:_ Nischala Balakrishna, _et al._ A Study to Correlate Diabetic Retinopathy with Diabetic Peripheral Neuropathy in Patients with Type 2 Diabetes Mellitus. *EC Ophthalmology* 11.5 (2020): 01-15.
A Study to Correlate Diabetic Retinopathy with Diabetic Peripheral Neuropathy in Patients with Type 2 Diabetes Mellitus

1) 6 symptoms: (absent = 0; present = 1)-pain, numbness, tingling, weakness, ataxia and upper-limb symptoms.

2) 5 sensory tests: (normal = 0; abnormal = 1)
   - Fine touch: tested with 10-gram Semmes Weinstein monofilament
   - Pain: tested with pinprick
   - Vibration: tested with a 128Hz tuning fork
   - Temperature: tested with test tubes of different temperatures and
   - Proprioception.

3) B/L Lower limb (knee and ankle) reflexes tested with a reflex hammer (normal = 0; reduced = 1; absent = 2).

Total scores range from 0 to 19 (maximum) and were interpreted as shown below:


The vibration perception threshold (VPT) was also assessed using a biothesiometer (Dhansai Lab, Mumbai, India) at 6 different sites (the great toe, first metatarsal, third metatarsal, fifth metatarsal, medial arch, heel, and dorsum of both feet) in a graduated manner from 0 volts onwards, and patients were asked to give a verbal response once they started appreciating the vibration sensation. A mean value > 15 volts was considered abnormal.

Nerve conduction studies and lower limb Doppler were done when VPT was more than 15 volts to confirm diagnosis and rule out peripheral arterial disease.

**Lab investigations:** The following investigations were done for all participants:

1. Fasting Lipid Profile: Patients were considered to have dyslipidaemia if any of the parameters were outside the American Diabetes Association (ADA) recommended targets (TG ≥ 150mg/dL, TC ≥ 200 mg/dL, LDL-C ≥ 130 mg/dl, HDL-C < 50 mg/dL in females and < 40 mg/dL in males).

2. Complete blood count and Haemoglobin (%).

3. Sugar profile: FBS, PPBS and HBA1C.

4. Serum Urea and Serum Creatinine.

5. Vitamin B12 assay.


7. Thyroid function test.

8. Urine microalbumin.

All patients were referred to the department of Endocrinology for systemic evaluation and management.

**Outcome variables:**

1. Prevalence of diabetic retinopathy and diabetic peripheral neuropathy
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2. Correlation between grade of diabetic retinopathy and severity of diabetic peripheral neuropathy.

Statistical analysis

Statistical analysis has been done using Statistical Package for Social Sciences [SPSS] for Windows Version 22.0.

Descriptive statistics: Descriptive analysis of all the explanatory parameters has been done using mean and standard deviation for quantitative variables and frequency and proportions for categorical variables.

Inferential statistics

Glycaemic index, duration of DM is compared with DR and DPN using the Chi Square Test. Similar tabulation to compare different grades of DR with varying severity of DPN has been performed.

The level of significance was set at \( P < 0.05 \).

Results

The present study to correlate the severity of diabetic retinopathy (DR) with severity of diabetic peripheral (DPN) and serum lipid profile in patients with type 2 DM included 214 patients who satisfied the selection criteria and gave written informed consent. For statistical analysis, the worse eye was considered and ETDRS grades of very mild and mild NPDR were grouped together and severe and very severe NPDR were grouped together.

Discussion

The present cross-sectional study was conducted in the Department of Ophthalmology, Vydehi Institute of Medical Sciences and Research Centre, Bangalore between January 2017 and June 2018, with the aim of correlating the grade of diabetic retinopathy (DR) with the severity of diabetic peripheral neuropathy (DPN) and assessing their association with dyslipidaemia. The study included 214 patients with type 2 DM who fulfilled the selection criteria and gave written informed consent.

In this study, DR was present in 21.5% (n = 46) of the patients and DPN was present in 24.8% (n = 53) of the patients.

In a cross-sectional study conducted by Kumar KH., et al. in India, out of 1529 type 2 diabetic patients, 17% had DR and 37% had DPN [14].

In the present study most of the patients with DR had milder grades of DR; out of the 46 patients with DR, 29 patients had very mild and mild NPDR, 12 patients had moderate NPDR, 4 patients had severe and very severe NPDR, 1 patient had PDR without HRC and none of the patients had PDR with HRC. CSME was present in 5 patients and non-CSME was present in 14 patients. In other words, out of the 214 subjects, 1.87% had severe and very severe NPDR, 0.5% had PDR, 8.87% had DME, 6.54% had non-CSME and 2.3% had CSME. Table 1 and graph 1 shows gender distribution in the study group.

<table>
<thead>
<tr>
<th></th>
<th>Number of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>151</td>
<td>70.6%</td>
</tr>
<tr>
<td>Female</td>
<td>63</td>
<td>29.4%</td>
</tr>
<tr>
<td>Total</td>
<td>214</td>
<td></td>
</tr>
</tbody>
</table>

*Table 1: Gender distribution in the study group.*
Table 2 and graph 2 shows the presence and distribution of diabetic retinopathy and DME.

**Graph 1**: Showing the percentage of the gender distribution in the study group. 70.6% of the patients were male and 29.4% were female.

**Graph 2**: Shows the presence of Diabetic Retinopathy in the study group. Out of 214 patients, 78.50% (168 patients) had no Diabetic Retinopathy and 21.50% (46 patients) had Diabetic Retinopathy.

<table>
<thead>
<tr>
<th>Presence of DR in the study group (n = 214)</th>
<th>Category</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No DR</td>
<td>168</td>
<td>78.5%</td>
</tr>
<tr>
<td></td>
<td>DR</td>
<td>46</td>
<td>21.5%</td>
</tr>
<tr>
<td>Distribution of ETDRS grades of DR (n = 46)</td>
<td>Very mild and mild NPDR</td>
<td>29</td>
<td>63.0%</td>
</tr>
<tr>
<td></td>
<td>Moderate NPDR</td>
<td>12</td>
<td>26.1%</td>
</tr>
<tr>
<td></td>
<td>Severe and Very Severe NPDR</td>
<td>4</td>
<td>8.7%</td>
</tr>
<tr>
<td></td>
<td>PDR with HRC</td>
<td>1</td>
<td>2.2%</td>
</tr>
<tr>
<td>DME in patients with DR (n = 46)</td>
<td>DR without DME</td>
<td>27</td>
<td>58.7%</td>
</tr>
<tr>
<td></td>
<td>DME-Non CSME</td>
<td>14</td>
<td>30.4%</td>
</tr>
<tr>
<td></td>
<td>DME-CSME</td>
<td>5</td>
<td>10.9%</td>
</tr>
</tbody>
</table>

**Table 2**: Presence and distribution of diabetic retinopathy and DME.

Graph 3 shows the distribution and grades of diabetic retinopathy and diabetic macular edema in patients with diabetic retinopathy.

Graph 3: Distribution of grades of Diabetic Retinopathy and Diabetic Macular Oedema in patients with Diabetic Retinopathy.

The first part of the graph shows the distribution of Diabetic Retinopathy graded as per the abbreviated ETDRS scale, out of the 46 patients with DR 29 patients had very mild NPDR, 12 patients had moderate NPDR, 4 patients had severe and very severe NPDR, 1 patient had PDR without HRC and none of the patients had PDR with high risk characteristics.

The second part of the graph shows the presence of DME in patients with DR, Out of the 46 patients with DR, 27 patients did not have DME, 14 patients had Non-CSME and 5 patients CSME.

In the Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetic Study (SN-DREAMS), the prevalence of DR in an urban south Indian population with 5,999 participants was 18% and in a rural south Indian population with 13,079 participants were 10.3%. The prevalence of sight threatening DR was 3.8%. In the SN-DREAMS Report Number 13, including 1414 diabetic subjects, the prevalence of DME was 31.76%, non-CSME was 25.49% and CSME was 6.27% [20-22].

In the present study most of the patients with DPN had mild DPN; out of the 53 patients with DPN, 37 patients had mild DPN, 10 had moderate DPN and 6 had severe DPN. In other words, out of the 214 subjects, 17.3% had mild DPN, 4.7% had moderate DPN and 2.8% had severe DPN.

In a cross-sectional study conducted in North India by Bansal D, et al. the overall prevalence of DPN was 29.2%; 33.7% in known cases of DM (n=1637) and 9.2% in newly diagnosed patients (n = 369). Prevalence of mild, moderate, and severe neuropathies was 8.06%, 14.55% and 6.63%, respectively [13].

In the present study, a statistically significant positive correlation was found between the presence of DR and presence of DPN. DPN was around 10 times more common in patients with DR than in those without DR; 85% of patients with DR and 8% of patients without DR had DPN.

In a prospective study conducted by Sharma VK, et al. including 100 patients with type 2 DM, the prevalence of DR was 2.75 times greater in patients with DPN (37%) than in those without DPN (14%) [17]. Bansal D., et al. found that the prevalence of DR was higher in patients with DPN (41.8%) than in those without DPN (18.3%) [13]. Table 3 and graph 4 shows the presence and distribution of diabetic peripheral neuropathy.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Category</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence of DPN in the study group (n = 214)</td>
<td>No DPN</td>
<td>161</td>
<td>75.2%</td>
</tr>
<tr>
<td></td>
<td>DPN</td>
<td>53</td>
<td>24.8%</td>
</tr>
<tr>
<td>Distribution DPN severity based on the TCNS score (n = 53)</td>
<td>Mild DPN</td>
<td>37</td>
<td>69.8%</td>
</tr>
<tr>
<td></td>
<td>Moderate DPN</td>
<td>10</td>
<td>18.9%</td>
</tr>
<tr>
<td></td>
<td>Severe DPN</td>
<td>6</td>
<td>11.3%</td>
</tr>
</tbody>
</table>

Table 3: Presence and distribution of diabetic peripheral neuropathy.

The table shows that out of the total number of patients in the study group, there were 161 patients with no DPN and 53 patients with DPN while the distribution DPN severity based on the TCNS score showed 37 patients with mild DPN, 10 with moderate DPN and 6 patients with severe DPN.
Table 4 shows the comparison of Age and BMI of patients with and without DR. Table 5 shows the comparison of Age and BMI of patients with and without DPN.

### Table 4: Shows the comparison of Age and BMI of patients with and without DR.

<table>
<thead>
<tr>
<th>Variables</th>
<th>DR</th>
<th>No DR</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>58.37</td>
<td>52.10</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.04</td>
<td>24.75</td>
<td>0.649</td>
</tr>
</tbody>
</table>

The mean age of patients with DR was 58.37 years and without DR was 52.10 years. The difference was statistically significant (P value < 0.001).

The mean BMI of patients with DR was 25.04 kg/m² and without DR was 24.75 kg/m². This difference was not statistically significant (P value = 0.649).

### Table 5: Shows the comparison of Age and BMI of patients with and without DPN.

<table>
<thead>
<tr>
<th>Variables</th>
<th>DPN</th>
<th>No DPN</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>54.8</td>
<td>53.0</td>
<td>0.228</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.1</td>
<td>24.7</td>
<td>0.596</td>
</tr>
</tbody>
</table>

The mean age of patients with DPN was 54.8 years and without DPN was 53 years. The difference was not statistically significant (P value = 0.228). The mean BMI of patients with DPN was 25.1 kg/m² and without DPN was 24.7 kg/m². The difference was not statistically significant (P value = 0.596).

In the present study, a statistically significant positive correlation was found between severity of DR and severity of DPN. All the patients without DR having DPN had mild DPN; 76% of the patients with mild NPDR had mild DPN and 24% had no DPN; 84% of the patients with moderate NPDR, had moderate DPN, 8% had mild DPN and 8% had severe DPN. All the patients with severe and very severe NPDR as well as those with PDR had severe DPN. The mean vibration perception threshold (VPT) was significantly higher in patients with

**Citation:** Nischala Balakrishna, *et al.* “A Study to Correlate Diabetic Retinopathy with Diabetic Peripheral Neuropathy in Patients with Type 2 Diabetes Mellitus.” *EC Ophthalmology* 11.5 (2020): 01-15.
more severe grades of DR. The mean VPT in patients without DR was 13.17 volts; in patients with very mild and mild NPDR was 20.87; in patients with moderate NPDR was 32.5 volts; in patients with severe and very severe NPDR was 45.71 volts and in patients with PDR was 53.4 volts.

<table>
<thead>
<tr>
<th>Duration of DM</th>
<th>Total</th>
<th>NO DR</th>
<th>DR</th>
<th>Chi square Value</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 - 10 years</td>
<td>184</td>
<td>161</td>
<td>23</td>
<td>63.696</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>11 - 15 years</td>
<td>22</td>
<td>6</td>
<td>16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 15 years</td>
<td>8</td>
<td>1</td>
<td>7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 6: Shows the association between duration of type 2 DM and presence of DR.

Out of the 184 patients with DM for 5 - 10 years, 23 patients (12.5%) had DR. Out of the 22 patients with DM for 11 - 15 years, 16 patients (72.2%) had DR and out of the 8 patients with DM for more than 15 years, 7 patients (87.5%) had DR. The above observations were found to be statistically significant (P value < 0.001).

Though previous studies in India have shown that DR is more common in the presence of DPN, Indian studies correlating severity of DR with severity of DPN are limited. Shen J, Hu Y., et al. found that in their cross-sectional study including 955 type 2 diabetic patients, a VPT value higher than 18 V was the optimal cut off for reflecting a high risk of sight-threatening DR [23].

Graph 5 shows the association between duration of type 2 DM and presence of DR. Table 7 and graph 6 shows the association between duration of type 2 DM and presence of DPN.

<table>
<thead>
<tr>
<th>Duration of DM</th>
<th>Total</th>
<th>NO DPN</th>
<th>DPN</th>
<th>Chi square Value</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 - 10 years</td>
<td>184</td>
<td>153</td>
<td>31</td>
<td>45.345</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>11 - 15 years</td>
<td>22</td>
<td>7</td>
<td>15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 15 years</td>
<td>8</td>
<td>1</td>
<td>7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 7: Shows the association between duration of type 2 DM and presence of DPN

Out of the 184 patients with DM for 5 to 10 years, 31 patients (16.8%) had DPN. Out of the 22 patients with DM for 10 to 15 years, 15 patients (68.2%) had DPN. And out of the 8 patients with DM for more than 15 years, 7 patients (87.5%) had DPN. The above observations were found to be statistically significant (P value < 0.001).
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Graph 6: Shows the association between duration of type 2 DM and presence of DPN.

Out of the 184 patients with DM for 5 to 10 years, 31 patients (16.8%) had DPN. Out of the 22 patients with DM for 10 to 15 years, 15 patients (68.2%) had DPN. And out of the 8 patients with DM for more than 15 years, 7 patients (87.5%) had DPN. The above observations were found to be statistically significant (P value < 0.001).

In the present study, 72.89% of the subjects had dyslipidaemia (n = 156). The presence of dyslipidaemia in patients with and without DR was 71.7% and 73.2% respectively. Dyslipidaemia was present in 66.7% of the patients with DR but no DME; 71.4% of the patients with non-CSME; and all the patients (100%) with CSME. The presence of dyslipidaemia in patients with and without DPN was 73.6% and 72.7% respectively. However, none of these observations were statistically significant. None of the serum lipid profile parameters (triglycerides, total cholesterol, HDL cholesterol, LDL cholesterol) were associated with DR or DME or DPN. Table 8 shows the association between glycaemic control and presence of DR. Graph 7 shows the association between glycaemic control and presence of DR.

Graph 7: Shows the association between glycaemic control and presence of DR.

Out of 46 patients with good glycaemic control 10 patients (21.7%) had DR. Out of the 142 patients with moderate glycaemic control, 24 patients (16.9%) had DR. And out of the 26 patients with poor glycaemic control, 12 patients (46.2%) had DR. The above observation was statistically significant (P value < 0.04).
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<table>
<thead>
<tr>
<th>Glycaemic Index</th>
<th>Total</th>
<th>NO DR</th>
<th>DR</th>
<th>Chi square Value</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>&lt; 7: Good control</td>
<td>46</td>
<td>36</td>
<td>78.3</td>
<td>10</td>
<td>21.7</td>
</tr>
<tr>
<td>7 - 10: Moderate control</td>
<td>142</td>
<td>118</td>
<td>83.1</td>
<td>24</td>
<td>16.9</td>
</tr>
<tr>
<td>&gt; 10: Poor control</td>
<td>26</td>
<td>14</td>
<td>53.8</td>
<td>12</td>
<td>46.2</td>
</tr>
</tbody>
</table>

Table 8: Shows the association between glycaemic control and presence of DR.

Out of 46 patients with good glycaemic control, 10 patients (21.7%) had DR. Out of the 142 patients with moderate glycaemic control, 24 patients (16.9%) had DR. And out of the 26 patients with poor glycaemic control, 12 patients (46.2%) had DR. The above observation was statistically significant (P value < 0.04).

Table 9: Shows the association between glycaemic control and presence of DPN.

Out of the 46 patients with good glycaemic control, 12 patients (26.1%) had DPN. Out of the 142 patients with moderate glycaemic control, 30 patients (21.1%) had DPN. And out of the 26 patients with poor glycaemic control, 11 patients (42.3%) had DPN. The above observation was not statistically significant (P value = 0.07).

Results of previous studies on the association of serum lipid profile with DR and DPN have been inconsistent. Timothy D., et al. found that in their cross-sectional study that a higher levels of triglycerides (but not total cholesterol, LDL cholesterol and HDL cholesterol) were associated with DPN [24]. In a cross-sectional study conducted in North India by Bansal D., et al. dyslipidaemia was found to be inversely associated with DPN (possibly due to better management of lipid profile among DPN patients) [13]. Kumar KH., et al. found that hypertriglyceridaemia was associated with retinopathy over other microangiopathies [14]. In the Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetic Study (SN-DREAMS) Report Number 13, non-CSME was related to high S.LDL-C, high S.non-HDL-C and a high cholesterol ratio. And CSME was related only to high TC [25].

Upon further analysis, we found a statistically significant association between longer duration of DM and the presence of both DR as well as DPN; in patients with 5 - 10 years of DM, 12% had DR and 17% had DPN; in patients with 10 - 15 years of DM, 73% had DR and 68% had DPN; in patients with DM for more than 15 years, 88% had DR as well as DPN. These results were consistent with previous studies. Increasing age and higher glycaemic index were associated with presence of DR but not DPN. BMI was not associated with either DR or DPN.

Sharma VK., et al. found that both DR and DPN were associated with longer duration of DM and poor glycaemic control but were not associated with BMI (obesity) [17]. Kumar KH., et al. found that increasing age, longer duration of DM and higher HBA1c were common risk factors for both DR and DPN while low body weight predisposed to retinopathy over DPN [14]. Nisar UM., et al. found that longer duration of DM, higher BMI and presence of CKD were associated with both DR and DPN. But, HBA1c and serum lipid profile were not associated with DPN [26]. Table 9 and graph 8 Shows the association between glycaemic control and presence of DPN. Table 10 shows presence of dyslipidaemia in different grades of DR and DME. Table 11 shows serum lipid profile in different grades of DR and DME.

Graph 8: Shows the association between glycaemic control and presence of DPN.

Out of the 46 patients with good glycaemic control, 12 patients (26.1%) had DPN. Out of the 142 patients with moderate glycaemic control, 30 patients (21.1%) had DPN. And out of the 26 patients with poor glycaemic control, 11 patients (42.3%) had DPN. The above observation was not statistically significant (P value = 0.07).

<table>
<thead>
<tr>
<th>Glycaemic Index</th>
<th>Total</th>
<th>NO DPN</th>
<th>DPN</th>
<th>Chi square Value</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>&lt; 7: Good control</td>
<td>46</td>
<td>34</td>
<td>73.9</td>
<td>12</td>
<td>26.1</td>
</tr>
<tr>
<td>7 - 10: Moderate control</td>
<td>142</td>
<td>112</td>
<td>78.9</td>
<td>30</td>
<td>21.1</td>
</tr>
<tr>
<td>&gt; 10: Poor control</td>
<td>26</td>
<td>15</td>
<td>57.7</td>
<td>11</td>
<td>42.3</td>
</tr>
</tbody>
</table>

Table 10: Shows the association between glycaemic control and presence of DPN.

Out of the 46 patients with good glycaemic control, 12 patients (26.1%) had DPN. Out of the 142 patients with moderate glycaemic control, 30 patients (21.1%) had DPN. And out of the 26 patients with poor glycaemic control, 11 patients (42.3%) had DPN. The above observation was not statistically significant (P value = 0.07).
A Study to Correlate Diabetic Retinopathy with Diabetic Peripheral Neuropathy in Patients with Type 2 Diabetes Mellitus

Citation: Nischala Balakrishna., et al "A Study to Correlate Diabetic Retinopathy with Diabetic Peripheral Neuropathy in Patients with Type 2 Diabetes Mellitus". EC Ophthalmology 11.5 (2020): 01-15.

<table>
<thead>
<tr>
<th>DR Grade</th>
<th>Dyslipidaemia (n = 156)</th>
<th>No dyslipidaemia (n = 58)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>No DR (n = 168)</td>
<td>123</td>
<td>73.2%</td>
</tr>
<tr>
<td>Very mild+ mild NPDR (n = 29)</td>
<td>21</td>
<td>72.4%</td>
</tr>
<tr>
<td>Moderate NPDR (n = 12)</td>
<td>8</td>
<td>66.7%</td>
</tr>
<tr>
<td>Severe+ Very severe NPDR (n = 4)</td>
<td>3</td>
<td>75.0%</td>
</tr>
<tr>
<td>PDR without HRC (n = 1)</td>
<td>1</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Table 10: Presence of dyslipidaemia in different grades of DR and DME.
Dyslipidaemia was present in 72.89% (n = 156) of the subjects.
The first part shows the presence of dyslipidaemia in different grades of DR. Dyslipidaemia was present in 73.2% of the patients without DR. 72.4% of the patients with very mild and mild NPDR, 66.7% of the patients with moderate NPDR, 75% of the patients with severe and very severe NPDR and the patients with PDR. This observation was not statistically significant (P value = 0.96). The second part shows that dyslipidaemia was present in 66.7% of the patients with DR but no DME. 71.4% of the patients with non CSME and all the patients (100%) with CSME. This observation was not statistically significant (P value = 0.49).

<table>
<thead>
<tr>
<th>Grade of DR</th>
<th>TG Mean (mg/dl)</th>
<th>SD</th>
<th>TC Mean (mg/dl)</th>
<th>SD</th>
<th>HDL-C Mean (mg/dl)</th>
<th>SD</th>
<th>LDL-C Mean (mg/dl)</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>No DR</td>
<td>159.66</td>
<td>125.87</td>
<td>191.73</td>
<td>46.65</td>
<td>43.38</td>
<td>10.74</td>
<td>102.35</td>
<td>35.41</td>
</tr>
<tr>
<td>V Mild+ Mild NPDR</td>
<td>152.72</td>
<td>88.09</td>
<td>186.17</td>
<td>45.58</td>
<td>43.69</td>
<td>10.14</td>
<td>102.71</td>
<td>29.36</td>
</tr>
<tr>
<td>Moderate NPDR</td>
<td>193.25</td>
<td>109.87</td>
<td>211.08</td>
<td>49.52</td>
<td>38.64</td>
<td>5.79</td>
<td>116.56</td>
<td>35.95</td>
</tr>
<tr>
<td>Severe + V Severe NPDR</td>
<td>9250</td>
<td>26.26</td>
<td>185.50</td>
<td>17.46</td>
<td>44.80</td>
<td>2.20</td>
<td>99.00</td>
<td>17.49</td>
</tr>
<tr>
<td>PDR without HRC</td>
<td>230.00</td>
<td>-</td>
<td>100.00</td>
<td>-</td>
<td>32.00</td>
<td>-</td>
<td>65.00</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 11: Serum lipid profile in different grades of DR and DME.
HRC was 159.66 (high), 152.72 (high), 193.25 (high), 92.5 (normal) and 230 (high) respectively.
This observation was not statistically significant (P = 0.62).
The mean serum total cholesterol (mg/dl) in patients with no DR, very mild and mild NPDR, moderate NPDR, severe and very severe NPDR and PDR without.
HRC was 191.73 (normal), 186.17 (normal), 211.08 (high), 185.5 (normal) and 100 (normal) respectively.
This observation was not statistically significant (P = 0.17).
The mean serum HDL cholesterol (mg/dl) in patients with no DR, very mild and mild NPDR, moderate NPDR, severe and very severe NPDR and PDR without.
HRC was 43.38 (normal), 43.69 (normal), 38.64 (low), 44.8 (normal) and 32 (low) respectively.
This observation was not statistically significant (P = 0.45).
The mean serum LDL cholesterol in patients with no DR, very mild and mild NPDR, moderate NPDR, severe and very severe NPDR and PDR without HRC was 102.35 (normal), 102.71 (normal), 116.56 (normal), 99 (normal) and 65 (normal) respectively.
This observation was not statistically significant (P = 0.53). The mean serum triglyceride level (mg/dl) in patients with DR without DME, with non-CSME and with CSME was 148.56 (normal), 175.36 (normal) and 176.40 (high) respectively.
This observation was not statistically significant (P = 0.63). The mean serum total cholesterol (mg/dl) in patients with DR without DME, with non-CSME and with CSME was 177.93 (normal), 215 (high) and 191.2 (normal) respectively.
This observation was not statistically significant (P = 0.05). The mean serum HDL cholesterol (mg/dl) in patients with DR without DME, with non-CSME and with CSME was 41.71 (normal), 43.62 (normal) and 41 (normal) respectively.
This observation was not statistically significant (P = 0.78). The mean serum LDL cholesterol (mg/dl) in patients with DR but no DME was 102 mg/dl (normal), non-CSME was 115 mg/dl (normal) and CSME was 94.38 mg/dl (high).
This observation was not statistically significant (P = 0.31).
Conclusion

In the present study, diabetic peripheral neuropathy (DPN) was significantly more common in patients with diabetic retinopathy (DR) than in those without DR. A statistically significant positive correlation was found between severity of DR and severity of DPN. The mean vibration perception threshold (VPT) was significantly higher in patients with more severe grades of DR.

No statistically significant association was found between presence of dyslipidaemia and presence of DR, DME or DPN. None of the traditional lipid parameters (TG, TC, HDL-C, LDL-C were found to be associated with DR, DME or DPN.

Longer duration of DM was a common risk factor for both DR and DPN. Increasing age and higher glycaemic index were associated with DR but not DPN. BMI was not associated with either DR or DPN.

This study, by demonstrating a strong association between severity of DR and severity of DPN, emphasizes the importance of inter-departmental references for the screening and evaluation of other microvascular complications of diabetes mellitus, irrespective of the patient’s symptoms and cause of attendance.

Compared to other Indian studies, in this study, the association between severity of DR and severity of DPN was stronger. This could be because the present study, unlike other studies excluded conditions such as, anaemia, CKD, vitamin B12 deficiency and peripheral arterial disease that may increase the presence and severity of one microangiopathy more than the other. Further studies are needed to understand the importance of screening patients with only DR, only DPN and those with disproportionate disease for these other conditions. As this was not a prospective study, the chronological order (if any) of appearance of DR and DPN was not investigated.

Identification of modifiable risk factors for DR and DPN and their subsequent control may prevent the onset and progression of these potentially devastating complications. Further investigation into the modifiable risk factors for DR and DPN in the Indian population.

Bibliography


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