Original Research Article

A study to estimate the occurrence of peripheral neuropathy among asymptomatic type 2 diabetic patients

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ABSTRACT

Background: Diabetes is a life long illness characterized by increased blood glucose levels. According to International Diabetes Federation, the number of diabetes already reached 451 million in 2017 and estimated that in 2045, 693 million people will have diabetes. Approximately, 27% of the direct medical cost of diabetes may be attributed to DPN. The objectives of the current study were to estimate the occurrence of peripheral neuropathy among asymptomatic type 2 diabetic patients. The data gained from this study can aid health care providers and primary care providers to understand the occurrence of diabetic peripheral neuropathy in asymptomatic type 2 diabetic patients.

Methods: Study was conducted on patients diagnosed with Type 2 Diabetes in hospitals attached to BMCRI. It is a Cross sectional Correlational study done from February 2019 to June 2019. 88 patients who consented for the study and diagnosed with T2DM for at least a period of 5 year were included. Recently diagnosed T2DM, T1DM, pregnant female, patients on chemotherapeutic agents, known case Peripheral neuropathy of any other cause and patients not willing to participate in the study were excluded.

Results: Total 57(64.77%) males and 31(35.22%) females with mean 41.12±15 years. Patients relevant history related to of diabetic peripheral neuropathy collected and Michigan peripheral neuropathy screening instrument (MNSI) assessment done using monofilament testing and vibrotherm (table 3). It was noted that 26.13% (23) patients had objective signs of peripheral neuropathy, 17.04% were males, and female (9.09%) and p value were statistically significant <0.001.

Conclusions: Our study concluded that, 26.13% occurrence of Peripheral neuropathy in asymptomatic patients with duration of T2DM >5 years. The neuropathy was independently associated with age and duration of symptoms of diabetes prior to the diagnosis.

Keywords: Biothesiometer, Diabetic peripheral neuropathy, Michigan peripheral neuropathy screening instrument, Type 2 Diabetes Mellitus

INTRODUCTION

Diabetes is a life long illness characterized by increased blood glucose levels and reduction in tissue repair that requires continuing medical care to prevent acute complications and to reduce the risk of long-term complications. Failure to achieve optimal glycemic control can cause damage to the body's small and large vessels and nerves, affect the functioning of many body organs and interfere with body metabolism. Globally, type 2 Diabetes mellitus (T2DM) is increasing in its occurrence.1
It is associated with significant morbidity, mortality, and increasing health care cost. According to International Diabetes Federation, the number of diabetes already reached 451 million in 2017 and estimated that in 2045, 693 million people will have diabetes.

Major complications of T2DM include diabetic foot and diabetic peripheral neuropathy (DPN); that constitutes an increasing public health problem with increasing admission rate, cost, amputation risk, and mortality in diabetic patients.

Approximately, 27% of the direct medical cost of diabetes may be attributed to DPN. Diabetic patients have a 15-25% lifetime risk of developing a diabetic foot ulcer and one out of 6 patients will have a lower-limb amputation, with an associated increase in mortality ranging from 47% to 70%. The symptoms of DPN show a discrepancy; between patients however, initially it begins with sensory loss that makes diabetic patients more liable to foot ulcers and increasing risk of leg amputation.

The practice of foot care measures such as daily foot washing and drying, daily foot examination, proper nail care, and footwear are important in regard to prevention and early detection of the expected complications. Patients with poor knowledge and practices about diabetic foot care with peripheral neuropathy have a higher incidence of diabetic foot complications.

Studies suggest that increasing awareness about diabetic foot care practices in patients with peripheral neuropathy may reduce diabetes related foot ulceration and amputations and facilitate healing of foot ulcers.

A significant proportion of patients with peripheral neuropathy have no known underlying cause. Therefore, a better understanding of the underlying causes is needed to inform the development of new disease modifying treatments. Multiple studies have implicated the metabolic syndrome (MetS) as a potential cause of peripheral neuropathy.

The objectives of the current study were to estimate the occurrence of peripheral neuropathy among asymptomatic type 2 diabetic patients. The data gained from this study can aid health care providers and primary care providers to understand the occurrence of diabetic peripheral neuropathy in asymptomatic type 2 diabetic patients and to target self-management education programs for people with diabetes about healthy foot care measures such as daily wash, drying feet after washing to decrease occurrence of diabetic foot complication like foot ulcers.

Aims and objectives of the study was to estimate the occurrence of peripheral neuropathy among asymptomatic Type 2 diabetic patients.

**METHODS**

Study was conducted on patients diagnosed with Type 2 Diabetes in hospitals attached to BMCRI who were willing to participate in the proposed study after taking informed written consent. It is a Cross sectional Correlational study done from February 2019 to June 2019. 88 patients who gave consent for the study and diagnosed with Type 2 Diabetes Mellitus for at least a period of 5 year were included. Recently diagnosed type 2 diabetes, type 1 Diabetes patients, pregnant female, patients on chemotherapeutic agents, known case Peripheral neuropathy of any other cause and patients not willing to participate in the study were excluded.

**Inclusion criteria**

- Patient diagnosed with Type 2 Diabetes Mellitus for at least a period of 5 years
- Patient willing to participate in the study after taking informed written consent.

**Exclusion criteria**

- Recently diagnosed Type 2 diabetes
- Type 1 Diabetes patients
- Pregnant females
- Patient on chemotherapeutic agents
- Known case Peripheral neuropathy of any other cause
- Patient not willing to participate in the study.

**Methodology of data collection**

After obtaining ethical clearance and approval from the Institutional Ethics Committee of BMCRI, written informed consent was taken from the patients.

Data regarding Peripheral neuropathy was collected by using a Michigan neuropathy screening instrument (MNSI) examination and questionnaire, Monofilament testing was performed with a Semmes Weinstein 5.07/10-g monofilament on the dorsum of the dominant great toe and 10 other sites on the sole of the foot, patient was subjected to neuro-thesiometer analysis, other relevant investigations was performed.

Data was entered in MS excel spreadsheet and analyzed using IBM SPSS version 24.0 software. Results were presented as descriptive statistics in the form of mean/ proportion and percentage and possible associations was derived by using suitable parametric and non-parametric tests of significance. Results was be presented as tables, charts and figures as applicable.

**Statistical significance**

- $<0.01$ highly significant at 99% CI.
- $0.01 \leq p < 0.05$ significant at 95% CI.
- $0.05 \leq p < 0.1$ significant at 90% CI.
RESULTS

Socio-demographic profile including age, occupation, gender is tabulated in the table (Table 1) and duration of diabetes and treatment details in (Figure 1 and 2) respectively. The mean age of patients is 41.12±15 years, 57(64.77%) were males and 31(35.22%) were females. All patients more than 5 years history of diabetes mellitus were included, in which 55.68% patients were belonging to category of diabetes from 5 to 10 years and males were predominant (33%) (Figure 1).

Patients treatment history were collected, and it was found that 60.22% were mainly on OHA’s, 14.7% on insulin and 25% were on both.

Table 1: Socio-demographic characteristics of patients on second line ART.

<table>
<thead>
<tr>
<th>Variables</th>
<th>No. of patients</th>
<th>% of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 31-39</td>
<td>6</td>
<td>6.81%</td>
</tr>
<tr>
<td>Age 40-49</td>
<td>44</td>
<td>50%</td>
</tr>
<tr>
<td>Age 50-59</td>
<td>16</td>
<td>18.18%</td>
</tr>
<tr>
<td>Age ≥60</td>
<td>22</td>
<td>25%</td>
</tr>
<tr>
<td>Mean age</td>
<td>41.12</td>
<td></td>
</tr>
<tr>
<td>SD</td>
<td>15.80</td>
<td></td>
</tr>
<tr>
<td>Gender Male</td>
<td>57</td>
<td>64.77%</td>
</tr>
<tr>
<td>Gender Female</td>
<td>31</td>
<td>35.22%</td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coolie</td>
<td>64</td>
<td>72.72%</td>
</tr>
<tr>
<td>Non-Coolie</td>
<td>24</td>
<td>27.27%</td>
</tr>
</tbody>
</table>

Table 2: Glycemic control.

<table>
<thead>
<tr>
<th>Cases</th>
<th>FBS (MEAN) mg/dl</th>
<th>SD mg/dl</th>
<th>PPBS (MEAN) mg/dl</th>
<th>SD mg/dl</th>
<th>HbAIC (MEAN) %</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>210</td>
<td>22.24</td>
<td>278</td>
<td>34.78</td>
<td>9.2</td>
<td>3.1</td>
</tr>
<tr>
<td>Female</td>
<td>186</td>
<td>26.81</td>
<td>234</td>
<td>36.43</td>
<td>8.6</td>
<td>2.4</td>
</tr>
<tr>
<td>Mean</td>
<td>198</td>
<td>24.52</td>
<td>256</td>
<td>35.605</td>
<td>8.9</td>
<td>2.75</td>
</tr>
<tr>
<td>p value</td>
<td>0.031</td>
<td>0.04</td>
<td>&lt;0.01</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3: Michigan peripheral neuropathy screening instrument (MNSI) assessment using biothesiometer.

<table>
<thead>
<tr>
<th>History</th>
<th>Physical examination</th>
<th>Monofilament</th>
<th>Vibrotherm</th>
<th>Total score (Mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>nil</td>
<td>36 (40.9%)</td>
<td>24 (27.27%)</td>
<td>35(39.77%)</td>
</tr>
<tr>
<td>Females</td>
<td>nil</td>
<td>22 (25%)</td>
<td>17(19.31%)</td>
<td>19(21.59%)</td>
</tr>
<tr>
<td>Total</td>
<td>nil</td>
<td>58 (65.90%)</td>
<td>41(46.59%)</td>
<td>54(61.36%)</td>
</tr>
<tr>
<td>p value</td>
<td>-</td>
<td>0.032</td>
<td>0.041</td>
<td>0.034</td>
</tr>
</tbody>
</table>

Table 4: Results of Michigan peripheral neuropathy screening instrument.

<table>
<thead>
<tr>
<th>Peripheral neuropathy</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>15</td>
<td>8</td>
<td>23</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Absent</td>
<td>42</td>
<td>23</td>
<td>65</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Glycemic control of the study patients were assessed by FBS, PPBS, HbA1c according to ADA guidelines. Since most of the patients were on irregular treatment it was found that HbA1c was in the uncontrolled limit >8%, that is 8.9±2.75 (Table 2). All the patients enrolled in the study relevant history related to diabetes were collected including symptoms of peripheral neuropathy and Michigan peripheral neuropathy screening instrument (MNSI) assessment were done using biothesiometer-which includes monofilament testing and vibrotherm (Table 3). 15 males (17.04%) and 8 females (9.09%) were having object evidence of peripheral neuropathy, inspite of being asymptomatic (Table 4).

It was noted that 26.13% (23) patients had objective signs of peripheral neuropathy, 17.04% were males, and female (9.09%) and p value were statistically significant <0.001(Figure 3).

<table>
<thead>
<tr>
<th>Column1</th>
<th>PN ABSENT</th>
<th>PN PRESENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEMALE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MALE</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 3: Percentage of peripheral neuropathy in asymptomatic Type 2 diabetes mellitus patients.

DISCUSSION

Diabetic neuropathies are the most prevalent chronic complications of diabetes. This heterogeneous group of conditions affects different parts of the nervous system and presents with diverse clinical manifestations. High frequency of distal peripheral neuropathy (DPN) in newly diagnosed patients as well as in asymptomatic patients with Type 2 Diabetes Mellitus (T2DM) patients were noted. However, a lower but significant proportion of healthy controls also had PN. DPN was independently associated with increasing age and duration of symptoms of diabetes prior to diagnosis. Simple clinical assessment and bio-thesiometer has a high sensitivity and specificity in detecting DPN. Among the various forms of diabetic neuropathy, distal symmetric polyneuropathy (DSPN) and diabetic autonomic neuropathies, particularly cardiovascular autonomic neuropathy (CAN), are by far the most studied.

Interestingly, it has been previously reported that both DPN and foot ulcers are lower in Indians compared with European Caucasians. In the current study, 26.13% of patients had DPN. Two earlier studies in Indians have reported on the occurrence of DPN in newly diagnosed T2DM of 19.5% and 29.0%. However, our study is first of its kind to estimate the occurrence of diabetic peripheral neuropathy in asymptomatic patients. In the latter study, the occurrence of DPN was measured by NSS and NDS in 100 newly diagnosed T2DM.

In a community-based study from Chennai, South India, Pradeepa et al. measured the occurrence of DPN using VPT by biothesiometer. The occurrence in newly diagnosed patients was 19.5% and 27.8% in those with known diabetes. However, the frequency of DPN in the subjects without diabetes and asymptomatic diabetes patients was not studied.

Monofilament sensation is a measure of protective sensations in the foot and is strongly associated with risk of foot ulceration. The occurrence of impaired monofilament sensation was 46.59%, considerably lower than that of DPN. This low frequency may be reflective of the fact that the 10-g (5.07) monofilament testing is appropriate for the clinical assessment of risk for foot ulceration 12 but not a sensitive means to detect occurrence of neuropathy. In the latter case, a monofilament of 1 g or less may be more appropriate.

Previous studies have identified several risk factors for DPN such as age, poor glycemic control, increasing diabetes, gender, height, body mass index, retinopathy, hypertension, smoking, and alcohol consumption. In the current study, age at diagnosis and duration of symptoms of diabetes prior to diagnosis were independent risk factors for DPN. Since elderly patients have other risk factors for foot ulcerations, such as vision abnormalities and vascular involvement, neuropathy screening assumes an even greater importance in this age group.

The occurrence of DPN increased with longer prediabetic period, as reflected by duration of symptoms attributable to diabetes. We could not demonstrate any association between HbA1c, but this may be partly due to the fact that most of our patients were already on treatment at the time of examination. Another proposed possibility is that any elevated glucose beyond a threshold will predispose to DPN.

The occurrence of DPN depends on the criteria and methods used. After a simple instrument such as Michigan neuropathy assessment, 26.13% of subjects had an increased threshold suggestive of PN even though they were asymptomatic. Thus a good clinical examination with objective assessment such a biothesiometer is a sensitive measure to diagnose PN and other studies have also suggested neuropathy scoring to be simple, inexpensive, easy, and sensitive method for PN detection. Limitations of the study was that it was clinic based and may not reflect the actual occurrence of DPN in the community and authors did not investigate metabolic causes of Peripheral neuropathy other than diabetes.
CONCLUSION

This study concluded that, 26.13% occurrence of Peripheral neuropathy in asymptomatic patients with duration of T2DM >5 years. The neuropathy was independently associated with age and duration of symptoms of diabetes prior to the diagnosis. Screening for DPN using simple clinical examination is cost-effective means to prevent foot ulceration and infections in Indian patients with T2DM. The strength of our study is that it was a prospective design, patient evaluation was done by a single physician, and the use of both qualitative and quantitative mode of assessment of neuropathy.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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