PREVALENCE AND ASSOCIATED RISK FACTORS OF DIABETIC PERIPHERAL NEUROPATHY AMONG DIABETIC PATIENTS IN NATIONAL CENTER OF DIABETES IN YEMEN

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ABSTRACT

Background: Diabetes mellitus is one of the important public health concerns challenging the world in the 21st century. Neuropathy is one of the most frequent complications of diabetes, and the most common type of neuropathy is the diabetic peripheral neuropathy. Diabetic peripheral neuropathy is common and frequent cause of morbidity and disability. In Yemen, the data on the prevalence and risk factors of diabetic peripheral neuropathy remains scarce.

Aim: The purpose of this study is to determine the prevalence and associated risk factors of diabetic peripheral neuropathy in the National Centre of Diabetes in Yemen.

Materials and Methods: A cross-sectional study of 306 diabetic patients was conducted in the National Centre of Diabetes in Yemen from February to May 2014. The diabetic peripheral neuropathy was assessed by using Neuropathy Symptoms Score and Neuropathy Disability Score.

Result: The prevalence of diabetic peripheral neuropathy was 56.2%, and it increased with diabetes duration, HbA1c (from 34.6% in patients with HbA1c <7% to 61.3% in patients with HbA1c >9%) and with increased in total cholesterol (P = 0.0001 95%CI 4.9 – 5.1). The diabetic peripheral neuropathy was less among obese patients (P = 0.03). There was no significant association between the diabetic peripheral neuropathy and diabetes type (P = 0.373) and hypertension (P = 0.08).

Conclusion: The prevalence of diabetic peripheral neuropathy among diabetic patients in the National Centre of Diabetes in Yemen was 56.2%. Diabetes duration, HbA1c, body mass index and total cholesterol were the associated risk factors of diabetic peripheral neuropathy.

Keywords: Diabetic peripheral neuropathy, risk factors
1.0 Introduction

Diabetes mellitus is one of the non-communicable diseases which become a real challenge of public health due to its epidemic proportion (Khatib, 2006). The World Health Organization estimates that 346 million people have diabetes mellitus worldwide (WHO, 2012) and this number increases continuously due to lifestyle changing (Shaw, 2010).

According to the International Diabetes Federation, the Middle East and North Africa Region has the greatest comparative prevalence of diabetes (10.9%), and the Africa Region has the lowest (5.7%). Yemen is one of the Middle East and North Africa countries and the prevalence of diabetes mellitus in this country is estimated to be 8.45% (International Diabetes Federation, 2013).

The long-term outcome of diabetes results from the progress of tissue complications, essentially microvascular and macrovascular disease. Diabetic neuropathy is one of the long term common complications of diabetes, as it affects 50% of patients (Boulton, Malik, Arezzo, & Sosenko, 2004). Peripheral neuropathy is the most common form of diabetic neuropathy (Boulton et al., 2004).

Diabetic peripheral neuropathy is defined as the presence of symptoms and/or signs of peripheral nerve dysfunction in patients with diabetes after excluded the other causes of dysfunction (Boulton, 2005). Diabetic peripheral neuropathy is common and frequent cause of morbidity and disability by predisposing the foot to ulceration and amputation. The development of diabetic peripheral neuropathy is influenced by age, diabetes duration, glycaemic control; and macrovascular disease risk factors such as smoking, hypertension, obesity, and hyperlipidaemia. It affects more than 50% of patients with long duration diabetes, with new cases occurring at annual incidence of about 2% (Veves & Malik, 2007).

The prevalence of diabetic peripheral neuropathy is varying widely in the literature and this is due to differences in the diagnostic criteria employed, the different methods of patient selection and the sample size (Edwards, Vincent, Cheng, & Feldman, 2008).

In Middle East Region, the prevalence of painful diabetic peripheral neuropathy in type 1 or 2 was 53.7% (Jambart et al. 2011). In Yemen, the data about the epidemiology of diabetic peripheral neuropathy and its risk factors remains poor, and there is little information available on this issue in the international literature. A study done in 1990s found that the prevalence of diabetic peripheral neuropathy was 40.7% (Gunaid, et al., 1997), and another study done between 2003 and 2006 found that the prevalence of diabetic peripheral neuropathy among type 2 diabetes patients was 64.50% (Ali, 2007).

The aims of this study are to determine the prevalence of diabetic peripheral neuropathy among the diabetic patients who registered in the National Centre of Diabetes in Yemen and to determine the association between the clinical profiles of the diabetic patients (diabetes type, diabetes duration, HbA1c, body mass index, hypertension, total cholesterol) and the diabetic peripheral neuropathy.
2.0 Materials and Methods

A cross-sectional study was conducted in National Centre of Diabetes, in Yemen that was inaugurated in March 2007 and hosted by the main referral hospital in Yemen, Al Thawra Modern General and Teaching Hospital. The hospital is located in Sana’a city, the capital of Yemen, and it is a tertiary hospital. The centre consists of two medical clinics, diabetic foot care clinic, laboratory, and centre hall for continuing medical education. The centre receives 50 to 60 patients per day.

Systematic random sampling method was used to select 306 diabetic patients, who attended the National Centre of Diabetes from February to May 2014. The inclusion criteria were local Yemeni diabetic patients above 18 years old with type 1 or type 2 diabetes. The exclusion criteria include patients with a foot ulcer; lower extremity amputation and any patient with a disease that causes peripheral neuropathy.

The data was collected by using questionnaire, medical examination of the foot and for measuring the blood pressure, anthropometric measurement of height and weight to measure body mass index and medical record to record latest HbA1c and fasting serum cholesterol.

The questionnaire was made of simple and obvious questions, and it was administrated by interview the diabetic patient. The participants were interviewed, after receiving their informed consent, for their socio-demographic data (age, gender) diabetes type and clinical history. The diabetic peripheral neuropathy was assessed by using Neuropathy Symptoms Score and Neuropathy Disability Score (Young et al., 1993).

The Neuropathy Symptom Score consists of five questions; each assigning points in order to estimate the total symptom score. The total maximum abnormal symptom score is nine points. The first question in the Neuropathy Symptoms Score is about the presence of following symptoms in the lower extremity (burning, numbness, tingling) these symptoms get two points, or (Fatigue, Cramping, Aching feelings) get one point. The second question is about which part of the lower extremity has the symptoms if the symptoms present in the feet, this get two points or in the calf one point. The third question is about the time of the exacerbation of the symptoms. If the symptoms exacerbate during the night; this gets two points or present equally at day and night one point. The fourth question is about the previous symptoms if they awaken the patient from sleep; yes answer gets one point. The last question is about the manoeuvres reduce the symptoms; walking gets two points; standing gets one point, and sitting gets zero.

The Neuropathy Disability Score consists of four clinical tests on both feet. The procedure was explained, and the tests were done on the patient’s hand prior to the test on feet. The patient was asked to close the eyes during the test. Every test was evaluated with points to estimate the total disability score. The total maximum abnormal disability score is ten points. The four clinical tests are ankle reflex, vibration perception, thermal sensation and tactile sensation.

The ankle reflex was done by using Babinski reflex hammer. If there is no jerk it considered (two points) for each side, jerk with reinforcement considered (one point) for each side. Normal ankle reflex considered (zero points).
The vibration perception was tested by using a 128-Hz vibrating fork. The fork was put on the first toe three times with at least one false application (not vibrating fork). The patient was asked to recognize which application that was vibrating or not. Two of three right responds set to be a correct answer (zero points); two of three wrong responds was an incorrect answer (one point) for each side.

The thermal sensation was done by using one cold and one room temperature sponge. The sponge was applied on the dorsum of the foot. The patients required to tell which application was cold or normal, a correct answer (zero points), an incorrect answer (one point) for each side.

Tactile sensation (pin-prick): The pin-prick was done at the first toe by using the reverse ends of the turning fork and tendon hammer. The patients asked to recognize which application was sharp or dull, a correct answer (zero points), an incorrect answer (one point) for each side.

“The total symptom score of 3-4 points considered as mild symptoms, 5-6 points as moderate symptoms and 7-9 points as severe symptoms. A total disability score 3-5 points considered mild disability, 6-8 points as moderate disability and 9-10 points as severe disability” (Young et al., 1993). According to Young et al. the minimum acceptable criteria for diagnosis of diabetic peripheral neuropathy were moderate disability, with or without symptoms, or mild disability with moderate symptoms (Young et al., 1993).

The questionnaire was translated to Arabic by an academic expert and then retranslated to English by another academic expert. Pre-test of the questionnaire was conducted in Yemen on 30 patients who were not included in the study. The face validity and content validity of the questionnaire were assessed. The sensitivity of neuropathy symptom score and neuropathy disability score is 71.1% and the specificity is 90%. (Chawla, Bhasin & Chawla, 2013).

The data was analysed by utilizing Statistical Package for the Social Sciences (SPSS) version 21. Descriptive statistics (frequency and percentage) was used to identify the prevalence of diabetic peripheral neuropathy and to summarize categorical data. Continuous variables (HbA1c and body mass index BMI) were converted into categorical. The good glycemic control defined as HbA1c less than 7% and poor glycemic control defined as HbA1c more than 9%. HbA1c between 7% and 9% was considered as fair glycemic control. In this study, non-obese were those with BMI less than 30 and obese were those with BMI ≥30.

The data was collected after obtaining the permission and approval from the Ethics Committee for Research involving Human Subjects of University Putra Malaysia and the National Centre of Diabetes in Yemen. The patients were informed about the purpose and objective of the study, and that they had the right to withdraw or restrict their data from analysis at any stage of the study.
Diabetic peripheral neuropathy was the dependent variable and diabetes type, diabetes duration, HbA1c, body mass index, hypertension and total cholesterol were the independent variables.

3.0 Results and Discussion

3.1 Patients’ characteristics

Out of three hundred and seven diabetic patients eligible to participate in this study, one patient refused to participate. The response rate was 99.7%, and analysis was done on the remaining three hundred and six patients. The mean age of the study population was 53.5 ± 11.1 years. There were 166 (54.2%) female and 140(45.8%) male.94.8% of the patients have type 2 diabetes. The mean duration of diabetes was 7.14 ± 5.7 years. The mean value of glycated haemoglobin (HbA1c) was 9.5 ± 2.5%. The mean body mass index was 27.1 ± 5.1Kg/m². Hypertension was present in 27.5% of the patients. The mean total cholesterol was 5.1± 1.3mmol/l. In this study, the overall prevalence of diabetic peripheral neuropathy was 56.2%.

3.2 Clinical profiles in patients with and without diabetic peripheral neuropathy

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients with DPN</th>
<th>Patients without DPN</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes Type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type1</td>
<td>4 (25%)</td>
<td>12 (75%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Type2</td>
<td>168(57.9%)</td>
<td>122 (42.1%)</td>
<td></td>
</tr>
<tr>
<td>Duration (years)</td>
<td>8.5±6 years</td>
<td>5.4±4 years</td>
<td></td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 7%</td>
<td>18 (34.6%)</td>
<td>34 (65.4%)</td>
<td>0.003</td>
</tr>
<tr>
<td>7% - 9%</td>
<td>62 (59.6%)</td>
<td>42 (40.4%)</td>
<td></td>
</tr>
<tr>
<td>&gt; 9%</td>
<td>92(61.3%)</td>
<td>58 (38.7%)</td>
<td></td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td></td>
<td></td>
<td>0.03</td>
</tr>
<tr>
<td>Obese</td>
<td>36 (46.2%)</td>
<td>42 (53.8%)</td>
<td></td>
</tr>
<tr>
<td>Non-obese</td>
<td>136 (59.6%)</td>
<td>92 (40.4%)</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td>0.08</td>
</tr>
<tr>
<td>Yes</td>
<td>54 (64.3%)</td>
<td>30 (35.7%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>188(53.2%)</td>
<td>104 (46.8%)</td>
<td></td>
</tr>
<tr>
<td>Total cholesterol (mmol/l)</td>
<td>5.2</td>
<td>4.8</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

The table 1 illustrates the differences of clinical profiles between patients with and without diabetic peripheral neuropathy. The table showed that the prevalence of diabetic peripheral neuropathy in patients with type 1 diabetes was 25% and 57.9% in patients with type2 diabetes. There was a significant association between diabetes type and the diabetic peripheral neuropathy (P = 0.01) and patients with type2 DM have a higher prevalence of diabetic peripheral neuropathy than patients with type1 DM (OR 4.1, 95%CI 1.3 – 13.1). The diabetes duration was significantly associated with the diabetic peripheral neuropathy (P = 0.0001). The mean duration of diabetes in patients without diabetic peripheral neuropathy was 5.4 years and for patients with diabetic peripheral neuropathy was 8.5 years. There was a
significant association between HbA1c and the diabetic peripheral neuropathy. The prevalence of diabetic peripheral neuropathy was increase with the increase in HbA1c. The prevalence of diabetic peripheral neuropathy in patients with HbA1c > 9% was higher (61.3%) than in patients with HbA1c less than 7% (34.6%) (P = 0.003). There was a significant association between body mass index and the diabetic peripheral neuropathy. The prevalence of diabetic peripheral neuropathy in obese patients (46.2%) is less than that in non-obese patients (59.6%) (P = 0.03, OR 0.58 95% CI 0.35 – 0.97). The prevalence of diabetic peripheral neuropathy among the hypertensive patients was 64.3% compared with 53.2% among normotensive patients. However, there was no significant association between hypertension and the diabetic peripheral neuropathy (P = 0.08, OR 1.6, 95% 0.95 – 2.7). There was a significant association between total cholesterol and the diabetic peripheral neuropathy (P = 0.0001). The prevalence of diabetic peripheral neuropathy was increased with increased in the total cholesterol. The mean total cholesterol in patients with diabetic peripheral neuropathy was 5.2mmol/l compared with 4.8mmol/l in patients without diabetic peripheral neuropathy (P = 0.01). The association between the clinical profiles and diabetic peripheral neuropathy was significant with type of diabetes, diabetes duration, HbA1c, body mass index, and total cholesterol and not significant with hypertension.

3.3 Risk factors of diabetic peripheral neuropathy

Table 2: Multiple Logistic Regression Analysis of Associated Risk Factors with Diabetic Peripheral Neuropathy

<table>
<thead>
<tr>
<th>Variables</th>
<th>B</th>
<th>P Value</th>
<th>* Odd Ratio</th>
<th>95% CI for Odd Ratio Lower</th>
<th>95% CI for Odd Ratio Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes type</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type 2</td>
<td>0.738</td>
<td>0.373</td>
<td>2.09</td>
<td>.413</td>
<td>10.59</td>
</tr>
<tr>
<td>Duration (years)</td>
<td>0.098</td>
<td>0.000</td>
<td>1.1</td>
<td>1.04</td>
<td>1.16</td>
</tr>
<tr>
<td>Glycaemic control</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HbA1c &lt; 7%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HbA1c 7%–9%</td>
<td>0.826</td>
<td>0.037</td>
<td>2.28</td>
<td>1.02</td>
<td>4.96</td>
</tr>
<tr>
<td>HbA1c &gt;9%</td>
<td>0.789</td>
<td>0.041</td>
<td>2.2</td>
<td>1.03</td>
<td>4.69</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-obese</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obese</td>
<td>-0.585</td>
<td>0.049</td>
<td>0.568</td>
<td>0.313</td>
<td>0.996</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol (mmol/l)</td>
<td>0.209</td>
<td>0.034</td>
<td>1.2</td>
<td>1.01</td>
<td>1.50</td>
</tr>
</tbody>
</table>

* Adjusted for age

Table 2 illustrates the risk factors of the diabetic peripheral neuropathy. Multiple logistic regression analysis was performed to determine the association between diabetic peripheral neuropathy and the clinical profile variables. The analysis showed that the diabetes type was not significantly associated with the diabetic peripheral neuropathy. The duration of diabetes was positively associated with the diabetic peripheral neuropathy (OR 1.1, 95% CI 1.04 - 1.16, P = 0.0001). Fair glycaemic control (HbA1c 7% - 9%) and poor glycaemic control (HbA1c > 9%) were significantly associated with diabetic peripheral neuropathy. The body mass index
was negatively associated with diabetic peripheral neuropathy (OR 0.558, 95% CI 0.313 – 0.996, P = 0.049) the diabetic peripheral neuropathy was high in non-obese patients. The hypertension was not significantly associated with the diabetic peripheral neuropathy. The total cholesterol was positively associated with the diabetic peripheral neuropathy (OR 1.2, 95%CI 1.01 - 1.5, P = 0.03).

3.4 Discussion

The diabetic peripheral neuropathy in this study was determined by neuropathy symptom score and neuropathy disability score, and its prevalence was compared with other studies used the same scores to assess the diabetic peripheral neuropathy.

The prevalence of diabetic peripheral neuropathy in this study was 56.2%. It was higher than the prevalence of diabetic peripheral neuropathy in Malaysia (50.7%) (Mimi et al., 2003) and Iran (45.7%) (Kiani et al., 2013). The prevalence of diabetic peripheral neuropathy among type2 diabetic patients was (57.9%) that was the highest compared with (49.3%) in Iran (Kiani et al., 2013), (19.7%) in Bangladesh (Mørkrid, et al., 2010) and (33.33%) in India (Pawde et al., 2013).

The explanation of high prevalence of diabetic peripheral neuropathy in this study was that (49%) of the patients had poor glycaemic control HbA1c > 9%, and (34%) had fair glycaemic control. 53.5% of patients with diabetic peripheral neuropathy were those who had poor glycaemic control and (36%) of patients with diabetic peripheral neuropathy were those who had fair glycaemic control. Poor and fair glycaemic control means that the blood glucose level is above the normal level for a long time. Hyperglycaemia causes activation of multiple biochemical pathways through induces oxidative stress in diabetic neurons and leads to nerve damage and neuronal ischemia (Edwards et al., 2008).

3.4.1 Association between clinical profiles and diabetic peripheral neuropathy

In this study the clinical profile of the patients consisted of diabetes type, duration of diabetes, HbA1c, body mass index, hypertension, and total cholesterol. This study found that the diabetic peripheral neuropathy was higher among patients with type2 diabetes compared with patients with type1 diabetes (57.9%, 25 % respectively, P = 0.01, OR 4.1, 95%CI 1.3 – 13.1), but in the logistic regression analysis the diabetes type was not significantly associated with diabetic peripheral neuropathy (P = 0.3, OR 2.09, 95%CI 0.4 – 10.59). This result was not similar to result in study done by Kiani et al. and found that the diabetic peripheral neuropathy was associated with type2 diabetes (P< 0.001) (Kiani et al., 2013).

The duration of diabetes was significantly associated with the prevalence of diabetic peripheral neuropathy (P = 0.0001, 95%CI 6.5- 7.8). This finding supported the same finding in many studies (Pawde et al., 2013, Mørkridet al., 2010, Mimi et al., 2003).

This study found that the prevalence of diabetic peripheral neuropathy was high among patients with fair and poor glycemic control compared (P= 0.003). A similar finding was found in different studies, in Al-Kaabi et al. study the diabetic peripheral neuropathy was high in patients with HbA1c ≥ 7% (P = 0.01,OR 3.41, 95% CI 1.15– 10.16) (Al-Kaabi et al., 2014). In Mørkrid et al., study the prevalence of diabetic peripheral neuropathy was increased with
increased the HbA1c (P < 0.01) (Mørkrid et al., 2010). Fair and poor glycemic control (HbA1c ≥ 7%) can cause nerve damage and neuronal ischemia (Edwards et al., 2008).

This study found that the obese patients had lower prevalence of diabetic peripheral neuropathy (46.2%) compared with non-obese patients (59.6%) (P = 0.03, OR 0.58 95%CI 0.35 – 0.97). Similar finding was found in different studies. A Mørkrid et al. study found that the diabetic peripheral neuropathy was more in non-obese patients (P < 0.01, OR 3.7, 95%CI 1.5- 9.3). A Katulanda et al. study that done in Sri Lanka found the similar result P <0.01 (2012). However, in the EURODIAB Prospective Complications Study that done in Europe found that the diabetic peripheral neuropathy increase with increased in body mass index (P< 0.001 RR 1.29, 95%CI 1.10, 1.51), but adjusted relative risk became not significant (RR1.04, 95%CI 0.86- 1.26) (Tesfaye et al., 1996). The explanation of this difference may be related to the differences between developing and developed countries and more studies are required to define the role of body mass index in diabetic peripheral neuropathy and if the culture and genetics can explain this differences.

This study found that hypertension was not associated with prevalence of diabetic peripheral neuropathy (P = 0.08, OR 1.6, 95% 0.95 – 2.7). This result was not similar to the finding in previous study. A study by Pawde et al. showed that the prevalence of diabetic peripheral neuropathy was high among the hypertensive patients (P<0.001, OR 2.95 95%CI 1.67-5.20) (Pawde et al., 2013).

In this study, the total cholesterol was significantly associated with diabetic peripheral neuropathy (P = 0.001 95%CI 4.9 – 5.1). Similar result was found in previous studies. In a study done by Pawde et al. Dyslipidaemia was a risk factor for diabetic peripheral neuropathy (P = 0.006 OR 3.18 95%CI 1.34-7.53) (Pawde et al., 2013).

4.0 Conclusion and recommendation

The current cross-sectional study was conducted in the National Center of Diabetes, in Yemen to study the prevalence and risk factors of diabetic peripheral neuropathy among diabetic patients. The overall prevalence of diabetic peripheral neuropathy was 56.2% this prevalence was high when compared with other countries. From the clinical profiles, diabetes duration, HbA1c, body mass index and total cholesterol were the associated risk factors of diabetic peripheral neuropathy. However, diabetes type and hypertension were not associated with diabetic peripheral neuropathy. The results of this study supported the finding of previous studies.

This study has some limitations. The major limitation is that the results cannot be generalized to all diabetic patients in Yemen because not all diabetic patients are registered in the National Centre of Diabetes. The study design is cross-sectional so the causal relationships cannot be investigated.

The results of this study can serve as a basis for future intervention programs to prevent diabetic peripheral neuropathy. The intervention programs should focus on the risk factors that identified in this study. For example fair and poor glycaemic controls were associated with diabetic peripheral neuropathy so the diabetic patients should be educated about the ways to control the blood glucose.
Acknowledgement

We would like to thank the Ethics Committee for Research involving Human Subjects of University Putra Malaysia and the director of National Centre of Diabetes in Yemen (Dr. Zaid Atef) for their permission to do this study. We fully acknowledge all people who participated and supported to complete this study.

Declaration

Authors declare that there is no conflict of interest regarding publication of this article.

Authors’ contribution

Author 1: Prepared draft of manuscript
Author 2: Editing draft and final manuscript
Author 3: Editing draft manuscript
Author 4: Prepared draft of manuscript

References


