

Screening for the Diagnosis of Diabetic Peripheral Neuropathy in Type-2 Diabetes Mellitus in Southwest Iran

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ABSTRACT

Diabetic Peripheral Neuropathy is a major debilitating complication in patients with diabetes. Evidence suggests that the early screening diagnosis of neuropathy can reduce the risk of diabetic foot ulcers and amputations. The present study was conducted to screen peripheral neuropathy in type-2 diabetes mellitus. This cross-sectional study was conducted on 200 patients with type-2 diabetes mellitus randomly recruited from a diabetes center in Khorramabad, Iran, in 2020. DPN was assessed using the Michigan Neuropathy Screening Instrument in two parts: interviews about neuropathic symptoms and clinical examinations. The validity and reliability of the tool have already been confirmed. Two hundred patients (110 men, 90 women) with type-2 diabetes mellitus were studied. A total of 57 (27%) of them had Diabetic Peripheral Neuropathy. The duration of the disease [OR: 4.01; 95% CI (2.1-5.2)], age [OR: 1.3; 95% CI (1.4-3.5)], BMI [OR: 3.1; 95% CI (1.5-5.7)] and smoking [OR: 2.8; 95% CI (1.8-4.9)] were the main risk factors that had significant positive correlations with neuropathy (P<0.05). The present findings emphasize the importance of screening for the early diagnosis of neuropathy in patients with diabetes. Foot examination is recommended to be incorporated into the routine management of diabetic patients in primary care centers.

Keywords: Diabetes; peripheral neuropathy; Screening

Introduction

Neuropathy is the most common cause of diabetic foot ulcers that is observed in 90% of the patients [1]. The nerves generally become involved in 7% of patients with diabetes within the first year of their diagnosis, and the prevalence of nerve involvement increases to over 50% as the duration of the disease increases to 25 years [2]. The loss of sensory modalities leads to a failure to sense minor trauma, altered plantar pressure, and deformity of the foot, leading to ulceration. According to the American Diabetes

Association, all patients with diabetes should be screened for neuropathy at the time of their diabetes diagnosis [3]. Proper care programs can help prevent or eliminate the risk factors so that diabetic patients can enjoy a normal life and that no high costs are imposed on the

community [4]. Studies have reported the worldwide prevalence of Diabetic Peripheral Neuropathy (DPN) as 15% to 83% [5-9]. Estimates of the prevalence of diabetic neuropathy vary to a large extent due to the differences in the type of patients, the neurological effects of aging, and the diagnostic methods and criteria used. A few studies have evaluated the prevalence of DPN in different regions of Iran and have reported it to range from 27% to 75% [10-14].

Given the large emphasis on the prevention and/or early diagnosis of DPN at the primary care level and given the very few studies on the frequency of diabetic neuropathy, especially since these few studies have only dealt with secondary and tertiary health centers and patients presenting to these centers do not

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represent all the diabetic patients in the community [10-14], the present study was conducted using simple standard tools in primary health centers to offer data that can help increase the awareness of those affected as well as health policy-makers.

Materials and Methods

This cross-sectional study was carried out in a referral diabetes clinic (a public primary care center) in Khorramabad, the capital of Lorestan Province, southwest Iran, in 2020, on 200 patients with type-2 diabetes mellitus who were randomly selected based on a sampling frame. Since all the patients consented to participate in the study, there were no withdrawals. The inclusion criteria for the case group consisted of having a diagnosis of Type-2 Diabetes Mellitus (T2DM) according to the 1999 World Health Organization criteria, receiving treatment with hypoglycemic agents, using no other medications for the treatment of neuropathy, and willingness to sign informed consent forms. The patients with foot ulcers, lower limb amputations, autoimmune diseases, severe osteoarthritis, and a background of hereditary neuropathy or underlying neuropathic diseases such as chronic uremia were excluded from the study based on their history, physical examination, and laboratory findings. The sample size was estimated based on the 30% prevalence of DPN among T2DM patients as detected through the MNSI with a 0.065 precision [10-11].

Data Collection and Instruments

After obtaining informed consent from the patients, a questionnaire inquiring about their general details, height (m), weight (Kg) and, BMI (Kg/m²), HbA1c, smoking history, and duration of diabetes was completed with the help of a trained and experienced investigator and the patients were screened for Diabetic Peripheral Neuropathy (DPN) using a standard questionnaire. The Michigan Neuropathy Screening Instrument (MNSI) was used to screen for DPN in two parts. It included an

interview and a clinical examination that evaluated four different factors in each leg, including the foot's appearance (inspecting signs of dry skin, callous formation, fissures, and deformities) [15]. The first part assessed neuropathic symptoms by history-taking through a form with 15 yes/no items on foot sensations such as pain, numbness, and temperature sensitivity. Two of these items were not scored because they screened patients with impaired peripheral blood circulation and general weakness. The second part was a brief physical examination involving an inspection of the feet (the appearance of the foot skin in terms of dryness, cracks, and deformities) and the evaluation of ankle reflexes (present =0, decreased = 0.5, absent =1), vibration perception in the feet with the use of a 128-Hz tuning fork on the big toe (present =0, decreased = 0.5, absent = 1) and foot sensations using a 10-g monofilament (present =0, reduced = 0.5, absent =1). The combination of two tests (the 128-Hz tuning fork test and the 10-g SWM monofilament) increased the sensitivity and accuracy of the responses by 89.5% and 86.5 [16]. Equipment calibration was not required for the examination, which has previously been validated against the San Antonio consensus criteria and found to be both highly specific (95%) and sensitive (80%); [16]. According to previous validations in different studies, neuropathy is defined operationally as seven or more positive responses on the MNSI or a score of 2 or higher on the examination part of the MNSI [9-16]. The validity and reliability of this tool have already been confirmed [10]. The present study also obtained a Cronbach's alpha coefficient of 0.91 and a test-retest reliability coefficient of 0.89 for the tool. The same investigator performed all the discussed tests to control for inter-rater reliability. The protocol received the ethical approval of the Human Research Ethics Committee of Lorestan University of Medical Sciences under the code LUMS. IRC.1393.19.

Statistical analysis

The data collected were analyzed in SPSS. The mean, standard deviation, and frequency were used to describe the data. The student's test, was used to analyze the variables with a normal distribution. The Chi-square test was performed to compare the qualitative variables between the groups. A logistic regression was used to predict the effects of the independent variables on neuropathic disorder and to control the confounding variables.

P<0.05 was set as the level of statistical significance.

Results

A total of 200 diabetic patients entered the study. The response rate was 100%. The data had a normal distribution, and there was no missing value.

The patients' age range was 31-67 years, and their Average age was 47±5.5 years. The minimum disease duration was 1.9 years, the

maximum was 16 years, and the mean was 9.3±1.71years. Table 1 presents the demographic details of the study population. Of the total of 200 diabetic patients screened in this research through the MNSI, 54 (27%) had diabetic neuropathy. Of those with DPN (27%), 20% met the criteria of the MNSI examination part for neuropathy (a score of 2 or higher in the examination part of the MNSI). No significant differences were observed between the two genders in terms of the frequency of diabetic neuropathy. The mean duration of the disease was 8.6±2.2 years in the patients with neuropathy and 5.4±1.7 in those without neuropathy (P=0.02). The mean age of the patients was 55.8±6.1 years in those with neuropathy and 44.7±4.8 in those without neuropathy (P=0.04), and the mean HbA1c was 8.01±2.34 in the patients with neuropathy and 7.61±2.01 in those without neuropathy (P=0.7). No statistically significant differences were observed between the groups in terms of education (P=0.326); however, a significant difference was observed between them in terms of BMI (P=0.016) and smoking history (P=0.022), as shown in Table 1.

Table 1: A comparison of the frequency distribution of neuropathy in the patients based on the study variables

Variable	Sub Categories	Neuropathy		P	OR [#]	CI (95%) [*]
		Negative N (%)	Positive N (%)			
Level of Education	Illiterate	11 (73.4)	4 (26.6)	0.32	1.54	0.99-2.1
	Secondary school	27 (69.3)	12 (30.7)			
	High school	48 (68.6)	22 (31.4)			
	Diploma	34 (77.3)	10 (22.7)			
	graduate	26 (77)	6 (23)			
Body Mass Index (BMI)	≤24.5	50 (86.3)	8 (13.7)	0.016	3.1	1.51-5.77
	24.6-29	72 (68)	34 (32)			
	Over 29	24 (66.7)	12 (33.3)			
Gender	Male	82 (74.6)	28 (25.4)	0.12	2.1	0.69-3.25
	Female	59 (65.6)	31 (34.4)			
Smoking status	Smoker	35 (58.4)	25 (41.6)	0.02	2.8	1.80-4.91
	Nonsmoker	111 (79.3)	29 (20.7)			
Duration of diabetes (mean±SD) [‡]		5.4±1.7	8.6±2.2	0.01	4.01	2.13-5.23
Age (mean±SD)		55.8±6.1	44.7±4.8	0.04	1.3	1.40-3.55
HbA1c(mean±SD)		7.61±2.01	8.01±2.34	0.7	1.2	0.82-3.67

[#]OR=Odds Ratio; ^{*}CI = Confidence Interval; [‡]SD = Standard deviation

Table 2: The frequency of the symptoms in the study of diabetics according to the diabetic neuropathy screening questionnaire

Questionnaire Item	N (%)
Are your legs and/or feet numb	98(49)
Have you ever felt burning pain in your legs and/or feet?	45(22.5)
Are your feet too sensitive to touch?	65(32.5)
Do you ever have any prickling feelings in your legs or feet?	68(34)
Does it hurt when the bed covers touch your skin?	42(21)
Have you ever had an open sore on your foot?	0(0)
Has your doctor ever told you that you have diabetic neuropathy?	5(2.5)
Are your symptoms worse at night?	39(19.5)
Do your legs hurt when you walk?	60(30)
Is the skin on your feet so dry that it cracks open?	90(45)
Have you ever had an amputation?	0(0)
When you get into the tub or shower, can you tell the hot water from the cold water?	19(9.5)
Are you able to sense your feet when you walk?	200(100)

In terms of the symptoms of neuropathy and according to the MNSI, numbness (49%) and skin cracks or dryness (45%) were the patients' most common complaints, respectively (Table 2).

In the backward stepwise regression analysis of the study variables, including age, duration of the disease, BMI, HbA1c, smoking history, and education, statistically significant differences were observed between the two groups in terms of the frequency of BMI over 29 [OR: 3.1, 95% CI (1.5-5.7), $P = 0.016$], smoking [OR: 2.8, 95% CI (1.8-4.9), $P = 0.022$], age [OR: 1.3 95% CI (1.4-3.5), $P = 0.04$] and duration of diabetes [OR: 4.01, 95% CI (2.1-5.2), $P = 0.01$], as shown in Table 1.

Discussion

Diabetic polyneuropathy is a highly debilitating and common complication of diabetes that deteriorates the quality of life. The Michigan Neuropathy Screening Instrument (MNSI) was used in the present study to screen 200 patients for peripheral neuropathy. A total of 27% of the patients had DPN. Tabatabaei et al. reported a frequency of 27% for neuropathy in diabetic patients presenting to Shariati Hospital in Tehran, Iran (11). A study conducted in Tehran reported a frequency of 30.9% for neuropathy using the

MNSI [10]. Another study conducted in Isfahan, Iran, found a frequency of 75% for neuropathy in diabetic patients based on their symptoms [11]. Clinical examinations and symptoms showed a frequency of 51.7% for neuropathy in Yazd, Iran, and 45.6% in Hamadan, Iran [13-14]. The disparity in findings on the frequency of neuropathy may be associated with differences in methods, demographic factors, care protocols, and screening programs.

Different results have also been reported in studies conducted abroad in Iran. The frequency of neuropathy was reported as 33.5% in South Korea, as 83% by Pham et al.,

as 15% by Bruce et al. in Canada and 22.7% in Spain [5-8]. In this study, according to the results obtained on the prevalence of neuropathy using MNSI, numbness was the most common complaint in the patients, which is consistent with the results obtained by Tabatabaei et al. [12]. A study conducted to investigate the value of patient complaints as a screening instrument showed that around 90% of the subjects under the age of 68 who did not complain of tingling feet also presented no symptoms in favor of diabetic neuropathy [17]. Generally, sensory neuropathy symptoms are recommended not to be used individually in diagnostic or even screening tools, as they should be utilized alongside annual foot examinations performed by physicians. The

level of hyperglycemia determined by measuring glycosylated hemoglobin was not associated with PN. However, other studies have shown evidence of a link between poor metabolic control and increased prevalence and severity of diabetic neuropathy [6, 8-9, 12]. Although these data have failed to confirm a relationship between metabolic control and the prevalence of PN, they in no way diminish the need for optimal glycemic control to prevent type-2 diabetes complications, which is a need demonstrated both epidemiologically and through interventions [18].

The present study found statistically significant differences in age between the patients with and without neuropathy, which is consistent with the results of other studies [5-6, 9, 12-13]; aging can be a risk factor for DPN.

Although the present findings are consistent with the results of other studies in reporting no significant differences between the two genders [19], some authors have found significant differences between men and women in terms of the emergence of neuropathy [9].

The present study also found positive relationships between the duration of diabetes and the risk of neuropathy, consistent with other studies [6, 8-9,12]. Factors affecting these relationships include the prolonged treatment of risk factors, the late diagnosis of neuropathy, and poor metabolic status control.

The present study found positive relationships between smoking and the risk of diabetic neuropathy, which is consistent with previous literature [20]. Smoking contributes to the progression of diabetic neuropathy through numerous mechanisms, such as increasing the level of carboxy hemoglobin and platelet adhesion and changing the level of blood lipids, thereby causing increased blood viscosity and reduced blood flow [20]. The present research also found relationships between BMI and neuropathy, consistent with other studies [21-22].

BMI and obesity can cause poor metabolic status control and, thereby, a higher prevalence of related complications [21]. The relationship

between obesity and insulin resistance is also well-understood. Endothelial dysfunction is a mediator between insulin resistance and microvascular complications, including neuropathy [22].

Strengths and Limitations of the Study

Considering the urgency of the problem and its increasing co-morbid complications, more primary data are needed on the subject to increase public awareness. Nonetheless, the complex and varying clinical manifestations of diabetic peripheral neuropathy and the lack of objective evaluation indexes make screening for this condition a challenge. The present study's findings show that neuropathy is less emphasized as a major health problem in healthcare centers.

It is recommended that foot examinations be included as a priority in the routine management of type 2 diabetic patients in health centers and diabetes centers.

Conclusion

Considering the urgency of the problem and its increasing co-morbid complications, more primary data are needed on the subject to increase public awareness. Nonetheless, the complex and varying clinical manifestations of diabetic peripheral neuropathy and the lack of objective evaluation indexes make screening for this condition a challenge. The present study's findings show that neuropathy is less emphasized as a major health problem in healthcare centers.

It is recommended that foot examinations be included as a priority in the routine management of type 2 diabetic patients in health centers and diabetes centers.

Conflict of Interests

Authors declare that they do not have any conflict interests.

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