Prevalence of Distal Symmetric Diabetic Neuropathy among Type 2 Diabetic Patients in Suez Canal University Hospital Outpatient Clinics in Ismailia

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Abstract

Background: **The World Health Organization describes diabetes mellitus as the most common endocrine disease in the world. Diabetes mellitus is the most common cause of neuropathy worldwide. About 25–50% of diabetic patients in developed countries have peripheral polyneuropathy. Prolonged B12 deficiency can lead to nerve degeneration and irreversible neurological damage.** *Aim:* **This study was conducted aiming at assessing the prevalence of peripheral neuropathy among type 2 diabetic patients attending Suez Canal University Outpatient clinics. A secondary objective of the study was to identify the relation between vitamin B and diabetic neuropathy.** *Patients and Methods:* **A convenience sample was used in this cross sectional study, which was conducted in Suez Canal University Outpatient clinics. A total of 362 type 2 diabetic patients, responded to questionnaire and screening examination, using the Michigan Neuropathy Screening Instrument (MNSI).** *Results:* **The present study showed that the mean age was 55.12 ± 9.26 and about 81.2% of the study population were females. More than, two-thirds (69.1%) were married. In addition, about 37%, had diabetes for over 10 years. The study revealed that 34% of the study population had peripheral neuropathy according to Michigan score results. The most frequent symptom was numbness (83.4 %). Vibration perception was absent in half of patients. Nearly monofilament was absent in one-third (34.5%) of patients. As regards vitamin B12 supplements, the results revealed that about 87.1% of neuropathic patients had taken vitamin B12.** *Conclusion:* **The result of the present study concluded that peripheral neuropathy is a very common problem in diabetic patients, which accounts 34% in our study.**

Keywords: Diabetic neuropathy;MNSI;vitamin B treatment

Introduction

Type 2 diabetes has reached epidemic levels in most populations and epidemiological evidence suggests that unless effective preventive measures are implemented, the prevalence continue to raise globally[1]. Egypt also is in the world's top 10 in terms of the highest number of people with diabetes (3.9 million) in 2003 and this number is expected to increase to 7.8 million by 2025[2]. The high economic burden of diabetes in the Eastern Mediterranean and Middle East region is due to the high prevalence rate coupled with the high cost of diabetes and limited resources. A less affluent country such as Egypt is estimated to spend between 486 and 892 million dollars on diabetes care[2]. In a cross-sectional multicenter study in Iran which aimed to

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study the overall prevalence of diabetic neuropathy reported that the diabetic neuropathy was 38% among type 2 diabetes mellitus[3].The early recognition and appropriate management of neuropathy in the patient with diabetes is important[4]. In 40-50% of people with diabetes mellitus type 1 or type 2, detectable peripheral neuropathy develops within 10 years of the onset of diabetes, and the neuropathic pain associated with symptomatic disease is frequently bothersome[5-6]. Vitamin B12 plays a vital role in the metabolism of fatty acids essential for the maintenance of nerve myelin. Prolonged B_{12} deficiency can lead to nerve degeneration and irreversible neurological damage[7]. The treatment of diabetic neuropathy can be a frustrating experience for both physicians and patients, and the clinical effectiveness of vitamin B12 therapy on diabetic peripheral neuropathy is still unclear. Role of family physician in early detection of peripheral diabetic neuropathy that he should educate all patients with diabetes about proper foot care &check their feet daily (grade C)[8].

Subjects and Methods

The current study is a cross sectional descriptive one. It was carried out at Suez Canal University Hospital outpatient clinic in Ismailia. A Semi-structured questionnaire was developed by the researcher revised by the supervisors and validated according to pilot study on 10 diabetic patient. The questionnaire is composed of four parts: *Part one:* contained some selected demographic variables as age, gender, residence, marital status, family size, address, occupation, Income sufficiency, educational background. *Part two:* questions about disease: duration of DM (<5 years, 5-10 years, >10 years), presence of diabetic complication. *Part three:* including complete drug history including; Antidiabetic drugs (duration,

form, frequency, regularity, dose). Antiplatelet drugs (duration, form, frequency, regularity, and dose). Supplements vitamin B6 and B12 (tablets, injections), Duration of usage (<1 month, 1-3 months, 3-6 months,>6 months), and frequency (regular or irregular). *Part four:* Michigan Neuropathy Screening Instrument (MNSI) questionnaire with cut off of ≥7 points (specificity 91%) and 10-g monofilament test. The 10g monofilament is an objective, simple instrument used in screening the diabetic foot for loss of protective sensation. The monofilaments produce a characteristic force perpendicular to the contacting surface. The force of downward contact increases linearly until the monofilament buckles. The ten-point monofilament test was applied on 10 different points on the sole and dorsum of the foot; the absence of sensation in one or more of these points was considered as peripheral neuropathy[9].

Statistical analysis

Gathered data were processed using SPSS version 15 (SPSS Inc., Chicago, IL, USA). Quantitative data were expressed as means ± SD while qualitative data were expressed as numbers and percentages (%). Student t test was used to test significance of difference for quantitative variables and Chi Square was used to test significance of difference for qualitative variables. To measure the effect size and the strength of association with cardiovascular risk factor among diabetic patients with and without DSN, odds ratios (OR) were calculate with 95% CI. A probability value of p-value < 0.05 was considered statistically significant.

Results

This study was carried on 362 type 2 diabetic patients attending Suez Canal University Hospital Outpatient Clinic in Ismailia. It was

obvious that of all subjects, more than 3/4th (81.2%) were females, the mean age was 55.12±9.26. According to the residence, about half (51.1%) of the patients were resident in urban areas. About 53.3% were illit-

erate, 35.2% of the patients could read and write. More than (2/3) 69.1% were married, 69.9 were not working. Regarding income the majority of them (80.4%) had sufficient income as shown in Table 1

Table 1: Socio demographic characteristics of study population (N=362)

		Frequency	Percent
Age groups (years)	30 -	14	3.9
	40 -	59	16.3
	50 -	168	46.4
	60 -	84	23.2
	≥ 70	37	10.2
	Mean ± SD (Range)	55.12 ± 9.26 (31 − 78)	
Sex	Female	294	81.2
	Male	68	18.8
Marital status	Single	7	1.9
	Married	250	69.1
	Divorced	12	3.3
	Widow	93	25.7
Residence	Urban	185	51.1
	Rural	177	48.9
Family size	1 − 2	39	10.8
	3 − 4	48	13.3
	5 - 6	176	48.6
	≥ 7	99	27.3
	Mean ± SD (Range)	5.37 ± 1.86 (1 - 10)	
Income	Insufficient	71	19.6
	Sufficient	291	80.4
Occupation	Not working (Housewife/not fit for work)	253	69.9
	Unskilled worker	60	16.6
	Skilled worker	27	7.5
	Clerk	22	6.1
Education	Illiterate	193	53.3
	Read & write	77	21.3
	Basic education	61	16.9
	High education	31	8.6

The prevalence of diabetic neuropathy patients according to Michigan score is shown in Figure (1). The range of Michigan score was 0–13 (mean= 5.53±2.3).while more than one third (34%) of studied population had peripheral neuropathy according to Michigan score Figure (2).By Illustrating the prevalence of neuropathy according to different screening tools. it was 34% (by using questionnaire), 45.3% (by using vibra

tion perception), while it was 26.8% (by monofilament) table (2). It was found that prevalence of neuropathy by using vibration sensation and monofilament was 23.5% while by questionnaire and vibration Sensation was 20.4%. Table (3) shows the diagnostic performance of different instruments used. The best tools were vibration sensation and monofilament together which had high sensitivity (87.6%) and
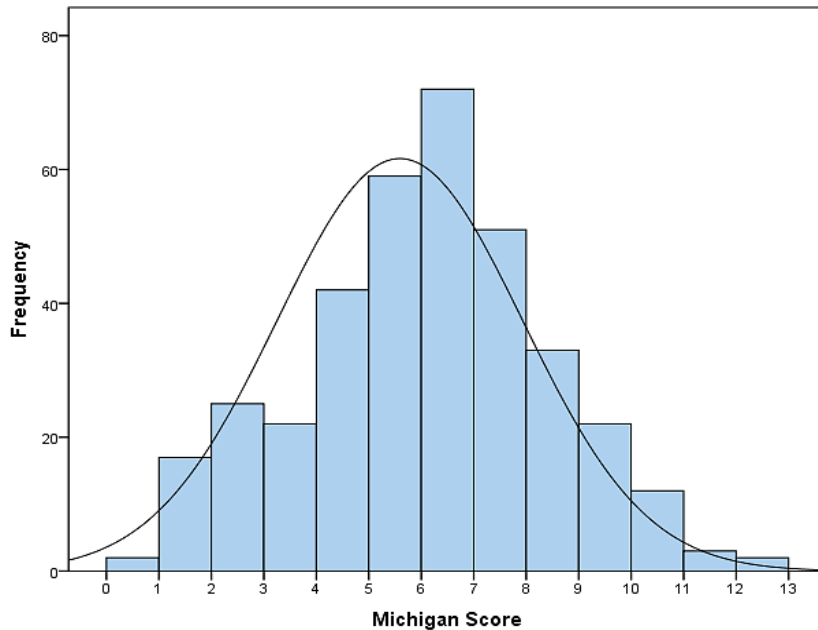
Figure 1: Distribution of diabetic patients according to Michigan score (range 0–13)
(mean= 5.53 ± 2.3).

high specificity (100%). The least sensitive (47.4%) and least specific (70.9%) instrument was questionnaire. To explain the relation between neuropathy & socio-demographic characteristic it was found that half (50.6%) of neuropathic patients were 50-60 years old. There was statistical-ly highly significant relationship between age and diabetic neuropathy (P<0.05). About gender, the majority of patients were females and this represents (81.2%). There was no statistically significant relationship between gender and diabetic neuropathy (p>0.05, Table 4).
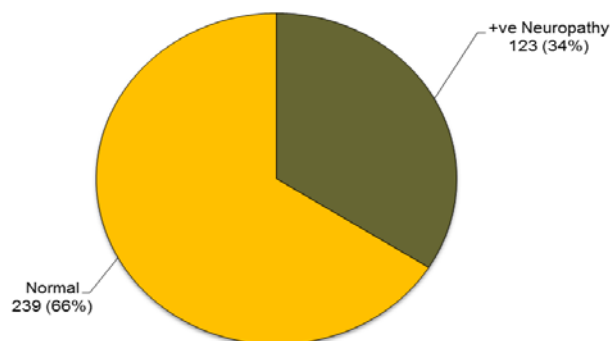
Figure 2: Frequency of peripheral neuropathy in the studied population
(according to Michigan questionnaire score)

While studying the relation between neuropathy and disease characteristics. Regards the relation between neuropathy and duration of diabetes mellitus in the studied population, more than half (61.2%) of patients who had neuropathy had diabe-

tes >10 years. There was statistically highly significant relationship between duration of DM and neuropathy (p<0.05). About 3/4th (74.1%) of neuropathic patients had complication. There was statistically no significant relationship between complication and diabetic neuropathy (p>0.05, table 5)**.** the relation between neuropathy and medications characteristics. Regarding antidiabetic drugs, neuropathic patients

Table 2: The prevalence of neuropathy according to different screening instruments (N=362)

Instruments	Frequency	%
Questionnaire	123	34.0%
Vibration perception	164	45.3%
Monofilament	97	26.8%
Vibration Sens. + Monofilament	85	23.5%
Questionnaire +Vibration Sens.	74	20.4%
Questionnaire + Monofilament	46	12.5%
Questionnaire +Vibration Sens. + Monofilament	85	23.5%

taking oral hypoglycemic drugs were nearly equal neuropathic patients taking insulin. There was statistically highly significant relationship between neuropathy anti-diabetic drugs (p<0.05). The relation between neuropathy and vitamin B12 reveals that more than 3/4th (87.1%) of neuropathic patients had taken vitamin B12 and more than 2/3rd (64.9%) of neuropathic patients had taken vitamin B12 regularly. There was statistically highly significant relationship between neuropathy and vitamin B12 drugs (p<0.05) as illustrated in table (6). While the predictors for diabetic neuropathy as age, marital status, family size, duration of diabetes and regularity for taking vitamin B was significant as showed in table (7).

Discussion

The study aimed to improve the quality of care for diabetic patients. The study had assessed the prevalence of diabetic distal symmetric neuropathy among 362 patients with type II diabetes attending Suez Canal university outpatient clinic in Ismailia city, Egypt. In the present study, the the prevalence of peripheral neuropathy was 34%

Table 3: Diagnostic performance of different instruments for screening of neuropathy (N=362)

	Sensitivity% (95% CI)	Specificity% (95% CI)	PPV% (95% CI)	NPV% (95% CI)
Questionnaire	47.4 (37.2 – 57.8)	70.9 (65.1 – 76.3)	37.4 (28.8 – 46.6)	78.7 (72.9 – 83.7)
Vibration Sens.	87.6 (79.4 – 93.4)	70.2 (64.3 – 75.6)	51.8 (43.9 – 59.7)	93.9 (89.6 – 96.8)
Vibration Sens. + Monofilament	87.6 (79.4 – 93.4)	100 (98.6 - 100)	100 (95.7 - 100)	95.7 (92.5 – 97.7)
Questionnaire + Vibration Sens.	42.3 (32.3 – 52.7)	87.5 (83.0 – 91.3)	55.4 (43.4 – 67.0)	80.6 (75.5 – 85.0)
Questionnaire + Monofilament	47.4 (37.2 – 57.8)	100 (98.6 – 100)	100 (92.3 - 100)	83.9 (79.3 – 87.7)

Monofilament is gold standard test

Table 4: Relation between neuropathy and sociodemographic characteristics (N=362)

		-ve neuropathy (n = 277)		+ ve neuropathy (n = 85)		p-value
		No.	%	No.	%	
Age groups (years)	30 -	14	5.1	0	0	<0.001*
	40 -	54	19.5	5	5.9	
	50 -	125	45.1	43	50.6	
	60 -	65	23.5	19	22.4	
	≥ 70	19	6.9	18	21.2	
Sex	Female	225	81.2	69	81.2	0.992
	Male	52	18.8	16	18.8	
Marital status	Single	5	1.8	2	2.4	0.01* Fisher
	Married	203	73.3	47	55.3	
	Divorced	7	2.5	5	5.9	
	Widow	62	22.4	31	36.5	
Residence	Urban	135	48.7	50	58.8	0.104
	Rural	142	51.3	35	41.2	
Family size	1 – 2	36	13.0	3	3.5	0.045*
	3 – 4	32	11.6	16	18.8	
	5 - 6	134	48.4	42	49.4	
	≥ 7	75	27.1	24	28.2	
Income	Insufficient	43	15.7	25	29.4	0.005*
	Sufficient	231	84.3	60	70.6	
Occupation	Not working	148	53.4	45	52.9	0.279
	Unskilled worker	54	19.5	23	27.1	
	Skilled worker	48	17.3	13	15.3	
	Clerk	27	9.7	4	4.7	
Education	Illiterate	148	53.5	45	52.9	0.279
	Read & write	54	19.5	23	27.1	
	Basic education	48	17.3	13	15.3	
	High education	27	9.7	4	4.7	

N.B. Neuropathy diagnosis based on combined vibration & monofilament results

according to Michigan score while the prevalence reported increased to 45.3% when evaluated by vibration perception and decreased to 26.8% when evaluated by monofilament test. In accordance to our study, an Iranian study had assessed the prevalence of peripheral neuropathy in diabetic patients using different evaluation methods, they detected diabetic neuropathy in 31.9% of studied diabetic patients (according to Michigan score), and according to 10-point monofilament test, peripheral diabetic neuropathy was detected in 31.7% of patients[3]. In a 25- years study performed on 4400 diabetics (1947-1973), the prevalence rate of neuropathy based on diagnostic criteria such as the absence of Achilles tendon reflex and the abnormal perception sensation was reported as 7.5% at the baseline, reached up to 50% in the end of study (after 25 years follow-up)[10]. We have found that best sensitivity and specificity for diagnosis of peripheral neuropathy is by combining both vibration perception test and monofilament test (87.6% sensitivity and 100% specificity).

Table 5: Relation between neuropathy and disease characteristics (N=362)

		- ve neuropathy (n= 277)		+ve neuropathy (n= 85)		p-value
		No.	%	No.	%	
Duration of DM (yrs)	< 5	99	35.7	16	18.8	<0.001*
	5 -10	96	34.7	17	20.0	
	> 10	82	29.6	52	61.2	
Complications	No	75	27.1	22	25.9	0.828
	Yes	202	72.9	63	74.1	
Co-morbid conditions	No	126	45.5	33	38.8	0.279
	Yes	151	54.5	52	61.2	

N.B. Neuropathy diagnosis based on combined vibration & monofilament results
CHD = Coronary Heart Diseases; CKD = Chronic Kidney Diseases

The prevalence of peripheral neuropathy was estimated to be 23.5% using these two tests. Similar to the present study, certain previous studies[11-13] have considered the combination of vibration perception test and the 10-point monofilament test as an accurate diagnostic tool in the early diagnosis of DPN. The present study has evaluated the influence of multiple demographic and social factors on incidence of peripheral neuropathy. We have found that older age, larger family size, irregular vitamin B intake and longer duration of disease are significant independent risk factors for peripheral diabetic neuropathy. Similarly, Tabatabaei-Malazy and colleagues[3] have also studied the influence of some demographic factors on prevalence of diabetic

Table 6: Relation between neuropathy and medications characteristics (N=362)

		-ve neuropathy (n = 277)		+ve neuropathy (n = 85)		p-value
		No.	%	No.	%	
Anti-Diabetic drugs	Oral	154	55.6	35	41.2	0.039 *
	Insulin	80	28.9	36	42.4	
	Mixed	39	14.1	14	16.5	
Regularity of Anti-Diabetic drugs	Irregular	4	1.4	0	0	0.576 Fisher
	Regular	269	97.1	85	100.0	
Anti-Platelet drugs	No	200	72.5	50	58.8	0.017*
	Yes	76	27.5	35	41.2	
Regularity of Anti-Platelet drugs	Irregular	18	23.7	3	8.6	0.063
	Regular	58	76.3	32	91.4	
Vitamin B12	No	71	25.6	11	12.9	0.014*
	Yes	206	74.4	74	87.1	
Regularity of Vitamin B12	Irregular	110	53.4	26	35.1	0.01*
	Regular	96	46.6	48	64.9	

N.B. Neuropathy diagnosis based on combined vibration & monofilament results

neuropathy as evaluated by different measurement tools. They have reported that male sex is associated with lower risk of neuropathy. However, age over 50, diabetes duration over 10 years were significant risk factors associated with increased risk of peripheral diabetic neuropathy[3]. Different studies evaluating the effect of various factors on diabetic neuropathy have reported controversial results. In a

case-control study conducted on some 110 diabetic patients in Dr. Shariati Hospital, Bouya et al.[14] assessed the prevalence of peripheral neuropathy and the factors influencing this rate using MNSI and the electro diagnostic methods (NCV, EMG).

Table 7: Multiple logistic regression analysis for the predictors of neuropathy (N=362)

	Coefficient	*p*-value	Adjusted Odds Ratio	95% Confidence Interval
– Age	0.048	0.010*	1.049	1.011 - 1.089
– Marital status	1.022	0.009*	2.780	1.289 - 5.993
– Family size	0.333	0.001*	1.395	1.138 - 1.710
– Income	0.724	0.070	2.062	0.942 - 4.515
– Duration of disease	0.630	0.008*	1.878	1.177 - 2.996
– Insulin	0.467	0.232	1.595	0.742 - 3.429
– Mixed (oral + insulin)	0.130	0.786	1.139	0.445 - 2.916
– Antiplatelet drugs	-0.044	0.895	0.957	0.498 - 1.840
– Regularity of vitamin B	1.014	0.002*	2.757	1.450 - 5.240
– Impaired circulation	0.403	0.237	1.497	0.767 - 2.922
– General asthenia	1.042	0.010*	2.834	1.287 - 6.242
– *Constant*	-7.574	<0.001*	0.001	

Reference categories: Marital status (married) Income (sufficient), form of anti-diabetic drugs (oral), anti-platelets (No), regularity of vit B (regular) impaired circulation (No), general asthenia (No).
Model fit, (χ^2=65.8; p< 0.001*), * Statistically significant at *p*<0.05

In this study, there was no statistically significant relation between smoking, the use of Angiotensin-Converting Enzyme inhibitors' drugs (ACEI drugs), hypertension, high cholesterol levels, diabetes treatment regimen and the prevalence of neuropathy; the influence of age, quality of diabetes control and duration of the disease on the development of neuropathy, however, was significant. The risk of developing neuropathy in men was 2.9 times higher than women. Poor controlled diabetes and every year increase in the duration of diabetes increased the risk of developing neuropathy by 0.3 and 1.1 times, respectively[15]. Similarly, Boru et al.[16] have found that age, the duration of diabetes, and poor controlled diabetes were the main risk factors contributing to the condition. In the Nigeria study[17], however, the duration of diabetes, age, the status of diabetes control, high blood pressure, retinopathy, and HbA1c level were the main factors increasing the risk of diabetic neuropathy by 1.34 times (r= 0.295). We conducted this cross-sectional study to explore the relation between vitamin B and diabetic peripheral neuropathy. It was conducted on 362 patients. More than 3/4th (77.3%) of them had taken vitamin B. More than half (57.9%) of them had been taken the vitamins in the injection form. About half (51.4%) of the patients had taken the vitamins regularly and about 2/3rd (70.0%) of them had taken the vitamins > 6 months. Our results revealed that about (87.1%) of neuropathic patients had taken vitamin B. Abbas (1997) was the largest study, accounting for 200 of the 488(41%) participants treated with vitamin B.[18] the age range of the participants was from 18 to74 years. Eleven studies were on diabetic neuropathy and two on alcoholic neuropathy[20-21]. None of the studies had documented vitamin B deficiency. one excluded participants with vitamin B12 deficiency[21]. The main results of this review showed in the comparison of vitamin B with placebo, two small trials showed no

significant short-term (3 months) benefit in pain intensity while one of trials showed a small significant benefit in vibration detection from oral benfotiamine, derivatives of thiamine. In the larges of two trials comparing different doses of vitamin B complex, there was some evidence that higher doses resulted in a significant short-term reduction in pain and improvement in parathesiae, in composite outcome combining pain, temperature and vibration and in a composite outcome combining pain, numbness and parathesiae.

Conclusion

In conclusion, peripheral diabetic neuropathy is a very common and serious problem among diabetic patients. A combination of both vibration perception test and 10-point filament test showed best sensitivity and specificity in detection of peripheral neuropathy. Other factors such as; older age and longer duration of diabetes must be taken in consideration.

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