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Prevalence and Determinants of Peripheral Neuropathy in Patients with Type 2 Diabetes Attending a Tertiary Care Center in the United Arab Emirates

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Abstract

Objective: This study was designed to estimate prevalence and identify relevant determinants of peripheral neuropathy in patients >18 years old with type 2 diabetes mellitus of at least 12 months.

Methods: Adults with type 2 diabetes mellitus (394 patients, age = 57 ± 12 yr, 67% females, duration of diabetes = 10.9 ± 7.9 yr) were randomly selected from the Diabetes Center at Tawam Hospital (Al Ain City, United Arab Emirates). The Michigan Neuropathy Screening Instrument (MNSI) history and sign scores were used to assess neuropathy. Stepwise logistic regression analysis was used to assess independent predictors of peripheral neuropathy on the Michigan score.

Results: Prevalence of peripheral neuropathy was 10.4% based on the MNSI-history score of ≥7 and 25.6% based on the MNSI-sign score of ≥ 3. Logistic regression analysis revealed that HbA1c [OR=3.41, 95% CI; 1.15–10.16] and physical activity [OR=4.99, 95% CI; 2.21–11.29] were significant predictors of the MNSI-history score. Age [OR=1.06, 95% CI; 1.03–1.09], height [OR=1.06, 95% CI; 1.02–1.10], systolic blood pressure [OR=1.03, 95% CI; 1.01–1.06] and duration of diabetes [OR=1.08, 95% CI; 1.04–1.13] were significant predictors of the MNSI-sign score.

Conclusion: Peripheral neuropathy was common in the studied diabetic patients and was associated with modifiable risk factors, such as glycemic control, blood pressure control and physical activity.

Keywords: Type 2 diabetes; Peripheral neuropathy; Prevalence; Michigan neuropathy screening instrument; United Arab Emirates

Abbreviations: BMI: Body Mass Index; MNSI: Michigan Neuropathy Screening Instrument; GFR: Glomerular Filtration Rate; HbA1c: Glycosylated Hemoglobin

Background

United Arab Emirates (UAE) is ranked among the world's top fifteen countries with the highest prevalence of type 2 diabetes (International Diabetes Federation report, 2013) [1]. Previously reported frequency of diabetic peripheral neuropathy in the UAE is about 35% [2,3]. The entity diabetic peripheral neuropathy is defined as symptoms and signs of nerve dysfunction in diabetic patients after other causes have been excluded [4]. This complication is common and may result in muscle atrophy, joint deformity, foot ulceration and limb amputation [5]. Its severity is usually linked to patient age, duration and control of diabetes and other risk factors, such as hypertension, dyslipidemia, obesity and smoking [2,3]. In addition, type 2 diabetes has been associated with adverse micro- and macro-vascular outcomes [6]. A complex array of metabolic, vascular and perhaps hormonal factors shifts the balance between nerve fiber damage and repair, favoring the former [5,7]. Risk factors related to diabetic neuropathy have not been adequately addressed in the Peninsular Arabs [2,3,8-10].

Distal symmetric polyneuropathy is the most common form of diabetic neuropathy. The disease is frequently insidious and may be asymptomatic. Prompt medical care and improved glycemic control may reduce its severity and progression [11].

This study was designed to investigate peripheral neuropathy in UAE adult patients with type 2 diabetes. The objectives were to estimate prevalence and identify relevant determinants of neuropathy in this population.

Subjects and Methods

Study population

The study was approved by Al Ain Medical District Human Research Ethics Committee. Subjects signed a written consent; a verbal consent was obtained from illiterate subjects. The questionnaire and clinical examination were piloted on ten patients to ensure feasibility of the study and clear understanding of the inquiries.

The inclusion criteria were adults (≥ 18 years) with type 2 diabetes for at least 12-months. Subjects with the followings conditions were excluded: type 1 diabetes, pregnancy, alcohol intake, malignancy,

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medication-induced neuropathy, liver disease, hypothyroidism, collagen vascular disease, vasculitis and other known causes of neuropathy.

Four hundred and twenty-two patients with type 2 diabetes were recruited from the Diabetes Centre at Tawam-Johns Hopkins Hospital (Al Ain, Abu Dhabi) between May 2007 and May 2008. This tertiary care facility accommodated about 20,000 diabetic visits per year. Twenty-eight patients were subsequently found to have type 1 diabetes and were excluded due to the known variation in the natural history of peripheral neuropathy between the two types of diabetes. Thus, the statistical analysis was performed on the 394 patients (264 females, 67%) with type 2 diabetes. Regular visits to the Center were defined as clinic consultations at least once every three months. A systematic random sampling approach was used to select these patients from the appointments list. Every third patient on the list was recruited. Of the 500 recruited patients, 422 consented to the study resulting in a response rate of 84%.

The Michigan Neuropathy Screening Instrument (MNSI) was used and the responses were added to attain a score [12]. A trained nurse (fluent in English and Arabic) facilitated completing the questionnaire that covered socio-demographics, medical history and physical activity. 'Yes' responses to questions 1–3, 5–6, 8–9, 11–12, and 14–15 were each counted as one point. 'No' responses to questions 7 and 13 were each counted as one point. Question 4 was a measure of impaired circulation and question 10 was a measure of asthenia. A score of ≥ 7 was considered abnormal [12].

Measurements

Patients were asked to wear light clothing without shoes. A portable digital scale and stadiometer were used to measure weight and height, respectively. Patients were asked to stand straight with their heads, backs and buttocks vertically aligned to the height gauge; their heights were then taken and rounded to the nearest 0.5 cm. Percent body fat was estimated by bioelectric impedance, using Tanita Body Composition Analyzer; model TBF-410 (Tanita Corporation, Tokyo, Japan). Abnormal fat composition on bioelectric impedance was defined in the instrument's protocol as >23% for males and >27% for females. Obesity was defined as body mass index (BMI) ≥ 30 kg/m^2. Blood pressure (systolic and phase-V diastolic) measurements recorded were the mean of three separate readings in a sitting position after 10 minutes of resting, using validated electronic sphygmomanometers (Omron Hem 907, Omron Healthcare, Kyoto, Japan). Hypertension was defined as a mean systolic blood pressure ≥130 mm Hg or diastolic blood pressure ≥ 80 mm Hg.

Foot examination

Neuropathy was assessed by MNSI history and examination. MNSI investigates aspects of both small (pain and hyperesthesia) and large (numbness and muscular) nerve fiber patency. Neuropathy was defined as MNSI-history score of ≥ 7 of a total possible score of 13, or MNSI-sign score of ≥ 3 of a total possible score of 10 [12]. A podiatrist assessed the feet for ulcers, callus, dry skin, fissures, infection, deformity, footwear, foot care and gait.

Both feet were examined for signs of peripheral neuropathy. Briefly, each foot with any abnormality received a score of one. An ulcer received a score of one. Ankle reflexes were elicited. If absent, the patient was asked to perform the Jendrassic manoeuver; if present, the reflex was designated present with reinforcement and scored 0.5. If absent with the Jendrassic manoeuver, the reflex was designated absent and scored 1.0. Vibration sensation was tested in the great toe, using a 128-Hz tuning fork (Rydel-Seiffer) exactly as per the MNSI protocol. The 10-gram Semmes-Weinstein monofilament was done in accordance with the MNSI [12].

Retinopathy

An ophthalmologist conducted eye examinations for cataract and retinopathy. Retinopathy was graded as none, non-proliferative (micro-aneurysms, hemorrhage and hard exudates) or proliferative (new blood vessels and/or scar tissue growing into the vitreous).

Laboratory

Venous blood (fasting) was collected to measure serum lipids, glycosylated hemoglobin (HbA1c), albumin and creatinine. A spot urine sample was collected for albumin and creatinine. The tests were performed on Beckman Coulter auto-analyzer DX800 (Beckman Instruments, Inc. Fullerton, CA, USA). Patients with HbA1c ≥ 7% were considered having uncontrolled diabetes [11]. Dyslipidemia was defined as triglycerides >150 mg/dl (1.7 mmol/l), low density lipoprotein-cholesterol (LDL-c) >100 mg/dl (2.6 mmol/L) or HDL cholesterol <40 mg/dl (1.0 mmol/l) in men and <50 mg/dl (1.3 mmol/l) in women.

Glomerular filtration rate (GFR) was estimated using the Cockcroft-Gault formula [eGFR = (140 – age) x mass (kg) × (0.85% if female)] / [72 x serum creatinine (mg/dL)] [13]. Diabetic nephropathy was considered if the GFR was <60 ml/min/1.73 m^2 or if the urinary albumin: creatinine ratio was ≥ 2.5 mg/mmol in males or ≥ 3.5 mg/mmol in females [14].

Statistical analysis

The Statistical Package for Social Sciences (SPSS) software version 19.0 for Windows was used. Logistic regression analysis was used to identify independent predictors of neuropathy. A *p*-value of <0.05 was significant.

Results

The clinical and laboratory values in all studied male and female patients are shown in Table 1. Sixty seven percent of the patients were females. Blood pressure and HbA1C were similar in both groups.

Based on MNSI-history score of ≥ 7, the prevalence of neuropathy

	Male (n=130)	Female (n=264)
Age (yr)	57 ± 12	52 ± 11
Height (cm)	167 ± 8	155 ± 6
Weight (kg)	81 ± 16	78 ± 17
Body mass index (kg/m^2)	29 ± 5	32 ± 6
Systolic blood pressure (mm Hg)	133 ± 15	133 ± 17
Diastolic blood pressure (mm Hg)	78 ± 9	76 ± 9
Body fat percentage	28.0 ± 7.9	40.3 ± 7.6
Hemoglobin A1c (%)	8.2 ± 1.9	8.2 ± 2.1
Total cholesterol (mmol/L)	4.4 ± 1.1	4.8 ± 1.1
Triglycerides (mmol/L)	1.5 ± 1.3	1.4 ± 1.1
HDL-cholesterol (mmol/L)	0.9 ± 0.2	1.1 ± 0.3
LDL-cholesterol (mmol/L)	2.9 ± 0.9	3.1 ± 0.9
Total cholesterol/HDL ratio	5.2 ± 1.5	4.6 ± 1.4
Serum creatinine (mmol/L)	96.7 ± 64.7	62.9 ± 21.6
Urinary albumin: creatinine ratio (mg/mmoL)	1.4 ± 0.6	1.3 ± 0.5
Estimated glomerular filtration rate (mL/min)	82.8 ± 37.9	102.3 ± 39.8

Table 1: The clinical and laboratory values (mean ± SD) in studied patients (n=394).

in males was 8.5% and in females was 11.4% (p=0.381). Based on MNSI-sign score of ≥ 3, the prevalence of neuropathy in males was 37.0% and in females was 20.1% (p<0.001), (Table 2). Smoking was more common in males (p<0.001) and body fat percentage was significantly elevated in females (p<0.001), (Table 2).

MNSI-history score ≥ 7 was significantly associated with being physically inactive (p<0.001), longer duration of diabetes (p=0.006), HbA1c ≥ 7 (p=0.014), abnormal body fat and higher BMI (p=0.042), (Table 3). The odds of abnormal MNSI-history score increased with each unit of increase in physically inactivity (6.36 fold) and HbA1c ≥7 (2.79 fold), (Table 3).

Variables	Male (n=130)	Female (n=264)	*p*-value [1]
Duration of diabetes (yr), mean ± SD	10.9 ± 7.9	9.4 ± 7.1	0.062
Duration of smoking (yr), mean ± SD	30.4 ± 13.7	10.3 ± 4.5	0.022
	n (%)	n (%)	*p*-value [2]
Education			<0.001
Illiterate	45 (34.6)	171 (64.8)	
Primary school	32 (24.6)	39 (14.8)	
Secondary school	39 (30.0)	35 (13.3)	
University	14 (10.8)	19 (7.2)	
Occupation			<0.001
Retired	73 (56.2)	2 (0.8)	
Employed	34 (26.2)	21 (8.0)	
Unemployed	23 (27.7)	14 (5.3)	
Housewife	0	227 (86.0)	
Smoking	24 (16.2)	3 (1.1)	<0.001
Regularly visiting the diabetes center	119 (93.7)	249 (95.8)	0.377
Physical activity			
Active	84 (65.1)	154 (58.6)	0.210
Inactive	45 (34.9)	109 (41.4)	
Abnormal percentage body fat	94 (73%)	254 (95%)	<0.001
Retinopathy	25 (20.7)	28 (10.8)	0.008
Mode of diabetes diagnosis			0.005
Screening	81 (63.3)	204 (78.8)	
Symptomatic	34 (24.2)	34 (13.1)	
Incidental	16 (12.5)	21 (8.1)	
Treatment			0.302
Lifestyle measures	5 (3.8)	10 (3.8)	
Oral hypoglycaemic agents	98 (75.4)	185 (70.1)	
Insulin added	27 (20.8)	69 (26.1)	
Michigan-history score			
Score <7	118 (91.5)	233 (88.6)	
Score ≥ 7	11 (8.5)	30 (11.4)	0.381
Michigan-sign score			
Score <3	75 (61.0)	202 (61.0)	
Score ≥ 3	48 (37.0)	53 (20.1)	<0.001

[1]P-value was based on independent samples t-test; [2]P-values were based on Pearson's chi-square test; n (%), number (percent) of patients. The percentage was calculated based on number of patients who had completed the test.

Table 2: Summary of the clinical variables in studied patients (n=394).

Variables	Coefficient	*p*-value	Odds Ratio	95%CI for OR
Age (yr)	0.02	0.229	1.02	0.99 – 1.05
Gender				
Female	0.32	0.374	1.38	0.67 – 2.85
Male (ref.)	-		-	-
Height (cm)	-0.016	0.436	0.98	0.94 – 1.03
Weight (kg)	0.01	0.311	1.01	0.99 – 1.03
Body mass index (kg/cm^2)	0.05	0.042	1.06	1.00 – 1.11
Systolic blood pressure (mm Hg)	0.01	0.296	1.01	0.99 – 1.03
Diastolic blood pressure (mm Hg)	-0.01	0.767	1.00	0.96 – 1.03
Total cholesterol (mmol/L)	0.17	0.271	1.18	0.88 – 1.58
Triglyceride (mmol/L)	0.12	0.359	1.13	0.88 – 1.45
LDL-cholesterol (mmol/L)	0.05	0.799	1.05	0.73 – 1.50
HDL-cholesterol (mmol/L)	0.42	0.492	1.52	0.47 – 4.88
HbA1c				
≥7%	1.03	0.014	2.79	1.13 – 6.85
<7%[2]	-		-	-
Education		0.306		
Illiterate	0.40	0.527	1.50	0.43 – 5.23
Primary school	-0.26	0.731	0.77	0.17 – 3.43
Secondary school	-0.32	0.673	0.73	0.16 – 3.23
University[2]	-	-	-	-
Occupation		0.753		
Unemployed	0.12	0.882	1.13	0.24 – 5.35
Retired	0.57	0.366	1.77	0.51 – 6.06
Housewife	0.46	0.411	1.59	0.53 – 4.76
Employed[2]	-	-	-	-
Smoking				
Yes	-0.27	0.717	0.77	0.17 – 3.39
No[2]	-		-	-
Duration of smoking	0.03	0.556	1.03	0.93 – 1.15
Duration of diabetes (yr)	0.06	0.006	1.06	1.02 – 1.10
Family history of diabetes				
Present	0.16	0.654	1.17	0.59 – 2.32
Absent[2]	-		-	-
Regularly visit of diabetes center				
Yes	-0.51	0.457	0.60	0.17 – 2.16
No[2]	-		-	-
Mode of diabetes diagnosis		0.989		
Incidental	0.04	0.995	1.00	0.27 – 3.69
Screening	-0.06	0.901	0.95	0.40 – 2.27
Symptomatic[2]	-	-	-	-
Treatment of diabetes				
Oral hypoglycaemic agents	-0.84	0.017	0.43	0.22 – 0.85
Insulin[2]	-	-	-	-
Physical activity				
Inactive	1.85	<0.001	6.36	2.94 – 13.78
Active[2]	-		-	-
Body fat composition				
Normal	-0.93	0.024	0.40	0.17 – 0.94
Abnormal[2]			-	-
Dyslipidemia				
Controlled	-0.004	0.994	1.00	0.37 – 2.70
Uncontrolled[2]	-		-	-
Estimated glomerular filtration rate				
<60	0.594	0.193	1.81	0.77 – 4.29

≥ 60[2]	-		-	-
Albuminuria				
Yes	0.59	0.193	1.81	0.77 – 4.29
No[2]	-		-	-
Retinopathy				
Yes	0.53	0.265	1.69	0.70 – 4.13
No[2]	-		-	-

(1) Caseness represented by a MNSI-history score ≥ 7
(2) Reference category (ref.)
OR: Odds Ratio; CI: Confidence Interval

Table 3: Simple logistic regression of MNSI-history score *vs.* selected predictors.

Variables	Coefficient	OR	95% CI	*p*-value
HbA1c (ref. = normal)	1.23	3.41	1.15 – 10.16	0.028
Physical activity (ref. = active)	1.61	4.99	2.21 – 11.29	<0.001

OR: Odds Ratio; CI: Confidence Interval
Likelihood ratio test of model significance: *p*-value <0.001.
Variables that were dropped out of the multivariable logistic regression using the stepwise-backward elimination method included body mass index, duration of diabetes, treatment of diabetes, and body fat composition.

Table 4. Subset of significant predictors of the odds of abnormal MNSI-history score.

Variables	Coefficient	*p*-value	Odds Ratio	95% CI for OR
Age (yr)	0.08	<0.001	1.08	1.06 – 1.11
Gender				
Female	-0.89	<0.001	0.410	0.26 – 0.66
Male[2]	-		-	-
Height (cm)	0.03	0.032	1.03	1.00 – 1.06
Weight (kg)	-0.004	0.548	1.00	0.98 – 1.01
Body mass index (kg/m^2)	-0.03	0.194	0.97	0.94 – 1.01
Systolic blood pressure (mm Hg)	0.03	<0.001	1.03	1.01 – 1.05
Diastolic blood pressure (mm Hg)	0.01	0.548	1.01	0.98 – 1.03
Total cholesterol (mmol/L)	-0.03	0.771	0.97	0.78 – 1.20
Triglyceride (mmol/L)	0.03	0.787	1.03	0.84 – 1.26
LDL-cholesterol (mmol/L)	0.02	0.864	1.02	0.79 – 1.32
HDL-cholesterol (mmol/L)	0.20	0.640	1.23	0.53 – 2.85
HbA1c				
≥7	0.52	0.055	1.68	0.98 – 2.88
<7%	-		-	-
Marital status		0.096		
Single	-1.61	0.156	0.20	0.02 – 1.85
Married	0.12	0.807	1.13	0.43 – 2.93
Divorced	0.92	0.232	2.50	0.56 – 11.25
Widowed[2]	-	-	-	-
Education				
Illiterate	0.47	0.301	1.60	0.77 – 4.44
Primary school	-0.01	0.988	0.99	0.44 – 3.14
Secondary school	-0.23	0.959	0.97	0.41 – 2.98
University[2]	-	-	-	-
Occupation				
Unemployed	1.88	0.001	6.53	2.24 – 19.10
Retired	1.80	<0.001	6.07	2.29 – 16.10
Housewife	0.88	0.056	2.42	0.98 – 5.97
Employed[2]	-	-	-	-
Smoking				
Yes	0.54	0.233	1.71	0.723 – 4.04
No[2]	-		-	-
Duration of smoking (yr)	0.04	0.197	1.04	0.98 – 1.11
Duration of diabetes (yr)	0.11	<0.001	1.12	1.08 – 1.16
Family history of diabetes				
Present	-0.44	0.064	0.64	0.40 – 1.03
Absent[2]	-		-	-
Regularly visiting diabetes center				
Yes	-1.31	0.008	0.27	0.10 – 0.71
No[2]	-		-	-
Mode of diabetes diagnosis				
Incidental	0.04	0.932	1.04	0.42 – 2.60
Screening	-0.01	0.969	0.99	0.53 – 1.83
Symptomatic[2]	-	-	-	-
Treatment of diabetes				
Oral hypoglycaemic agents	-0.59	0.057	0.61	0.36 – 1.01
Insulin				
Physical activity				
Inactive	1.02	<0.001	2.76	1.73 – 4.42
Active [(2)]	-		-	-
Body fat composition				
Normal	0.59	0.018	1.80	1.11 – 2.93
Abnormal [(2)]	-		-	-
Dyslipidemia				
Controlled	-0.06	0.861	0.94	0.48 – 1.86
Uncontrolled[2]	-		-	-
Estimated glomerular filtration rate				
<60	1.14	<0.001	3.13	1.73 – 5.65
≥ 60[2]	-		-	-
Albuminuria				
Yes	1.14	<0.001	3.13	1.73 – 5.65
No[(2)]	-		-	-
Retinopathy				
Yes	0.98	0.003	2.65	1.41 – 5.00
No[(2)]	-		-	-

(1) Caseness represented by MNSI-sign score ≥3
(2) Reference category (ref.)
OR: Odds Ratio; CI: Confidence Interval

Table 5: Simple logistic regression of MNSI-sign score *vs.* selected predictors.

Table 4 shows the results of multivariate stepwise logistic regression analysis to determine the best subset of predictors of MNSI-history score ≥ 7. The six significant predictors in Table 3 were entered in the model based on a forward Likelihood ratio method. HbA1c and physical activity were the only significant predictors of abnormal MNSI-history score (Table 4).

MNSI-sign score ≥ 3 was significantly associated with several variables including advanced patient age, increased height, male gender, higher systolic blood pressure, longer duration of diabetes, albuminuria and retinopathy (Table 5, $p<0.001$ for each). The odds of MNSI-sign score ≥ 3 increased with each unit of increase in duration of diabetes (12%), age (8%), height (3%) and systolic blood pressure (3%), (Table 5).

Variables	Coefficient	OR	95% CI	*p*-value
Age	0.06	1.06	1.03 – 1.09	<0.001
Height	0.05	1.06	1.02 – 1.10	0.005
Systolic blood pressure	0.03	1.03	1.01 – 1.06	0.002
Duration of diabetes (yr)	0.08	1.08	1.04 – 1.13	<0.001

OR: Odds Ratio; CI: Confidence Interval
Likelihood ratio test of model significance: *p*-value <0.001
Variables that were dropped out of the multivariable logistic regression using the stepwise-backward elimination method included gender, HbA1c, occupation, regular visits to the diabetic clinic, treatment of diabetes, physical activity, body fat composition, eGFR, albuminuria and retinopathy.

Table 6: Subset of significant predictors of the odds of abnormal MNSI-sign score.

	Percent of Patients with Abnormal Symptom
Are your legs/feet numb?	44%
Do you have burning pain in your legs/feet?	47%
Are your feet too sensitive to touch?	14%
Do you have prickling feelings in your legs/feet?	40%
Does it hurt when the bed covers touch your legs/feet?	11%
Can you tell hot water from cold water in the tub/shower?	5%
Have you had open sore on your foot?	12%
Has your doctor ever told you that you have neuropathy?	7%
Are your symptoms worse at night?	43%
Do your legs/feet hurt when you walk?	42%
Are you able to sense your legs/feet when you walk?	28%
Is the skin on your legs/feet so dry that it cracks open?	12%
Have you had an amputation?	<1%

Table 7: Summary of patients' responses to the MNSI-history questionnaire.

Table 6 shows the results of multivariate stepwise logistic regression analysis to determine the best subset of predictors of MNSI-sign score ≥ 3. The significant predictors in Table 5 were entered in the model based on a forward likelihood ratio method. Age, height, systolic blood pressure and duration of diabetes were the only significant predictors of abnormal MNSI-sign score (Table 6).

Table 7 summarizes the patients' responses to the MNSI-history questionnaire. The most prevalent leg/foot complaints were numbness, burning pain, prickling feeling and pain with walking (each occurring in ≥ 40% of the patients).

Discussion

The reported prevalence of diabetic peripheral neuropathy varies with the diagnostic tools used and the criteria applied. In this study, the MNSI history (questionnaire) and sign (lower extremity examination) scores were used, yielding prevalences of 10.4% and 25.6%, respectively. The sign score value is similar to previous reports from UAE (35%), Saudi Arabia (38%), Bahrain (37%), Egypt (20%), and United Kingdom (29%) [2,3,8,15-17]. In a prospective study in Finland involving newly diagnosed patients with type 2 diabetes, the prevalence of definite or probable neuropathy increased from 8.3% at baseline to 41.9% at 10 years; the corresponding values for healthy individuals were 2.1% and 5.8%, respectively [18].

A definite diagnosis of peripheral neuropathy requires nerve conduction studies [19]. These gold standard tests, however, are not readily available in most outpatient settings. For routine clinical practice, simpler approaches have been used including the United Kingdom Screening Test and the Michigan Neuropathy Screening Instrument [12,17]. A more detailed testing is also available (e.g., Toronto criteria, San Antonio Consensus and Mayo Clinic criteria) [4,20,21].

The neuropathy complaints are subjective and a constellation of symptoms is often more reliable than a single complaint (Table 7). In this study, 10.4% of the patients were abnormally symptomatic (MSNI-history score ≥ 7). In these patients, use of sandals as normal daily footwear might result in more skin dryness, callus formation and cracks over of heals (~72% of the patients); these findings might lead to a score of 2 out of 10 on the MNSI-sign. Any additional foot examination abnormality would raise the MNSI-sign score to the neuropathy range (defined ≥ 3). Nevertheless, the prevalence of neuropathy based on MNSI-sign score (25.6%) was relatively more objective and, thus, more reliable than that based on subjective MNSI-history score (10.4%). Furthermore, the prevalence of neuropathy based on MNSI-sign score was more consistent with previous studies (20-38%) [2,3,8,15-17,22,23]. Future studies are needed to assess the most appropriate MNSI-history and sign cutoff scores for defining neuropathy in the UAE population.

Limited amount of studies have addressed diabetes-associated symptoms of neuropathy in the Peninsular Arabs. Forty-seven percent of our patients had symptoms of painful neuropathy (Table 7). Higher prevalences were reported in a study from Saudi Arabia (65%) and in a multi-center study from Middle East (54%) [10,24]. This value, however, was less than reported in Australian patients (26%) [25].

Typical determinants of diabetic neuropathy include patient age, duration of diabetes, glycemic control, hypertension, smoking, obesity and dyslipidemia. In this study, the subset of significant predictors for odds of MSNI-history score ≥ 7 was abnormal HbA1C (odds ratio, 3.41) and inactive physical activity (odds ratio, 3.41), (Table 4). The subset of significant predictors for odds of MSNI-sign score ≥ 3 was patients age (odds ratio, 1.06), height (odds ratio, 1.06), systolic blood pressure (odds ratio, 1.03) and duration of diabetes (odds ratio, 1.08), (Table 6). The results confirm the need for optimal glycemic control. In the European Diabetes Perspective Complications Study, the rate of deterioration of glycemic control contributed markedly to the risk of neuropathy, independently of the glycosylated hemoglobin value at baseline [6]. Previous cross-sectional and cohort studies have also reported hypertension as a significant risk factor for diabetic neuropathy [26,27]. In rodents, the additive effect of hypertension on diabetic neuropathy was attributed to damages in Schwann cells and myelin sheaths around exons. These results endorse the relationship between diabetic neuropathy and its microvascular complications [28,29].

Lack of physical activity was also found to be associated with neuropathy in other studies [30-32]. Height may act in concert with poor glycemic control, which is postulated to contribute to capillary basement membrane thickening, possibly due to greater pressure and decreased capillary blood flow in the lower extremities [23,33-35]. Consistent with previous studies, male gender was a risk factor for the MSNI-sign score ($p<0.001$, Table 5) [36,37].

Association between abnormal body fat percentage and neuropathy has been shown in previous studies [48-40]. This association was noted here (Tables 3 and 5); however, it disappeared in the regression (Tables 4 and 6). Current evidence supports that the metabolic syndrome and obesity are risks factor of neuropathy. Proposed mechanisms for this nerve damage include fat deposition, extracellular protein glycation, mitochondrial dysfunction, oxidative stress and activation of counter-regulatory signaling pathways leading to chronic metabolic inflammation [38-40].

In this study, 95% of the patients regularly attended the diabetes center. The presence of high illiteracy rate (55%, Table 2) may have contributed to less health education and suboptimal foot care

practices. This report addressed the extent of diabetic neuropathy in UAE patients. The study, however, has limitations that include lack of nerve conduction studies (the definite tool for diagnosing neuropathy), causality determination (e.g., vitamin B12 or folic acid deficiency) and lack of patients from other centers in the country. These issues are logical goals in subsequent follow-up studies. Sixteen percent of patients have declined to participate. This problem may produce a selection bias, especially since patients with relevant symptoms are more likely to be included than asymptomatic patients. Thus, the prevalence of neuropathy may be somewhat lower than that shown here.

Conclusion

Diabetic neuropathy is common in UAE patients. This complication is shown here to be associated with poor glycemic control, hypertension and lack of physical activity. The results highlight the need for intensive programs aiming at early detection and prompt implementation of health education.

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