DR. ADNAN KHAN (Orcid ID : 0000-0003-4647-6672)

PROF. RAYAZ A. MALIK (Orcid ID : 0000-0002-7188-8903)

Article type : Original Article

Manuscript category: Original article

Prevalence and risk factors for painful diabetic neuropathy in secondary health care in Qatar

Short title: Painful diabetic neuropathy in Qatar

Georgios Ponirakis MPhil[1,4], Tarik Elhadd MD[2,3], Subitha Chinnaiyan ND[2], Zeinab Dabbous MD[2], Mashhood Siddiqui MD[2], Hamad Al-muhannadi[1], Ioannis Petropoulos PhD[1], Adnan Khan PhD[1], Khaled A. E. Ashawesh MD[3], Khaled M. O. Dukhan MD[3], Ziyad R. Mahfoud PhD[1], Christopher Murgatroyd PhD[4], Mark Slevin PhD[4], Rayaz A. Malik MB ChB[1, 2, 4, 5]

[1]Weill Cornell Medicine-Qatar, Qatar Foundation, Education City, Doha, Qatar

[2]National Diabetes & Endocrine Centre, Hamad General Hospital, Hamad Medical Corporation, Doha, Qatar

[3]National Diabetes & Endocrine Centre, Al-Wakra Hospital, Hamad Medical Corporation, Doha, Qatar

[4]Manchester Metropolitan University, Faculty of Science and Engineering, Manchester, UK

[5]Institute of Cardiovascular Science, University of Manchester, Manchester, UK.

Corresponding author:
Professor Rayaz. A. Malik,
Weill Cornell Medicine-Qatar,
Qatar Foundation,
Education City.
Doha, PO Box: 24144, Qatar
Tel: +974-4492-8256
E Mail: ram2045@qatar-med.cornell.edu

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/jdi.13037

Abstract

Aims/Introduction: Painful diabetic peripheral neuropathy (PDPN) has a significant impact on the patient's quality of life. The prevalence of PDPN in the Middle East and North Africa (MENA) region has been reported to be almost double that of populations in the UK. We sought to determine the prevalence of PDPN and its associated factors in T2DM patients attending secondary care in Qatar.

Materials and Methods: This is a cross-sectional study of 1095 participants with T2DM attending Qatar's two national diabetes centers. PDPN and impaired vibration perception on the pulp of the large toes were assessed using the DN4 questionnaire with a cut-off ≥4 and the Neurothesiometer with a cut-off ≥15V, respectively.

Results: The prevalence of PDPN was 34.5% (95% CI: 31.7%-37.3%), but 80% of these patients had not previously been diagnosed or treated for this condition. Arabs had a higher prevalence of PDPN compared to South Asians (P<0.05). PDPN was associated with impaired vibration perception AOR=4.42 (95%CI: 2.92-6.70), smoking AOR=2.43 (95%CI: 1.43-4.15), obesity AOR=1.74 (95%CI: 1.13-2.66), being female AOR=1.65 (95%CI: 1.03-2.64) and duration of diabetes AOR=1.08 (95%CI: 1.05-1.11). Age, poor glycemic control, hypertension, physical activity and proteinuria showed no association with PDPN.

Conclusions: PDPN occurs in 1/3 of T2DM patients attending secondary care in Qatar, but the majority have not been diagnosed. Arabs are at higher risk for PDPN. Impaired vibration perception, obesity and smoking are associated with PDPN in Qatar.

Keywords: Painful diabetic peripheral neuropathy; Obesity; Type 2 Diabetes

Introduction

Painful diabetic peripheral neuropathy (PDPN) has a significant impact on the patient's quality of life[1-3] as it is accompanied by depression, anxiety and sleep disturbance[2]. Estimates of the prevalence of PDPN in patients with T2DM vary and range from 17.9%-65.3%[1, 4-6]. In a large population-based study (n=15,692) from the UK [4], we previously showed that PDPN occurred in 21.5% of patients with T2DM and was more common in South Asians. In the Middle East and North Africa (MENA) region, Jambart *et al.* [5] reported a much higher prevalence of PDPN of 61.3% in Egypt, 57.5% in Jordan, 53.9% in Lebanon and 37.1% in the United Arab Emirates.

Despite having a serious impact on the patient's quality of life, PDPN is underdiagnosed and undertreated[7, 8]. Patients with painful symptoms are often unaware that the pain is related to diabetes and do not report it to their clinician[8, 9]. Screening patients at high risk for PDPN should allow timely identification and treatment. Previous studies have shown that older age, a longer duration of diabetes, being female and the presence of diabetic peripheral neuropathy (DPN) increases the risk for PDPN[1, 4-6, 10, 11]. Additionally, obesity[1, 5, 7, 12], low physical activity[13, 14], smoking[4, 12], poor glycemic control [15, 16], low HDL cholesterol[1], raised LDL cholesterol, triglycerides and creatinine[13], are also independent risk factors of PDPN.

The aim of this study was to establish the prevalence of PDPN in patients with T2DM in secondary care in Qatar and explore the association with ethnicity and risk factors for this condition. We have undertaken a large cross-sectional cohort study using DN4, a validated and highly sensitive and specific questionnaire for the diagnosis of PDPN[17].

Materials and Methods

This is a cross-sectional cohort study. Patients with diabetes aged 18 years and above were recruited from the two National Diabetes & Endocrine Centers in Qatar, Hamad General Hospital and Al-Wakra Hospital. Participating clinicians reported on all patients satisfying the inclusion criteria, examined between March 2017 to March 2018. No refusals were recorded as the procedure was quick, simple and potentially valuable to the patient health. Participants with other causes of neuropathy including vitamin B12 deficiency, hypothyroidism, HIV infection, leprosy, hepatitis C and chemotherapy were excluded from the study. We enrolled 1,163 individuals and after excluding 66 patients with T1DM and 2 patients who did not complete the assessments were left with a sample size of 1,095.

This study was approved by the Institutional Review Board (IRB) of WCM-Q and HMC and all participants gave informed consent to take part in the study. The research adhered to the tenets of the declaration of Helsinki.

Demographic and metabolic measures

Age, gender, duration of diabetes, height, weight and BMI were recorded. Ethnicity was categorized as Qatari Arabs, other Arabs, South Asians, and other ethnic groups. The average of two readings of the systolic (SBP) and diastolic (DBP) blood pressure taken from the subject's left arm while seated with his/her arm at heart level, using a standard zero mercury sphygmomanometer after 10-15 minutes of rest was obtained. A non-fasting blood sample of 10 ml was collected through venepuncture from each participant into vacutainer tubes containing EDTA. The samples were kept at room temperature and transported within 2 hours to a central certified laboratory at Hamad General Hospital, HMC, Doha, Qatar. Glycated haemoglobin (HbA1c), total cholesterol, HDL, LDL and triglycerides were measured by an autoanalyzer (Hitachi 747 autoanalyzer, Japan). Urinary albumin

and creatinine levels were assessed on a random spot urine sample to evaluate the albumin-to-creatinine ratio (ACR). Patients with an HbA1c ≥9% were considered to be poorly controlled. Hypertension was defined according to either an average systolic blood pressure (SBP) ≥ 140 mmHg and/or the use of antihypertensive medication, as described in the WHO/ISH Guidelines[18]. Current cigarette smoking was defined as having smoked at least one cigarette every day for 30 days preceding the study visit. Physical activity was defined as doing physical activity including walking for 30 minutes or more in a day for at least 3 times a week. Obesity was classified according to WHO criteria[19] with a BMI ≥30 Kg/m^2. Proteinuria was defined as an ACR >30mg/g.

Painful diabetic peripheral neuropathy assessment

The Douleur Neuropathique en 4 (DN4) questionnaire has been validated for painful diabetic peripheral neuropathy (PDPN)[20] and can distinguish between nociceptive and neuropathic pain[21]. It consists of 10 questions: 7 questions relating to the pain description (burning, painful cold, electric shocks) and associated abnormal sensations (tingling, pins and needles, numbness, itching) and the other 3 questions relate to a neurological examination in the painful area (hypoesthesia to touch and prick using disposable examination pins and allodynia to brushing). The scoring is based on a yes (1 point) or no (0 point) answer and each question is equally weighted. A score ≥4 has a high sensitivity (80%) and specificity (92%) for PDPN[20]. The questionnaire was administered by the investigator spoken in either English or Arabic. Previously diagnosed PDPN was self-reported. Medications for painful neuropathy were recorded.

Impaired vibration perception assessment

Vibration perception threshold (VPT) was measured bilaterally on the pulp of the large toe using a Neurothesiometer (Horwell, Scientific Laboratory Supplies, Wilford, Nottingham, UK). The strength of the vibration stimulus was gradually increased from null intensity to a value in voltage at which vibration was first detected by the participant. The test was repeated three times and the average value was recorded. The range for VPT readings is 1 to 50V. Iimpaired vibration perception was defined on a mean VPT ≥15V [22, 23].

Statistical analysis

Patients' demographic and clinical characteristics were summarized using means and standard deviations for numeric variables and frequency distribution for categorical variables. Variables were compared between patients with and without PDPN using an unpaired t-test or Mann-Whitney test when the distribution was highly skewed for numeric variables and the Chi-squared test or Fisher's exact test when expected cell counts fell below 5 for categorical variables.

Binary and multiple logistic regression analysis was performed with age, duration of diabetes, diabetic neuropathy, gender, poor glycemic control, hypertension, obesity, physical activity, smoking, proteinuria and ethnic groups as independent variables, and PDPN as the dependent variable. The multiple logistic regression model included all variables with p-value of 0.10 or less at the bivariate level. Adjusted odds ratios and their corresponding 95% confidence intervals are presented.

Demographic and clinical characteristics of the patients were compared between the different ethnic groups using the chi-square test for categorical variables such as hypertension and one-way ANOVA for numeric variables such as age. Multiple comparisons when needed were done using the Bonferroni's method.

All analyses were performed using IBM-SPSS (version 23; SPSS Inc, Armonk NY). A two-tailed P value of ≤0.05 was considered significant.

Results

Prevalence of PDPN

The cohort (n=1095) was aged 20 to 86 years (mean [SD], 54.3 [11.4]), 60.6% were male. The clinical and demographic characteristics of T2DM subjects with and without painful diabetic peripheral neuropathy (PDPN) are compared in Table 1. The prevalence of PDPN was 34.5% (95% CI: 31.7%-37.3%). 80.2% of the subjects with PDPN had not been previously diagnosed with this condition and 86.0% had not been treated.

Factors associated with PDPN

Subjects with PDPN had a higher mean age (P<0.0001), duration of diabetes (P<0.0001), HbA1c (P=0.02), systolic blood pressure (P<0.001), weight (P<0.0001) and BMI (P<0.0001), compared to subjects without PDPN. Vibration perception threshold (VPT) was significantly higher (17.4V vs 9.8V, P<0.0001). Total cholesterol, triglycerides, HDL, LDL and diastolic blood pressure were comparable between the two groups. Subjects with PDPN had a higher percentage of subjects with impaired vibration perception (60.9% vs 23.2%, P<0.0001), a greater proportion of females (39.3% vs 31.3%, P<0.01), poorer glycemic control (39.6% vs 32.4%, P<0.05), more hypertension (39.0% vs 28.5%, P=0.001), greater proportion with proteinuria (48.4% vs 32.9%, P<0.01), more obesity (39.8% vs 26.7%, P<0.0001) and a lower percentage of those undertaking physical activity (25.5% vs 36.8%, P=0.001).

Logistic regression analysis showed that five factors were independently and significantly associated with PDPN (Table 2). Impaired vibration perception adjusted odds ratio (AOR)=4.42 (95%CI: 2.92-6.70), smoking AOR=2.43 (95%CI: 1.43-4.15), obesity AOR=1.74 (95%CI: 1.13-2.66), being female AOR=1.65 (95%CI: 1.03-2.64) and duration of diabetes =1.08 (95%CI: 1.05-1.11) were associated with PDPN. Age, poor glycemic control, hypertension, physical activity, proteinuria and ethnicity showed no association with PDPN.

Ethnicity and PDPN

The prevalence of PDPN differed between ethnic groups (Figure 1 and Table 3). Qataris (45.3%) and other Arabs (35.7%) had a higher prevalence of PDPN compared to South Asians (25.8%). However, the prevalence of impaired vibration perception was comparable between ethnic groups. The prevalence of obesity was comparable between Qataris (66.8%) and other Arabs (70.9%), but significantly higher than in South Asians (34.2%). The percentage of Qataris (20.8%) and other Arabs (35.5%) who undertook physical activity was significantly lower than in South Asians (54.3%). The percentage of Qataris with proteinuria was significantly higher than in South Asians (9.4% vs 3.0%) and comparable with other Arabs and other ethnicities. Qataris were significantly older than other Arabs, South Asians and other ethnicities (58.2 vs 53.8 vs 51.8 and 52.5 years, respectively) and had a significantly longer duration of diabetes (13.4 vs 9.1 vs 8.1 and 9.9 years, respectively). The percentage of Qataris with hypertension was significantly higher than other Arabs (65.3% vs 53.9%). There were significantly less smokers amongst Qataris compared to other Arabs (10.4% vs 23.9%).

Discussion

This is the first large observational study to establish the prevalence of painful diabetic peripheral neuropathy (PDPN) and its associated factors in secondary care in Qatar. PDPN occurs in approximately one third of patients with T2DM, however, alarmingly, 4/5 had not been previously diagnosed or treated. PDPN, a manifestation of small fiber damage[24-26], occurred in more than one in four patients without impaired vibration perception, and in one in two patients with impaired vibration perception. Impaired vibration perception, obesity and smoking were associated with PDPN. Arabs also have a higher prevalence of PDPN compared to Asians. This may be attributed to the higher percentage of women and obesity, and a lower percentage undertaking physical activity in the Arab population.

The prevalence of PDPN in T2DM patients in Qatar was lower than previous studies from the MENA region, even though they also used the Douleur Neuropathique 4 (DN4) pain questionnaire and showed that the prevalence of PDPN was 65.3% in Saudi Arabia[6], 61.3% in Egypt[5], 57.5% in Jordan, 53.9% in Lebanon and 37.1% in United Arab Emirates and Kuwait. This difference could be attributed to different populations and control of various risk factors, although age, duration of diabetes and the percentage of those with obesity were comparable to this study. However, the percentage of those with poor glycemic control in Saudi Arabia was higher compared to the current study (59.5% vs 39.6%)[27]. Poor glycemic control is common in the Middle East [27-30] and has been reported to be a significant risk factor for both DPN and PDPN[15, 16]. In the UK, the prevalence of PDPN in T2DM patients is lower (21.5% - 26.4%) than in Qatar[4, 10] and may be attributed to a lower HbA1c (7.26% vs 8.14%) and shorter duration of diabetes (4-8 years vs 10.1 years). One of the earlier UK studies [10] was conducted in patients with T1DM and T2DM in primary care and the prevalence of PDPN is known to be lower in primary care[12] and in T1DM patients[1, 4, 7].

The physical quality of life of patients with PDPN decreases at a significantly faster rate over 3 years compared to T2DM patients without PDPN[3]. Patients with PDPN are also at high risk for depression, anxiety and sleep disturbance[2]. However, the under-diagnosis and treatment of PDPN continues to pose a considerable problem for patients. Other studies have also reported that a large proportion of patients with PDPN were not diagnosed, 61.5% in Germany[7] and 12.5% in the UK[8]. Major hurdles limiting the diagnosis of PDPN are that patients with painful symptoms do not attribute them to diabetes and fail to report them to their physician[8, 9] and of course screening is not currently advocated for PDPN, only for those at high risk of foot ulceration [31]. Given that we have identified age, duration of diabetes and the presence of impaired vibration perception as major determinants for PDPN[1, 5, 6, 10] one could advocate screening for PDPN in at least diabetic patients who are older, have a longer duration of diabetes and impaired vibration perception. Furthermore, we have identified that obesity is associated with PDPN, which has also been reported in some[1, 5, 7, 12], but not other studies [6, 11]. Low physical activity has been reported as a risk factor[13, 14], but in this study we show no association after adjusting for other risk factors. Smoking has also been associated with PDPN in some[4, 12] but not other studies[1, 4-6, 11]. Improved glycemic control reduces the development and progression of DPN in T1DM[32], but has shown limited benefit in T2DM[33]. Low HDL cholesterol, raised LDL cholesterol and triglycerides have been independently associated with PDPN[1]. Creatinine is associated with PDPN, whilst albuminuria[13] and proteinuria have no association. A previous study of subjects with pre-diabetes showed that lifestyle intervention reduced neuropathic symptoms and improved small fiber function and structure[14].

The prevalence of painful neuropathic symptoms[4] and PDPN[9] differs between ethnic groups. In our previous study in the UK [4], we showed that South Asians were 50% more likely to have painful neuropathic symptoms compared to Europeans and Afro-Caribbeans, after adjusting for age and duration of diabetes. However, in the present study, South Asians had a lower prevalence of PDPN compared to Qatari Arabs and other Arabs, which may be attributed to a lower proportion with obesity, less women and higher physical activity in this group. Indeed this and other studies[4, 5] have

shown that women have a 50-65% increase in the odds for PDPN. The ethnic difference may also reflect genetic differences in the prevalence of abnormalities in voltage gated channels on nociceptors in different ethnic groups[34, 35].

We recognise that recruiting patients with diabetes from secondary health care centers and not primary care centers as a major limitation of this study and limits the generalizability of the results to all people with diabetes in Qatar. However, those two hospitals are the only National Diabetes & Endocrine Centres in Qatar and the recruited participants were of diverse backgrounds. The cross sectional design of this study also limits the interpretation of cause and effect in relation to risk factors. The strength of this study is the large sample size and the inclusion of a wide range of risk factors to identify those associated independently with PDPN. Furthermore, PDPN was diagnosed using the DN4 questionnaire, which has been validated in Arabic [21] and used in other studies in the MENA region to establish the prevalence of PDPN [5, 6].

In conclusion, one in three patients with T2DM attending secondary care in Qatar have PDPN. It remains a neglected complication of diabetes as ~80% of patients were not diagnosed or treated for this condition. Impaired vibration perception, obesity and smoking are associated with PDPN, suggesting that patients with these risk factors should be screened for PDPN and treated for relief of symptoms and with life style interventions to limit progression.

Acknowledgement:

We thank all the participants for their efforts, will and commitment to be involved in the study.

Disclosure:
No conflict of interest

Research funding:

Funding source: *Qatar National Research Fund*, Funding ID: *Grant BMRP-5726113101* Funding source: *Pfizer Gulf FZ LLC*, Funding ID: *W1230787*

References

1. Van Acker K, Bouhassira D, De Bacquer D, et al. Prevalence and impact on quality of life of peripheral neuropathy with or without neuropathic pain in type 1 and type 2 diabetic patients attending hospital outpatients clinics. *Diabetes Metab.* 2009;35(3): 206-213.
2. Bohlega S, Alsaadi T, Amir A, et al. Guidelines for the pharmacological treatment of peripheral neuropathic pain: expert panel recommendations for the middle East region. *J Int Med Res.* 2010;38(2): 295-317.
3. daCosta DiBonaventura M, Cappelleri JC, Joshi AV. A longitudinal assessment of painful diabetic peripheral neuropathy on health status, productivity, and health care utilization and cost. *Pain Med.* 2011;12(1): 118-126.
4. Abbott CA, Malik RA, van Ross ER, Kulkarni J, Boulton AJ. Prevalence and characteristics of painful diabetic neuropathy in a large community-based diabetic population in the U.K. *Diabetes Care.* 2011;34(10): 2220-2224.
5. Jambart S, Ammache Z, Haddad F, et al. Prevalence of painful diabetic peripheral neuropathy among patients with diabetes mellitus in the Middle East region. *J Int Med Res.* 2011;39(2): 366-377.
6. Halawa MR, Karawagh A, Zeidan A, Mahmoud AE, Sakr M, Hegazy A. Prevalence of painful diabetic peripheral neuropathy among patients suffering from diabetes mellitus in Saudi Arabia. *Curr Med Res Opin.* 2010;26(2): 337-343.
7. Ziegler D, Landgraf R, Lobmann R, et al. Painful and painless neuropathies are distinct and largely undiagnosed entities in subjects participating in an educational initiative (PROTECT study). *Diabetes research and clinical practice.* 2018;139: 147-154.
8. Daousi C, MacFarlane IA, Woodward A, Nurmikko TJ, Bundred PE, Benbow SJ. Chronic painful peripheral neuropathy in an urban community: a controlled comparison of people with and without diabetes. *Diabet Med.* 2004;21(9): 976-982.
9. Eichholz M, Alexander AH, Cappelleri JC, et al. Perspectives on the impact of painful diabetic peripheral neuropathy in a multicultural population. *Clinical diabetes and endocrinology.* 2017;3: 12.
10. Davies M, Brophy S, Williams R, Taylor A. The prevalence, severity, and impact of painful diabetic peripheral neuropathy in type 2 diabetes. *Diabetes Care.* 2006;29(7): 1518-1522.
11. Jacovides A, Bogoshi M, Distiller LA, et al. An epidemiological study to assess the prevalence of diabetic peripheral neuropathic pain among adults with diabetes attending private and institutional outpatient clinics in South Africa. *J Int Med Res.* 2014;42(4): 1018-1028.
12. Aslam A, Singh J, Rajbhandari S. Prevalence of Painful Diabetic Neuropathy Using the Self-Completed Leeds Assessment of Neuropathic Symptoms and Signs Questionnaire in a Population with Diabetes. *Can J Diabetes.* 2015;39(4): 285-295.
13. Ziegler D, Rathmann W, Meisinger C, Dickhaus T, Mielck A, Group KS. Prevalence and risk factors of neuropathic pain in survivors of myocardial infarction with pre-diabetes and diabetes. The KORA Myocardial Infarction Registry. *Eur J Pain.* 2009;13(6): 582-587.
14. Smith AG, Russell J, Feldman EL, et al. Lifestyle intervention for pre-diabetic neuropathy. *Diabetes Care.* 2006;29(6): 1294-1299.

15. Harris M, Eastman R, Cowie C. Symptoms of sensory neuropathy in adults with NIDDM in the U.S. population. *Diabetes Care.* 1993;16(11): 1446-1452.
16. Smith AG, Singleton JR. Impaired glucose tolerance and neuropathy. *Neurologist.* 2008;14(1): 23-29.
17. Unal-Cevik I, Sarioglu-Ay S, Evcik D. A comparison of the DN4 and LANSS questionnaires in the assessment of neuropathic pain: validity and reliability of the Turkish version of DN4. *J Pain.* 2010;11(11): 1129-1135.
18. Moser M. World Health Organization-International Society of Hypertension Guidelines for the Management of Hypertension-Do These Differ From the U.S. Recommendations? Which Guidelines Should the Practicing Physician Follow? *J Clin Hypertens (Greenwich).* 1999;1(1): 48-54.
19. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. *World Health Organ Tech Rep Ser.* 2000;894: i-xii, 1-253.
20. Spallone V, Morganti R, D'Amato C, Greco C, Cacciotti L, Marfia GA. Validation of DN4 as a screening tool for neuropathic pain in painful diabetic polyneuropathy. *Diabet Med.* 2012;29(5): 578-585.
21. Harifi G, Ouilki I, El Bouchti I, et al. Validity and reliability of the Arabic adapted version of the DN4 questionnaire (Douleur Neuropathique 4 Questions) for differential diagnosis of pain syndromes with a neuropathic or somatic component. *Pain Pract.* 2011;11(2): 139-147.
22. Wiles PG, Pearce SM, Rice PJ, Mitchell JM. Vibration perception threshold: influence of age, height, sex, and smoking, and calculation of accurate centile values. *Diabet Med.* 1991;8(2): 157-161.
23. Garrow AP, Boulton AJ. Vibration perception threshold--a valuable assessment of neural dysfunction in people with diabetes. *Diabetes Metab Res Rev.* 2006;22(5): 411-419.
24. Sorensen L, Molyneaux L, Yue DK. The relationship among pain, sensory loss, and small nerve fibers in diabetes. *Diabetes Care.* 2006;29(4): 883-887.
25. Vlckova-Moravcova E, Bednarik J, Belobradkova J, Sommer C. Small-fibre involvement in diabetic patients with neuropathic foot pain. *Diabet Med.* 2008;25(6): 692-699.
26. Quattrini C, Tavakoli M, Jeziorska M, et al. Surrogate markers of small fiber damage in human diabetic neuropathy. *Diabetes.* 2007;56(8): 2148-2154.
27. Akbar DH, Mira SA, Zawawi TH, Malibary HM. Subclinical diabetic neuropathy. A common complication in Saudi diabetics. *Neurosciences (Riyadh).* 2000;5(2): 110-114.
28. Youssef AA, El Mahalli AA, Akl OA, Zaghloul AA. Quality of diabetes care in primary care setting in egypt: an example of health sector reform in developing countries. *J Egypt Public Health Assoc.* 2006;81(5-6): 301-320.
29. Uddin I, Ahmad TJ, Kurkuman AR, Iftikhar R. Diabetes education: its effects on glycemic control. *Ann Saudi Med.* 2001;21(1-2): 120-122.
30. Habib SS, Aslam M. Risk factors, knowledge and health status in diabetic patients. *Saudi Med J.* 2003;24(11): 1219-1224.
31. Pop-Busui R, Boulton AJ, Feldman EL, et al. Diabetic Neuropathy: A Position Statement by the American Diabetes Association. *Diabetes Care.* 2017;40(1): 136-154.
32. Klein R, Klein BE, Moss SE. Relation of glycemic control to diabetic microvascular complications in diabetes mellitus. *Ann Intern Med.* 1996;124(1 Pt 2): 90-96.
33. Callaghan BC, Little AA, Feldman EL, Hughes RA. Enhanced glucose control for preventing and treating diabetic neuropathy. *Cochrane Database Syst Rev.* 2012(6): CD007543.
34. Wadhawan S, Pant S, Golhar R, et al. NaV channel variants in patients with painful and nonpainful peripheral neuropathy. *Neurology Genetics.* 2017;3(6): e207.

35. Blesneac I, Themistocleous AC, Fratter C, et al. Rare NaV1.7 variants associated with painful diabetic peripheral neuropathy. *International journal of endocrinology.* 2018;159(3): 469-480.

Figure 1. Prevalence of painful diabetic peripheral neuropathy between ethnic groups.

Table 1. Demographic characteristics of adults with T2DM stratified by painful diabetic peripheral neuropathy (PDPN) status. Patients' demographic and clinical characteristics summarized using means and standard deviations for numeric variables and frequency distribution for categorical variables. Continues parametric and non-parametric variables were compared using unpaired t-test and (*) Mann-Whitney test, respectively. Categorical variables were compared using x^2.

		Painful diabetic neuropathy				
		No		Yes		P value
n (%)		717	(65.5)	378	(34.5)	N/A
Age, years, mean (SD)		52.6	± 11.4	57.5	± 10.7	<0.0001*
Gender, n (%)	Male	453	(68.7)	206	(31.3)	<0.01
	Female	261	(60.7)	169	(39.3)	
Diabetes duration, years, mean (SD)		8.2	± 7.0	13.6	± 7.9	<0.0001*
HbA1c, mean (SD)	%	8.0	± 2.0	8.4	± 2.0	0.02
	mmol/mol	64.9	± 22.3	67.9	± 21.8	0.02
Poor glycemic control	Yes	174	(60.4)	114	(39.6)	<0.05
	No	474	(67.6)	227	(32.4)	
Cholesterol, mmol/l, mean (SD)		4.5	± 1.2	4.4	± 1.1	NS
Triglyceride, mmol/l, mean (SD)		1.9	± 1.3	1.7	± 1.0	NS*
HDL, mmol/l, mean (SD)		1.3	± 0.2	1.1	± 0.0	NS
LDL, mmol/l, mean (SD)		2.6	± 0.0	2.5	± 0.0	NS
Systolic blood pressure, mmHg, mean (SD)		131.1	± 17.7	135.4	± 18.3	<0.001
Diastolic blood pressure, mmHg, mean (SD)		78.5	± 10.5	77.6	± 9.5	NS
Hypertension, n (%)	Yes	371	(61.0)	237	(39.0)	0.001
	No	294	(71.5)	117	(28.5)	
Weight, Kg, mean (SD)		83.4	± 21.4	87.6	± 18.6	<0.0001*

BMI, Kg/m^2, mean (SD)		30.7	± 6.8	32.7	± 7.0	<0.0001
Obesity, n (%), n (%)	Yes	314	(60.2)	208	(39.8)	<0.0001
	No	318	(73.3)	116	(26.7)	
Physical activity, n (%)	Yes	240	(74.5)	82	(25.5)	0.001
	No	330	(63.2)	192	(36.8)	
Smoking, n (%)	Yes	107	(69.0)	48	(31.0)	NS
	No	501	(67.2)	244	(32.8)	
Proteinuria, n (%)	Yes	33	(51.6)	31	(48.4)	<0.01
	No	300	(67.1)	147	(32.9)	
Vibration perception threshold, V, mean (SD)		9.8	± 7.5	17.4	± 10.6	<0.0001
Impaired vibration perception, n (%)	Yes	126	(39.1)	196	(60.9)	<0.0001
	No	586	(76.8)	177	(23.2)	
Previously diagnosed with PDPN, n (%)		28	(4.0)	73	(19.8)	<0.0001
Treated for PDPN, n (%)		22	(3.1)	53	(14.0)	<0.0001
Ethnic groups, n (%)	Qataris	181	(54.7)	150	(45.3)	<0.0001
	Other Arabs	196	(64.3)	109	(35.7)	
	South Asians	299	(74.2)	104	(25.8)	
	Others	41	(73.2)	15	(26.8)	

Table 2. Logistic regression analysis between painful diabetic peripheral neuropathy and risk factors. Outcome variable: Painful diabetic peripheral neuropathy. Independent variables: Age, duration of diabetes, impaired vibration perception, female, poor glycemic control, hypertension, obesity, physical activity, smoking, proteinuria and ethnic groups were considered in the fitted model with a P value ≤0.05.

	OR	(95% CI)		P value
Age	1.01	(0.99 -	1.03)	NS
Duration of diabetes	1.08	(1.05 -	1.11)	<0.0001
impaired vibration perception	4.42	(2.92 -	6.70)	<0.0001
Female	1.65	(1.03 -	2.64)	<0.05
Poor glycemic control	1.40	(0.93 -	2.11)	NS
Hypertension	1.16	(0.77 -	1.76)	NS
Obesity	1.74	(1.13 -	2.66)	<0.01
Physical activity	0.83	(0.55 -	1.26)	NS
Smoking	2.43	(1.43 -	4.15)	0.001
Proteinuria	1.04	(0.51 -	2.16)	NS
Ethnic groups				
Qataris	1			NS
Other Arabs	1.05	(0.64 -	1.73)	NS
South Asians	0.95	(0.57 -	1.59)	NS
Others	0.81	(0.31 -	2.07)	NS

Table 3. Differences in the prevalence of painful diabetic peripheral neuropathy and other risk factors between different ethnic groups. a,b,c,d within each row, columns with similar letters are not statistically significant and those with different letters are significantly different.

	Qataris	Other Arabs	South Asians	Others
n	331	305	403	56
Painful DPN, n (%)	150 (45.3)[a]	109 (35.7)[a]	104 (25.8)[b]	15 (26.8)[ab]
Age, years, mean (SD)	58.2 (12.0)[a]	53.8 (11.7)[b]	51.8 (9.7)[b]	52.5 (10.5)[b]
Duration of diabetes, years, mean (SD)	13.4 (7.8)[a]	9.1 (7.2)[b]	8.1 (7.0)[b]	9.9 (8.4)[b]
Impaired vibration perception, n (%)	108 (33.0)[a]	91 (30.0)[a]	102 (25.6)[a]	21 (37.5)[a]
Female, n (%)	211 (64.1)[a]	109 (35.9)[b]	89 (22.3)[c]	21 (39.5)[bc]
Poor glycemic control, n (%)	100 (33.8)[a]	86 (31.5)[a]	152 (41.4)[a]	21 (39.6)[a]
Hypertension, n (%)	196 (65.3)[a]	153 (53.9)[b]	229 (59.9)[ab]	30 (56.6)[ab]
Obesity, n (%)	185 (66.8)[ab]	188 (70.9)[b]	125 (34.2)[c]	24 (49.0)[ac]
Physical activity, n (%)	52 (20.8)[a]	87 (35.5)[b]	170 (54.3)[c]	13 (36.1)[abc]
Smoking, n (%)	27 (10.4)[a]	62 (23.9)[b]	57 (16.9)[ab]	9 (20.5)[ab]
Proteinuria, n (%)	31 (9.4)[a]	15 (4.9)[a,b]	12 (3.0)[b]	6 (10.7)[a]