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Prevalence and Treatment Options for Diabetic Neuropathic Pain in Kuwait

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Abstract
Epidemiological data on Painful diabetic peripheral neuropathy (PDPN) is scarce in Kuwait. We aimed to study the prevalence of PDPN among diabetic patients and to assess its treatment modalities in Kuwait. This cross-sectional study collected data from 5 clinics in the primary, secondary and tertiary centres. Diabetic patients aged ≥18 years were included. PDPN was diagnosed based on combination of history of typical pain in extremities and objective neurological examination. Socio-demographic data and treatment modalities were extracted from the medical records. Questionnaires of patients` and practitioners` perceptions were collected from patients` and care health providers respectively. Descriptive and chi-square analyses were used to measure the statistical significance.A total of 202 diabetic participants; 109 were diagnosed as PDPN, representing a prevalence of 53.9% [95% confidence interval (CI), 50.7% – 58.5%] of the studied sample. The PDPN cohort had a mean age of 52.77±12.2 years. Patients with PDPN were older (39.6% versus 21.3%; p <0.005), taller (37.1% versus 23.8%; P <0.013), had longer disease duration (35.1% versus 21.8%; P <0.011), had body mass index > 30 (42.6% versus 26.2%; P <0.001) and higher fasting blood glucose (29.7% versus 18.8%; P <0.044) compared with patients without PDPN. The most commonly prescribed pain treatments were Non-steroidal anti-inflammatory drugs (25.68%) and anticonvulsants (22.93%).We concluded thatdisease duration, poor glycemic control and high BMI were associated with increased risk of PDPN. Patient education and management of neuropathic pain control need to be optimized.
Keywords: *Painful Peripheral neuropathy, Diabetes mellitus, Kuwait.*

Introduction

Peripheral neuropathy is one of the most common complications in patients with long-standing diabetes, since approximately 50 % of patients develop diabetic peripheral neuropathy (DPN) by 25 years after diagnosis[1]. Patients with DPN often experience chronic pain defined as painful diabetic peripheral neuropathy (PDPN), which starts in both feet and often leads to involving calves, fingers, and hands (glove and stocking distribution pattern)[2]. The pain associated with DPN is a major cause of morbidity among diabetic patients, which could have a profound impact on their activity of daily living and well being[3]. Previous studies reported that, the prevalence of PDPN ranges from 40% to 50% of those with diabetic neuropathies[4]. Despite its high prevalence, there is no definite treatment for the condition apart from improving the glycemic control[3]. Several controlled studies demonstrated that antidepressants, anticonvulsants, tramadol, opioids, topical medications (analgesic patches, anesthetic patches, capsaicin cream, clonidine), aldose reductase inhibitors, and protein kinase C beta inhibitors could be used as treatment of neuropathic pain [5].

There have been no previous studies conducted in Kuwait to assess the epidemiology of diabetic neuropathic pain. Therefore, our study aimed to measure the prevalence of diabetic neuropathic pain amongst diabetic patients, to assess the available treatment modalities of PDPN, and to evaluate the perceived patient level of satisfaction in Kuwait.

Methods

This cross-sectional study assessed patients from outpatients in two primary care clinics, two secondary hospitals and one diabetes tertiary centre in Kuwait. Eligibility was limited to adult diabetic patients (≥ 18 years). Patients who had other neurologic disorders, pain conditions unrelated to diabetic peripheral neuropathy, diabetic gangrene, peripheral artery disease, spine disease, psychological disorders, malignancy, or alcohol abuse was excluded. Patient records were accessed in order to collect specific information about those patients who participated in the study.

Neuropathy was assessed using 10-g Semmes-Weinstein monofilament (Huntleigh Diagnostics, Cardiff, United Kingdom)[6,7], pinprick sensations [7], vibration perception threshold (VPT) test measured by neurothesiometer[8], and ankle reflexes. PDPN diagnosis was confirmed by the neurologist if one or more abnormal finding of 10-g monofilament, pinprick sensations, reduced vibration perception and lost ankle reflexes and pain in extremties. The assessment was conducted by neurologists experienced in managing patients with diabetic neuropathies.

Healthcare Practitioner Questionnaire and Pain ratings of patients, were used with patients to determine their experience of PDPN and their perceptions of pain[9]. Healthcare Practitioner Questionnaire, was sent to pharmacists and physicians to determine their views about how they would deal with patients with painful peripheral neuropathy[10].

The participant's body weight was measured to the nearest of 0.1 kg by an electronic weighing scale (Seca, Birmingham, United Kingdom). Height was measured without shoes to the nearest of 0.5 cm using a stadiometer (Seca, Birmingham, United Kingdom). Body mass index (BMI) was calculated as weight (kg) divided by height (m) squared (kg/m2). The cutoff points of BMI recommended by the World Health Organization (WHO) were used to define obesity (≥30 kg/m2) [11].

Collected data was analyzed to assess the prevalence of PDPN. Statistical Package for the Social Sciences (SPSS) for Windows version 18 was used. Simple descriptive statistical tests (Mean and Standard deviation) are used to describe the numerical values of the sample and frequency described, and the number and percentage of the non-numerical values. A comparison of variables was performed using the chisquare (χ 2) test for non-numeric variables. A $P < 0.05$ was regarded as significant.

Ethical clearance was obtained from the Human Ethics committee from Kuwait Institute for Medical Specialization; Ministry of Health.

Results

Among the 202 studied participants, 109 were diagnosed as PDPN, representing a prevalence of 53.9% [95% confidence interval (CI), 50.7% – 58.5%].The majority of the participants were of Kuwait nationality (72.5% versus 27.5%). The mean age of this cohort was 52.77±12.2 (range 18-91 years). Most Patients with PDPN were 50 years or higher (39.6 versus 21.3%; p <0.005), had height ≥ 158 cm (37.1% versus 23.8%; P <0.013), had longer duration of diabetes of more than 5 years (35.1% versus 21.8%; P <0.011), BMI > 30 (42.6% versus 26.2%; P <0.001) and fasting blood glucose higher than 10 mmol/L (29.7% versus 18.8%; P <0.044) compared with their counterparts without PDPN. Type 2 diabetes was significantly higher in PDPN patients (44.6% versus 32.2%; P <0.034).The majority of participants with PDPN had Glycosylated haemoglobin (HbA1c) reading above the normal threshold (39.1% versus 25.7%; P <0.015), which raises a concern (table 1).

Pain scale was the most common parameter of the diagnostic criteria used by physicians (40%). The most common types of reported symptoms were burning pain and numbness 66.1%, 88.1% respectively. Non-steroidal anti-inflammatory drugs (25.68%) and anticonvulsants (22.93%) were the most commonly prescribed painkillers. The minority of PDPN used opioids (2.75%) and (4.59%) was not on treatment (table 2). Twenty-seven patients (24.77%) had complete treatment response by taking the medication(s) and nine patients (8.26%) had no relief.

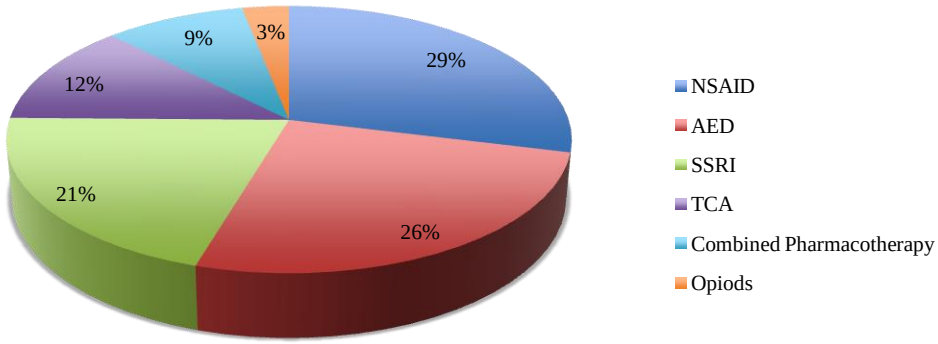
Table 1: Socio-demographic and clinical characteristics of the patients according to diabetic peripheral neuropathy (n=202)

Variables	PDPN (No=109) Number (%)	Non- PDPN (No=93) Number (%)	P
Gender			
• Males	55 (56.1)	43 (43.9)	0.550
• Females	54 (51.9)	50 (48.1)	
Age (in years)			
• <30	4 (2)	5 (2.5)	
• 30-39	7 (3.7)	15 (7.4)	0.005*
• 40-49	18 (8.9)	30 (14.9)	
• 50-59	50 (24.8)	25 (12.4)	
• 60-69	15 (7.4)	11 (5.4)	
• ≥70	15 (7.4)	7 (3.5)	
Height in centimeter			0.013*
• 157 centimeter or less	34 (16.8)	45 (22.3)	
• 158 centimeter or more	75 (37.1)	48 (23.8)	
Body weight in kilogram			
• Less than 70 Kilogram	31 (15.3)	42 (20.8)	0.014*
• 70 kilogram or more	78 (38.6)	51 (25.2)	
BMI range			0.001*
• 30 or less	23 (11.4)	40 (19.8)	
• More 30	86 (42.6)	53 (26.2)	
Types of DM			
• Type 1DM	19 (9.4)	28 (13.9)	0.034*
• Type 2 DM	90 (44.6)	65 (32.2)	
Duration since diagnosis of diabetes mellitus			0.011*
• 5 years or less	38 (18.8)	49 (24.3)	
• More than5 years	71 (35.1)	44 (21.8)	
Fasting blood glucose levels			
• less than or equal to 10 mmol/L	49 (24.3)	55 (27.2)	0.044*
• Mores than 10 mmol/L	60 (29.7)	38 (18.8)	
HbA1c			
• Not done	9 (4.5)	6 (3)	
• Less or 8	21(10.4)	35 (17.3)	0.015*
• 8.1% or more	79 (39.1)	52 (25.7)	

Table 2: Classes of painkillers commonly prescribed for PDPN

Medication	Number	Percentage (%)
Non-steroidal anti-inflammatory drugs	28	25.68
Anticonvulsants: Carbamazebine, Pregabalin, and Gabapentin	25	22.93
Serotonin norepinephrine reuptake inhibitor	20	18.35
Tricyclic antidepressants	12	11.01
Combined Pharmacotherapy	9	8.26
Opioids	3	2.75
Not on treatment	12	11.01

Figure 1: Therapeutic options of PDPN



Discussion

The prevalence rate of PDPN in our study is 53.9%, which is similar to that reported in previous Middle-Eastern studies in Lebanon (53.9%) and Jordan (57.5%) but lower than Egypt (61.3%) and in Saudi Arabia (65.3%)[12,13]. Studies conducted in western countries (Europe and the USA), reported lower prevalence rates between 15% and 25% [14–18] which was similar to a Japanese study (22.1%) [2]. The difference in prevalence of PDPN across the studies can be attributed to differences in disease duration of diabetes, study designs, population studied and different types of scales used to assess the magnitude of PDPN.

The higher prevalence of PDPN in eastern populations could be explained by low diabetes-related knowledge and poor glycaemic control among diabetics compared to Western populations [19,20], which highlights the importance of adequate blood sugar control among diabetics.

Patients with PDPN were older, taller, had longer disease duration, Body mass index > 30 and higher HbA1c compared with patients without PDPN.

Our results are consistent with previous findings [21,22] that observed a strong association between longer duration of diabetes and PDPN. We are also in agreement with previous studies, which suggested that elevated level of HbA1c, a maker for long-term chronic glycemic exposure, strongly predicted risk of PDPN [22-24]. Older age and BMI higher than 30 in our study were associated with risk of PDPN as in other eastern countries [12].

Burning pain and numbness were the most frequently reported problem associated with patients who have PDPN. Our findings were consistent with a previous study that concluded that PDPN patients frequently reported burning pain and numbness as a characteristic of neuropathic pain[9]. In our study the diagnostic criteria for pain in neuropathy found to be used by physicians and pharmacists was the pain scale

visual analogue scale (VAS). 17.9% of the healthcare providers were using a pain scale and questionnaire to diagnose patients with PDPN. Furthermore, 32.1% were using other ways to diagnose patients with PDPN but these were not stated which raises a concern. From this study it can suggest that diagnostic criteria may exist but used incorrectly or not used at all.

One study, "Talk beyond pain: understanding diabetic nerve pain" (2007) identified that 66% of physicians surveyed in the United Kingdom believed that the most commonly cited reasons for a misdiagnosis of PDPN was due to the lack of information they received from their patients. The National Pain Foundation (NPF) and Eli Lilly and Company, (2007) study suggests that it is necessary to educate patients in order to reduce misdiagnosis[25]. Such a practice could be used within Kuwait to educate patients, but Arabic literature would need to be made available for patients to find out more about what symptoms to look for and what is important to report to the doctor regarding their pain.

Most published practice guidelines recommend pregabalin and gabapentin as first-line treatments for painful DPN, with duloxetine as a second-line treatment[26,27]. Nevertheless, carbamazepine and NSAIDs continue to be prescribed as was notable in our study.

Non-steroidal anti-inflammatory drugs was the most frequent prescribed painkiller in our study. Ziegler et al. reported that 40% received NSAIDs for PDPN[28]. The ease of administration, the availability and relatively less accompanied adverse events were potential factors for initiating NSAIDs[29]. The general practitioners who were familiar with NSAIDs rather than antiepileptic and antidepressant drugs managed most of our patients. This would imply that education of healthcare providers plays a more role in the administration of adequate medications for PDPN. This would explain why only 25% of our cohorts had complete pain response.

There are several limitations in this study. First, this study was cross-sectional which does not allow longitudinal assessment over time. Second, data from only few clinics were included contributing to referral and selection bias which would limit generalization. Finally, patient-reported questionnaires might be subjected to recall bias.

In conclusion, the present study demonstrated a high rate of PDPN among diabetic patients in Kuwait. In line with previous studies, diabetes duration, glycemic control higher BMI were strongly associated with PDPN. Patients with diabetic neuropathies need better education with respect to their glycemic control while physicians treating PDPN are advised to use other treatment modalities as per the established practice guidelines.

The authors declare that there is no conflict of interest regarding publication of this paper.

This work was conducted at 5 clinics in the primary, secondary and tertiary centres in Kuwait.

Significance of the study: Painful diabetic neuropathy is underestimated in Kuwait. We wanted to recognize the problem and how it was managed. We want to highlight this disease and emphasis patient education about their illness and education of general physician who are the first physician who mange this disease.

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