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Peripheral Neuropathy in Patients with Diabetes: Prevalence, Compliance and Quality of life

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Abstract

Aims: This study aimed to assess prevalence of diabetes peripheral neuropathy (PN) and quality of life (QOL) and their associated factors among patients with diabetes in Kuwait. Patients with diabetes PN were anticipated to report worse QOL than those without.

Methods: A cross-sectional study was conducted among 630 adult patients with diabetes. Participants' socio-demographic, and medical history data was collected. The Diabetes Self-Management Questionnaire (DSMQ), and SF-36 QOL tool were employed. Chi-square, student-t, ANOVA tests, and binary logistic and multiple linear regressions were performed.

Results: Diabetes PN prevalence was 54.3%. Mean scores of DSM and QOL were (6.2/10) and (64.8/100) respectively. PN patients showed lower DSM and QOL mean scores than those without (5.8vs.6.5 and 59.2vs.71.5 respectively). Multivariate analysis revealed that mixed diabetic medication, increased number of diabetes complications and co-morbidities, and poor DSM were significant correlates to existing PN and poor QOL. Female patients, long diabetes duration, and poor glycemic control were additional significant correlates to presence of PN.

Conclusion: Diabetes PN was highly prevalent and negatively associated with DSM and QOL. Female gender, clinical history, and DSM contributed significantly to the presence of PN and poor QOL. Further research about PN and DSM based on gender is needed.

***Keywords:** Diabetes mellitus type 2; Peripheral neuropathy, Quality of life, Diabetes self-management*

1. Introduction

Globally, the number of people with diabetes mellitus has quadrupled in the past three decades, and diabetes mellitus is the ninth major cause of death. Worldwide, about one in eleven adults has diabetes mellitus, 90% of them have type 2 diabetes mellitus (T2DM). Asia is a major area of the rapidly emerging T2DM global epidemic [1]. On a smaller scale, the Gulf region shows high competition in the racing prevalence of T2DM, for instance, it is about 24% in Saudi Arabia, 23% in Kuwait, 23% in Qatar, and 22% in Bahrain [2]. In Kuwait (the focus of this paper), according to the International Diabetes Federation, there are 441 thousand diabetics aged from 20 to 79 [3]. The high prevalence of T2DM is highly related to the rapid increase in economic development and per capital income that took place after oil discovery. This was accompanied by

a similar speedy change in lifestyle, in the form of high consumption of high-calorie foods, unhealthy diet and increased obesity and physical inactivity [2]. There is scarce information about the quality of life in adult patients with T2DM in general and who developed diabetes complications in particular in Kuwait, and this is the premise of this paper.

1.1 Diabetes self-management (DSM) and development of complications

Glucose self-monitoring, exercise regimen, maintaining a healthy diet, and foot care are the main principles of diabetes self-management [4]. The cornerstone of diabetes care, as indicated by international and national guidelines, is to maintain good glycemic control. Inconsistency to follow this regimen can accelerate the development of long-term micro- and macrovascular complications [6].Consequently, many patients with type 2 diabetes are on a complex regimen of medications (oral hypoglycemic, insulin injections, or mixed) targeting better glycemic control. The World Health Organization (WHO) has shown that adherence to long-term therapy for chronic illnesses, such as diabetes mellitus, in developed countries averages around 50% [7]. In addition, more than half of patients with diabetes decline either to adhere to the management regimen or to achieve recommended glycemic control [8]. This uncontrolled hyperglycemia enhances the development of long-term complications and increase premature death, along with a substantial increase in financial healthcare burden.

Peripheral neuropathy (PN) is one of the common micro-vascular complications of diabetes, and the focus of this study. Distal symmetric sensorimotor polyneuropathy is the most common type, which starts in the distal extremities and extends proximally; it causes sensory loss in a glove and stocking patterns [9]. PN can be presented in different forms depending on the type of nerves that are affected. Pain of different severity is a common complaint in patients with diabetic PN, in addition to muscle weakness, and altered sensation such as numbness or tingling. If autonomic nerves are affected, patients can suffer from blood pressure changes, heat intolerance, and bowel or bladder dysfunction [10]. Moreover, it is reported that 26% of people with T2DM have evidence of nerve damage at the time that diabetes is diagnosed [11]. Moreover, when diabetic patients lose their ability to sense pain and temperature, they are at increased risk of developing foot and skin injuries [10]. The duration and severity of glycemic variability are major risk factors for the development of diabetic neuropathy [12]. Other risk factors such as age, dyslipidemia, hypertension, and smoking are well-documented [13].

1.2 Quality of life (QOL) and diabetes mellitus

QOL is difficult to define, but it covers many aspects of a person's life measuring satisfaction with one's health, employment, housing, family and other social relationships [14]. Additionally WHO defined quality of life as "individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns."[15].

Previous studies have shown that the quality of life amid patients with diabetes deteriorated with the progression of disease [16]. Several studies revealed that the development of diabetes complication(s) lowers diabetics' quality of life. Patients with PN due to diabetes, on the other hand, had lower health specific quality of life than those without diabetic PN [9]. Furthermore, patients with diabetes have significant impairment in all aspects of QOL [17]. It specifically affects the physical side especially in patients with coexisting morbidities. It can affect the psychological aspect in younger patients and in patients with coexisting depression. In addition, it can destroy family ties and friendships affecting the social aspect. Finally,

diabetes can affect the mental cognitive component particularly when the patient suffers from dementia as well [15]. The progression of disease and the risk of developing complications are in favor of deteriorating diabetics' QOL. Therefore, patients with diabetes have to control their glycemic levels to avoid long-term complications and to insure a better QOL [17].

Kuwait is one of the Gulf countries with a population of 4.5 million, where almost 30% are nationals and the rest are non-nationals who reside in the country for working purposes [18]. According to the body of literature, there is no published data about QOL among adult patients with diabetes in general or with PN in Kuwait. Therefore, the main objectives of this study were to assess the prevalence of diabetic PN, to evaluate the level and factors associated with diabetes self-management (DSM) and quality of life (QOL) according to presence/absence of PN among patients with diabetes attending primary health care (PHC) diabetes clinics in Kuwait. The findings of this study help in filling the gap of knowledge about this area in Kuwait; and are of great importance to patients with diabetes, family medicine physicians, diabetologists, and policy makers. The latter can adopt designing health promotion programs to protect patients with diabetes from developing diabetes complications such as PN, which in turn would improve their QOL.

2. Methods

2.1 Study design and study population

This cross-sectional study was conducted among adult patients with diabetes attending PHC diabetes clinics in Kuwait. To obtain a representative sample of all adult patients with diabetes in Kuwait's six governorates, a stratified random sample technique was employed. A list of all diabetes clinics in the PHC (81 clinics) was obtained from the Ministry of Health. A probability proportional to size sampling method was applied based on the assumption that the number of diabetes clinics in each governorate reflected the population density and therefore the number of patients with diabetes in the corresponding governorate, since the number of patients with diabetes in each governorate was not available. Accordingly, in each governorate, a random number of diabetes clinics proportional to the number of clinics in each governorate was selected. In each diabetes clinic, a purposive convenient sampling procedure was employed to collect data from 630 patients with diabetes who participated in the study and the response rate was 85.1%. The study included 32 diabetes clinics, which represented 39.5% of the PHC diabetes clinics in Kuwait.

2.2 Ethical approval

The Health Sciences Center Ethics Committee approved the study for Research. Furthermore, permission was obtained from the director of each health region. Additionally, each participant signed a written informed consent form, explaining the study objectives prior to his/her participation. The consent form emphasized that the patients' participation was voluntary and they had the right to withdraw at any time of the study without affecting their course of treatment in the clinic.

2.3 The study tool

A self-administered questionnaire was developed in both Arabic and English for convenience sake. It consisted of 28 items divided into four parts, the first (10 questions) contained participants' socio-demographic characteristics such as age, gender, nationality, level of education, family monthly income, working and marital status.

The second section (13 questions) included clinical characteristics of diabetes such as age of disease onset, type of medication (oral, insulin injection, or mixed), and presence of diagnosed diabetes peripheral neuropathy (PN). The duration of the latter was further assessed and the pain intensity was evaluated by using the Numerical Rating Scale (NRS) from 0-10 where "0 = No pain" and "10 = Worst possible pain". The pain scale was further divided to "0: No pain", "1-3: Mild pain", "4-6: Moderate pain", and "7-10: Severe pain". It also included presence of other diabetes complications such as foot ulcer, amputation, retinopathy, nephropathy, and hospitalization. In addition, presence of co-morbidities such as hypertension, hypercholesterolemia, cardiovascular diseases, cancer, and history of stroke, asthma, and arthritis were assessed.

Diabetes Self-Management Questionnaire (DSMQ) was the third section in the form of one stem question. It consists of 16 statements that assess patient's self-care behavior in controlling diabetes during the last eight weeks prior to the study. The test has high reliability (Cronbach's alpha = 0.84) and high validity compared with other scales [19]. Each statement was formulated as a behavioral description from the patient's own point of view and is scored on a 4-point Likert scale that ranges from "0-does not apply to me" to "3-applies to me very much". The total score range is 0-48, and the higher scores indicate a desirable diabetes self-management behavior. The questionnaire generates five sum scores: the 'Sum Scale (SS)' all the 16 statements, as well as four subscale scores, which are labelled as 'Glucose Management (GM)', 'Dietary Control (DC)', 'Physical Activity (PA)', and 'Health-Care Use (HU)'. The score is calculated as sum of the corresponding item scores and then it is converted to a raw score with a scale ranging from 0 to 10, with 10 being the theoretical maximum score indicating the best self-rating of the assessed behavior [20]. The DSMQ was originally developed in English, translation and back translation to Arabic took place to assure precision and accuracy.

As for the last section of the questionnaire, the SF-36 was used (as a stem question) to assess patients' quality of life. The SF-36 covers eight health concepts: physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning, energy/fatigue, and general health perceptions [21]. It also provides an indication of any perceived change in health with one single item out of the 36. Scoring the SF-36 necessitates recoding of the original response into another value from a scoring key that ranges from 0 to 100, where the higher score defines a more favorable health status. In addition, items of the corresponding sub-scores are averaged together to obtain the eight scale scores. The validated English and Arabic versions were used in the study.

In addition to the questionnaire, participant's latest HbA1c, height, and weight were obtained from his/her medical record through the help of the physician or the nurse.

2.4 Statistical methods

The collected data from January to April, 2018 was analyzed using the Statistical Package for Social sciences (SPSS, version 25, IBM, U.S.A.). For descriptive analysis, frequencies, and mean and standard deviation (SD) were considered. The normality of distribution of continuous variables was examined using Shapiro-Wilk test. Both total scores of DSM and QOL were normally distributed.

Participants' HbA1c were divided according to the American Diabetes Association (ADA). HbA1c of <7.0 was considered "Good", values between 7-<9 were categorized as "Moderate", and "Poor" for values ≥ 9. Additionally, the body mass index

(BMI) of participants was calculated according to the World Health Organization (weight in kilograms/square height in meters). The BMI was further divided to underweight (<18.5), normal (18.5-24.9), overweight (25.0-29.9), and obese (30.0+).

To examine the association between presence/absence of PN and socio-demographic as well as medical history characteristics, Chi-square test, student-t, and ANOVA tests were computed. Moreover, Pearson correlation test was calculated to examine the association between DSM and QOL total scores. Furthermore, in order to examine the association between the dependent variable presence/absence of PN and the independent socio-demographic, medical history characteristics, and DSM of respondents, after ruling out the effect of confounders, binary logistic regression model was implemented. Presence of PN was scored as "1" and its absence was scored as "0". In addition, to scrutinize the association between the other outcome variable QOL total score and socio-demographic characteristics, medical history characteristics, and DSM of respondents after adjustment for confounders, multiple linear regression was implemented (residual errors of QOL total score were checked for normality and homoscedasticity did not show a specific pattern). A p-value of <0.05 and Confidence Interval [CI] at 95% were considered statistically significant.

3. Results

The prevalence of diabetes peripheral neuropathy (PN) among study participants was 54.3%. The socio-demographic and medical history characteristics of participants according to the presence or absence of PN is illustrated in TABLE 1. The mean age of participants was 52.3 ± 11.6 years, 53.7% were males, 54.1% were Kuwaitis, and 53.8% were employed. The mean duration of diabetes was 10.8 ± 9.04 years, which was significantly higher among patients with PN than those without. The prevalence of PN was higher among female diabetics than male diabetics (61.3% vs. 48.2% respectively, p=0.001). Most of participants (65.9%) were on oral medication only, which was significantly less among patients with PN (60.5%) than those without (72.2%). The opposite picture is shown in regards to insulin injection as a line of treatment. Poor level of HbA1c (9.0+) was prevalent significantly more among patients with PN than those without (66.7% vs. 33.3% respectively). Moreover, severity of pain, number of diabetes complications other than PN (2+) and number of co-morbidities (3+) were also significantly higher among patients with PN than those without.

TABLE 1. **Association between socio-demographic characteristics and the presence or absence of peripheral neuropathy (PN) among patients with diabetes attending diabetes clinics in PHC (n=630).**

Characteristic	**Total**		**Diabetes with PN (n=342)**		**Diabetes (n=288)**		**p-value**
	n	**(%)**	**n**	**(%)**	**n**	**(%)**	
Age (years)							0.329
<45	171	(27.2)	85	(49.7)	86	(50.3)	
45-59	276	(43.9)	157	(56.9)	119	(43.1)	
60+	182	(28.9)	100	(54.9)	82	(45.1)	
Mean ± SD	*52.3 ± 11.6*		*53.2 ± 11.3*		*51.3 ± 11.9*		0.054
Gender							**0.001**
Male	338	(53.7)	163	(48.2)	175	(51.8)	

Female	292	(46.3)	179	(61.3)	113	(38.7)	
Nationality							**0.056**
Kuwaiti	341	(54.1)	197	(57.8)	144	(42.2)	
Non-Kuwaiti	289	(45.9)	154	(50.2)	144	(49.8)	
Marital status							0.332
Married	517	(82.1)	276	(53.4)	241	(46.6)	
Not married	113	(17.9)	66	(58.4)	47	(41.6)	
Monthly income (KD)							0.582
< 1000	331	(52.5)	180	(54.4)	151	(45.6)	
1000-<2000	169	(26.8)	96	(56.8)	73	(43.2)	
2000+	130	(20.6)	66	(50.8)	64	(49.2)	
Educational level							0.531
Up to high school	313	(49.7)	166	(53.0)	147	(47.0)	
Diploma/University	317	(50.3)	176	(55.5)	141	(44.5)	
Working status							**0.024**
Working	339	(53.8)	170	(50.1)	169	(49.9)	
Non-Working	291	(46.2)	172	(59.1)	119	(40.9)	
Smoking status							0.511
Smoking	107	(17.0)	55	(51.4)	52	(48.6)	
Not Smoking	523	(83.0)	287	(54.9)	236	(44.1)	
BMI							0.118
Normal	116	(18.4)	60	(51.7)	56	(48.3)	
Overweight	237	(37.6)	120	(50.6)	117	(49.4)	
Obese	277	(44.0)	162	(58.5)	115	(41.5)	

TABLE 1: **(Cont).**

Characteristic	**Total**		**Diabetes with PN (n=342)**		**Diabetes (n=288)**		**p-value**
	n	**(%)**	**n**	**(%)**	**n**	**(%)**	
Duration of disease (years)							**<0.001**
≤ 5	222	(35.4)	94	(27.6)	128	(44.8)	
6-10	144	(23.0)	79	(23.2)	65	(22.7)	
10+	261	(41.6)	168	(49.3)	93	(32.5)	
Mean ± SD	*10.8 ± 9.0*		*53.2 ± 11.3*		*8.8 ± 7.9*		**<0.001**
Type of medication							**<0.001**
Oral only	415	(65.9)	207	(60.5)	208	(72.2)	
Injections only	79	(12.5)	40	(11.7)	39	(13.5)	
Mixed	136	(21.6)	95	(27.8)	41	(14.2)	
HbA1c							**0.001**
Good (<7.0)	152	(26.5)	75	(49.3)	77	(50.7)	
Moderate (7.0-<9.0)	248	(43.2)	129	(52.0)	119	(48.0)	
Poor (9.0+)	174	(30.3)	116	(66.7)	58	(33.3)	

Pain level in hands and feet							**<0.001**
No pain	293	(46.5)	49	(14.3)	244	(84.7)	
Mild	99	(15.7)	73	(21.3)	26	(9.0)	
Moderate	199	(31.6)	183	(53.5)	16	(5.6)	
Severe	39	(6.2)	37	(10.8)	2	(0.7)	
Number of diabetes complications other than PN							**<0.001**
0	354	(56.2)	149	(43.6)	205	(71.2)	
1	167	(26.5)	104	(30.4)	63	(21.9)	
2+	109	(17.3)	89	(26.0)	20	(6.9)	
Number of comorbidities							**<0.001**
0	111	(17.6)	41	(12.0)	70	(24.3)	
1	143	(22.7)	69	(20.2)	74	(25.7)	
2	183	(29.0)	88	(25.7)	95	(33.0)	
3+	193	(30.6)	144	(42.1)	49	(17.0)	

In addition, diabetes self-management (DSM) mean of sum score and sub-scores according to the presence or absence of PN were portrayed in FIG. 1. The mean DSM sum score was 6.2/10 among participants. Patients with diabetes and PN showed significantly lower DSM means than those with PN in the sum score (5.8 vs. 6.5), glucose monitoring (6.6 vs. 7.0), diet control (4.9 vs. 5.8), physical activity (4.7 vs. 5.2), and health care utilization (6.7 vs. 7.8) respectively. Further analysis of DSM sub-scores according to gender showed that male patients reported better DSM mean scores than females in regards to DC (5.5 vs. 5.1, p=0.008), PA (5.2 vs. 4.7, p=0.01), and the overall SS (6.3 vs. 6.0, p=0.004) respectively.

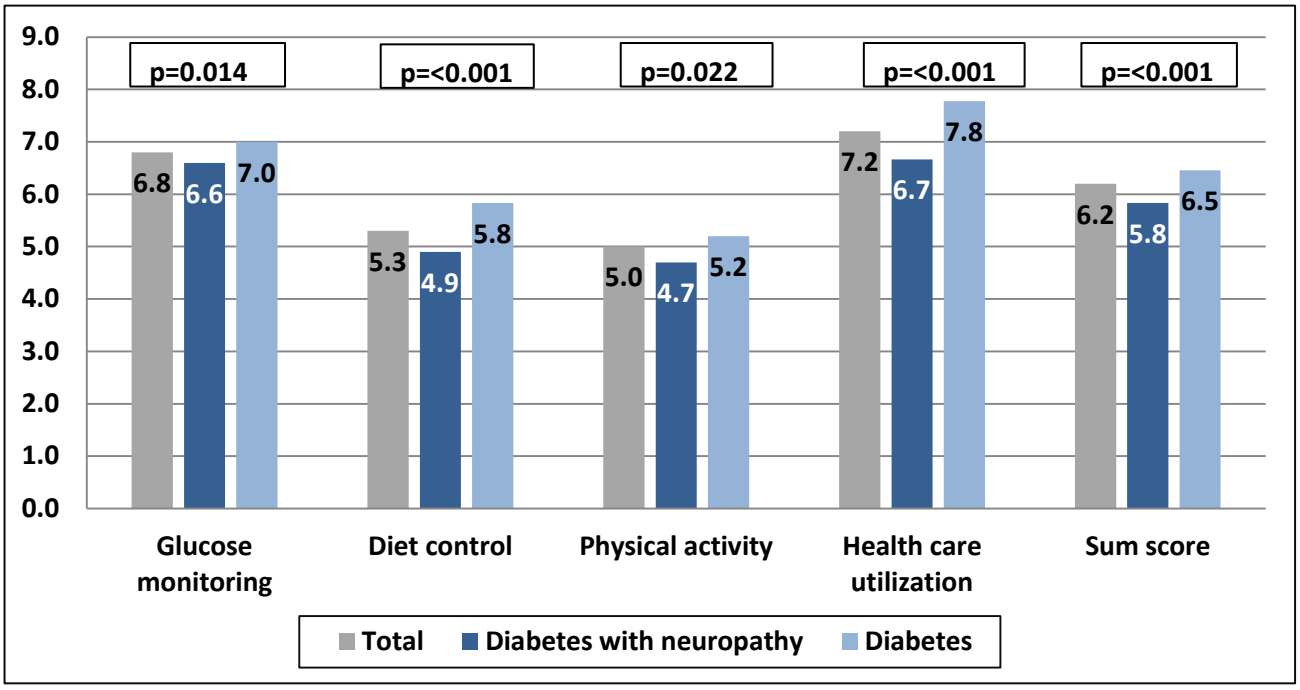

FIG. 1. **Means of Diabetes Self-Management sum score and sub-scores according to the presence or absence of PN among patients with diabetes attending diabetes clinics in PHC (n=630).**

Furthermore, FIG. 2 demonstrated the means of quality of life (QOL) total score and sub-scores according to the presence or absence of PN among participants. Patients with diabetes without PN showed significantly better quality of life than those with PN in regards to QOL total mean score (71.5 vs. 59.2 respectively) and all sub-categories mean scores with a p<0.001 for each.

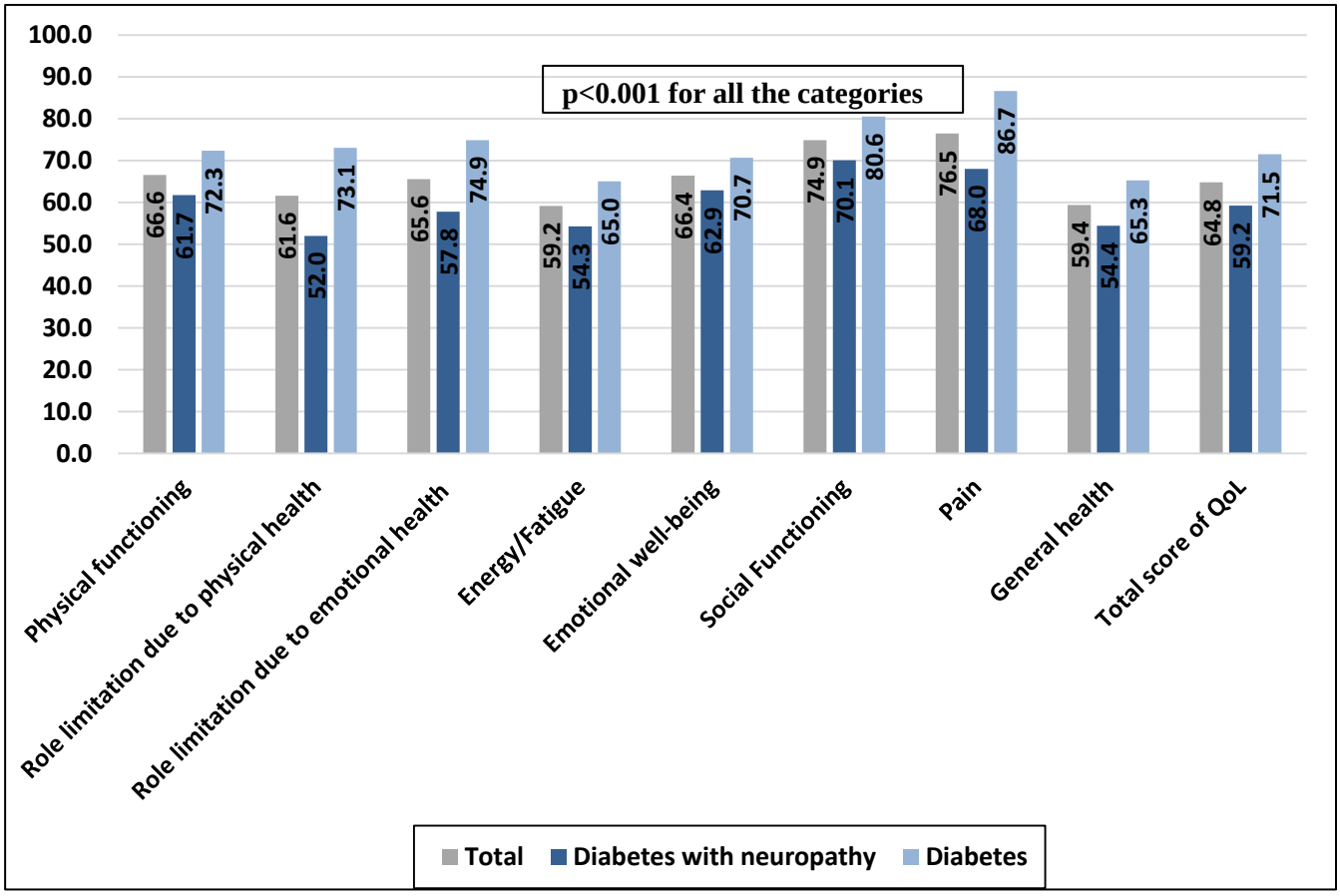

FIG. 2. **Means of Quality of life total score and sub-scores according to the presence or absence of PN among patients with diabetes attending diabetes clinics in PHC (n=630).**

The Pearson correlation between DSM sum score and QOL total score showed a good positive significant correlation between both of them (r=0.354, p<0.001). This meant that the more the DSM among patients with diabetes, the better would be their QOL.

Moreover, the association between the means of QOL total score and socio-demographic as well as medical history characteristics of participants is presented in TABLE 2. For socio-demographic characteristics, relatively young participants (<45 years old), male patients, non-Kuwaitis, patients with monthly income of >2000 KD (Kuwaiti Dinar =3.3 $ US), working participants, and those who have normal BMI showed better QOL mean total score than other correspondents. In regards to medical history characteristics, there was a significant gradual inverse association between mean of QOL total score and duration of diabetes, level of HbA1c, level of pain, number of diabetes complications other than PN (e.g. nephropathy, retinopathy, etc.), and number of comorbidities. Additionally, being on only oral medication and absence of PN were associated with better QOL mean scores.

TABLE 2**: Association between quality of life (QOL) mean total score and socio-demographic, and medical history characteristics among patients with diabetes attending diabetes clinics in PHC (n=630).**

Socio-demographic Characteristics	QOL Mean ± SD	p-value	Medical history Characteristics	QOL Mean ± SD	p-value
Age (years)		**0.016**	**Duration of disease (years)**		**0.001**
<45	65.7 ± 18.3		≤ 5	67.6 ± 18.5	
46-59	66.4 ± 16.3		6-10	65.9 ± 16.1	
60+	64.8 ± 19.4		10+	61.7 ± 17.9	
Gender		**<0.001**	**Type of medication**		**<0.001**
Male	67.8 ± 16.4		Oral only	67.3 ± 17.1	
Female	61.4 ± 18.8		Injections only	61.2 ± 17.9	
			Mixed	59.4 ± 18.7	
Nationality		**0.001**			
Kuwaiti	62.8 ± 19.5		**HbA1c**		**0.002**
Non-Kuwaiti	67.3 ± 15.4		Good (<7)	68.4 ± 17.5	
			Moderate (7-<9)	63.7 ± 17.3	
Marital status		0.120	Poor (9+)	61.5 ± 18.7	
Not married	62.2 ± 20				
Married	65.4 ± 17.3		**Presence of diabetic PN**		**<0.001**
			No	71.5 ± 15.9	
Education level		0.210	Yes	59.2 ± 17.5	
Up to high school	63.9 ± 18.2				
Diploma/university	65.7 ± 17.5		**Pain level in hands and feet**		**<0.001**
			No pain	71.6 ± 16.1	
Working status		**<0.001**	Mild	62.8 ± 18.0	
Working	67.6 ± 16.7		Moderate	59.8 ± 15.0	
Not working	61.3 ± 18.7		Severe	45.0 ± 19.9	
Smoking status		0.387	**Number of diabetes complications**		**<0.001**
No	64.6 ± 18.1		0	69.9 ± 15.7	
Yes	66.2 ± 16.9		1	63.3 ± 17.8	
			2+	50.8 ± 16.7	
Monthly income (KD)		**0.048**			
<1000	65.4 ± 16.5		**Number of comorbidities**		**<0.001**
1000-2000	62.1 ± 18.8		0	72.3 ± 16.7	
2000+	66.9 ± 19.6		1	69.5 ± 16.0	
			2	66.8 ± 16.2	
BMI		**0.003**	3+	55.2 ± 17.4	
Normal	67.4 ± 17.8				
Overweight	66.8 ± 16.2				
Obese	62.1 ± 19.0				

TABLE 3 illustrated the binary logistic regression of significant factors correlated with the presence of PN among participants after adjustment for confounders. The table revealed that gender significantly correlated to reporting PN. Female patients with diabetes were 1.55 times more likely to report PN than males [95% CI: 1.06-2.28, p=0.025]. Moreover, duration of diabetes was a significant correlate to reporting PN. Patients who had diabetes for 10 or more years were 1.81 higher odds to report PN than those who had diabetes for less than five years [95% CI: 1.17-2.82, p=0.026]. In addition, compared to those on oral medication, patients on mixed medication were 1.7 times more likely to report PN [95% CI: 1.03-2.83, p=0.04]. Regarding HbA1C, patients with poor diabetes control (HbA1c=9+) were 1.82 times more likely to report PN than those with good glycemic control (HbA1c<7). Additionally, participants who reported one and 2+ diabetes complications other than PN (e.g. nephropathy, retinopathy, etc.) were 2.04 and 3.99 times (respectively) more likely to report PN compared to their counterparts who did not report any diabetes complications. Furthermore, participants who reported 3+ comorbidities were at 3.12 higher risk to reporting PN compared to those who did not report any comorbidities [95% CI: 1.74-5.57, p<0.001]. Additionally, the table showed that DSM was an independent correlate to reporting PN. One-unit increase in the DSM sum score was associated with 86% lower risk to report PN, p=0.019.

TABLE 3**. Binary logistic regression of significant factors associated with presence of peripheral neuropathy (PN) among patients with diabetes attending diabetes clinics in PHC (n=630).**

Characteristics	Sub-group n	Crude OR for presence of PN			Adjusted[a] OR for presence of PN		
		OR	[95% CI]	p-value	OR	[95% CI]	p-value
Socio-demographic Characteristics							
Gender				0.001			0.025[a]
Males	338	1	[RG*]		1	[RG]	
Females	292	1.7	[1.24-2.34]		1.55	[1.06-2.28]	
Medical history Characteristics							
Duration of diabetes (years)				<0.001			0.026[b]
≤ 5	222	1	[RG]		1	[RG]	
6-10	144	1.66	[1.09-2.53]	0.019	1.53	[0.94-2.51]	0.091
10+	261	2.46	[1.70-3.55]	<0.001	1.81	[1.17-2.82]	0.008
Type of medication				<0.001			0.024[b]
Oral only	415	1	[RG]		1	[RG]	
Injections only	79	1.03	[0.64-1.67]	0.902	0.67	[0.37-1.23]	0.192[b]
Mixed	136	2.33	[1.54-3.52]	<0.001	1.7	[1.03-2.83]	0.040[b]

Number of diabetes complications (other than PN)				<0.001			<0.001[b]
0	354	1	[RG]		1	[RG]	
1	167	2.27	[1.56-3.31]	<0.001	2.04	[1.32-3.13]	0.001[b]
2+	109	6.12	[3.61-10.39]	**<0.001**	3.99	[2.09-7.64]	**<0.001[b]**
No. of comorbidities				**<0.001**			**<0.001[b]**
0	111	1	[RG]		1	[RG]	
1	143	1.59	[0.96-2.64]	0.072	1.37	[0.76-2.45]	0.293[b]
2	183	1.58	[0.98-2.56]	0.063	1.1	[0.63-1.90]	0.745[b]
3+	193	5.02	[3.03-8.30]	**<0.001**	3.12	[1.74-5.57]	**<0.001[b]**
HbA1C				**0.002**			**0.025[b]**
<7 (good)	152	1	[RG]		1	[RG]	
7-<9 (moderate)	248	1.11	[0.74-1.67]	0.604	1	[0.64-1.57]	0.998[b]
9+ (poor)	174	2.05	[1.31-3.21]	**0.002**	1.82	[1.09-3.04]	**0.023[b]**
Diabetes Self-Management (DSM)							
DSM (Sum Score)	630	0.74	[0.66-0.83]	**<0.001**	0.86	[0.76-0.98]	**0.019[c]**

[*]RG = Reference group

[a]Model 1: covariates included age, gender, nationality, marital status, monthly income, educational level, and BMI

[b]Model 2: covariates in model 1 and duration of disease, type of medication, HbA1c, level of pain, number of diabetes complications (other than diabetic PN) and comorbidities

[c]Model 3: covariates in model 2 and DSM sum score.

TABLE 4 illustrated the multiple linear regression of significant factors associated with QOL total score among participants. Shifting from oral medication to injections or mixed medications was associated with a decrease in the QOL by 3.61 [95% CI: -6.28 - -0.94, p=0.008]. The table also showed that for each unit increase in pain score (0-10), participant's QOL was reduced by 1.31, [95% CI: -1.82 - -0.80, p<0.001]. In addition, QOL was decreased by 3.18 for the unit increase in the number of diabetes complications [95% CI: -4.55 - -1.81, p<0.001], and by 2.78 for every unit increase in the number of

comorbidities [95% CI: -3.72 - -1.83, p<0.001]. Furthermore, one unit increase in DSM sum score was associated with improvement in participant's QOL by 2.27 [95% CI: 1.44 - 3.11, p<0.001].

TABLE 4**. Multiple linear regression of significant factors associated with QOL total score among patients with diabetes attending diabetes clinics in PHC (n=630).**

Characteristics	Adjusted difference[a] in mean		
	QOL total score		
	Coefficient β	[95% CI]	p-value
Medication (oral* vs. others**)	-3.61	[-6.28 - -0.94]	0.008 [b]
Pain score	-1.31	[-1.82 - -0.80]	<0.001[b]
Number of diabetes complications	-3.18	[-4.55 - -1.81]	<0.001[b]
Numbers of comorbidities	-2.78	[-3.72 - -1.83]	<0.001[b]
Diabetes Self-Management (DSM) (Sum Score)	2.27	[1.44 - 3.11]	<0.001[d]

*Reference group, **Injections and mixed types of medications

[a]Model 1: covariates included age, gender, nationality, marital status, monthly income, educational level, and BMI

[b]Model 2: covariates in model 1 and duration of disease, type of medication, HbA1c, level of pain, number of diabetes complications and comorbidities

[c]Model 3: covariates in model 1 and duration of disease, type of medication, HbA1c, level of pain, diabetic PN, and number of comorbidities

[d]Model 4: covariates in model 2 and DSM sum score

4. Discussion

This cross-sectional study conducted amid 630 patients with diabetes attending PHC diabetes clinics in Kuwait revealed that the prevalence of diabetic PN was 54.3%, participants generally showed a modest level of DSM and QOL, while those with PN arrayed poorer levels of DSM and QOL than those without. The multivariate analysis revealed that female gender, duration of diabetes (≥10 years), taking mixed medications (oral and injections), poor HbA1c, having two or more diabetes complications (other than diabetic PN), having three or more comorbidities, and poor DSM were significant correlates to the presence of diabetic PN. In addition, the multiple linear regressions revealed that being on diabetes mixed medication, increased level of pain, increased number of diabetes complications and comorbidities were significant independent correlates to poor QOL in patients with diabetes. Moreover, DSM was positively correlated with better QOL.

4.1 Prevalence of Diabetic Peripheral Neuropathy (PN)

Diabetic PN was prevalent among more than half of patients with diabetes in this study. This prevalence is in agreement with the 53.7% prevalence of diabetic PN in a study conducted in the Middle East [22]. Additional published studies in the Gulf Region have reported prevalence of 65.3% in Saudi Arabia [23], and 35%in UAE [24]. However, a study conducted in United Kingdom concluded a much lower prevalence of 28.5% [25]. This noticeable difference might be related to poor glycemic control among patients with diabetes in the Gulf region.

4.2 Factors associated with diabetic PN

An important finding in this study that female gender was a significant independent correlate to the presence of diabetic PN. This finding is in concordance with the findings of preceding studies conducted in the Middle East region [22,26]. However, other studies found that the male gender was a significant predictor for diabetic PN rather than female gender [27,28]. Significant gender dimorphisms in the responsiveness of patients to anti-diabetic drugs might explain this debate [29]. Then it may be hypothesized that earlier interventions in the female population may improve disease outcomes. In addition, females in this study showed poorer level of DSM than males on the bivariate level in the diet control and physical activity sub-categories. However, after adjustment for confounders, female gender was a persistent contributor to the presence of PN. Further qualitative gender based research is required to understand the cultural and subjective barriers for practicing good DSM.

Another finding in this study was that the long duration of diabetes (≥ 10 years) significantly contributed to the presence of diabetic PN. This finding was also in concordance with preceding studies conducted in Belgium [26], in the Middle East [22], in UAE [27], and in Iran [28]. The latter reported that the risk of microvascular diabetic PN is directly proportional to the duration of hyperglycemia and that of diabetes. This was an anticipated finding since long exposure to poor glycemic control would precipitate the development of microvascular complications as previously mentioned [30].

In addition, this study found that diabetes mixed medication was an independent contributor to the presence of diabetic PN, rather than oral medication only. This was also an expected result; since diabetics particularly type 2 diabetes have to add insulin injections on top of oral tablets when the glycemic control was very difficult and associated with high HbA1c for long period (≥10 years) as the study depicted. This finding is well reported as it might be harder for patients on both medications to be compliant which makes them more prone to develop diabetic PN [22,31]. In addition, this might be explained by the fact that patients who take mixed medications are at a worse stage of the disease than those using either. In addition, in a 10-year follow-up study of people with normal glucose tolerance, impaired glucose tolerance and type 2 diabetes, found an association between HbA1c and peripheral neuropathy [32]. They also reported that as HbA1c increases by 1%, the amplitude of sural nerve function decreases by 1%, regardless of the group classification.

Moreover, the more reported diabetes complications (other than diabetic PN such as nephropathy, retinopathy, foot ulcers, amputations, and hospitalization due to diabetes), the higher the chance of reporting diabetic PN in this study. This result is matching with another study which concludes that the more number of diabetic complications the patient has, the more likely he/she will complain of diabetes PN [33]. In addition, another study conducted in the United States found a positive

association between both retinopathy and nephropathy with neuropathy [34].This could be explained as evidenced that neuropathy, as well as both retinopathy and nephropathy are all microvascular complications of diabetes and have similar pathogenesis. The mechanism of this pathogenesis occurs due to chronic hyperglycemia and is characterized by production of advanced glycation end products (AGEs), pro inflammatory microenvironment, and oxidative stress [35]
Additionally, in this study patients who reported having three or more other comorbidities (hypertension, CVS, stroke, cancer, etc.), reported diabetes PN more than those with less number did. This could be explained that some of these comorbidities such as stroke and cardiovascular diseases share the same risk factors for diabetes. Some of these shared risk factors are obesity, poor diet, and sedentary life style as reported earlier [36]. This result is backed by a previous study, which showed that cardiovascular disease is more common in diabetic hypertensive patients than in diabetics alone; it also mentioned that combined comorbidities accelerates the development of microvascular and macro vascular complications among diabetics [37].

4.3 Factors associated with QOL in patients with diabetes

This study illustrated that overall, participants showed modest level of QOL and it was better among patients with diabetes and without PN than those with PN. This finding is supported by a study which shows that diabetes PN has a statistically significant negative impact on the quality of life [38].

Furthermore, this study revealed that shifting from oral to mixed diabetes medication (oral and injections) was associated with poor QOL amid patients with diabetes. This was an expected finding since patients with diabetes on oral medication have most probably better glycemic control, which in turn protect them from developing diabetes complications, which deteriorate the patients' QOL in many domains.

This finding is in agreement with a previous study, which found that a better QOL in patients with diabetes treated with oral hypoglycemic medication, than those on mixed medication [39]. Additionally, an earlier study recorded that as the treatment intensity increases, hence moving from diet to oral medications to insulin, the quality of life decreases [40].

Moreover, the reverse association between the level of pain reported by patients with diabetes and their QOL was another finding in this study. This result is well documented in previous studies. For instance, [41] Bair et al. found that pain was prevalent among more than half of patients with diabetes and it was strongly associated with poor health-related quality of life. Another study conducted to assess the nature and extent of pain in diabetes PN patients, also found that pain had a negative impact on the QOL of diabetic patients by interfering with their sleep, enjoyment of life, recreational activities, normal work, mobility, general activity, social activities, and mood [42].

In addition, this study revealed that the number of diabetes complications was inversely associated with diabetics' QOL. This expected result is supported by a study among patients with diabetes in the United Kingdom [40]. Furthermore, a Norwegian study shows that patients with two or more diabetes complications report much lower QOL than patients with one complication [43]. Diabetes complications such as PN, retinopathy, nephropathy, foot ulcers, amputations or others would definitely crumble the patients' QOL in a way or another.

Although this study revealed that diabetics with PN showed poorer QOL than those without in all QOL domains, it is important to disclose that diabetes PN by itself was not a significant correlate to poor QOL in this study rather than the number of diabetes complications, regardless its nature, after adjustment for confounders. This points out that PN, which is usually associated with pain and in many instances with other diabetes complications, would affect the diabetics' QOL negatively. In other words, the higher the number of diabetes complications the patient would suffer from, the poorer QOL the patient would certainly have, irrespective to the type of diabetes complications.

Furthermore, majority of participants (82%) in this study reported at least one co-morbidity, and almost one third had three or more. This finding is matching with the results of another study which reports that most of patients with diabetes in their study have at least one comorbid disease and 40% have at least three[44].

In addition, this study pointed out that the number of co-morbidities was a significant correlate to lower level of quality of life among patients with diabetes. Several preceding studies support this finding. For example, a study concluded that as the number of comorbidities increased, the QOL decreased among patients with diabetes [45]. Another study showed that the number of comorbidities is one of the most important predictors of a negative QOL among patients with diabetes [35].

4.4 Diabetes Self-Management and diabetes PN and QOL

A significant finding in this study was that poor DSM, was a significant independent correlate to reporting diabetes PN. DSM is explained in the form of diabetes monitoring, diet control, physical activity, beside to adherence to regular diabetologist visit and compliance with medication. Patients with diabetes PN in this study showed lower level of DSM than those without in all subcategories. This suggests that better DSM protects diabetics from developing PN.

This anticipated finding is supported by Giugliano et al. (2018) who concluded that poor adherence to medication amid patients with diabetes affects the microvascular complications such as, retinopathy, nephropathy, and neuropathy development. They added that groups with more intense glucose control avoided 2% of the risk of developing PN than those with less intense glucose management [46]. Compliance to diabetes medication and lifestyle modification play an important role in preventing or delaying the development of diabetes complications.

This was reported in a previous study in the US, which showed that compliance affects the level of neuropathic pain and its progression in patients with diabetes [47]. In addition, another study established that poor physical activity and nutritional factors are associated with acquiring diabetes complications [48].

For DSM and QOL, this study found that proper diabetes self-management (DSM) was positively correlated to better QOL and a significant contributor to better QOL after adjustment for confounders. This finding is consistent with the results of a previous study conducted in Thailand among patients with type 2 diabetes, and found that DSM program improved the QOL of those patients [49]. Another study concluded that physical inactivity (a subcategory of DSM) is related to poor QOL and should be considered as effective measure together with diet control in improving the QOL of patients with diabetes [50].

This study encountered some limitations. The study design was cross-sectional; therefore, causation inferences are limited. Severe cases of patients with complications were missed due to their inability to attend PHC centers; rather they go directly to the secondary health care centers (hospitals). This might have underestimated the prevalence of diabetes PN in this study.

5. Conclusions

Diabetic peripheral neuropathy was prevalent alarmingly high among diabetic patients attending primary health care diabetes clinics in Kuwait. Diabetic participants reported modest levels of DSM and QOL; and those with PN showed worse levels of DSM and QOL than those without. Patients' gender as well as diabetic and medical history characteristics were significant contributors to the presence of diabetes PN and poor QOL. Health planners, policy makers, and family physicians ought to set holistic diabetes management strategies to prevent the development of diabetes complications and promote adopting healthy lifestyle among patients with diabetes in Kuwait. Future studies to examine the barriers behind proper DSM care separately by presence of PN and gender based are needed.

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