# Prevalence of Peripheral Neuropathic Pain among Adult Diabetic Patients (T2DM) with Peripheral Neuropathy and Quality of Life of the Patients with Peripheral Neuropathic Pain

**Jawad Ahmad Abu-Shennar** ( jawad_0799@yahoo.com )
Near East University: Yakin Dogu Universitesi https://orcid.org/0000-0002-0505-5356

**Nurhan Bayraktar**
Near East University: Yakin Dogu Universitesi

**Hatic Bebis**
Near East University: Yakin Dogu Universitesi

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# Abstract

**Aim** The aim of the study was to assess the prevalence of diabetic peripheral neuropathic pain (DPNP) among adult patients suffering from type 2 diabetes mellitus (T2DM) with diabetic peripheral neuropathy (DPN) as well as to determine the quality of life of patients with DPNP.

**Materials and method** The study designed in cross-sectional research model was conducted at the Jordanian Ministry of Health in Jordan, Amman during the period from 15 June 2019 to 5 October 2019. A total of 400 adult T2DM patients with DNP were recruited for the study. Data were collected by way of an assessment tool package, including descriptive data (demographics, anthropometric measurements, laboratory measurements, and clinical data), the Douleur Neuropathique4 (DN4) questionnaire, physical exam, Quality of Life Questionnaire (EQ-5D), and Numeric Pain Rating Scale (NRS). To analyze study data descriptive and inferential statistics were used.

**Results** Results of the current study showed that the prevalence of DPNP among adult T2DM patients with DPN was high (47.8%). About half of the participants had mild or moderate pain with the most frequently reported symptoms of tingling and burning. Uncontrolled diabetes was found to be the main predictor of DPNP among patients with DPN. Participants who had DPNP reported having problems in connection with mobility, self-care, routine activities, discomfort, and anxiety or/and depression, and they had a significantly lower quality of life with poorer self-rated health status than those without DPNP. Besides, the effect of pain on their quality of life was found to be significant.

**Conclusion** The study recommends, in accordance with the results, that strategies should be developed for an effective management of painful DPN with an integrated and interdisciplinary approach. Current clinical guideline recommendations should be followed to improve patient care and reduce the burden of the disease.


# Introduction

Diabetes mellitus is a common, chronic medical condition worldwide. Due to an aging population, and changes in diet and lifestyle, it is rapidly becoming more widespread [1]. T2DM and its complications constitute a main public health problem, affecting people in both developed and developing countries with high rates of diabetes-related mortality and morbidity [2]. International Diabetic Federation in most recent estimates indicates that 8.3% (382 million people) of the world population have diabetes, and the number of people suffering from the disease is set to rise beyond 592 million (10.1%) by 2035, with the majority of patients between 40 to 59 years of age, and 80% living in low and middle-income countries [3]. The incidence of diabetes mellitus in the Middle East Region has also increased over the previous decade [4]. In Jordan, the prevalence of T2DM and impaired fasting glucose (IFG) were 17.1% and 7.8%, respectively [5]. In the Kingdom of Saudi Arabia, the prevalence of DM was 30% [6]; In respect of DM prevalence, Saudi Arabia, Kuwait, and Qatar have ranked among the top 10 (at positions 7, 8 and 9) in the world with a prevalence of 24%, 23% and 23%, respectively [3].

Diabetic peripheral neuropathy (DPN) is the most common complication of diabetes mellitus, affecting up to 50% of patients [7]. This complication is defined as the presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes [8, 9, 10]. DPN is associated with significant morbidity and mortality, and is a very common cause of non-traumatic amputations, increased hospitalizations, and increased health-related costs [1, 7, 11, 12, 13].

Diabetic peripheral neuropathic pain (DPNP) is an important problem among patients with DPN [14]. Many studies in Europe have shown that the global prevalence of DPN range between 40 and 50% [15]. Additionally, according to data from a Cohort study among almost 7.5 million individuals contributing 38,118,838 individual-years of observations in the UK, 6,779 new cases of DPNP were identified, yielding an incidence rate of 17.8 per 100,000 individual-years [16].

International Association for the Study of Pain defined DPNP as pain arising as a direct consequence of abnormalities in the peripheral somatosensory system in people with diabetes [7]. DPNP often involves sensations such as burning, tingling, electric shock, sharp shooting, and lancinating [1, 17]. This problem is associated with a high degree of functional impairment, deterioration in health-related quality of life, and activities of daily living [4]. The pain usually interferes with daily living activities, mood, work, mobility, and social relations. The impaired health could have a negative impact on the patients' quality of life (QoL) with poor self-rated health status and may cause sleep disruption and depression in some cases. Diabetic neuropathic pain causes higher societal and health care costs compared to diabetes without neuropathic pain [1, 17]. As this condition progresses, the damage to peripheral nerves can be permanent, with loss of sensation leading to sores, ulcers, and lower limb amputation [18, 19, 20].

Effective management of DPNP is necessary to prevent the negative impacts of DPNP on the patients' QoL. Guidelines for clinical practices for patients with diabetes recommend screening of all patients diagnosed with DM for neuropathy, maintenance of glycemic control, and pain management to improve outcomes and the quality of life in those patients [1, 2]. Thus, early detection in primary care settings is necessary to increase awareness of patients to initiate measures to prevent further complications, which may lead to improved planning and selection of the appropriate interventions [2].

The determination of the prevalence of DPNP among diabetic patients with DPN and Quality of Life of the Patients with DPNP is important for a rational planning and allocation of resources. Clearer knowledge of DPNP and its impact on patients' quality of life (QoL) would be of major importance for the appropriate strategies to deliver optimal patient care and prevent the related problems. Although there is a growing awareness among health care professionals regarding DPNP, there remains a lack of information that is crucial for improving the management of DPNP. Furthermore, the fact that DPNP is an often underdiagnosed and undertreated disease raises the need for further research on this subject.

The primary objectives of the present study were to determine the prevalence of DPNP among diabetic patients with DPN and quality of life of the patients with DPNP in Jordan. The secondary objectives were to assess the socio-demographic and clinical-laboratory characteristics of patients with DPN, nature and

severity of pain among patients with DPNP, and associated factors with DPNP including socio-demographic factors, anthropometric measurements, and clinical data from the patients.

# Methodology

### Study design

The study designed in cross-sectional survey model was performed on adult T2DM patients diagnosed with DPN in a time-span between 15 June 2019 and 5 October 2019.

### Setting

The study was conducted at the Jordanian Ministry of Health. The three hospitals involved function under the Ministry of Health of Jordan. The researcher chose this setting because it receives referrals from all medical sectors in different parts of Jordan, based particularly on the assumption that the selected setting would provide a profile of patients with diabetes from different parts of Jordan. This center was established in 1921 in Jordan, Amman with an annual admission rate of 25,000 patients of all disease types, and provides services to all patients from all around Jordan. It also provides screening services for each patient presenting to the centers (clinics and hospitals) functioning under the Ministry of Health of Jordan. The services include the monitoring of patients with diabetes mellitus every three months, and in addition routine measurements of blood glucose HbA1c, blood pressure, weight, height, and waist circumference that are performed during each visit. Every day the medical staff responsible for records in each clinic pick up the patients' medical files, and put them available for use on the nursing desk. Once the patients show up, they are received by a qualified nurse who performs some physical examinations required before the examination and treatment by the physician. There are also several clinics in centers specialized in addressing the complications of diabetes.

### Sampling And Sample Size

The target population for this study consisted of adult patients (T2DM) having a DPN. The accessible population included all the patients presenting to the Ministry of Health of Jordan during the period between 15 June 2019 and 5 October 2019, and those who were ≥ 18 years of age and had been regularly monitored in the hospitals for at least six months were included in the study.

The sample size for this study was calculated using the equation ($n=(Za/2)^2 Pq / ^{2)}$ with a confidence level (CL) of 95%, expected prevalence of 50%, and margin error of 5%. The calculation indicated a sample size of 375 participants [21]. The researcher accordingly increased the sample size to 100% to compensate for the attrition rate and missing data. As a result, the final estimated sample included 400 participants.

Patients with T1DM were not included because they were beyond the purpose of the study. Adult patients who had undergone an amputation were also excluded from the study due to limited possibilities to

perform a physical examination on them. Besides, patients who did not give consent or failed to respond to the questionnaire were not included in the study as well.

## Study Instruments

An assessment tool package consisting of five tools, namely (1) descriptive data (demographics, anthropometric measurements, laboratory measurements, and clinical data, (2) Douleur Neuropathique4 (DN4) questionnaire, (3) Physical exam (second section from the DN4 questioner), (4) Quality of Life Questionnaire (EQ-5D), (5) Numeric Pain Rating Scale (NRS) were used in the research project.

The first tool was developed by the researcher and consisted of the patients' demographic data (such as file number, age, gender, marital status, income, working status, and level of education. Smoking status [22] included the categories of current smoker (namely one who has smoked 100 cigarettes in his/her lifetime), ex-smoker (adults who have smoked more than 100 cigarettes in their lifetime, but have not smoked in the last 28 days), and non-smokers (being an adult who has never smoked or one who has smoked less than 100 cigarettes in his/her lifetime). Besides, it also includes the type of treatment (which includes insulin, oral hypoglycemic agents (OHA's) or both OHA's and insulin) and type of medication (which includes metformin, anti-hypertensive treatment, and statin). Data regarding anthropometric measurements (based on the latest reading), laboratory measurements (also based on the latest reading), and clinical data were obtained from the clinical records of the subjects. These data procedures followed the following process:

## Anthropometric Measurements

Anthropometric measurements made under the following criteria included weight, height, waist circumference, and blood pressure systolic/diastolic.

### Weight

Weight was measured for each patient; it was taken barefooted with light clothing rounded down to the nearest 0.5 kg using an electronic scale.

### Height

Height was measured in standing position without shoes rounded down to the nearest 0.5 cm using a stadiometer with the shoulder in a relaxed position and the arms hanging freely.

### Waist circumference

Waist circumference was measured in cm rounded down to the nearest cm using a non-stretchable tailor's measuring tape at the midway level between the lower rib margin and the iliac crest in the horizontal plane. According to the adult treatment panel III (ATP III) criteria for metabolic syndrome, people with a waist circumference of ≥ 102 cm for men and ≥ 88 cm for women are considered to have abdominal obesity [23].

### Body mass index (BMI)

Body mass index was obtained by dividing the weight in kilograms by the square of height in meters, and classified according to criteria set forth by the American Diabetes Association (ADA) [23], it included the categories of underweight (< 18.5 Kg/$m^2$), normal weight (18.5-24.99 Kg/$m^2$), overweight (25 -29.9 Kg/ $m^2$), and weight evaluated as obesity (≥ 30 Kg/ $m^2$).

**Blood pressure**

Blood pressure was measured in sitting position with the arm at heart level, after 5 minutes of rest, after which time the cuff was deflated at the rate of 2–3 mmHg per second, systolic blood pressure was taken upon the heart first sound, and diastolic blood pressure taken upon complete disappearance of KorotK of sound (phase V). It was measured by using a standardized sphygmo-manometer EN1060 (Riester) with a cuff circumference of 24–32 cm to cover 80% of the upper arm (for obese patients larger cuff circumference was used (42–50 cm)).

Correspondingly, the anthropometric measurements were documented according to the latest reading of the medical file that was taken at the end of the interview. These measurements were documented by qualified staff nurses working in the involved hospitals in conformity with the standardized measuring standards set out by the Ministry of Health of Jordan.

**Laboratory Measurements**

Laboratory measurements made under the following criteria included the latest recorded values of glycosylated hemoglobin (HbA1c), fasting blood glucose (FBG), or random blood glucose (RBG). Besides, total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL), vitamin B12 levels, and low-density lipoprotein (LDL) were also assessed.

**Glycosylated Hemoglobin (HbA1c%) levels**

The latest record of HbA1c was taken from the medical file after the participants had been examined by the physician. HbA1c was classified into two categories according to ADA [23]: controlled if HbA1c < 7, uncontrolled if HbA1c ≥ 7.

**Fasting blood glucose (FBG) and random blood glucose (RBG) levels**

To measure the level of blood glucose, patients were asked not to eat anything or drink no fluid other than water for at least 8 hours (fasting). It is considered to be abnormal if the patient has FPG ≥ 126 mg/dl (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 hours according to ADA. According to ADA, it is considered to be abnormal if the patient has RBG ≥ 200 mg/dl (11.1 mmol/L) [23]. FBG or RBG was analyzed by the enzymatic reference method with hexokinase supplied by COBAS INTEGRA systems provided by Roche Diagnostics.

**Plasma lipid profile levels**

According to the Ministry of Health of Jordan, total cholesterol (TC) levels below 200 mg/dl are classified as "desirable blood cholesterol", and those 200 mg/dl and above as "high blood cholesterol". Triglyceride (TG) levels below 150 mg/dl, on the other hand, are classified as "desirable blood Triglyceride", and those

150 mg/dl and above as "high blood triglyceride". Low-density lipoprotein (LDL) levels below 100 mg/dl and those above this value are classified as "desirable blood lipoprotein " and "high blood lipoprotein ", respectively. While high-density lipoprotein (HDL) levels of < 40 mg/dl in men or those of < 50 mg/dl in women are classified as "undesirable blood lipoprotein ", and those of ≥ 40 mg/dl in men or ≥ 50 mg/dl in women are classified as “desirable blood lipoprotein ".

**Vitamin B12 levels**

Serum vitamin B12 level was measured by ARCHITECT B12 assay which is a chemiluminescent micro-particle intrinsic factor assay for the quantitative determination of vitamin B12 in human serum or plasma. Normal level ranges between (208–963 pg/ml). In cases when the patient is already on a vitamin B12 treatment, it is taken within 6 months.

Consistently, the laboratory measurements were documented according to the latest reading from the medical file that was taken at the end of the interview. These measurements were documented according to the standardized measurement rules set by the Ministry of Health of Jordan.

**Clinical Data**

Clinical data included complications of diabetes and comorbidities. The complications of diabetes were neuropathy, nephropathy, and retinopathy. Comorbidities included hypertension, dyslipidemia, and cardiovascular disease described under the following criteria:

**Hypertension**

Hypertension is defined as a condition when the patient is already on antihypertensive drugs, or have a blood pressure of ≥ 130 mmHg systolic and/or ≥ 80 mmHg diastolic on at least two occasions according to ADA [23].

**Retinopathy**

Retinopathy was diagnosed as positive if it was so documented by either the ophthalmologist or the treating physician in the medical records.

**Nephropathy**

Nephropathy was diagnosed as positive if it was so documented by either the nephrologists or the treating physician in the medical records.

**Dyslipidemia**

The patients were considered to have dyslipidemia in cases where the TC of the patient is ≥ 200 mg/dl, TG ≥ 150 mg/dl, LDL ≥ 100 mg/dl and HDL < 40 mg/dl in men or < 50 mg/dl in women or where the patients are on medications for any of the above conditions, according to ADA [23].

**Cardiovascular diseases**

Cardiovascular diseases were considered to be positive if there was a history of heart diseases such as angina, myocardial infarction, heart failure, coronary artery disease, arrhythmias, congenital heart failure,

and atherosclerosis as well as an ongoing treatment with drugs prescribed for cardiovascular diseases, or the presence of a pathological electrocardiogram.

Correspondingly, the clinical data were documented according to the physician's diagnosis, with duration of diabetes, type of treatment, and type of medication that was documented in the medical file.

The second tool is Douleur Neuropathique4 DN4, an interview questionnaire [24]. The questionnaire diagnosis of DPNP among adult T2DM patients with DPN was made by a score of ≥ 3. The DN4 score was derived by counting the number of positive responses to each of the first 7 items in the questionnaire, which included burning sensation, painful cold sensation, electric shocks, tingling, pins and needles, numbness, itching, hypoesthesia to touch, hypoesthesia to prick, and brushing [24]. Only those who completed all 10 items of the DN4 questionnaire were included in the analysis performed to estimate the prevalence of DPNP. The responses to the questionnaire were either yes or no. Scores ≥ 3 with a sensitivity of 89.9% were used to identify the patients with DPNP among adult T2DM patients with DPN, while using a cut-off score point of 3 items out of 7 had a sensitivity 78% and specificity of 81.2% in identifying patients with DPNP [24]. This questionnaire was reported by the International Association for the Study of Pain in 2004 by Bouhassira et al. (2005) [24]. The analysis of the psychometric properties of the DN4 questionnaire included face validity, factor analysis, and logistic regression to identify the discriminate properties of items or combinations of items for the diagnosis of neuropathic pain. The reliability and validity studies of the DN4 questionnaire in Arabic was performed by Terkawi et al. in 2017. The results showed Arabic DN4 to have a good diagnostic accuracy, with an area under the curve of 0.88. As with the original version, a score of ≥ 4 was found to be the best cut-off for the diagnosis of DPN, with a sensitivity of 88.31%, the specificity of 74.47%, a positive predictive value of 85%, and a negative predictive value of 80%. The Cronbach's alpha value of the revised scale was 0.67 [25].

The third tool is the physical examination that is the second section in the DN4 questionnaire; it includes hypoesthesia to touch, hypoesthesia to prick, and brushing [24]. The researcher filled in each questionnaire using face to face interviews in Arabic language.

The fourth tool is the quality of life questionnaire titled EQ-5D [26]. This standardized instrument includes four domains that measure the QoL, namely mobility, self-care, routine activities, discomfort, and anxiety /depression. Each dimension has five levels, namely no problems, slight problems, moderate problems, severe problems, and extreme problems. The participants were asked how good or bad they self-rated their health status. Responses were rated on a scale ranging from 0 to 100, with 100 indicating the best self-rated health status, and 0 indicating the poorest one [26]. The EQ-5D was translated by the researcher and checked by two professional academic instructors working in the field of nursing to ensure the consistency of the information obtained in the interviews. The reliability and validity studies of the EQ-5D in Jordan were performed by Abu-Shennar, Bebis, and Bayraktar in 2020. The Cronbach's alpha value of the revised scale was 0.88 [27].

In addition to the above measurements, the researcher measured the intensity of pain using the Numeric Pain Rating Scale (NRS). Each patient was asked to indicate the number that represented the intensity of

his/her current pain experience.

### Data Collection

Data were collected in five stages in the following way:

- Each weekday, the researcher assessed the adult T2DM participants with DPN who met the criteria of inclusion in the study.
- A face-to-face structured interview was performed with the adult T2DM patients with DPN while waiting for his/her turn to be treated by the physician after their laboratory check and nursing examination. Descriptive data were obtained, and Douleur Neuropathique4 DN4 was administered to evaluate DPNP. Each interview took about 10 to15 minutes.
- After the interviews, a physical examination was performed on each participant using the second section of the DN4 for evaluation of DPNP, and patients with DPNP were determined.
- The intensity of pain was measured using the Numeric Pain Rating Scale (NRS) among the DPNP patients.
- Finally, the quality of life questionnaires titled EQ-5D were collected from the patients having DPNP.

### Statistical analysis

Statistical analysis was carried out using the Statistical Package for Social Sciences (SPSS, version 25). Descriptive statistics were obtained such as mean and stander deviation values for continuous and proportions for categorical variables. Chi-square was used to test the independent distribution of categorical variables where appropriate. Spearman's Rank-Order Association Coefficient (Spearman's Rho) was also used to measure the direction and strength of the correlation between the two variables. The Kolmogorov-Smirnov test and the Shapiro-Wilk test were used to measure the value of the Shapiro-Wilk Test. While values greater than 0.05 indicated the normality of data, those below 0.05 indicated that the data significantly deviated from a normal distribution. Binary logistic regressions were also used to examine the net effect for each of the proposed variables on DPNP. P-values smaller than 0.05 were considered to be statistically significant.

### Ethical Considerations

Data were collected after approval by the ethical committee in the Ministry of Health of Jordan. We obtained approval from a consultant specialized in neurology to administer the DN4 as required by the Ethical Committee of the Ministry of Health of Jordan The data were only used for scientific research. Since the study was based on data obtained from medical records and structured questionnaires, it inflicted no harm at all on adult patients (T2DM) with DPN. Verbal consent was obtained from those eligible to participate, who were assured about the confidentiality of information.

# Results

In this cross-sectional study, the age of participants ranged between 30 and 38 years with a mean age of 58.2 years (SD = ± 9.4). Around half of the participants were male (87.5%), and the majority (93.2%) married. While 53.3% of the participants had never smoked, 33% were current smokers. While 37.3% had had T2DM for less than five years, the participants who had been suffering from diabetes for a time-span between 5 and 11 years accounted for 32% with a mean length of time of 9.7 years (SD = ± 7.3) (Table 1).

**Table 1: Socio-demographic characteristics of the participants n=400**

| Participants' characteristics | n (%) | Mean (SD) |
|---|---|---|
| **Age (year)** | | 58.2 ± 9.4 |
| < 50 | 56 (14) | |
| 50-69 | 291 (72.8) | |
| ≥70 | 53 (13.3) | |
| **Gender** | | |
| Male | 350 (87.5) | |
| Female | 50 (12.5) | |
| **Marital status** | | |
| Single / Divorced /Widowed | 27 (6.8) | |
| Married | 373 (93.3) | |
| **Working status** | | |
| Unemployed | 49 (12.3) | |
| Employed | 172 (43.0) | |
| Retired | 179 (44.8) | |
| **Level of Education** | | |
| High school or less | 140 (35.0) | |
| Diploma college | 86 (21.5) | |
| Bachelor degree or higher | 174 (43.5) | |
| **Medical insurance:** | | |
| Not insured | 23 (5.8) | |
| Have any insurance | 373 (94.3) | |
| **Smoking status** | | |
| Not smoker | 231 (53.3) | |
| Ex-smoker | 55 (13.8) | |
| current smoker | 132 (33.0) | |
| **Duration of diabetes** | | 9.7 ± 7.3 |
| < 5 years | 149 (37.3) | |
| 5-11 years | 128 (32.0) | |
| ≥12 years | 123 (30.8) | |

Regarding the clinical and laboratory findings of the study participants (Table 2), the results showed that the mean BMI was 31.7 kg/m$^2$ (SD ± 5.4), and more than half of the participants, namely 59.3%, were obese and 32.8% overweight. Most of the participants had comorbid diseases such as hypertension (85%), dyslipidemia (87.8%), cardiovascular disease (32.5%), retinopathy (10%), and nephropathy (5.5%. Also, 65% of the participants had uncontrolled HbA1c with the mean HbA1c of 7.6% (SD ± 1.5). Regarding the modality of treatment for T2DM, 19.8%, 51.7%, and 28.5% of the study participants were on a treatment with insulin only, with oral hypoglycemic agents only, and with oral hypoglycemic agents with insulin, respectively.

**Table 2: Clinical and laboratory characteristic of the participants n= 400**

| Participants' characteristics | n (%) | Mean (SD) |
|---|---|---|
| **Body mass index (BMI) (Kg/ $m^2$)*** | | 31.7± 5.4 |
| Normal | 32 (8.0) | |
| Overweight | 131 (32.8) | |
| Obese | 237 (59.3) | |
| **Comorbid diseases \ conditions** | | |
| Hypertension | 340 (85.0) | |
| Dyslipidemia | 351 (87.8) | |
| Retinopathy | 40 (10.0) | |
| Nephropathy | 22 (5.5) | |
| Cardiovascular diseases | 130 (32.5) | |
| **Modality of treatment** | | |
| Insulin only | 79 (19.8) | |
| Oral hypoglycemia agents only | 207 (51.7) | |
| Oral hypoglycemia agents & Insulin | 114 (28.5) | |
| **HbA1C (%)** | | 7.6 ± 1.5 |
| Controlled <7% | 140 (35.0) | |
| Uncontrolled ≥7% | 260 (65.0) | |

**** = Normal: 18.5-24.9 kg/$m^2$; overweight: 25-29.9 kg/$m^2$; obese: ≥30 kg/$m^2$***

The researcher used the criteria based on the DN4 questionnaire, in accordance which the participants who obtained scores ≥ 3 with at least one symptom were considered to have DPNP. Accordingly, the results of the study revealed that the overall prevalence of DPNP based on the DN4 questionnaire among adult T2DM patients with DPN (n = 400) was 47.8% (n = 191).

Using the NRS measurement of pain intensity (Table 4), we observed that while more than half of the participants, namely 50.3%, had mild pain, 45% had moderate pain and 4.7% severe pain. The most frequently reported symptoms were tingling (78.5%) and burning (63.9%), and the least reported ones were painful cold (15.7%) and itching (16.2%), a result which reflected the aspects of pain in participants with DPN.

Table 3 shows the relationship between DPNP and the selected socio-demographic and clinical data. Of the participants, 36.1% who had diabetes for longer than 12 years, 31.4% with a duration between 5–11 years, and 32.5% suffering from diabetes for less than 5 years reported experiencing pain ($p < 0.05$). Results showed that 71.2% of the patients with uncontrolled diabetes mellitus and 28.8% of those with controlled diabetes mellitus suffered from pain ($p < 0.05$). With respect to comorbid diseases/conditions, 88.5% of the patients with hypertension and dyslipidemia reported having pain. On the other hand, 24.6%,

40.8%, and 34.6% of the patients treated with insulin only, oral hypoglycemia agents only, and oral hypoglycemia agents & insulin, respectively, also reported experiencing pain, a difference that was found to be statistically significant ($p < 0.05$) (Table 3).

**Table 3: Relationship between DPNP and the selected socio-demographic and clinical data of the participants n= 400**

| Variables | Neuropathy status | | p-value |
|---|---|---|---|
| | Pain N=191 n (%) | Without pain N=209 n (%) | |
| **Gender** | | | |
| Male | 171 (89.5) | 179 (85.6) | 0.241 |
| Female | 20 (10.5) | 30 (14.4) | |
| **Age** | | | |
| 50< | 25 (13.1) | 31 (14.8) | 0.869 |
| 50-69 | 141 (73.8) | 150 (71.8) | |
| ≥70 | 25 (13.1) | 28 (13.4) | |
| **Employment** | | | |
| Not employed | 26 (13.6) | 23 (11.0) | 0.249 |
| Employed | 74 (38.7) | 98 (46.9) | |
| Retired | 91 (47.6) | 88 (42.1) | |
| **Smoking status** | | | |
| Not smoker | 98 (51.3) | 115 (55.0) | 0.690 |
| Ex-smoker | 26 (13.6) | 29 (13.9) | |
| Current smoker | 67 (35.1) | 65 (31.1) | |
| **Body mass index (BMI) (Kg/ $m^2$)** | | | |
| Normal | 17 (8.6) | 15 (7.2) | 0.565 |
| Overweight | 58 (30.4) | 73 (34.9) | |
| Obese | 116 (60.7) | 121 (57.9) | |
| **Duration of diabetes** | | | |
| < 5 years | 62 (32.5) | 87 (41.6) | 0.057 |
| 5-11 years | 60 (31.4) | 68 (32.5) | |
| ≥ 12 years | 69 (36.1) | 54 (25.8) | |
| **(%)HbA1c** | | | **0.013 |
| Controlled <7% | 55 (28.8) | 85 (40.7) | |
| Uncontrolled ≥7% | 136 (71.2) | 124 (59.3) | |
| **Marital status** | | | |
| Widowed/ Divorced /Single | 16 (8.4) | 11 (5.3) | 0.215 |
| Married | 175 (91.6) | 198 (94.7) | |
| **Level of Education** | | | |
| High school or less than | 72 (37.7) | 68 (32.5) | 0.184 |
| Diploma collage | 45 (23.6) | 41 (19.6) | |
| Bachelor degree or higher | 74 (38.7) | 100 (47.8) | |
| **Comorbid diseases \ conditions** | | | |
| **Hypertension** | | | |
| Yes | 169 (88.5) | 171 (81.8) | 0.062 |
| No | 22 (11.5) | 38 (18.2) | |
| **Nephropathy** | | | |
| Yes | 15 (7.9) | 7 (3.3) | *0.048 |
| No | 176 (92.1) | 202 (96.7) | |
| **Cardiovascular disease** | | | |
| Yes | 69 (36.1) | 61 (29.2) | 0.139 |
| No | 122 (63.9) | 148 (70.8) | |
| **Dyslipidemia** | | | |
| Yes | 169 (88.5) | 182 (87.1) | 0.670 |
| No | 22 (11.5) | 27 (12.9) | |
| **Retinopathy** | | | |
| Yes | 25 (13.1) | 15 (7.2) | *0.049 |
| No | 166 (86.9) | 194 (92.8) | |

| Type of treatment | | | |
|---|---|---|---|
| Insulin only | 47 (24.6) | 32 (15.3) | **0.001 |
| Oral hypoglycemia agents only | 78 (40.8) | 129 (61.7) | |
| Oral hypoglycemia agents & Insulin | 66 (34.6) | 48 (23.0) | |

**** = significance level 0.05; ** = significance level 0.01***

Regarding the quality of life of the participants who had DPNP, the participants in this group reported having problems in mobility (1%), self-care (2.6%), routine activities (29.8%), discomfort (97.50%), and anxiety /depression (48.1%), with the mean self-rated health status of 78.27 (SD ± 12.31), which was found to be statistically significant ($p < 0.05$) (Table 4).

The participants who had DPNP and reported having problems in mobility, self-care, routine activities, discomfort, and anxiety or/and depression had significantly lower QoL with a poorer self-rated health status than those without DPNP (Spearman correlation coefficients (Spearman's Rho) $r = 0.606$, $p = 0.001$) at a moderate level (50–69). Besides, with the group in homogenate structure and data with a normal distribution, the Kolmogorov-Smirnov test and the Shapiro-Wilk test showed that the effect of pain on the life quality of the patients in the group was statistically significant (Df) = 399 ($p < 0.05$) (Table 5).

**Table 5: Spearman's rho correlation coefficient between patients' quality of life, health status imagines and DPNP of the Participants**

| Variables | The correlation coefficient of DPNP | The correlation coefficient of QOL | The correlation coefficient of Health Status Imagine |
|---|---|---|---|
| Total DPNP score | 1.000 | 0.507* | -0.404* |
| Total QOL score | 0.507* | 1.000 | -0.724* |
| Total Health Status Imagine score | -0.404* | -0.724* | 1.000 |

**** = Spearman's rho correlation coefficient is significant at the 0.01 level (2-tailed)***

| Variables | Kolmogorov-Smirnov* | | Shapiro-Wilk | | p-value |
|---|---|---|---|---|---|
| | Statistic | The number *of degrees of freedom* (Df) | Statistic | The number *of degrees of freedom* (Df) | |
| Total DPNP score | 0.188 | 399 | 0.922 | 399 | 0.001 |

****Lilliefors significance correlation.***

The binary logistic regression analysis was used to identify the impact of the demographic, clinical, and laboratory variables on the DPNP using the entry system. The value of $p < 0.05$ indicated a significant influence of any demographic, clinical, and laboratory variables on the DPNP. Besides, the odds ratios

mentioned in the table indicate how likely given variables could contribute to the DPNP in adult patients (T2DM) with DPN. The result showed that subjects with uncontrolled diabetes were 1.48 times more likely to have DPNP compared to those with controlled diabetes (OR = 1.48, CI; 0.948–2.331; p = 0.015) (Table 6).

**Table (6): Logistic regression analysis of significant factors associated with DPNP of the Participants**

| riables | Odds Ratios (OR) | 95% Confidence Interval (Lower – Upper) | p-value |
|---|---|---|---|
| **nder** | | | |
| ıle | 1 | | 0.319 |
| male | 0.728 | (0.390-1.358) | |
| **ɔA1c (%)** | | | |
| ntrolled <7% | 1 | | 0.015* |
| ıcontrolled ≥7% | 1.48 | (0.948-2.331) | |
| **dy mass index (BMI) (Kg/ m$^2$)** | | | |
| ɔrmal | 1 | | |
| erweight | 0.715 | (0.324-1.578) | 0.406 |
| ɔese | 0.861 | (0.406-1.826) | 0.697 |
| **ıration of diabetes** | | | |
| 5 years | 1 | | |
| 1 1 years | 1.088 | 1.088 (0.663-1.784) | 0.738 |
| 2 years | 1.464 | 1.464 (0.870-2.464) | 0.152 |

*1 = References group.*

** = significance level 0.05; ** = significance level 0.01*

# Discussion

DPNP is a common disorder that is difficult to manage due to complications arising from diabetes. Many studies have shown that the prevalence of DPNP ranges between 40 and 50% [15]. The current study reported the overall prevalence of DPNP among adult patients (T2DM) with DPN as 47.8%, a result which can be considered high. The results of this study are contrary to the results of a recent study conducted in South Africa, which found a DPNP prevalence of 30% among patients with DPN [7]. The results are not also consistent with an observational study performed in England by Abbott et al. (2011), in which a DPNP prevalence of 34.5% was observed among T2DM patients [11]. A comprehensive national survey study conducted in France with a sample of 24.497 patients with diabetes to estimate the prevalence of chronic pain with or without neuropathic characteristics reported that 7,522 (31.7%) of the involved

patients had pain in different intensity. However, neuropathic characteristics were reported by only 1,631 (6.9%) of the patients surveyed [28]. Another study conducted in Saudi Arabia reported that the prevalence of DPNP was 65.3% among 1039 patients with T2DM and T1DM [1], a result higher than the ones we observed in the present study. In another study, Jambart et al. (2011) investigated the prevalence of DPNP in 3989 patients with T2DM or T1DM in outpatient clinics across the Middle East using the DN4 instrument [4]. Their results revealed that 53.7% of the patients met the criteria for painful DPNP (with Douleur Neuropathique-4 (DN4) scores ≥ 4). This study showed a difference in the prevalence of DPNP among patients with diabetes mellitus. The involved countries in the study were Egypt (n = 783), Gulf States (n = 639), Jordan (n = 1194) and Lebanon (n = 1373) [4]. The results showed that the prevalence in Jordan was 57.5%, a value less than the one observed in Egypt (61.3%), however, higher than the result observed in the Gulf States and Lebanon (37.1% and 53.9% respectively). This higher prevalence of the previous study from Jordan can be explained by the fact that the study included patients with T1DM and T2DM. However, patients with T1DM were 1.59 times more likely to have DPNP than patients with T2DM, more or less than 0.05. The difference in the reported prevalence from all over the world can be related to different populations of the studies, different screening tools, and different scores for DN4 used to assess DPNP. Another possible explanation for this association could be the existence of different lifestyles among patients with DPNP including weight gain and less physical activity.

Results showed that the most frequently reported symptoms were tingling, and burning, and the least reported ones painful cold and itching. Several studies evaluated the nature of pain among adult patients (T2DM) with DPNP, in which burning, pins, and needles and numbness were the most frequently reported symptoms of diabetic patients with DPNP [4, 13, 16, 26, 27]. In a cross-sectional study performed in France with the inclusion of 885 patients with T1DM and T2DM, while, on the one hand, numbness and burning were the most frequently reported symptoms with T2DM, tingling and numbness were, on the other, the most frequently reported ones among patients with T1DM [12]. A DN4 questionnaire survey among 4097 patients with T2DM from several countries in the Middle East including Jordan reported that, in a nearby country (Saudi Arabia), while burning, numbness, and tingling were the most common symptoms of DPN in cases of establishing DPNP [1], burning, numbness, tingling, pins, and needles were the most frequently reported symptoms [4].

In the present study, participants reported having pain in different intensities ranging from mild to moderate, with more than half, however, reporting experiencing pain of mild intensity. In a cross-sectional study conducted with 1111 patients in Brussels, Belgium, 61% of the patients reported having pain of moderate-intensity (776 T1DM, 344 T2DM) [29]. The investigators in this trial used a visual analog scale (VAS) for the assessment of pain intensity, while in our study, in which NRS measurement was used to assess pain intensity, 45% of patients with DPNP reported having moderate pain. Another study from the same region conducted in French by Bouhassira et al. (2013) using the NRS showed that 76.2% of patients reported having pain of moderate to severe intensity [12]. The reported differences in the assessment of pain intensity can be related to the use of different tools to assess pain intensity. In a study performed in the USA, in which Brief Pain Inventory (BPI-DPN) was used to assess pain intensity,

researchers reported a pain intensity ranging from moderate to severe in 71.4% of patients with DPNP [30].

Regarding the quality of life of the patients with DPNP, EQ5 questionnaire findings showed that the patients (T2DM) with DPN who had DPNP reported having problems in mobility, self-care, routine activities, discomfort, and experiencing anxiety or/and depression, with the self-rated bad health status. There has been little research that has specifically assessed the impact of neuropathic pain on the health-related quality of life among patients with diabetes mellitus. These results were concordant with those from other epidemiological studies, where adult patients (T2DM) with DPNP had significantly lower QoL with poorer self-rated health status than those without DPNP. For example, Davies et al. (2006) assessed the impact of neuropathic pain on the quality of life of patients with T2DM. They found that the patients who developed DPNP had poorer quality of life [13]. Similar results were found in a study conducted in Belgium by Van Acker et al. (2009) on 1111 patients diagnosed with diabetes (767 T2DM and 344 T1DM). The results revealed that patients with DPNP were more likely to report problems regarding physical activities and mental alterations than those without DPNP, a result which may account for their lower QOL scores [29]. In a more recent study conducted in France to estimate the impact of DPNP on the QoL of 766 diabetic patients (38.7% with T1DM, 44.8% with T2DM), the results showed that DPNP was associated with disturbances in sleep, higher anxiety levels, and depression [12]. Another study that agrees with the results of our study was performed in South Africa, which reported results suggesting that DPNP had a negative impact on QoL of 1036 patients with diabetes from 50 health care clinics [7]. To conclude, comparing these results with the current study results, we have found that there is a consensus that DPNP has a statistically significant negative effect on the QoL of adult patients (T2DM) with DPN including both physical and mental status.

The results of the present study showed that the participants' HbA1c, BMI, hypertension, dyslipidemia, duration of diabetes, and treatment modality were the main factors associated with the incidence of DPNP in adult patients (T2DM) with DPN. The findings have also shown that the DPNP is related to uncontrolled diabetes. Another study result is that the patients with HbA1c ≥ 7% are 1.48 times more likely to have DPNP. Consistent with the results of this study is the finding observed in a cross sectional survey that was conducted in the UK to determine the severity of DPNP and its impacts on quality of life [13], which showed that the degree of neuropathy was associated with the degree of diabetes control, with OR for HbA1c found as 1.28 (CI: 1.08–1.52; P-value = 0.004).

# Conclusion

The current study showed that the prevalence of DPNP among adult T2DM patients with DPN was high. Around half of the participants reported having mild or moderate pain. The most frequently reported symptoms were tingling and burning. Uncontrolled diabetes was found to be the main predictor of DPNP among patients with DPN. The long duration of the disease, dyslipidemia, obesity, and hypertension and treatment with only oral hypoglycemia agents were significant factors associated with DPNP. Regarding the quality of life of the participants having DPNP, the patients reported having problems in mobility, self-

care, routine activities, discomfort, and experiencing anxiety or/and depression, and they had significantly lower QoL, with a self-rated bad health status poorer than those without DPNP. Besides, the effect of pain on their quality of life was found to be significant. Identification of patients with DPNP highlights the need for improved awareness, health education, early detection, and intervention for the patients, and may eventually lead to a significant improvement in the management of these health problems and reduction of its adverse consequences.

In conclusion, the results of the study provide an insight to the health burden of diabetes mellitus in Jordan and useful information on the prevalence of DPNP and life quality among the patients with diabetes mellitus and associated factors. In accordance with the results, it can be recommended that strategies should be developed for an effective management of painful DPN with an integrated and interdisciplinary approach. Recommendations set out in current clinical guidelines should be followed to improve patient care and reduce the burden of the disease. There is a need to enhance patients' awareness and provide them education with respect to lifestyle interventions such as appropriate diet, exercise, and importance of regular visits to treating physicians to promote tighter blood glycemic control, manage weight, and hypertension. Furthermore, early detection and appropriate management are important in improving the HRQoL of patients with DPNP. Screening could improve the early diagnosis of DPNP in diabetic patients.

# Limitations

The results of this study are subject to certain limitations. Even though the focus of the study was to assess the prevalence of PDNP among adult patients (T2DM) with DPN, the study is limited by the lack of data in cases where patients received a pain therapy through pharmacological and non-pharmacological means. Another limitation is the lack of detailed data and comparison regarding identification of the complications of the T2DM such as chronic kidney disease in nephropathy. It is recommended that further research should be undertaken with samples consisting of patients from different health care facilities in Jordan with a greater focus on the collection of more detailed data on the patients.

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