The Egyptian Journal of Hospital Medicine (April 2024) Vol. 95, Page 1608- 1618

Prevalence, Pattern and Factors Associated with Diabetic Peripheral Neuropathy in Benha City, Egypt

Ahmed Khedr Mohammed*, Rasha O. Abdelmoniem, Mohammed S. Saleh, Ayman M. Elbadawy, Walaa M. Ibrahim

Internal Medicine Department, Faculty of Medicine, Banha University, Banha, Egypt

***Corresponding Author:** Ahmed Khedr Mohammed**, Mobile:** (+20) 01014716843**, Email:** ahmedkhedrmohammed@gmail.com

ABSTRACT

Background: Diabetic peripheral neuropathy (DPN) is the most frequent kind of neuropathy globally. DPN is one of the most prevalent and serious microvascular consequences of diabetes. **Objective:** To assess prevalence of DPN, its pattern, severity and associated risk factors in Benha City, Egypt. **Patients and methods:** This cross-sectional observational study was conducted on 500 diabetic patients (type 1 and type 2). All patients were subjected to complications of diabetes especially microvascular and macrovascular complications, diabetic foot and history of previous operations, physical examinations (general, neurological, sensory examination and Toronto clinical scoring system (TCSS)) and laboratory investigations (CBC, hemoglobin A1c (HbA1c), kidney function tests, liver function tests, serum thyroid-stimulating hormone and lipogram). **Results:** Body mass index (BMI), height, duration of diabetes, HbA1c, and thyroid-stimulating hormone (TSH) had a strong positive significant correlation with TCSS score (r=0.338, P< 0.001; r=0.335, P< 0.001; r=0.630, P< 0.001; r=0.806, P< 0.001; r=0.332, P< 0.001 respectively). Low-density lipoprotein-cholesterol (LDL-C) level and triglycerides level had no significant correlation with TCSS score (r= 0.015, P= 0.743; r= 0.074, P= 0.097 respectively). **Conclusions:** The primary risk factors include higher BMI, height, hard working, smoking, poor glycemic management, extended diabetes mellitus (DM), metformin use, chronic kidney disease (CKD), and an abnormal thyroid profile. After documenting these findings, a greater effort should be made to lower the frequency and severity of PDN in diabetic patients by education emphasising regular foot care, strict glucose control, and lifestyle adjustment.

Keywords: Prevalence, Pattern, Factors, DPN.

INTRODUCTION

One serious problem for public health is DM. Globally, 451 million individuals were diagnosed with diabetes in 2017; by 2045, that figure is expected to rise to 693 million [1]. The most prevalent kind of neuropathy in the world is DPN [2]. One of the most prevalent and serious microvascular consequences of diabetes is DPN [3]. In diabetic people, DPN exacerbates the chances of impairment and lowers quality of life [4]. The characteristic of neuropathies is a gradual decrease of nerve fibre function. "The presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after exclusion of other causes" is a commonly recognised definition of diabetic peripheral neuropathy [5].

It is well acknowledged that there are several factors at play. The onset of symptoms is contingent upon several circumstances, including the overall amount of hyperglycemic exposure and additional risk factors including high blood pressure, raised cholesterol, smoking, increased height, and excessive exposure to other potentially neurotoxic chemicals like ethanol. There may be a genetic component as well [6].

Damage from DPN can be catastrophic. A foot ulcer will occur in around 50% of diabetics at some point in their lives, and diabetes is a major factor in lower limb amputations. Neuropathic pain and diminished sensation have been linked to a number of negative consequences, such as depression symptoms, falls, reduced quality of life, and limitations in everyday activities [7]. Distal symmetric polyneuropathy, which makes up around 75% of all diabetic neuropathies, is the most prevalent kind of DPN. It can be categorised as mostly small-fiber, primarily big-fiber, or mixed small and large fibre [7]. Atypical types of DPN include mononeuropathies (e.g., mononeuritis multiplex), (poly)radiculopathies, and treatment-induced neuropathies [8]. According to most estimates, DPN will impact almost half of all persons with diabetes during their lifetime [9].

In their Canadian study, **Mai *et al.*** [10] discovered that almost one-third of the patients with painful diabetic neuropathy (DN) receiving tertiary care had shown a substantial improvement in pain and function at the 12-month follow-up. This included functional improvement (reduction of 1 or more on the Pain Interference Scale) in 51.2% of patients, pain reduction of 30% or more in 37.2% of patients, and attainment of both of these criteria in 30.2% of patients. They discovered that the use of analgesic antidepressants, anticonvulsants, and polypharmacy is crucial for managing symptoms.

This work's objective was to assess prevalence of DPN, its pattern, severity and associated risk factors in Benha City, Egypt.

PATIENTS AND METHODS

This cross-sectional observational study was conducted on 500 diabetic patients (type 1 and type 2) who attend Benha University Hospital.

Exclusion criteria were diabetic patients with other possible causes of peripheral neuropathy e.g., hereditary polyneuropathy, malignancy, drugs, and post inflammatory neuropathy.

All patients were subjected to complete history taking (Personal history, complaint and its duration, history of duration of diabetes, modality of treatment, medication adherence, history of currently prescribed

Received: 09/11/2023
Accepted: 09/01/2024

medication, other comorbidities [cardiac problems, hypertension, chest diseases, renal diseases, liver diseases, blood diseases or bleeding tendency], complications of diabetes especially microvascular and macrovascular complications, diabetic foot and history of previous operations), physical examinations (general, neurological, and sensory examination, and TCSS, anthropometric measurements (Weight, height, waist circumference, and hip circumference and BMI), and laboratory investigations (CBC, HbA1c, kidney function tests, liver function tests, serum thyroid-stimulating hormone (TSH), and lipogram).

Neurological Examination: Mental Status and Cranial Nerves: Assessing the patient's mental status, orientation, and cognition. Examining cranial nerves, especially assessing pupillary reflexes and eye dryness.

Motor Examination: Evaluating muscle strength and tone in all four limbs. Checking for any signs of muscle atrophy or weakness, which may be related to autonomic neuropathy.

Reflexes: Testing deep tendon reflexes (e.g., patellar reflex, Achilles reflex) to assess for abnormalities. Observing for the presence of hyperreflexia or areflexia, which can be indicative of autonomic neuropathy.

Sensory Examination: Assessing sensory perception, including light touch, temperature, and pinprick sensation.

Coordination and Balance: Evaluating coordination and balance by performing tests such as finger-to-nose and heel-to-shin maneuvers.

Gait Examination: Observing the patient's gait and looking for any abnormalities, such as ataxia or instability.

Toronto clinical scoring system (TCSS): Diagnosis of peripheral neuropathy and assessment of severity was based on TCSS. TCSS was calculated for each patient with DM to detect pattern and progression of peripheral neuropathy in each patient. This was done by taking careful history about pain, numbness, tingling, weakness, ataxia and upper limb symptoms.

Examination of superficial sensation including pinprick, light touch, temperature sensations and deep sensations including vibration, joint movement sensations. Examination of motor system including power, tone and reflexes.

TCSS:

Symptom scores: Foot pain, Numbness, Tingling, Weakness, Ataxia, Upper-limb symptoms.

Sensory test scores: Pinprick, Temperature, Light touch, Vibration, Joint position.

Reflex scores: Knee reflexes, Ankle reflexes.

Symptom scores: present = 1; absent = 0.

Sensory test score: abnormal = 1. normal = 0

Reflex scores: absent = 2; reduced = 1, normal = 0.

Total scores range from normal = 0 to maximum of 19.

The individual patient's TCSS score was documented out of a total of 19. Severity of neuropathy was classified based on the score as: No neuropathy (0 to 5), mild neuropathy (6 to 8), moderate (9 to 11) and severe DN (12 to 19).

Sample Size Calculation:

OpenEpi, version3, open-source calculator-cross sectional study was used to calculate the least required sample size at 0.05 alpha error, power of 0.80 and prevalence 10% for DM type I and 90% for DM type II % (reference). The least number was 139 patients.

Ethical approval:

Prior to their enrolment in the study, participants gave their informed permission. The Benha Faculty of Medicine's Research Ethics Committee gave its clearance. The Helsinki Declaration was observed at all stages of the study.

Statistical analysis

The collected data were presented in tables and analyzed by SPSS. Quantitative variables were expressed as mean ± SD, and range. Qualitative variables were expressed as frequency and percentage. The level of significance was $p<0.05$.

RESULTS

Table 1 shows demographic data, DM characteristics and treatment of the studied patients.

Table (1): Demographic data, DM characteristics and treatment of the studied patients

		n=500
Age (years)		54.4 ± 10.89
Sex	Male	140 (28%)
	Female	360 (72%)
Marital status	Single	112 (22.4%)
	Married	388 (77.6%)
Weight (Kg)		68.8 ± 15.87
Height (cm)		176 ± 9.91
BMI (Kg/m^2)		28.02 ± 3.89
Residence	Rural	272 (54.4%)
	Urban	228 (45.6%)
Occupation	Sedentary	268 (53.6%)
	Mental worker	123 (24.6%)
	Hard worker	109 (21.8%)
Smoking	Nonsmoker	458 (91.6%)
	Light smoker	20 (4%)
	Heavy smoker	22 (4.4%)
DM characteristics		
Type of diabetes		
Type 1	50 (10%)	
Type 2	450 (90%)	
Treatment		
Oral	260 (52%)	
Insulin	160 (32%)	
Oral and Insulin	80 (16%)	
Duration of diabetes	5 (3 - 10)	

Data are presented as mean ± SD, Median (IQR) or frequency (%).

Table 2 shows laboratory parameters tests results and clinical manifestations of peripheral neuropathy among the studied patients.

Table (2): Laboratory parameters tests results, and clinical manifestations of peripheral neuropathy among the studied patients

	n=500
FBS (mg/dL)	176.44 ± 43.11
PPS (mg/dL)	262.18 ± 63.31
HBA1c (%)	8.54 ± 1.75
Hb (g/dL)	12.06 ± 1.79
Platelets (x 10^9)/L	259.9 ± 28.78
INR	1.13 ± 0.26
Creatinine (mg/dL)	1.37 ± 0.31
Total cholesterol (mg/dL)	204.2 ± 46.05
Triglycerides (mg/dL)	160.27 ± 38.20
LDL (mg/dL)	120.11 ± 30.10
Albumin (g/dL)	3.6 ± 0.44
AST (U/L)	33.1 ± 5.1
ALT (U/L)	33.07 ± 7.98
TSH (mU/L)	2.90±0.64
Albumin / creatinine ratio	10±2.41
Clinical manifestations of peripheral neuropathy	
Pain	350 (70%)
Numbness	257 (51.4%)
Tingling	309 (61.8%)
Weakness	158 (31.6%)
Ataxia	60 (12%)
	163 (32.6%)

Data are presented as mean ± SD, Median (IQR) or frequency (%), FBS: fasting blood sugar, PPS: post prandial blood sugar, Hb: Hemoglobin, INR: International normalized ratio, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, AST: Aspartate aminotransferase, ALT: Alanine transaminase, TSH: Thyroid stimulating hormone, UL: upper limb.

Table 3 shows results of examination of sensory system and results of examination of deep reflexes among the studied patients.

Table (3): Results of examination of sensory system and results of examination of deep reflexes among the studied patients

	Studied patients (n = 500)
Pinprick	
Normal (pin prick sensation intact)	260 (52%)
Abnormal (pinprick sensation lost)	240 (48%)
Temperature	
Normal (temperature sensation intact)	400 (80%)
Abnormal (temperature sensation lost)	100 (20%)
Light touch	
Normal (light touch sensation intact)	248 (49.6%)
Abnormal (light touch sensation lost)	252 (50.4%)
Vibration	
Normal (vibration sensation intact)	340 (68%)
Abnormal (vibration sensation lost)	160 (32%)
Joint position	
Normal (joint position sensation intact)	353 (70.6%)
Abnormal (joint position sensation lost)	147 (29.4%)
Results of examination of deep reflexes	
Rt Knee Reflex	
Normal	379 (75.8%)
Reduced	80 (16%)
Absent	41 (8.2%)
Lt Knee Reflex	
Normal	380 (76%)
Reduced	80 (16%)
Absent	40 (8%)
Rt Ankle reflex	
Normal	321 (64.2%)
Reduced	64 (12.8%)
Absent	115 (23%)
Lt Ankle reflex	
Normal	330 (66%)
Reduced	60 (12%)
Absent	110 (22%)

Body mass index, height, duration of diabetes, HbA1c, and TSH had a strong positive significant correlation with TCSS score. LDL-C level and triglycerides level had no significant correlation with TCSS score **(Table 4).**

Table (4): Prevalence of DN among the studied patients according to TCSS and correlation between risk factors and TCSS score

TCSS score result		
	Frequency	**Percentage**
No DN	250	50%
Mild DN	80	16%
Moderate DN	60	12%
Severe DN	110	22%
Total	500	100%
Correlation between risk factors and TCSS score		**TCSS score**
BMI	R	0.338
	P-value	< 0.001*
Height	R	0.335
	P-value	< 0.001*
Duration of diabetes	R	0.630
	P-value	< 0.001*
HbA1c	R	0.806
	P-value	< 0.001*
TSH	R	0.332
	P-value	< 0.001*
LDL-C	R	0.015
	P-value	0.743
Triglycerides	R	0.074
	P-value	0.097

*: Significant

Table 5 shows distribution of DN according to risk factors.

Table (5): Distribution of DN according to risk factors.

Score result		**No diabetic neuropathy**	**Diabetic neuropathy**
Type of diabetes	Type 1	20	30
	Type 2	230	220
BMI (Kg/m^2)	Normal	140	40
	Overweight	50	112
	Obese	60	98
Height (cm)	Short	82	50
	Average	150	77
	Tall	18	123
Duration result	<=5y	230	60
	6 to 10y	20	110
	>=11y	0	80
HbA1c result	<=7	90	10
	7 to 8	130	20
	8.1 to 9	30	42
	>9	0	178
Metformin	Not on metformin	150	72
	On metformin	100	178
GFR result	No nephropathy	230	90
	G1 CKD	5	49
	G2 CKD	5	42
	G3a CKD	7	44
	G3b CKD	2	11
	G4 CKD	1	8
	G5 CKD	0	6
TSH (mU/L)	Euthyroid	210	130
	Hypothyroidism	30	90
	Hyperthyroidism	10	30
LDL-C (mg/dL)	Optimal Level	147	147
	Intermediate elevation	43	61
	High elevation	36	21
	Very High elevation	24	21
Triglycerides (mg/dL)	Optimal Level	146	134
	Intermediate elevation	71	65
	High elevation	26	40
	Very High elevation	7	11
Residence	Rural areas	130	142
	Urban areas	120	108
Smoking	Nonsmoker	244	214
	Light smoker	4	16
	Heavy smoker	2	20
Occupation	Sedentary Life	154	114
	Mental Worker	73	50
	Hard Worker	23	86

Table 6 shows distribution of DN according to risk factors depending on severity.

Table (6): shows distribution of DN according to risk factors depending on severity.

Score result		No DN	Mild DN	Moderate DN	Severe DN
BMI Result	**Normal**	140	10	20	10
	Overweight	50	62	20	30
	Obese	60	8	20	70
Height	**Short**	82	32	5	13
	Average	150	27	39	11
	Tall	18	21	16	86
Duration of diabetes	**<=5 y**	230	40	0	20
	6 to 10y	20	30	30	50
	>=11y	0	10	30	40
HbA1c (%)	**<=7**	90	10	0	0
	7 to 8	130	20	0	0
	8.1 to 9	30	12	20	10
	>9	0	38	40	100
Metformin	**Not on metformin**	150	22	20	30
	On metformin	100	58	40	80
GFR	**No nephropathy**	230	60	20	10
	G1 CKD	5	8	22	19
	G2 CKD	5	2	8	32
	G3a CKD	7	7	8	29
	G3b CKD	2	2	1	8
	G4 CKD	1	1	1	6
	G5 CKD	0	0	0	6
TSH (mU/L)	**Euthyroid**	210	40	30	60
	Hypothyroidism	30	30	20	40
	Hyperthyroidism	10	10	10	10
LDL-C (mg/dL)	**High elevation**	8	3	36	10
	Intermediate elevation	10	19	43	32
	Optimal level	59	38	147	50
	Very-high elevation	3	0	24	18
Triglycerides (mg/dL)	**Optimal level**	146	36	37	61
	Intermediate elevation	71	37	19	9
	High elevation	26	2	2	36
	Very-high elevation	7	5	2	4

DISCUSSION

This was a cross-sectional observational study conducted on 500 diabetic patients (type 1 and type 2) to assess prevalence of DPN, its pattern, severity, and associated risk factors in Benha City, Egypt. In our study, prevalence, pattern and severity of DN among the studied patients were detected based on TCSS.

In the present study, we found that prevalence of diabetic patients who presented with no peripheral neuropathy in the studied patients was 50% and prevalence of diabetic patients who presented with peripheral neuropathy in the studied patients was 50%. Thirty-two percent of neuropathic patients presented with mild peripheral neuropathy. Twenty-four percent of neuropathic patients presented with moderate peripheral neuropathy. Forty-four percent of neuropathic patients presented with severe peripheral neuropathy. The prevalence of patients who presented with type 1 diabetes in the studied patients was 10% and prevalence of patients who presented with type 2 diabetes in the studied patients was 90%. Forty percent of patients who presented with type 1 diabetes in the studied patients had no peripheral neuropathy while sixty percent of patients who presented with type 1 diabetes in the studied patients had peripheral neuropathy. About fifty-one percent of patients who presented with type 2 diabetes in the studied patients had no peripheral neuropathy while forty-nine percent of patients who presented with type 2 diabetes in the studied patients had peripheral neuropathy.

Parallel to our results, **Amour *et al.* [11],** used TCSS to detect DPN and found that twenty-six percent of diabetic patients in the studied patients presented with mild peripheral neuropathy. Nineteen percent of diabetic patients in the studied patients presented with moderate peripheral neuropathy. Fifty-five percent of diabetic patients in the studied patients presented with severe peripheral neuropathy. **Gurbakhshani *et al.* [12],** used TCSS to detect DPN and its severity and found that prevalence of mild, moderate and severe peripheral neuropathy in a total of 237 diabetic patients was 26%, 19%, 55% respectively.

Regarding clinical manifestations of DPN in diabetic patients in the studied patients, we found that seventy percent presented with pain of feet. About fifty-one percent presented with numbness. About sixty-two percent presented with tingling. About thirty-two percent presented with weakness. Twelve percent presented with ataxia. About thirty-three percent presented with upper limb symptoms. Fifty-two percent presented with intact pinprick sensation and forty-eight percent presented with lost pinprick sensation. Eighty percent presented with intact temperature sensation and twenty percent presented with lost temperature sensation. About fifty percent presented with intact light touch sensation and about fifty percent presented with lost light touch sensation. Sixty-eight percent presented with intact vibration sensation and thirty-two percent presented with lost vibration sensation. About seventy-one percent presented with intact joint position sensation and about twenty-nine percent presented with lost joint position sensation. About seventy-six percent presented with normal Rt knee reflex, sixteen percent presented with reduced Rt knee reflex and about eight percent presented with absent Rt knee reflex. Seventy-six percent presented with normal Lt knee reflex, sixteen percent presented with reduced Lt knee reflex and eight percent presented with absent Lt knee reflex. About sixty-four percent presented with normal Rt ankle reflex, about thirteen percent presented with reduced Rt ankle reflex and twenty-three percent presented with absent Rt ankle reflex. Sixty-six percent presented with normal Lt ankle reflex, twelve percent presented with reduced Lt ankle reflex and twenty-two percent presented with absent Lt ankle reflex.

In parallel with our results, **Katulanda *et al.* [13],** found that about thirty-two percent of diabetic patients in the studied patients presented with burning, aching pain or tenderness of feet. About thirty-seven percent presented with numbness of feet. About thirty percent presented with prickling sensation of feet. About Twenty-five percent presented with unsteadiness. About forty percent presented with impaired big-toe pin prick sensation. About thirty-eight percent presented with impaired light touch sensation. About twenty-six percent presented with impaired vibration sensation. About seventeen percent presented with impaired joint position sensation. About eight percent presented with impaired temperature sensation. About twenty-eight percent presented with absent or diminished ankle reflex. About twelve percent presented with absent or diminished knee reflex.

Regarding impact of height on DPN, our study showed that height is an important risk factor for development and severity of DPN, this could be inferred from the following:

In the present study, we found that the prevalence of short, average, and tall diabetic patients in the studied patients was 26.4%, 45.4%, and 28.2% respectively. About sixty-two percent of short diabetic patients in the studied patients had no peripheral neuropathy while about thirty-eight percent had peripheral neuropathy. About sixty-six percent of diabetic patients with average height had no peripheral neuropathy while about thirty-four percent had peripheral neuropathy. About thirteen percent of tall diabetic patients in the studied patients had no peripheral neuropathy while about eighty-seven percent had peripheral neuropathy. About seventy percent of tall neuropathic patients presented with severe form of DPN.

Our study found that height had a strong positive significant correlation with TCSS score ($r=0.335$, $P< 0.001$). Agreed with our findings, **Davis *et al.* [14]**, stating that height was linked in the

pathophysiology of diabetic sensorimotor polyneuropathy (DSPN) due to the disease's length-dependent pattern. In contrast, **Franklin *et al.*[15]** discovered no link between height and the incidence of DSPN in a population sample in southern Colorado.

Regarding impact of BMI on DPN, our study showed that obesity is an important risk factor for development and severity of DPN, this could be inferred from the following:

In the present study, we found that the prevalence of diabetic patients with normal BMI, overweight, and obese in the studied patients was 36%, 32.4%, and 31.6% respectively. About seventy-eight percent of diabetic patients with normal BMI in the studied patients had no peripheral neuropathy while about twenty-two had peripheral neuropathy. About thirty-one of overweight diabetic patients in the studied patients had no peripheral neuropathy while about sixty-nine had peripheral neuropathy. Thirty-eight percent of obese diabetic patients in the studied patients had no peripheral neuropathy while sixty-two percent had peripheral neuropathy. About seventy-one percent of obese neuropathic patients in the studied patients presented with severe form of DPN. Our study found that BMI had a strong positive significant correlation with TCSS score (r=0.338, P< 0.001). In agreement with our study, increased BMI was substantially related with the development of DPSN in diabetic individuals in a multivariate study [16-18].

Regarding impact of residence on DPN, our study showed that residence isn't a significant risk factor for development and severity of DPN, this could be inferred from the following:

In the current study, we discovered that the prevalence of diabetes patients in rural regions was 54.4% and in urban areas was 45.6%. Our study found that there was no correlation between DPN and residence because about forty-eight percent of diabetic patients who live in rural areas in the studied patients had no peripheral neuropathy and about fifty-two percent had peripheral neuropathy. About fifty-three percent of diabetic patients who live in urban areas in the studied patients had no peripheral neuropathy while about forty-seven percent had peripheral neuropathy. In contrast to our study, lower household income and living in a rural area were linked to the presence of DPN. One reason for the phenomena would be because those in poverty have lower rates of health service utilisation, which might lead to delayed diagnosis and inadequate management of diabetes mellitus [19].

Regarding impact of life style on DPN, our study showed that hard working is an important risk factor for development of DPN, this could be inferred from the following:

In the present study, we found that the prevalence of patients who had sedentary life was 53.6%. The prevalence of mental worker patients was 24.6%. The prevalence of hard worker patients was 21.8%. Our study found that there was no correlation between sedentary life and DPN because about fifty-seven percent of patients who have sedentary life in the studied patients had no peripheral neuropathy while about forty-three percent had peripheral neuropathy. Our study found that there was no correlation between mental working and DPN because about fifty-nine percent of mental worker patients in the studied patients had no peripheral neuropathy while about forty-one percent had peripheral neuropathy. Our study found that there was positive correlation between hard working and DPN because about twenty-one percent of hard worker patients in the studied patients had no peripheral neuropathy while about seventy-nine percent had peripheral neuropathy.

Regarding impact of smoking on DPN, our study showed that smoking is an important risk factor for development and severity of DPN, this could be inferred from the following:

In present study, we found that prevalence of non-smoker patients was 91.6%. The prevalence of light smoker patients was 4%. The prevalence of heavy smoker patients was 4.4%. About fifty-three percent of non-smoker diabetic patients in the studied patients had no peripheral neuropathy while about forty-seven percent had peripheral neuropathy. Twenty percent of light smoker diabetic patients in the studied patients had no peripheral neuropathy while eighty percent had peripheral neuropathy. About nine percent of heavy smoker diabetic patients in the studied patients had no peripheral neuropathy while about ninety-one percent had peripheral neuropathy. About fifty-five percent of heavy smoker neuropathic patients in the studied patients presented with severe form of DPN.

In consistent with our findings **Soheilykhah *et al.*** [20] showed a substantial association ($p < 0.001$) between current smoking status and the prevalence of DN. **Jaiswal *et al.*** [21] discovered a link between the development of peripheral neuropathy and smoking (p-value 0.012), which might be explained by the fact that smoking reduces blood flow to microvascular nerve cells, which causes nerve damage.

Regarding impact of glycemic state on DPN, our study showed that poor glycemic control is an important risk factor for development and severity of DPN, this could be inferred from the following:

In current study, we found that the prevalence of diabetic patients who presented with HbA1c $\leq$ 7, between 7 to 8, between 8.1 to 9, more than 9 was 20%, 30%, 14.4%, 35.6% respectively. Ninety percent of diabetic patients with HbA1c is $\leq$7 in the studied patients had no peripheral neuropathy while ten percent had peripheral neuropathy. About eighty-seven percent of diabetic patients with HbA1c between 7 to 8 in the studied patients had no peripheral neuropathy while about thirteen percent had peripheral neuropathy. About forty-two percent of diabetic patients with HbA1c between 8.1 to 9 in the studied

patients had no peripheral neuropathy while about fifty-eight percent had peripheral neuropathy. All diabetic patients with HbA1c more than 9 in the studied patients had peripheral neuropathy. About fifty-six percent of neuropathic patients with HbA1c more than 9 in the studied patients presented with severe form of DPN. Our study found that HbA1c had a strong positive significant correlation with TCSS score (r=0.806, P< 0.001).

In keeping with our findings, **Ziegler *et al.*** [22] conducted a 24-year follow-up analysis of type 1 diabetic patients and discovered that the prevalence of verified clinical DSPN in insufficiently treated individuals was 64%, compared to 0% in stringently controlled patients. **Elmagboul** [23] discovered that maintaining adequate glycemic control reduces the chance of developing peripheral neuropathy.

Regarding impact of duration of diabetes on DPN, our study showed that prolonged hyperglycemia is an important risk factor for development and severity of DPN, this could be inferred from the following:

In the present study, we found that the prevalence of patients who were diabetic for ≤5 years was 58%, for 6 to 10 years was 26%, and for ≥11 years was 16%. About seventy-nine percent of patients who were diabetic for ≤5 years in the studied patients had no peripheral neuropathy while about twenty-one percent had peripheral neuropathy. About fifteen percent of patients who were diabetic for 6 to 10 years the studied patients had no peripheral neuropathy while about eighty-five percent had peripheral neuropathy. All patients who were diabetic for ≥11 years in the studied patients had peripheral neuropathy. Fifty percent of neuropathic patients who were diabetic for ≥11 years in the studied patients presented with severe form of DPN. Our study found that duration of diabetes had a strong positive significant correlation with TCSS score (r=0.630, P< 0.001).

In keeping with our findings, **Ziegler *et al.*** [24] indicated that diabetes duration is a significant and well-known risk factor for DPN. In all kinds of diabetes, the link between DPN and diabetes duration is independent of patient age. Although the actual incidence of DPN varies depending on the diagnostic methods employed and the population chosen (for example, hospital-based vs. outpatient-based vs. community-based), its relationship with diabetes duration is still considerable.

Regarding impact of medical therapy on DPN, our study showed that metformin intake is an important risk factor for development and severity of DPN, this could be inferred from the following:

In the current study, we observed that the prevalence of diabetes patients who were not using metformin was 44.4%. The prevalence of diabetic patients who were on metformin was 55.6%. About sixty-eight percent of diabetic patients who were not on metformin in the studied patients had no peripheral neuropathy while about thirty-two percent had peripheral neuropathy. About thirty-six percent of diabetic patients who were on metformin in the studied patients had no peripheral neuropathy while about sixty-four percent had peripheral neuropathy. About forty-four percent of neuropathic patients who were on metformin in the studied patients presented with severe form of DPN. In agreement with our study, metformin-associated cobalamin insufficiency may add to DPN's clinical burden [25], and the association is dependent on metformin dosage and duration [26].

Regarding impact of thyroid profile on DPN, our study showed that abnormal thyroid profile -either hypothyroidism or hyperthyroidism- is an important risk factor for development of DPN, this could be inferred from the following:

In our investigation, we discovered that the prevalence of euthyroid, hypothyroid, and hyperthyroid patients was 68%, 24%, and 8% respectively. About sixty-two percent of euthyroid diabetic patients in the studied patients had no peripheral neuropathy while about thirty-eight percent had peripheral neuropathy. Twenty-five percent of diabetic patients who presented with hypothyroidism in the studied patients had no peripheral neuropathy while seventy-five percent had peripheral neuropathy. Twenty-five percent of diabetic patients who presented with hyperthyroidism in the studied patients had no peripheral neuropathy while seventy-five percent had peripheral neuropathy. Our study found that TSH had a strong positive significant correlation with TCSS score (r=0.332, P< 0.001).

In agreement with our findings, **Zhao *et al.*** [27] conducted research on 605 type 2 diabetes mellitus (T2DM) patients and discovered that serum TSH levels were considerably higher in DPN compared to non-DPN T2DM patients. Subclinical hypothyroidism (SCH) people had a greater prevalence and symptoms of DPN compared to euthyroid individuals (both P<0.01). According to Spearman's correlation analysis, serum TSH levels were positively related with DPN (r=0.172, P<0.01). Multiple logistic regression study revealed a significant independent connection between TSH and DPN after correcting for relevant factors [odds ratio (OR)=1.365, P<0.01].

Regarding impact of lipid profile on DPN, our study showed that dyslipidemia isn't a significant risk factor for development of DPN, this could be inferred from the following:

In the current investigation, we discovered the frequency of diabetic patients who presented with optimal, intermediately elevated, highly elevated, very highly elevated LDL-C level was 58.8%, 20.8%, 11.4%, 9% respectively. Also, the prevalence of diabetic patients who presented with optimal, intermediately elevated, highly elevated, very highly elevated triglycerides level was 56%, 27.2%, 13.2%, 3.6% respectively. Our study found that there was no significant association between dyslipidemia and

peripheral neuropathy because the prevalence of peripheral neuropathy in diabetic patients who presented with optimal, intermediately elevated, highly elevated, very highly elevated of LDL-C level was 50%, 58.7%, 36.8%, 46.7% respectively and the prevalence of peripheral neuropathy in diabetic patients who presented with optimal, intermediately elevated, highly elevated, very highly elevated of triglycerides level was 47.9%, 47.8%, 60.6%, 61.2% respectively. Our study found that LDL-C and triglycerides level had no significant correlation with TCSS score (r= 0.015, P= 0.743).

In consistence with our findings, **Agrawal *et al.*'s**[28] findings showed that neuropathy and aberrant lipid profiles in type 2 diabetes did not significantly correlate with one another. In contrast to our study, **Davis *et al*.**[14] found that dyslipidemia is a risk factor for peripheral neuropathy because DSPN has been shown to correlate with high cholesterol and triglycerides after adjustment for metabolic control & other risk factors and also found that In Type2 diabetes, fibrate use (hazard ratio (HR): 0.52, 95% CI: 0.27-0.98) and statin use (HR: 0.65, 95% CI: 0.46-0.93) significantly reduced the incidence of DSPN over 5 years.

Regarding impact of kidney function tests on DPN, our study showed that CKD is an important risk factor for development and severity of DPN, this could be inferred from the following:

In the current investigation, we discovered the frequency of diabetic patients who presented with no nephropathy, grade1 CKD, grade2 CKD, grade3a CKD, grade3b CKD, grade4 CKD, grade5 CKD was 64%, 10.8%, 9.4%, 10.2%, 2.6%, 1.8%, 1.2% respectively. The prevalence of peripheral neuropathy in diabetic patients who presented with no nephropathy, grade1 CKD, grade2 CKD, grade3a CKD, grade3b CKD, grade4 CKD, grade5 CKD was 28.2%, 90%, 89.4%, 86.3%, 84.7%, 88.9%, 100% respectively. All patients who presented with grade 5 CKD in the studied patients presented with severe form DN. In agreement with our study, **He *et al.*** [29] conducted a meta-analysis and found that a low estimated glomerular filtration rate (eGFR) was a significant risk factor for developing DPN (SMD, − 0.45; 95% CI, − 0.63 to − 0.27; P < 0.01).

Strength of the study:

Our findings look at the frequency of DPN, its pattern, severity, and related risk factors in Benha City, Egypt.

The limitations of the study:

1. The study's methodology was cross-sectional, making it difficult to establish causal relationships between chronic renal failure and thyroid dysfunction.
2. The research sample size was modest, which may limit the findings' generalizability to broader groups.
3. The study did not look at other factors that might impact thyroid hormone malfunction, such as dietary habits, medication usage, or other comorbidities.
4. The absence of electro-diagnostic procedures, nerve conduction velocity (NCV), which are the definitive and conventional approaches for identifying neuropathy, might alter the course of these presentations. Finally, other unusual causes of neuropathy, such as vasculitis and vitamin B insufficiency, were not ruled out.

CONCLUSIONS

DPN is common in our context, affecting half of the patients who visit the diabetic clinic, with more than half suffering from severe cases. The key risk factors include age, increasing BMI, duration of diabetes, HTN, and oral hypoglycemic agent (OHGA). After documenting these findings, a greater effort should be made to reduce the incidence and severity of PDN in diabetic patients by education that emphasises regular foot care, strict glucose control, blood pressure reduction, and lifestyle adjustment. In addition, a simple bedside screening method may now be used to detect DPN and quantify its severity in diabetic patients.

ABBREVIATIONS

ALT	Alanine transaminase
AST	Aspartate aminotransferase
BMI	Body mass index
CKD	chronic kidney disease
DM	Diabetes mellitus
DN	Diabetic neuropathy
DPN	Diabetic peripheral neuropathy
DSPN	Diabetic Sensorimotor Polyneuropathy
eGFR	Estimated Glomerular filtration rate
FBS	fasting blood sugar
HbA1c	Hemoglobin A1c
HDL	High-density lipoprotein
INR	International normalized ratio
LDL	Low-density lipoprotein
Lt	Left
NCV	Nerve conduction velocity
OHGA	Oral hypoglycemic agent
Rt	Right
SCH	Subclinical hypothyroidism
T1DM	Type1 diabetes
T2DM	Type2 diabetes
TCSS	Toronto clinical scoring system
TSH	Thyroid-stimulating hormone
UL	Upper limb

Conflict of interest: None declared.
Fund: Non-fundable.

REFERENCES

1. **Cho N, Shaw J, Karuranga S *et al.* (2018):** IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes Res Clin Pract., 138:271-81.
2. **Iqbal Z, Azmi S, Yadav R *et al.* (2018):** Diabetic peripheral neuropathy: Epidemiology, diagnosis, and pharmacotherapy. Clin Ther., 40(6):828-49.
3. **Callaghan B, Cheng H, Stables C *et al.* (2012):** Diabetic neuropathy: clinical manifestations and current treatments. Lancet Neurol., 11(6):521-34.
4. **Lu Y, Xing P, Cai X *et al.* (2020):** Prevalence and risk factors for diabetic peripheral neuropathy in type 2 diabetic patients from 14 countries: Estimates of the INTERPRET-DD Study. Front Public Health, 8: 534372. Doi:10.3389/fpubh.2020.534372.
5. **Juster-Switlyk K, Smith A (2016):** Updates in diabetic peripheral neuropathy. F1000Res., 5:6898. Doi:10.12688/f1000research.7898.1.
6. **Pop-Busui R, Boulton A, Feldman E *et al.* (2017):** Diabetic Neuropathy: A Position Statement by the American Diabetes Association. Diabetes Care, 40(1):136-54.
7. **Hicks C, Selvin E (2019):** Epidemiology of peripheral neuropathy and lower extremity disease in diabetes. Curr Diab Rep., 19(10):86. Doi:10.1007/s11892-019-1212-8.
8. **Tavakkoly-Bazzaz J, Amoli M, Pravica V *et al.* (2010):** VEGF gene polymorphism association with diabetic neuropathy. Mol Biol Rep., 37(7):3625-30.
9. **Jende J, Groener J, Oikonomou D *et al.* (2018):** Diabetic neuropathy differs between type 1 and type 2 diabetes: Insights from magnetic resonance neurography. Ann Neurol., 83(3):588-98.
10. **Mai L, Clark A, Gordon A *et al.* (2017):** Long-term outcomes in the management of painful diabetic neuropathy. Can J Neurol Sci., 44(4):337-42.
11. **Amour A, Chamba N, Kayandabila J *et al.* (2019):** Prevalence, patterns, and factors associated with peripheral neuropathies among diabetic patients at tertiary hospital in the Kilimanjaro Region: descriptive cross-sectional study from north-eastern Tanzania. Int J Endocrinol., 19:34-44.
12. **Gurbakhshani M, Shaikh B, Gurbakhshani K (2020):** Peripheral neuropathies its prevalence, patterns and associated factors among diabetic patients at tertiary hospital in Larkana, Sindh: Descriptive cross-sectional study. Diabetologia, 20: 1-4.
13. **Katulanda P, Ranasinghe P, Jayawardena R *et al.* (2012):** The prevalence, patterns and predictors of diabetic peripheral neuropathy in a developing country. Diabetol Metab Syndr., 4: 1-8.
14. **Davis T, Yeap B, Davis W *et al.* (2008):** Lipid-lowering therapy and peripheral sensory neuropathy in type 2 diabetes: the Fremantle Diabetes Study. Diabetologia, 51:562-6.
15. **Franklin G, Shetterly S, Cohen J *et al.* (1994):** Risk factors for distal symmetric neuropathy in NIDDM: the San Luis Valley Diabetes Study. Diabetes Care, 17(10): 1172-77.
16. **Jacovides A, Bogoshi M, Distiller L *et al.* (2014):** An epidemiological study to assess the prevalence of diabetic peripheral neuropathic pain among adults with diabetes attending private and institutional outpatient clinics in South Africa. Int J Med Res., 42(4):1018-28.
17. **Al-Kaabi J, Al Maskari F, Zoubeidi T *et al.* (2014):** Prevalence and determinants of peripheral neuropathy in patients with type 2 diabetes attending a tertiary care center in the United Arab Emirates. J Diabetes Metab., 5(346):2-12.
18. **Kiani J, Moghimbeigi A, Azizkhani H *et al.* (2013):** The prevalence and associated risk factors of peripheral diabetic neuropathy in Hamedan, Iran. Arch Iran Med., 16(1):10-23.
19. **Group D (1988):** Factors in development of diabetic neuropathy: baseline analysis of neuropathy in feasibility phase of Diabetes Control and Complications Trial (DCCT). J Diabetes, 37(4):476-81.
20. **Soheilykhah S, Rashidi M, Dehghan F *et al.* (2013):** Prevalence of peripheral neuropathy in diabetic patients. Iran J Basic Med Sci., 5: 107-13.
21. **Jaiswal M, Divers J, Dabelea D *et al.* (2017):** Prevalence of and risk factors for diabetic peripheral neuropathy in youth with type 1 and type 2 diabetes: SEARCH for diabetes in youth study. Diabetes Care, 40: 1226-32.
22. **Ziegler D, Behler M, Schroers-Teuber M *et al.* (2015):** Near-normoglycaemia and development of neuropathy: a 24-year prospective study from diagnosis of type 1 diabetes. BMJ Open, 5: 23-33.
23. **Elmagboul N (2020):** Prevalence and associated risk factors of peripheral neuropathy in diabetic patients attending the primary health care centers in Khartoum locality, Khartoum State, Sudan at 2019. J Diabetes Res., 2: 1-7.
24. **Ziegler D, Papanas N, Vinik A *et al.* (2014):** Epidemiology of polyneuropathy in diabetes and prediabetes. Handb Clin Neurol., 126: 3-22.
25. **Wulffele M, Kooy A, Lehert P *et al.* (2003):** Effects of short-term treatment with metformin on serum concentrations of homocysteine, folate and vitamin B12 in type 2 diabetes mellitus: a randomized, placebo-controlled trial. J Intern Med., 254(5):455-63.
26. **Ting R, Szeto C, Chan M *et al.* (2006):** Risk factors of vitamin B12 deficiency in patients receiving metformin. Arch Intern Med., 166(18):1975-9.
27. **Zhao W, Zeng H, Zhang X *et al.* (2016):** A high thyroid stimulating hormone level is associated with diabetic peripheral neuropathy in type 2 diabetes patients. Diabetes Res Clin Pract., 115:122-9.
28. **Agrawal R, Sharma P, Pal M *et al.* (2006):** Magnitude of dyslipedemia and its association with micro and macro vascular complications in type 2 diabetes: a hospital based study from Bikaner (Northwest India). Diabetes Res Clin Pract., 73: 211-4.
29. **He Q, Zeng Z, Zhao M *et al.* (2003):** Association between thyroid function and diabetes peripheral neuropathy in euthyroid type 2 diabetes mellitus patients. Sci Rep., 13(1):13499-505.