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Detection of diabetic polyneuropathy in a family medicine clinic by using monofilament

Detekcija dijabetesne polineuropatije u ambulanti porodične medicine korišćenjem monofilamenta

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Abstract

Background/Aim. Diabetic polyneuropathy (DPN) is the most common microvascular complication of diabetes mellitus (DM), which may be present at the time of disease detection. Screening for DPN is performed for the patients with type 2 diabetes at the time of diagnosis and for type 1 diabetes 5 years after diagnosis. The primary aim of this study was to determine the prevalence of DNP among family medicine patients with DM aged 18 to 70 years using nylon monofilament. **Methods.** The cross-sectional study estimated the prevalence of DPN among primary care patients with DM in Banja Luka, Republic of Srpska, Bosnia and Herzegovina. Semmes-Weinstein nylon 10 g monofilament was used to detect DPN. Age, gender, duration of DM, type of therapy, symptoms, glycosylated hemoglobin (HbA1c), and risk factors (hypertension, smoking, dyslipidemia, obesity, physical inactivity) were analyzed. Data collection took place from June 1st, 2017 to May 31st, 2018. **Results.** The study included 228 patients, 132 (57.9%) men and 96 (42.1%) women. There was a statistically significant difference in the presence of all symptoms of DPN (tingling, burning, light burning, and stinging) among patients with different duration of DM ($p < 0.01$). Multivariate logistic regression revealed that patients who had hypertension [odds ratio (OR) = 26.2; 95% confidence interval (CI): 4.070–168.488; $p = 0.001$], used oral antidiabetic therapy (OR = 12.3; 95% CI: 1.300–116.309; $p = 0.029$), had tingling (OR = 5.2; 95% CI: 1.431–18.571; $p = 0.012$) and a longer duration of diabetes (OR = 4.27; 95% CI: 1.983–9.175; $p = 0.000$) were more likely to have DPN. **Conclusion.** The prevalence of DPN in family medicine patients with DM using nylon monofilament was 24.2%. Determinants of DNP were the presence of symptoms of tingling, duration of diabetes, hypertension, and the use of oral antidiabetic therapy alone.

Key words:
bosnia and herzegovina; diabetes mellitus, type 2; diabetic neuropathies; prevalence; primary health care; risk factors.

Apstrakt

Uvod/Cilj. Dijabetesna polineuropatija (DPN) je najčešća mikrovaskularna komplikacija dijabetesa melitusa (DM) koja može da bude prisutna i u trenutku samog otkrivanja bolesti. *Screening* na DPN se radi svim obolelim od DM tipa 2 u trenutku postavljanja dijagnoze, a kod DM tipa 1, 5 godina od postavljene dijagnoze. Osnovni cilj ovog istraživanja bio je da se utvrdi prevalencija DPN kod bolesnika sa DM korišćenjem najlonskog monofilamenta u ambulanti porodične medicine. **Metode.** U istraživanju sprovedenom po tipu studije preseka praćena je učestalost DPN kod bolesnika sa DM na području Banja Luke. Za detekciju DPN korišćen je *Semmes-Weinstein* najlonski monofilament od 10 g. Analizirani su dob, pol, trajanje DM, simptomi, vrsta terapije, glikozilirani hemoglobin (HbA1c) i faktori rizika (hipertenzija, pušenje, dislipidemija, gojaznost, fizička neaktivnost). Podaci su prikupljani u periodu od 01. juna 2017. do 31. maja 2018. godine. **Rezultati**. Istraživanje je obuhvatilo 228 pacijenata, 132 (57,9%) muškarca i 96 (42,1%) žena. Utvrđena je statistički značajna razlika u prisustvu svih simptoma DPN (trnjenje, gorenje, peckanje i žarenje) kod bolesnika sa različitim trajanjem DM ($p < 0,01$). Multivarijantnom logističkom regresijom utvrđeno je da najveću verovatnoću pojave DPN ima bolesnik sa hipertenzijom [*odds ratio* (OR) = 26,2; 95% *confidence interval* (CI): 4,070–168,488; $p = 0,001$], koji koristi oralnu antidijabetesnu terapiju (OR = 12,3; 95% CI: 1,300–116,309; $p = 0,029$), ima simptom trnjenje (OR = 5,2; 95% CI: 1,431–18,571; $p = 0,012$) i duže trajanje DM (OR = 4,27; 95% CI: 1,983–9,175; $p = 0,000$). **Zaključak.** Prevalencija DPN kod bolesnika sa DM, korišćenjem najlonskog mono

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filamenta u ambulanti porodične medicine, iznosila je 24,2%. DPN je bila udružena sa prisustvom simptoma trnjenja, trajanjem dijabetesa, hipertenzijom i upotrebom samo oralne antidijabetesne terapije.

Ključne reči:
bosna i hercegovina; dijabetes melitus, tip 2; dijabetičke neuropatije; prevalenca; zdravstvena nega, primarna; faktori rizika.

Introduction

Diabetic polyneuropathy (DPN) is the most common microvascular complication of diabetes mellitus (DM), which may also be present at the time of disease detection. It is mainly distal sensorimotor polyneuropathy, which is responsible, in 75% of cases, for the early amputation of parts of the extremities and whole extremities in patients with diabetes [1–4].

A study conducted in England found the onset of symptoms of painful neuropathy in one-third of the total number of diabetic patients at the community level examined [5].

Small A-delta and C fibers become damaged first. Initially, the disease is asymptomatic in 50% of cases [6], but later on, there are symptoms such as tingling, burning, loss of sensation of touch, temperature or pain, trophic changes on the skin with the onset of ulcer development. The intensity of symptoms is greatest when resting, especially at night. DPN is the leading cause of foot ulceration, as well as a prerequisite for the development of Charcot's neuropathy or Charcot's foot, also increasing the risk of falls and fractures [7, 8]. It was found that 45–60% of diabetic foot ulcers are of neuropathic origin, and patients with DM are 3.5 times more likely to develop ulcers than non-diabetic patients.

The American Diabetes Association (ADA) [9] recommends DNP screening for all patients with type 2 DM at the time of diagnosis and with type 1 DM, 5 years after diagnosis. According to the International Diabetes Federation (IDF), every family physician should provide foot examination at least once a year to his/her patients [10]. There are several clinical diagnostic modalities for diagnosing DPN. Quantitative sensory testing (QST) has been available for more than 2 decades using cold and warmth thresholds to detect small fiber neuropathies. Semmes-Weinstein 10 g monofilament test is commonly used to detect DNP in family medicine setting. Further evaluation includes clinical imaging and nerve conduction studies (NCS). The study by Park and Kim [11] established the need for simple and non-invasive tests, including a Semmes-Weinstein 10 g monofilament test for DPN in patients with type 2 DM.

According to the previous studies, DPN can develop as early as in pre-diabetes (glucose tolerance impairment – IGT) [12, 13]. In addition to hyperglycemia, one of the important factors involved in the pathogenetic mechanism of DPN is hyperlipidemia [14, 15].

Many prospective studies have confirmed that loss of pressure sensitivity by 10 g monofilament is an important predictor of possible onset ulceration and diabetic foot leading to possible lower limb amputations [16, 17]. The monofilament test is the best choice for DPN detection because it is portable, fast, non-invasive, inexpensive, and patient-friendly.

The epidemiological research found that the prevalence of DPN in the world is greater than 50% when adjusted for diabetes duration and age [18–20]. However, data for diabetes patients in the Republic of Srpska are lacking. The primary aim of this study was to determine the prevalence of DNP among family medicine patients with DM aged 18 to 70 years by using nylon monofilament. The secondary aim was to determine the risk factors (hypertension, smoking, dyslipidemia, obesity, physical inactivity), duration of diabetes, type of therapy, and regulation of DM (glycosylated hemoglobin – HbA1c) associated with DNP.

Methods

The cross-sectional study explored the prevalence of DPN in patients with DM registered with the family practices and affiliated with Primary Health Center in Banja Luka, Republic of Srpska, Bosnia and Herzegovina. With a population size of 15,617 diabetic patients, an error of 5%, confidence level of 95% and confidence interval (CI) of 6.44, the estimated sample size was 228. Patients were selected randomly from the electronic registry of patients with DM. Data collection took place between June 2017 and May 2018.

Inclusion criteria were as follows: age 18 to 70, type 1 and type 2 DM diagnosis according to International Classification of Diseases (ICD), and written consent to participate in the study obtained from each respondent. Patients with DM who had ulcers or amputations, associated peripheral arterial disease, and those with multiple complications of diabetes were excluded from the study. Written and electronic records of DM patients were used in the data collection.

For this research, a checklist was created for each participant individually. The participants underwent inspection, palpation, and physical examination of the foot. Semmes-Weinstein nylon 10 g monofilament was used to detect DPN.

The examiner demonstrated first the strength of the monofilament touch on each participant's arm, then asked them to close their eyes and performed testing on both feet. The examined points included the first metatarsal-phalangeal joint of the thumb, the dorsum of the thumb, the plantar side of the thumb, and the plantar side of the heel. The participant should relay when he or she feels the touch. The total score is eight. According to a previous study, more than four wrong answers screened positive for DPN [4]. Moreover, data on subclinical manifestations (tingling, burning, light burning, and stinging) of DPN are collected in an interview with each participant (Yes, No).

Age, gender, duration of diabetes, type of therapy, glycemic regulation (HbA1c), and risk factors (hypertension, smoking, dyslipidemia, obesity, physical inactivity) were recorded for each participant.

Participants were divided into 4 age groups: 20–30, 31–40, 41–50, and 51–60 years. They were also divided into 4

groups according to the duration of diabetes: duration of diabetes up to 5, 10, 20 years, and over 20 years.

According to the type of therapy, they were divided into 3 groups: those using oral antidiabetic therapy, insulin therapy, and combination therapy. For glycemic control assessment, HbA1c was used. HbA1c levels were evaluated in the central laboratory of the Primary Health Center in Banja Luka (Bioanalyzer Arhitekt c 8000). HbA1c < 7% was considered good glycemic control and HbA1c ≥ 7% as poor glycemic control. Blood pressure values greater than 130/80 mmHg were considered unregulated hypertension. Dyslipidemia was diagnosed if total cholesterol value was > 4 mmol/L, and/or LDL cholesterol > 2.6 mmol/L and/or triglyceride > 1.7 mmol/L [21, 22]. Obesity was recorded if the participant's body mass index (BMI) was > 30 kg/m^2 and waist circumference (WC) > 94 cm for men and 80 cm for women. According to physical activity, participants were rated as inactive, moderately active, and extremely physically active [23].

The consent of the institutional Ethics Committee was obtained for this research.

Statistical analysis

All analyzes were performed using SPSS version 25 (SPSS Inc., Chicago, IL, USA). The results were analyzed and presented using descriptive statistics (absolute and relative numbers, measures of central tendency, standard deviation). Demographic data and risk factors in the respondents were analyzed using adequate statistical tests (χ^2-test and Student's *t*-test of independent samples). Univariate and multivariate logistic regression were used to determine the association between DNP and risk factors. A probability level or *p*-value of less than 0.05 ($p < 0.05$) was considered statistically significant.

Results

The study included 228 patients, 132 (57.9%) men and 96 (42.1%) women. The average age of the participants was 55.8 ± 9.2 years. The prevalence of DNP among our participants with DM, using nylon monofilament, was 24.2%.

Participants with a longer duration of diabetes and report-

Table 1

Frequency of DPN according to gender, age, HbA1c, duration of diabetes, presence of symptoms (tingling, burning, light burning, and stinging), and type of therapy

Parameter	Presence of DPN, n (%)		*p*
	yes	no	
Gender			
male	38 (69.1)	94 (54.7)	0.059
female	17 (30.9)	78 (45.3)	
Age (years)			
< 18	0 (0.0)	0 (0.0)	
18–30	1 (1.8)	6 (3.5)	
31–40	2 (3.6)	10 (5.8)	
41–50	54 (7.3)	21 (12.2)	0.712
51–60	25 (45.5)	73 (42.4)	
61–70	23 (41.8)	62 (36.0)	
> 70	0 (0.0)	0 (0.0)	
HbA1c (%)			
≤ 7.00	20 (36.4)	64 (37.4)	0.007
> 7.00	35 (63.6)	107 (62.6)	
Duration of diabetes (years)			
5–10	19 (34.5)	106 (61.6)	
10–15	11 (20.0)	41 (23.8)	< 0.001
15–20	13 (23.6)	18 (10.5)	
> 20	12 (21.8)	7 (4.1)	
Presence of symptoms			
tingling			
yes	44 (80.0)	55 (32.0)	< 0.001
no	11 (20.0)	117 (4.1)	
burning			
yes	27 (49.1)	26 (15.1)	< 0.001
no	28 (50.9)	146 (84.9)	
light burning/stinging			
yes	32 (58.2)	38 (22.1)	< 0.001
no	23 (41.8)	134 (77.9)	
Therapy			
oral antidiabetics			
yes	13 (23.6)	30 (17.4)	0.307
no	42 (76.4)	142 (82.6)	
insulin			
yes	33 (60.0)	70 (40.7)	0.012
no	22 (40.0)	102 (59.3)	

DPN – diabetic polyneuropathy; HbA1c – glycosylated hemoglobin.

ing all symptoms of DPN (tingling, burning, burning, and burning) were more likely to have DNP in comparison with those without symptoms and short disease duration ($p < 0.001$). The statistically significant difference in the DNP presence was found among patients on insulin therapy and those who used other types of therapy ($p = 0.012$). No statistically significant dofference was found between patients with lower and higher HbA1c than 7%, nor between both types of diabetes with respect to the occurrence of polyneuropathy (Table 1).

Differences in DNP presence were not found regarding hypertension ($p = 0.276$) and smoking ($p = 0.607$). However, DNP was more frequently found among participants with dyslipidemia compared to those without it ($p = 0.046$) (Table 2).

The multivariate logistic regression model was adequate for the data available ($\chi^2 = 80.794$, $p < 0.001$), with 63.6% of the variability of the dependent variable explained by the selected model. Additionally, when predicting polyneuropathy using the characteristics of patients who entered the model, 85.9% of cases would be successful.

In univariate regression models, associations were found between DNP and the following variables: the presence of symptoms of tingling (8.509), burning (5.415), light burning and stinging (4.906), hypertension (3.380), and the use of insulin therapy (2.075) (Table 3).

Table 2

Frequency of risk factors in a patient with and without DPN

Risk factor	Presence of DPN		*p*
	yes	no	
Hypertension > 130/80 mmHg, n (%)			
yes	19 (34.5)	46 (26.9)	0.276
no	36 (65.5)	125 (73.1)	
Smoking, n (%)			
ex-smoker	9 (16.4)	35 (20.3)	0.607
smoker	14 (25.5)	34 (19.8)	
non-smoker	32 (58.2)	103 (59.9)	
Dyslipidemia, n (%)			
yes	30 (57.7)	111 (72.5)	0.046
no	22 (42.3)	42 (27.5)	
LDL (mmol/L), mean ± SD	2.939 ± 0.95	3.353 ± 1.019	0.012
HDL (mmol/L), mean ± SD	1.3075 ± 0.397	1.293 ± 0.435	0.825
CHOL (mmol/L), mean ± SD	5.1172 ± 1.152	5.468 ± 1.248	0.068
Tg (mmol/L), mean ± SD	2.007 ± 1.45	2.1605 ± 1.509	0.516
Obesity (BMI > 30 kg/m^2), n (%)			
yes	24 (44.4)	56 (33.7)	0.155
no	30 (55.6)	110 (66.3)	
Physical activity, n (%)			
inactive	13 (23.6)	35 (20.3)	0.857
moderately physically active	34 (61.8)	109 (63.4)	
extremely physically active	8 (14.5)	28 (16.3)	

DPN – diabetic polyneuropathy; LDL – low density lipoprotein; HDL – high density lipoprotein; CHOL – cholesterol; Tg – triglycerides; BMI – body mass index; SD – standard deviation.

Table 3

Univariate and multivariate logistic regression of DPN-related variables

Variable	Univariate logistic regression				Multivariate logistic regression			
	p	OR	95% CI for OR		*p*	OR	95% CI for OR	
			lower	upper			lower	upper
Gender	0.061	0.539	0.283	1.029	0.790	0.850	0.257	2.813
Duration of diabetes	0.000	2.085	1.534	2.833	0.000	4.266	1.983	9.175
Presence of symptoms								
tingling	0.000	8.509	4.083	17.733	0.012	5.155	1.431	18.571
burning	0.000	5.415	2.761	10.618	0.105	3.368	0.777	14.600
light burning, stinging	0.000	4.906	2.572	9.357	0.066	4.054	0.914	17.980
HbA1c	0.097	1.153	0.975	1.365	0.407	1.159	0.817	1.645
Cholesterol	0.070	0.787	0.607	1.020	0.150	0.556	0.250	1.238
LDL	0.013	0.641	0.450	0.912	0.077	0.440	0.177	1.093
CCr	0.107	0.637	0.368	1.103	0.133	0.516	0.218	1.222
AvgTA	0.008	1.033	1.008	1.058	0.028	0.934	0.879	0.993
Hypertension > 130/80 mmHg	0.001	3.380	1.667	6.852	0.001	26.186	4.070	168.488
Oral antidiabetic therapy	0.045	0.526	0.282	0.985	0.029	12.296	1.300	116.309
Insulin therapy	0.025	2.075	1.098	3.919	0.069	6.014	0.870	41.578

DPN – diabetic polyneuropathy; OR – odds ratio; CI – confidence interval; HbA1c – glycosylated hemoglobin; LDL – low density lipoprotein; CCr – creatinine clearance; AvgTA – average blood pressure.

Multivariate logistic regression revealed that patients who had hypertension [odds ratio (OR) = 26.2; 95% CI: 4.070–168.488; $p = 0.001$], used oral antidiabetic therapy (OR = 12.3; 95% CI: 1.300–116.309; $p = 0.029$), had tingling (OR = 5.2; 95% CI: 1.431–18.571 $p = 0.012$;) and a longer duration of diabetes (OR = 4.27; 95% CI: 1.983–9.175; $p = 0.000$) were more likely to have DPN (Table 3).

Discussion

The prevalence of DNP among family medicine patients with DM aged 18 to 70 years, using nylon monofilament, was 24.2%. The determinants of DNP were hypertension, using oral antidiabetic therapy, having tingling, and a longer duration of diabetes.

The prevalence found in the current study was lower than in previously conducted research. Salvotelli et al. [24], investigating DPN in patients with type 2 DM, based on a clinical examination of the foot, detected a prevalence of 30%. A study conducted in Tanzania found that more than half of patients included in that study had neuropathy with a severe form, and the main risk factors were: increasing age, increasing duration of diabetes, obesity, and hypertension [25].

Age and gender were not associated with the prevalence of DNP, which is in disagreement with a study by Gill et al. [26] in which the association between prevalence of DPN, and age, and duration of symptoms was found.

A study by Abbott et al. [5] from North West England showed that type 2 DM patients, women, and the South Asian population have a higher incidence of DNP. Studies in Jordan and England have found a prevalence of DPN of 30.3–39.5% in patients with type 2 DM over the age of 18. Furthermore, they detected higher prevalence in the secondary health care versus primary health care setting level, as well as a higher occurrence of DPN among patients with type 2 DM compared to the patients with type 1 DM [27, 28]. Our study showed no association between glycemic control via HbA1c and the presence of DPN, even though a greater number of patients with DPN had HbA1c greater than 7% (average HbA1c = 7.98 ± 2.07%).

Although statistical analyses showed that participants with dyslipidemia have a higher prevalence of DNP, no associations between DNP and lipid serum levels were found in multivariate regression analysis. A meta-analysis of several observational studies has demonstrated an association between LDL cholesterol fraction and systolic blood pressure with DPN [29]. Moreover, a study done in Jordan found a significant association of dyslipidemia with increased OR for DPN [27].

A Chinese study carried out on patients with type 2 DM found a higher prevalence of DNP among overweight and obese patients (33.1%) compared to patients who had optimal BMI [30]. On the other hand, a recent Indian study found no associations between obesity and DNP, which corroborates our findings [31].

Considering the type of therapy, this study found that the use of oral antidiabetic therapy alone was a predictor of DPN together with the duration of diabetes and hypertension as the present risk factor (OR = 12.296, 95% CI: 1.300–116.309; $p < 0.05$). A cross-sectional study conducted in Peru found that patients who were on both oral and insulin therapy were 40% more likely to have DPN than those with a diabetes duration longer than 10 years [32].

Several limitations need to be considered. Only Semmes-Weinstein nylon 10 g monofilament test was used to detect DNP. Although this test presents a good, inexpensive and accessible screening tool, more objective diagnostic procedures are required to confirm the diagnosis of DNP. The study measured HbA1c at a single point in time, which may not reflect the real level of glycemic control. The study was carried out in one region of the Republic of Srpska, Bosnia and Herzegovina, and the results may not be generalized to the whole country.

Conclusion

The prevalence of DPN in family medicine diabetic patients was 24.2%. DPN was associated with hypertension, the presence of symptoms (tingling), the duration of diabetes, and the use of oral antidiabetic therapy alone. Screening of diabetic polyneuropathy is justified in a family medicine setting. Early and rigorous management of diabetes and associated risk factors may have an essential role in the prevention of diabetic complication development and progression.

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