

# Assessment of Diabetic Polyneuropathy in Inpatient Care: Fasting Blood Glucose, HbA1c, Electroneuromyography and Diabetes Risk Factors

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## Original paper SUMMARY

**Goal:** The goals of this study are to: a) determine the prevalence of diabetic polyneuropathy (DPNP) in hospitalized patients with diabetes mellitus (DM) type 2; b) determine the frequency of DPNP in hospitalized patients with type 2 DM in relation to gender, duration of diabetes, fasting blood glucose and HbA1c; c) identify the dominant DPNP symptoms and the presence of variable risk factors in hospitalized patients; and d) determine the frequency and motor nerve conduction velocity of n. peroneus (electroneuromyography) in relation to the treatment of type 2 DM in hospitalized patients with DPNP. **Material and methods:** The study was conducted on 141 patients diagnosed with type 2 diabetes who were hospitalized at the Neurological clinic of Clinical Center of Sarajevo University in the period from June 1 2009 to June 1 2010. All patients included in the study were older than 18. Values determined for all subjects are: age, sex, dominant symptoms, duration of type 2 DM, fasting blood glucose, HbA1c, motor conduction velocity of n. peroneus, diabetes risk factors (hyperlipidemia, hypertension, smoking, alcoholism, obesity) and DM treatment type. **Results:** Of 141 patients with type 2 DM, DPNP was confirmed in 50 patients (35.5%).

Men were slightly more represented in the total sample (51.8%). In a sample of patients with DPNP, there were slightly more male patients (n=26; 52%). The average age of patients with DPNP was higher in men (58.3±12.5) (p<0.05). The average age of the patients with DPNP was 55.1± 13.2. Average values of fasting glucose was higher in the group of patients with DPNP (11.032±5.4 mmol/l) compared to patients without DPNP (9.7±2.8 mmol/l) (p<0.05). Mean values of HbA1C were higher in patients with DPNP (8.212±3.3%) compared to patients without DPNP (6.9±2.6%) (p<0.05). Analysis of DM duration between patients with and without DPNP did not show statistically significant difference (chi-square=3.858, p>0.05). In both groups, most of the patients had duration of DM over 10 years, with a minimum duration of DM of 12 months. There are statistically significant differences in applied DM therapy by gender (chi-square=11.939, p<0.05). Hypertension was more frequent in women (79.2%:69.2%), hyperlipidemia was equally presented in both sexes (50%:50%), obesity was more prevalent among women (25%:7.7%), while alcoholism and smoking were more frequent in men (7.7%:0%; 34.6%:8.3%). There are statistically significant differences in the prevalence of risk factors by gender (chi-square=10.013, p<0.05).

**Conclusions:** The DPNP incidence was higher in patients with longer duration of the disease, but without significant gender differences. Fasting blood glucose and HbA1c were significantly higher in patients with DPNP compared to patients without DPNP (p<0.05). The dominant symptoms of DPNP were paresthesia (44%) and hypoesthesia (28%). Regarding variable risk factors, the most common were hypertension and hyperlipidemia, without statistical significance in gender distribution, while smoking was significantly more common in men than women (34.6%:8.3%). DPNP was present in 43.2% of men who use insulin therapy, while 54.2% of women with DPNP used oral therapy. The lowest frequency of DPNP was found in patients treated with combined therapy. Motor conduction velocity of n. peroneus was significantly lower in men using insulin therapy and/or combined therapy (p<0.05), whereas in patients on oral therapy there was no significant gender difference. Timely DM type 2 diagnosis with proper treatment and electromyoneurographic monitoring (especially in older men) can prevent onset of diabetic polyneuropathy and contribute to its successful treatment.

**Keywords:** diabetic polyneuropathy, diabetes mellitus, ENMG, electroneuromyography, HbA1c, inpatient, fasting blood glucose, inpatient.

## 1. INTRODUCTION

Diabetes mellitus is most simply defined as absolute or relative lack of insulin which results in hyperglycemia. As the consequences of long-term hyperglycemia, late complications of diabetes can occur on small and large blood vessels, nerves, and basal membranes of different tissues (1).

Globally, the prevalence of diabetes is 5.9%. It is believed that this number will exceed to 7.1% in 2025 (2). In Bosnia and Herzegovina, the incidence of diabetes mellitus is 7.4/100000 inhabitants (3).

Diabetic polyneuropathy is one of the most common complications

of diabetic disease which includes peripheral nerves damage. Diabetic polyneuropathy is generally more or less progressive and is developing for weeks, months or even years (3). It occurs in patients with diabetes mellitus types 1 and 2, as well as in patients with so-called secondary diabetes as part of other diseases which indicates that chronic hyperglycemia is the major factor in the development of polyneuropathy (4).

Diabetic polyneuropathy is defined as the presence of symptoms and/or signs of peripheral nerve dysfunction in patients with diabetes mellitus after exclusion of other possible causes of dysfunction (5). Sub-

clinical neuropathy indicates the state of electro-physiologically verified neuropathy with absence of subjective and objective neurological signs. It occurs in about 20% of patients with diabetes (6). Distal, predominantly sensitive, motor (vegetative) or sensor-motor (vegetative) polyneuropathy, are the most common forms of the peripheral nervous system damage in diabetes mellitus. Symptoms and signs of sensory fibers affection are most pronounced in the distal parts of the extremities.

In patients with poorly controlled diabetes, syndromes such as paresthesia, dysesthesia or pain in the legs can occur - they quickly disappear

after hyperglycemia correction (7). Common symptoms are symmetrical paresthesia and burning pain that most frequently occurs distally in the legs, with the highest intensity during night (in bed). In nighttime, very painful spasms in the lower legs can also occur. Achilles reflex is typically absent. Very often, sense of vibration is impaired, less commonly sense of position. Motility disturbances are rare. The easiest form occurs in elderly diabetes, while the worst manifests in juvenile DM. Disorders of the autonomic nervous system are manifested primarily by bladder atonia and sphincter insufficiency. Further symptoms include tachycardia, orthostatic hypotonia, arthropathy and osteopathy with osteolytic foci in tibiotarsal or tarsometatarsal joints (8).

Data on prevalence of diabetic polyneuropathy depends heavily on diagnostic criteria, as well as the subjects (groups) characteristics. We can say that neuropathic symptoms are present in 20-40% of patients with diabetes mellitus. The most common symptoms are in the form of distal sensibility disorders. The symptoms of pain are more common in proximal and unilateral muscle groups (3). In some European countries, like United Kingdom, the prevalence of polyneuropathy in hospitalized patients with diabetes mellitus is 29% (9).

In the monitoring and treatment of diabetes mellitus, fasting blood glucose and HbA1c are regularly determined, while it is necessary to monitor and treat risk factors (hypertension, smoking, alcoholism and obesity). For assessment of diabetic polyneuropathy, besides clinical assessment, electromyoneurography (ENMG) is used for measurement of motor nerve conduction velocity of peripheral nerves.

## 2. GOALS

The goals of this study are: To determine the incidence of diabetic polyneuropathy in hospitalized patients with diabetes mellitus type 2; To determine the incidence of diabetic polyneuropathy in hospitalized patients with diabetes mellitus type 2 compared to gender, duration of diabetes, fasting blood glu-

cose and HbA1c values; Identify the dominant symptoms of diabetic polyneuropathy and the presence of additional variable risk factors in hospitalized patients; To determine the incidence of diabetic polyneuropathy and motor nerve conduction velocity of n. peroneus (electromyoneurography) in relation to the treatment of type 2 diabetes in hospitalized patients.

## 3. MATERIAL AND METHODS

Study was conducted on 141 patients diagnosed with type 2 diabetes mellitus who were hospitalized at the Neurology clinic, Clinical Center of Sarajevo University. A retrospective study was conducted which used medical records of patients who were hospitalized in the period from June 1, 2009 to June 1, 2010. All patients included in the study were older than 18.

Elevated values of fasting glucose was considered for values over 7 mmol/L, while elevated HbA1c values were considered if they were over 6.5%. As for pathological motor nerve conduction velocity of n. peroneus, values lower than 40m/s were considered as significant sign of DPNP. Only diastolic blood pressure values were noted. High blood pressure was considered if diastolic blood pressure was over 95 mmHg. Elevated blood lipids was considered if cholesterol level was over 6.4 mmol/L and triglyceride level over 2.2 mmol/L.

Classification of patients was made in relation to: fasting blood glucose, HbA1c, dominant symptoms, duration of type 2 diabetes, motor nerve conduction velocities of n. peroneus, presence of risk factors and medical treatment of DM type 2.

## 4. RESULTS

From total of 141 patients diagnosed with type 2 diabetes mellitus that were treated at the Neurology clinic from June 1 2009 to June 1 2010, 50 patients had confirmed diabetic neuropathy, which amounts to 35.5%.

Men were slightly more represented in the total sample (51.8%). In the total sample of patients with diabetic polyneuropathy we found more male patients (n=26; 52%) than

|                   |   | Male   | Female | Total |
|-------------------|---|--------|--------|-------|
| Normal findings   | N | 1      | 3      | 4     |
|                   | % | 3.9    | 12.5   | 8.0   |
| Paresthesia       | N | 13     | 9      | 22    |
|                   | % | 50.0   | 37.5   | 44.0  |
| Dysesthesia       | N | 3      | 2      | 5     |
|                   | % | 11.5   | 8.3    | 10.0  |
| Spasms            | N | 1      | 4      | 5     |
|                   | % | 3.9    | 16.7   | 10.0  |
| Hypoesthesia      | N | 8      | 6      | 14    |
|                   | % | 30.8   | 25.0   | 28.0  |
| Total             | N | 26     | 24     | 50    |
|                   | % | 52.0   | 48.0   | 100.0 |
| Chi-square=13.939 |   | p<0.05 |        |       |

**Table 1.** The dominant symptoms in patients with diabetic polyneuropathy

|                   |   | With DPNP | Without DPNP | Total |
|-------------------|---|-----------|--------------|-------|
| <6 months         | N | 2         | 3            | 5     |
|                   | % | 4.0       | 3.3          | 3.6   |
| 6-12 months       | N | 1         | 2            | 3     |
|                   | % | 2.0       | 2.2          | 2.1   |
| 1-5 years         | N | 3         | 14           | 17    |
|                   | % | 6.0       | 15.4         | 12.1  |
| 6-10 years        | N | 15        | 18           | 33    |
|                   | % | 30.0      | 19.8         | 23.4  |
| >10 years         | N | 29        | 54           | 83    |
|                   | % | 58.0      | 59.3         | 58.9  |
| Total             | N | 50        | 91           | 141   |
|                   | % | 35.5      | 64.5         | 100.0 |
| Chi-square =3.858 |   | p>0.05    |              |       |

**Table 2.** Duration of diabetes in patients with and without diabetic polyneuropathy women (n=24; 48%).

Overview of the average age of patients with diabetic polyneuropathy shows that the average age was higher in men (58.3±12.5) than women (48.4±15.6). Statistical analysis using the Student t-test shows that there are statistically significant differences (p<0.05). The average age of patients with diabetic neuropathy in our sample was 55.1±13.2 years, with the youngest patient aged 33 and the oldest at the age of 64. Overview of fasting glucose values in patients with and without diabetic polyneuropathy shows that the average value are higher in the group of patients with DPNP (11.032±5.4 mmol/l) compared to patients without DPNP (9.7±2.8 mmol/l). Statistical analysis using the Student t-test shows that there are statistically significant differences (p<0.05).

Overview of HbA1c values in patients with and without diabetic polyneuropathy indicates a higher mean values in patients with diabetic polyneuropathy (8.212±3.3%) compared

|                    |   | Male | Female | Total |
|--------------------|---|------|--------|-------|
| Insulin            | N | 11   | 7      | 18    |
|                    | % | 42.3 | 29.2   | 36.0  |
| Oral antidiabetics | N | 9    | 13     | 22    |
|                    | % | 34.6 | 54.2   | 44.0  |
| Combined therapy   | N | 6    | 4      | 10    |
|                    | % | 23.1 | 16.7   | 20.0  |
| Total              | N | 26   | 24     | 50    |
|                    | % | 52.0 | 48.0   | 100.0 |

Chi-square =11.939 p<0.05

**Table 3.** The treatment of patients with polyneuropathy

|        |                    | Mean | Standard deviation | Standard error mean | Range     |
|--------|--------------------|------|--------------------|---------------------|-----------|
| Male   | Insulin            | 33.7 | 12.5               | 3.2                 | 21.2-46.2 |
|        | Oral antidiabetics | 35.2 | 11.6               | 2.6                 | 23.6-46.8 |
|        | Combined therapy   | 32.5 | 9.52               | 2.3                 | 23-42     |
| Female | Insulin            | 36.4 | 12.4               | 3.4                 | 24-48.8   |
|        | Oral antidiabetics | 35.5 | 11.3               | 2.8                 | 24.2-46.8 |
|        | Combined therapy   | 36.8 | 9.6                | 2.1                 | 27.2-46.4 |

**Table 4.** Mean conduction velocity of n. peroneus in patients with diabetic polyneuropathy in relation to the administered therapy. t-insulin=6.254, p<0.05, t-peros=0.524, p>0.05, t-comb.=3.478, p<0.05

to patients without diabetic polyneuropathy (6.9±2.6%). Statistical analysis using the Student t-test shows that there are statistically significant differences (p<0.05). Analysis of predominant symptoms shows that normal findings are often seen in women (n=3; 12.5%) than men (n=1; 3.9%). Almost all symptoms were more present in men, except spasms that was more dominant in female patients (16.7%:3.9%) (Table 1). Statistical analysis using the chi-square test shows that there are statistically significant differences in the prevalence of symptoms by gender (p<0.05). Motor nerve conduction velocity of n. peroneus was somewhat lower in men (12.5±34.273 m/s) compared to women (35.875±15.2 m/s). Statistical analysis using the Student t-test showed that there were no statistically significant differences (p>0.05).

Analysis of diabetes duration between patients with and without DPNP shows no statistically significant difference (chi-square=3.858, p>0.05) (Table 2). In both groups, most patients were with diabetes duration of more than 10 years, with a minimum duration of diabetes up to 12 months.

Analysis of diabetes duration by gender shows no statistically significant difference (chi-square=3.360, p>0.05) and diabetes duration of more than 10 years was more present

in both sexes, with a minimum duration of diabetes up to 12 months. Overview of applied diabetes therapy in patients with diabetic polyneuropathy shows that men more commonly used insulin (n=11; 42.3%) while women used oral anti-diabetics (n=13; 54.2%) (Table 3). Statistical analysis shows that there are statistically significant differences in applied treatment of diabetes by gender (chi-square=11.939, p<0.05).

Review of the presence of risk factors (one respondent could have had more than one risk factor), shows that hypertension is more frequent in women (79.2%:69.2%), hyperlipidemia equally in both sexes (50%:50%), obesity is more prevalent among women (25%:7.7%), whereas alcohol use and smoking are more frequent among men (7.7%:0% for alcohol use; 34.6%:8.3% for smoking). Statistical analysis shows that there are statistically significant differences in the prevalence of risk factors by gender (chi-square=10.013, p<0.05). Analysis of motor nerve conduction velocity of n. peroneus between sexes and according to applied treatment of diabetes, showed that women had higher average velocity (Table 4).

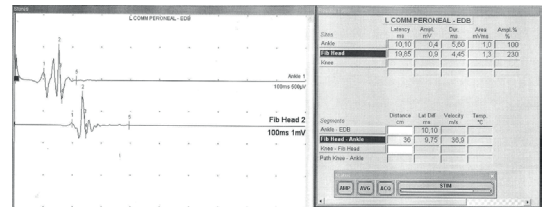
### 5. DISCUSSION

In our sample, the incidence of diabetic polyneuropathy was 35.5%, which is at the level of findings by F. Liu and associates, who found DPNP in 32% of patients with diagnosed diabetes mellitus (10). In the study by Morkrid and associates in 2010, DPNP prevalence was 19.7%, which was significantly lower than in the other European studies, but the authors suggest the possibility that it was a case of different criteria (11). When analyzing the gender structure in patients with diabetic polyneuropathy, we find equal proportion in both sexes, as well as in study conducted by Morkrid and associates (11).

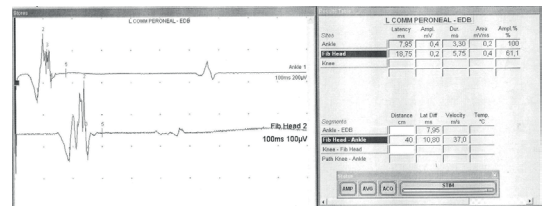
Analysis of age in patients with diabetic polyneuropathy showed that men were slightly older (58.3±12.5) than women (48.4±15.6). Similar results reached Morkrid and associates in 2010, where women were also significantly younger than men (48.7±10.7:53.1±9.9) (11). In our sample, the fasting blood glucose values were significantly higher in patients with diabetic polyneuropathy than in patients without polyneuropathy. Similar results were presented by a group of Turkish researchers (Ovayolu et al, 2008) (12).

In our sample, mean HbA1c values were significantly higher in patients with diabetic polyneuropathy than in patients without polyneuropathy, which corresponds to the study of

Booy et al. (2005) where mean values of HbA1c in patients with DPNP was 8.2±2.5 and in patients without DPNP 7.4±2.7 (13). In our study, the predominant symptom in both sexes were paresthesia followed by hypoaesthesia, and higher incidence of almost all symptoms was recorded in men, except for spasms that was more frequent in women. Although essentially there are no significant differences in the duration of diabetes in patients with and without DPNP in our study, more patients with disease duration of 6-10 years are in the group with DPNP (compared to the group without DPNP). This leads us to the conclusion that the duration of



**Image 1.** Electroneuromyography in assesment of diabetic polyneuropathy (36,9m/s)



**Image 2.** Electroneuromyography in assesment of diabetic polyneuropathy (37,0 m/s)

illness is an important factor for the development of diabetic polyneuropathy. Similar results reached Morkrid et al (2010) which showed a mean duration of diabetes in patients with DPNP of 12±8 years (11).

In our sample of patients with DPNP, the largest number of male patients used insulin therapy, while women were mostly using oral antidiabetics. The smallest number of patients in both sexes is of those using combined therapy. The study of Morkrid et al. (2010), as in our study, found that hypertension and hyperlipidemia are important risk factors for diabetic polyneuropathy (11). However, they are not identified as statistically significant risk factors, as is the case of a study by Bor et al from 2004 (14). In our study, the mean motor nerve conduction velocity of n. peroneus in patients with DPNP was somewhat lower in men (not significant). The same results was found by Kiziltan et al in 2008 (15). There are slightly lower motor conduction velocities of n. peroneus among men in our study and this is probably caused by the fact that men were significantly older than women, although the duration of diabetes was equal in both sexes. Analysis of mean motor nerve conduction velocity of n. peroneus in relation to the type of therapy shows that the average value was higher in women than in men, which is also found in the study by Kiziltan et al. from 2008 (15).

Our data suggest that the occurrence of diabetic polyneuropathy increases in case of poor disease treatment, or poor blood glucose level control, as well as in terms of longer duration of diabetes.

## 6. CONCLUSION

On the basis of this retrospective study (period from June 1 2009 to June 1 2010) conducted at the Neurology clinic, Clinical Center of Sarajevo University, we came to the following conclusions:

Diabetic polyneuropathy in hospitalized patients with type 2 diabetes mellitus was present in 35.5% of patients, with equal representation in both sexes, but men were significantly older with an average age of 58.3 (SD 12.5) compared to women

with an average age of 48.4 (SD 15.6).

DPNP frequency was higher in patients with longer duration of disease, but without significant gender differences; fasting blood glucose and HbA1c was significantly higher in the patients with DPNP compared to patients without DPNP ( $p < 0.05$ ).

Dominant symptoms of DPNP were paresthesia (44%) and hypoesthesia (28%), with significantly higher percentage of normal findings in women compared to men (12.5%:3.9%).

Among variable risk factors, the most common are hypertension (two thirds of the respondents), hyperlipidemia (half of the respondents) and without statistical significant difference in gender distribution, while smoking was significantly more common in males compared to females (34.6%:8.3%) and alcoholism recorded only in males (15.4%).

Diabetic polyneuropathy was present in 43.2% of men who use insulin therapy, while 54.2% of women with DPNP used oral therapy. The lowest frequency of diabetic polyneuropathy was recorded in patients treated with combined therapy.

Mean values of motor nerve conduction velocities of n. peroneus were significantly lower in men on insulin therapy and/or combined therapy ( $p < 0.05$ ), whereas in patients on oral therapy there are no significant gender differences. Women with type 2 diabetes mellitus have higher mean values of motor nerve conduction velocity of n. peroneus.

Timely DM type 2 diagnosis with proper treatment and electromyoneurographic monitoring (especially in older men) can prevent onset of diabetic polyneuropathy and contribute to its successful treatment.

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