



Gender differences in Diabetic Peripheral Neuropathy

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Abstract

Diabetic peripheral neuropathy (DPN) is one of the most common disabling complications of diabetes mellitus. **Aim:** To find out gender based differences in frequency of DM, duration of DM, neurologic examination and electrophysiological patterns. **Methodology:** cross sectional study was conducted at Neurology department, Beni-Suef university hospital, Egypt. Patients fulfilling the ADA criteria for DM, and DPN were included in the study. All patients were submitted to Michigan Neuropathy Screening Instrument physical examination. **Results:** A total of 25 patients were included in the study with 9/25 (36%) males and 16/25 (64%) females. Although mean age of females [53.50+11.90yrs.] was lower than that of males [56.556+12.99 yrs.] but this difference was also not significant ($p=.569$). There was no significant difference ($p=.311$) in the mean duration of DM in men (10.11+8.23 yrs) and women (6.81+5.99 yrs). Insignificant difference in the mean of glycemic control between males (7.889+1.00) and females (8.219+.9050) ($p=.427$). There was no association between males (4.333+1.93) and females (4.25+1.34) in MNSI physical examination ($p=.911$). **Conclusion:** In our study, gender based differences in DPN are statistically not significant with respect to age at diagnosis of diabetes, duration of DM, HbA1c level, MNSI and electrophysiological patterns. More studies are required to settle whether gender based differences in onset and progression of diabetic neuropathy exist.

Keywords: Diabetic Peripheral Neuropathy; MNSI.

1. Introduction:

Diabetic polyneuropathy is defined as the presence of clinical or subclinical symptoms and/or signs of peripheral nerve damage in patients with diabetes mellitus in the absence of the other causes of peripheral neuropathy [1]. It is one of the most common and most important

complications of diabetes, and one of the most frequent polyneuropathies in developed countries [2]. The reported prevalence of diabetic neuropathy varies from less than 5 to 60 percent with average standing at 26.4% [3]. Approximately 40-50% of the patients developing DPN

further develop painful neuropathy [4]. DPN has a statistically significant negative impact on the quality of life [5]. Patients with DPN usually have increased risks of disability, cardiovascular diseases, and mortality [6]. The distal symmetrical polyneuropathy (DSPN) is the commonest clinical form of diabetic neuropathy, affecting more than 90% of the patients [7]. Diabetic peripheral neuropathy is well known to be the most common cause of non traumatic Lower limb amputation [8]. The prevalence of foot ulcers ranges from 4% to 10% among persons diagnosed with diabetes mellitus [9]. The mechanisms that lead to DNP are not fully understood, although there is a consensus that toxic effects of hyperglycemia represent an important factor for the development of this complication [10]. Pain intensity normally is not associated with neuropathy severity, and can occur even in the absence of nerve injuries [11]. Very little data on onset and progression of diabetic peripheral neuropathy with reference to gender is available in international literature [12]. Studies from Western countries suggest that male gender is more prone to diabetic neuropathy than females [13]. From Pakistan, study was led to identify gender based differences in DPN. They have tried to find out gender based differences in prevalence, age at diagnosis of DM and subsequent onset of DPN and

finally duration of both DM and DPN symptoms. Gender based differences in electrophysiological patterns were also sorted out [12]. We tried to study how can gender difference affect clinical neuropathy and electrophysiologic patterns.

2. Patients and Methods

This was a cross sectional study performed in Beni-Suef university hospital six months from January to July 2017 involving 25 diabetes mellitus patients. Verbal consents were obtained.

2.1 Inclusion criteria:

Diabetic patients diagnosed according to American Diabetic Association criteria 2015 when one of the following criteria fulfilled:

- Fasting plasma glucose (FPG) ≥ 126 mg/dL (7.0 mmol/L) Fasting is defined as no caloric intake for ≥ 8 hours.
- 2 Hours plasma glucose (2-hr PG) ≥ 200 mg/dL (11.1 mmol/L) during oral glucose tolerance test (OGTT), Using a glucose load containing the equivalent of 75g anhydrous glucose dissolved in water.
- Hemoglobin A1C $\geq 6.5\%$ (48 mmol/l).
- Random plasma glucose (PG) ≥ 200 mg/dL (11.1 mmol/L) In individuals with symptoms of hyperglycemia.

2. 2 Exclusion criteria:

- Past history of malignancy and degenerative disease of the nervous system .
- Diabetic macrovascular complication.

- Chronic hepatitis, pregnancy, and history of drug abuse
- Renal impairment with renal replacement therapy.

2.3 All patients were subjected to:

1-Detailed History taking: focusing on duration of Diabetes Mellitus, onset of neuropathy symptoms and other microvascular complications of Diabetes Mellitus.

2-Through neurological examination according to the neurology sheet currently used in neurology department, Beni-Suef University.

3- Michigan Neuropathy Screening Instrument Physical Assessment

1) Inspection of the feet for deformities, dry skin, hair or nail abnormalities, callous or infection.

2) Semi-quantitative assessment of vibration sensation at the dorsum of the great toe

3) Grading of ankle reflexes.

4) monofilament testing.

Patients screening positive on the clinical portion of the MNSI (greater than 2 points on a 10 point scale) are considered neuropathic.

4. Laboratory investigations includes:

A-Fasting and 2 hours post prandial test.
Hemoglobin A1c test

Nerve Conduction Study: Using Nihon kohden equipment in Neurophysiology department Beni-Suef University hospital . The NCS assessed the number of nerves with abnormal

conduction velocities and amplitudes. The NCS in combination with the Neurological exam could quantitate the severity of the nerve pathology. Standardized techniques for nerve conduction study (NCS) with temperature control and fixed distances were applied. Measurements of latencies, amplitudes and conduction velocities were done in the following nerves of upper and lower limbs) median nerve sensory and motor parts ,ulnar nerve sensory and motor parts, tibial nerve, peroneal nerve, sural nerve)

Statistical methodology

- Analysis of data was done using SPSS (statistical program for social science) as follows;
- Description of quantitative variables as mean, SD and range.
- Description of qualitative variables as number and percentage.
- Unpaired t-test was used to compare quantitative variables, in parametric data (SD < 50 % mean)
 - P value > 0.05 insignificant
 - P < 0.05 significant
 - P < 0.01 highly significant [20].

3- Results

The current study was conducted at Beni-Suef university hospital within six months from January to July 2017. A total of 25 diabetic peripheral neuropathy patients were grouped into two groups, 16/25 female patients group (64%) and 9/25 male patients Group (36%)

with a male: female ratio = 1:1.77. The age of Diabetic Peripheral Neuropathy patients in this study ranged from 19 to 73 years with a mean value of sample 54.6 years \pm 12.12 years with mean age of females 53.50 \pm 11.90 years and of males 56.55 \pm 12.99 years. Though mean age of female diabetics in the sample was less than that in males implying early onset of DM & DPN but this gender based difference was statistically not significant (P = .0689). Mean

duration of diabetes in males was 10.11 \pm 8.23 years and 6.81 \pm 5.99 years in females (p=0.311). Mean level of HbA1C in males was 7.88 \pm 1.00 and 8.21 \pm 0.90 in females showing insignificant association P value 0.409. Table (2) showed that mean value of MNSI in males 4.333 \pm 1.93 and 4.25 \pm 1.34 in females P value = 0.911.

Table (3) electrophysiologic pattern differences in both genders were insignificant

Table (1): Comparison between groups as regards age at presentation, diabetes mellitus duration and HbA1c.

	Male group	Female group	P value
Age (Year) Mean \pm SD	56.55 \pm 12.99	53.50 \pm 11.90	0.689
Disease duration Mean \pm SD	10.11 \pm 8.23	6.81 \pm 5.99	0.311
HbA1c Mean \pm SD	7.88 \pm 1.00	8.21 \pm 0.90	0.409

P-value > 0.05 (Non-significant)

Table (2): Comparison between the two studied groups as regards MNSI

	Male group	Female group	P value
MNSI	4.333 \pm 1.93	4.25 \pm 1.34	0.911

P-value > 0.05 (Non-significant)

Table (3): Comparison between the two studied groups as regards the nerve conduction study.

		Male group MV(SD)	Female group MV(SD)	P value
Median (M)	Velocity	48.11 \pm 8.161	51.281 \pm 8.70	0.375
	Amplitude	6.722 \pm 2.29	7.306 \pm 3.31	0.610
	Latency	5.58 \pm 1.67	4.95 \pm 1.55	0.366
Median (S)	Velocity	36.83 \pm 8.23	41.14 \pm 9.98	0.259
	Amplitude	19.08 \pm 10.95	17.15 \pm 11.89	0.686
	Latency	4.65 \pm 1.55	4.50 \pm 1.59	0.822
Ulnar (M)	Velocity	49.44 \pm 6.53	53.83 \pm 7.42	0.142
	Amplitude	7.26 \pm 1.81	8.31 \pm 1.81	0.183
	Latency	3.722 \pm 1.08	4.23 \pm 1.60	0.356
Ulnar (S)	Velocity	46.44 \pm 6.83	49.48 \pm 8.18	0.333
	Amplitude	12.81 \pm 7.52	19.35 \pm 12.85	0.122
	Latency	2.97 \pm 0.58	2.69 \pm 0.53	0.251
Peroneal (M)	Velocity	40.11 \pm 7.78	43.62 \pm 6.43	0.269
	Amplitude	2.35 \pm 1.69	3.48 \pm 1.60	0.125
	Latency	5.64 \pm 2.33	7.65 \pm 3.36	0.094
Tibial(M)	Velocity	37.66 \pm 6.70	39.53 \pm 6.32	0.506
	Amplitude	5.33 \pm 4.01	6.70 \pm 3.20	0.393
	Latency	6.45 \pm 4.54	7.16 \pm 3.68	0.696
Sural (S)	Velocity	39.33 \pm 11.21	40.94 \pm 7.85	0.709
	Amplitude	5.32 \pm 5.40	6.90 \pm 4.75	0.475

	Latency	4.70 ±1.43	4.86 ±2.19	0.825
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P-value > 0.05 (Non-significant).

4- Discussion

Only few studies have been published internationally so far addressing the gender based differences in DPN suggesting that male being more affected by diabetic neuropathy than females [14]. The primary risk factor for the development of diabetic neuropathy is related to duration and severity of hyperglycemia [15]. In our study diabetic peripheral neuropathy male to female patients were 1:1.77. Similar to our study Aaberg & colleagues (2008) found that there were more female patients (59%) than male patients (41%) [14]. Our study revealed insignificant difference between both genders regarding mean age at presentation. In a multicenter study on the prevalence of diabetic neuropathy, the average ages in Italy ranged from 56 years. In men & 58 years. in women (sample age: 57 mean yrs.) [15]. Javed A 2014 found that the difference in the mean ages of both sexes is statistically not significant ($P < 0.504$) [12].

The current study found insignificant difference between both male and female groups regarding disease duration. The study included 25 diabetes mellitus patients diagnosed according to ADA criteria

Jarmuzewska E 2000 found that about 50% of diabetics suffer from neuropathy between 25-30 years after the diagnosis of DM [17]. In a multicenter study, patients with disease duration of 12.4 yrs. (+ 8.4) had mild neuropathy & those with duration of 15.6 yrs.

(+ 9.7) had severe neuropathy. Fraser et al 1979 found that no consistent relationship exists between onset of neuropathy and age, sex & duration of diabetes mellitus. Javed et al., 2014 found significant difference in mean duration of diabetes & duration of symptoms of DPN after onset is less in female gender than in males.

Our study also revealed insignificant difference between male and female group as regards the HbA1c level. Similarly Khan H et al 2007 reported no significant differences between males and females for the levels of HbA1C

In contrast MA et al., 2016 also found that HbA1c levels of male individuals were significantly higher than those of females in the 30–59 years age-groups ($P < 0.05$) [20]. Abudawood et al 2017 also stated that HbA1C differed significantly between male and female subjects [21]. It is most likely due to factors such as blood pressure and blood lipids of males in this age-group have worse control conditions, and women may be easily affected by physiological cycle.

In our Study, there was no significant difference between males and females in MNSI physical examination (P value 0.911). In accordance with our findings as, Anbarasu D et al., 2016 et al conducted a study on 72 diabetic patients. 18% were found to have a MNSI score of more than 2 suggesting the presence of peripheral neuropathy. Of these 72 patients with peripheral neuropathy, 38 (52.7%) were males and 34 (47.22%) were females ($p > 0.05$) [23]. Additionally, Mohamad S et al., 2016 failed to detect a significant

differences between both sexes in patient group as regard the neuropathy severity measured by TCSS [24].

Our study agreed with Javed A et al 2014 who stated that gender had no significant association with electrophysiological patterns ($p < 0.098$).

5- Conclusion and Recommendations

In conclusion, our study showed that gender based differences in DPN are statistically not significant with respect to frequency of diabetes, age at presentation, duration of DM and electrophysiological patterns. Larger studies are required to settle whether gender based differences in onset and progression of diabetic neuropathy exist.

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