Pakistan Journal of Neurological Sciences (PJNS)

Volume 9 | Issue 4 Article 6

12-2014

Gender based differences in diabetic peripheral neuropathy

Athar Javed
King Edward Medical University/Mayo Hospital, Lahore., dratharjaved59@gmail.com

Ahmad Furqan
King Edward Medical University / Mayo Hospital, Lahore

Mohsin Zaheer
King Edward Medical University / Mayo Hospital, Lahore

Naeem Kasuri
King Edward Medical University / Mayo Hospital, Lahore

GENDER BASED DIFFERENCES IN DIABETIC PERIPHERAL NEUROPATHY

Dr. Athar Javed, Dr. Ahmad Furqan, Dr. Mohsin Zaheer, Dr. Naeem Kasuri
Department of Neurology, King Edward Medical University/Mayo Hospital, Lahore.

Correspondence to: *Dr. Muhammad Athar Javed, Associate Professor, Department of Neurology, KEMU/Mayo Hospital, Lahore-54000. Email: dratharjaved59@gmail.com*
Date of submission: *December 15, 2014,* ***Date of revision:*** *December 22, 2014,* ***Date of acceptance:*** *December 23, 2014*

ABSTRACT

Introduction: Diabetic peripheral neuropathy (DPN) is one of the common complications of diabetes mellitus. **Aim:** To find out gender based differences in frequency of DM, age at diagnosis of DM and subsequent onset of DPN, duration of DM and DPN and electrophysiological patterns. **Methodology:** On the basis of non-probability purposive sampling, a cross sectional study was conducted at Neurology department, Mayo Hospital, Lahore. Patients fulfilling the ADA criteria for DM, and DPN were included in the study. Data was analyzed using SPSS 16 version. **Results:** A total of 125 patients were included in the study with 57/125 (45.6%) males and 68/125 (54.4%) females. This difference in gender based frequency was not statistically significant ($p<0.324$]. Although mean age of females [51.83+10.04 yrs.] was lower than that of males [53.29+9.39 yrs.] but this difference was also not significant ($p<0.504$). There was no significant difference ($p<0.685$) in the mean age at onset of DM in men (42.03+9.97yrs) and women (41.24+10.62yrs). Both genders took a mean period of 08 yrs to develop DPN. The mean age of onset of DPN was 50.87+9.43yrs in men and 49.25+10.62yrs in women and this was not statistically significant ($p<0.374$). Sensory-motor mixed polyneuropathy was the commonest electrophysiological pattern (51%) seen in both the genders. **Conclusion:** In our study, gender based differences in DPN are statistically not significant with respect to frequency of diabetes, age at diagnosis of diabetes or at onset of DPN, duration of DM before onset of DPN and electrophysiological patterns. More studies are required to settle whether gender based differences in onset and progression of diabetic neuropathy exist.

Key Words: Diabetic Peripheral Neuropathy (DPN); Electrophysiology.

INTRODUCTION

'Diabetic Peripheral Neuropathy (DPN)' is one of the most common complications of diabetes (both type-1 & type-2 diabetes). DPN is defined as 'The presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after exclusion of other causes'. DPN may be asymptomatic[1]. Diagnosis of DPN is both on clinical basis & electrodiagnostic analysis. The management includes both non-pharmacologic & pharmacologic approaches. Studies about DPN have reported a wide range of prevalence estimates. The reported prevalence of diabetic neuropathy varies from less than 5 to 60 percent [2] 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]. Very little data on onset and progression of diabetic peripheral neuropathy with reference to gender is available in international literature. Studies from Western countries suggest that male gender is more prone to diabetic neuropathy than females [6;7]. Few data are available in Asian populations. From Pakistan,ours is probably the first study on gender based differences in DPN. We 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.

MATERIALS AND METHODS

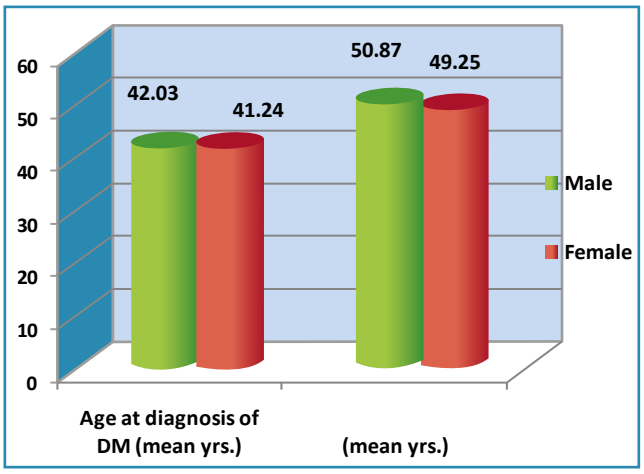
This was a retrospective cross sectional study carried out at Department of Neurology, Mayo Hospital, Lahore, over a period of six months from September, 2011 to February, 2012. Patients fulfilling the inclusion criteria were enrolled on the basis of non-probability purposive sampling technique. Diabetes mellitus was diagnosed as per American Diabetes Association (ADA) guidelines i.e. random blood sugar >200mg/dL or fasting blood sugar > 126 mg/dL. Diabetic neuropathy was diagnosed by the combination of more than one abnormal result of 10-gm monofilament, pinprick sensations, vibration perception and ankle reflexes [8]. Electrophysiological diagnosis of DPN was based on American Academy of Neurology (AAN), American Association of Electrodiagnostic Medicine (AAEM), and American Academy of Physical Medicine and Rehabilitation (AAPM&R) guide-

line [9]. After taking consent, patients were subjected to electrophysiology. Standardized techniques for nerve conduction study (NCS) with temperature control and fixed distances were applied. Measurements of latencies, amplitudes, conduction velocities and F-waves were done in nerves of upper and lower limbs. Inclusion criteria consisted of: (1) Diagnosed patients of diabetes mellitus (Type 1 or 2) with symptoms of peripheral neuropathy (2) Both males & females. (3) ADA clinical criteria for DPN. (4) Electrophysiological criteria for DPN as mentioned above. Exclusion criteria were based on History, examination or investigations showing: (1) Hereditary neuropathies. (2) Chronic Inflammatory Demyelinating Polyradiculopathy. (3) Renal or Thyroid disease. (4) Alcoholics or toxic drug intake; Nutritional deficiencies. (5) Malignancy or an autoimmune disorder. Data was collected on a Performa which included: (a) History. Onset & duration of DM & DPN were equated with the date of first symptom identification (b) Physical examination. (c) Electrodiagnostic test. Statistical analysis of data was done using independent Student's t-test (SPSS-16). Data has been presented as the mean with standard deviation (SD). Gender based differences in DPN have been studied with respect to:-

1. Gender vs. Frequency of DM.
2. Gender vs. Age of sample.
3. Gender vs. Age at diagnosisof DM & at onset of DPN.
4. Gender vs. Duration of both DM & DPN (symptomatic).
5. Gender vs. Electrophysiological patterns in DM.

Diagram-1

Gender vs. Age at diagnosis of DM & onset of DPN



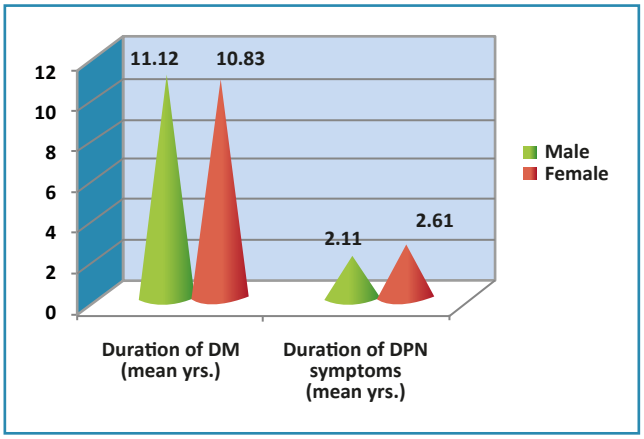
RESULTS

One hundred and thirty one patients of symptomatic DPN were selected from amongst those visiting the hospital OPD. There was drop out of six cases. So, one hundred and twenty five patients (n=125) went through the study, out of which 57/125 (45.6%) were male and 68/125 (54.4%) were female. Male/Female ratio was 1:1.1. Though, frequency of DM was more in female gender but this conclusion was'statistically not significant (P < 0.324)'. Mean age of the entire sample (n=125) was 52.52+9.05 yrs. with mean age of females 51.8+10.04 yrs and of male gender 53.29 + 9.39 yrs. 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 < 0.504). Age at diagnosis of DM was 42.03+9.97yrs. in males while in female gender it was 41.24+10.62yrs (Diagram-1). However, in statistical terms, this gender based difference in age at diagnosis of DM was found to be 'not significant (P < 0.685)'. The age of onset of DPN was 50.87+9.43 yrs. in males and 49.25+10.6yr in females but this difference was also 'statistically insignificant (P < 0.374) (Diagram 1. Mean duration of diabetes before onset of DPN in males was 8.83 +6.89 yrs. (p<.000) and 8.01+6.06 yrs in females (p<.001). On comparing this data, both genders took same period before the onset of symptomatic DPN (Diagram-1). Difference in mean duration of diabetes and mean duration of symptoms of DPN after onset was less [8.21 mean yrs. (+ 6.06); p <.004] in females than in male gender [9.01 mean yrs. (+ 6.99); p <.075]. This difference also points that females are more susceptible to an early onset of DPN (Diagram-2). Duration taken for the development of DPN was calculated by subtracting the age at diagnosis of DM from the age at diagnosis of DPN. Considering the electrophysiological patterns with reference to gender, five major neuropathic patterns constituted more than 92% of entire electrophysiological profile (Diagram-2). The commonest electrophysiological pattern was sensory-motor mainly axonal polyneuropathy and found in 51% (63/125) cases with almost an equal number of males (33/63 i.e. 52.38%) and females (30/63 i.e.47.62%). Second commonest pattern of 'sensory axonal polyneuropathy' was found in 22% (28/125) cases, again more frequent in female (17/28 i.e. 60.72%) than in male diabetics (11/28 i.e. 39.28%). Sensory-motor demyelinating polyneuropathy was found in 3% (4/125) of cases. This was more frequent in female (3/4 i.e. 66.67%) than in male gender (1/4 i.e. 33.33%). Normal electrophysiology was seen in 13% (16/125) of symptomatic DPN patients with more females (9/16 i.e. 56.25%) than males (7/16 i.e. 43.75%). Carpal Tunnel Syndrome (CTS) had predilection for female gender. CTS mainly manifested as part of polyneuropathy but in 3% females (4/125), it presented as mononeuropathy alone. While considering the entire electrophysiology, statistics do not yield any significant

relationship (P < 0.098) between gender & rest of the electrophysiological profile.

Diagram-2

Gender vs. Duration of DM & DPN



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 [6,7]. The primary risk factor for the development of diabetic neuropathy is related to duration and severity of hyperglycemia [10]. This is first study on gender based differences in diabetic peripheral neuropathy from Pakistan. We studied the gender based differences with respect to frequency of DM, age at diagnosis of DM and subsequent onset of DPN with respect to duration of DM, and electrophysiological patterns. We also compared our results with previously published studies.

Gender vs. frequency of DM: Regarding frequency of diabetes, factors like age, socioeconomic status & occupation have higher correlation with the occurrence of diabetes among both sexes. According to a study by Kaur & Bishoni (2010), reproductive status has significant impact on the occurrence of type-2 diabetes among female individuals [11]. Indians have the highest prevalence of diabetes among Asian countries [12]. In 2001, a study by Gale and Gillespie revealed that regarding gender based prevalence of diabetes mellitus, male excess is a consistent finding in populations of European origin. However, populations mostly of non-European origin, characteristically show a female bias [13]. In a study conducted by Aaberg & colleagues (2008), out of 376 reviewed charts of diabetics, there were more females (59%) than males (41%) [7]. Our study supports the findings of these studies. Though in our study male-female ratio is 1: 1.1 i.e. diabetes is more prevalent in female (54%) than in male gender (46%) but this finding is statistically not significant (P<0.324).

Gender vs. Age: Irrespective of gender, prevalence of diabetes increases with increasing age. Age-standardized prevalence of diabetes and prediabetes in both sexes is 9.7% [14]. In a multicenter study on the prevalence of diabetic neuropathy, the average ages in Italy ranged from 56 yrs.in men & 58yrs. in women (sample age:57 mean yrs.) [15]. In an Indian study, average ages in diabetics ranged from 57 yrs. in men to 54 yrs. in women (sample age:55 mean yrs.) [11]. In our study, as well, age of males in the sample is 53 mean yrs. while it is lesser(earlier) in female gender i.e. 52 mean yrs. (sample age: 52.5 mean yrs.). Our values are even lesser to those in the Indian study. So, one may conclude that in Asians mean age of diabetics is lesser than that in the Europeans. Interestingly, in both the Asian studies, mean age of female gender is less than that in males. This implies an early onset of DM & DPN in female gender. However, in our sample, the difference in the mean ages of both sexes is statistically not significant (P < 0.504).

Gender vs. Age at diagnosis of DM: Gender related factors are involved in the onset & transmission of diabetes from one generation to the next. Age at onset is an indicator of genetic susceptibility. The stronger the genetic component, the earlier is the onset of the disease and the greater the risk in the first degree relatives. Male gender seems to be more susceptible to gestational events predisposing to type-1 diabetes [16]. Studies reveal that age at diagnosis of diabetes in Indian males is 48.07 yrs. (+ 6.80) while in female gender it is 46.05 yrs. (+ 5.61). In Iranian population mean age at diagnosis of DM stands at 44.5 yrs.[10]. As compared to international data, in our study the mean age of the sample(41.63 mean yrs.) as well as mean ages in both the genders [Male: 42.03 yrs. (+ 9.97); Female: 41.24yrs. (+10.62)] at diagnosis of DM are low with a lower (earlier) mean age in females. Considering above statistics, amongst Asian countries are we even more susceptible than Iranian & Indian population in contracting diabetes at an earlier age? Age of diagnosis of DM in female gender is even lesser than that in males which means an earlier onset of DM in females. However, in our sample, gender based difference in age at diagnosis of DM is not significant (P<0.685).

Gender vs. Age at onset of DPN: In study, standard ADA criteria have been used for the diagnosis of DPN. Onset of DPN is equated with the date of first identification of neuropathy symptom. Deteriorating levels of glycemic control are associated with increasing likelihood of DPN. A difference in the progression of diabetic neuropathy between men & women may exist. Fedele D et al (1997) state that severity of neuropathy increases

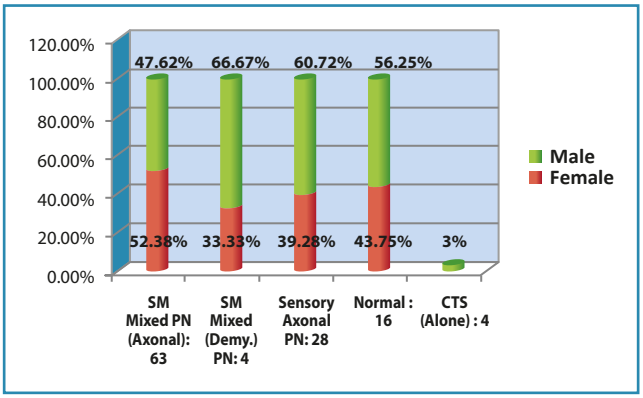
both with age and duration of diabetes [15]. However, Straub & colleagues (1996) state that there is no age related impact of duration of diabetes on cardiovascular autonomic nervous function [17]. As per international data, mean age of onset of DPN is 08 yrs. after the diagnosis / onset of DM. In 7.5% cases, age of onset of DPN is same as age of diagnosis of DM. According to Davies & Katulanda et al, increased frequency of DPN is seen in females [3;18]. In our study, in both genders, there was a significant difference (P<0.001) in the age at diagnosis of DM (42.03 mean yrs. in male & 41.24 mean yrs. in female gender) and age at onset of DPN (50.87 mean yrs. in male & 49.25 mean yrs. in female gender). Both genders, after the onset of diabetes, took almost an equal mean period of about eight years before there was onset of symptoms of DPN. So, the gender based difference in age at onset of DPN is not statistically significant (P<0.374). Gregersen et al have also reported no sex-specific difference in the onset of DPN [19].

Gender vs. duration of DM & duration of DPN: In prognostic terms, about 50% of diabetics suffer from neuropathy between 25-30 yrs. after the diagnosis of DM [20]. Prevalence of sensorimotor neuropathy is significantly high in patients with long duration of DM [16]. 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 [15]. Nevertheless, Fraser & colleagues state that no consistent relationship exists between onset of neuropathy and age, sex & duration of diabetes [21]. In our study, difference in mean duration of diabetes & duration of symptoms of DPN after onset is less in female gender than in males. Is this statistically significant (P<0.004) difference points to more susceptibility of female gender to DPN?

Gender vs. Electrophysiological patterns: Diabetic peripheral neuropathy (DPN) also known as 'Distal Symmetric neuropathy' is the most commonly recognized electrophysiological form of diabetic neuropathy [22]. According to an Indian study, irrespective of gender, commonest electrophysiological pattern in diabetics is that of sensory-motor mixed polyneuropathy [23]. Bloomgarden also states that the most commontype of diabetic neuropathy is distal symmetrical mixed motor and sensory neuropathy, comprising almost 70% of cases of diabetic neuropathy [24]. In our study, as well, sensory-motor mixed polyneuropathy (SM Mixed PN) is almost equally common in both the genders and constitutes more than 51% of entire electrophysiological spectrum. CTS has predilection for female gender. As a whole, gender had no significant association with electrophysiological patterns (p<0.098).

Diagram-3

Gender vs. Electrophysiological Profile



CONCLUSION

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

REFERENCES

1. Quan D. Preventing Diabetic Neuropathy. www.neuropathy.org/site/News2?id=7159.
2. Thomas PK, Eliasson SG: Diabetic neuropathy. In: Peripheral Neuropathy. 2nd Edition. P.J.Dyck, P.K.Thomas, E.H. Lambert and R. Bunge. Eds. Philadelphia: Saunders 1984; pp1773-18103.
3. Davies-M, Brophy-S, Williams-R, Taylor-A. The prevalence, Severity, and Impact of Painful Diabetic Peripheral Neuropathy in Type-2 Diabetes. Diabetes Care. July 2006. Volume 29. No.7. 1518-1522.
4. Veves A, Backonja M, Malik RA. Painful diabetic neuropathy: epidemiology, natural history, early diagnosis, and treatment options. Pain Med 2008; 9: 660–674.2.
5. Archer AG, Watkins PJ, Thomas PK, Sharma AK, Payan J. The natural history of acute painful neuropathy in diabetes mellitus. J Diabetes Complications 1999;13 (5-6):307-13. Boulton AJ. In: Dyck PJ, Thomas PK, editors. Diabetic neuropathy. 2nd ed. Philadelphia: WB Saunders, 1999:517-29.
6. Booya F, Bandarian F, Larijani B, Pajouhi M, et al. (2005) Potential risk factors for diabetic neuropathy: a case control study. BMC Neurology. 5:24.
7. Aaberg ML, Burch DM, Hud ZR, Zacharias MP. Gender differences in the onset of diabetic neuropathy. Journal of Diabetes and Its Complications.

March, 2008. Volume 22, Issue 2: 83-87.
8. Bansal D, Gudala K, Muthyala H, Esam HP, et al. Prevalence and risk factors of development of peripheral diabetic neuropathy in type 2 diabetes mellitus in a tertiary care setting. Journal of Diabetes Investigation. 2014; 5; 714-721.
9. Ref. England JD, Gronseth GS, Franklin G, Miller RG, Asbury AK, Carter GT, Cohen JA, Fisher MA, Howard JF, Kinsella LJ, Latov N, Lewis RA, Low PA, Sumner AJ, American Academy of Neurology, American Association of Electrodiagnostic Medicine, American Academy of PhysicalMedicine and Rehabilitation. Distal symmetric polyneuropathy: a definition for clinical research: report of the American Academy of Neurology, the American Association of Electrodiagnostic Medicine,and the American Academy of PhysicalMedicine and Rehabilitation. Neurology 2005;64:199–207
10. Adler AI, Boyko EJ, Ahroni JH, Stensel V, et al. Risk factors for diabetic peripheral sensory neuropathy. Results of the Seattle Prospective Diabetic Foot Study. Diabetes Care. 1997. 20:1162-1167.
11. Kaur T, Bishnoi D. Effect of sex on prevalence of type 2 diabetes mellitus (T2DM) with respect to blood pressure, BMI and WHR among Punjabi population. International Journal of Medicine and Medical Sciences. Sept., 2010 Vol. 2 (9), pp. 263-270.
12. DECODA Study Group. Age- and Sex-Specific Prevalence of Diabetes and Impaired Glucose Regulation in 11 Asian Cohorts. Diabetes Care. May, 2003. Vol. 26. no. 6. 1770-1780. (http://care.diabetesjournals.org.)
13. Gale EA, Gillespie KM. Diabetes and gender.Diabetologia. 2001. Jan;44(1):3-1.
14. Yang W, Lu J, Weng J, Jia W, et al.Prevalence of Diabetes among Men and Women in China. N Engl J Med. March. 2010; 362:1090-1101.
15. Fedele D, Comi G, Coscelli C, Cucinotta D, et al. A multicenter study on the prevalence of diabetic neuropathy in Italy. Italian Diabetic Neuropathy Committee. Diabetes Care. May, 1997; 20 (5): 836-843.
16. Harjutsalo V, Lammi N, Karvonen M, and Groop PH. Age at onset of Type 1 Diabetes in Parents and recurrence in Offspring. Diabetes. 2010 January; 59 (1): 210–214.
17. Straub RH, Zietz B, Palitzsch KD, Schölmerich J. Impact of disease duration on cardiovascular and pupillary autonomic nervous function in IDDM and NIDDM patients. Diabetes Care. 1996. Sept. 19 (9): 960-7.
18. Katulanda P, Ranasinghe P, Jawardena R, et al. The prevalence, patterns and predictions of diabetic peripheral neuropathy in a developing country. Diabetol Metab Syndr. 2012; 4; 21.
19. Gregersen G. Diabetic neuropathy; Influence of age, sex, metabolic control and duration of diabetes on motor conduction velocity. Neurology 1967; 17: 972-980.
20. Jarmuzewska EA, Ghidoni A. Study of the onset and progression of peripheral neuropathy and hypertension in NIDDM. Minerva Med. 2000 Jan-Feb; 91(1-2): 1-15.
21. Fraser DM, Campbell IW, Ewing DJ, Clarke BF. Mononeuropathy in diabetes mellitus. Diabetes. February 1979. vol. 28 no. 2 96-101.
22. MediFocus Guide from Medifocus.com, Inc.www.medifocus.com. January 19, 2012. (800) 965-3002:25.
23. Misra UK, Kalita J, Nair PP. Diagnostic approach to peripheral neuropathy. Ann Indian Acad Neurol.v. 2008 Apr-Jun; 11(2): 89–97.
24. Bloomgarden ZT. Diabetic neuropathy. Diabetes Care. May, 2008; 31 (3): 616-21.

Conflict of interest: Author declares no conflict of interest.

Funding disclosure: Nil

Author's contribution:
Dr. Athar Javed: Study concept and design, protocol writing, data collection, data analysis, manuscript writing, manuscript review
Dr. Ahmed Firqan: Study concept and design, protocol writing, data collection, data analysis, manuscript writing, manuscript review
Dr. Mohsin Zaheer: Study concept and design, protocol writing, data collection, data analysis, manuscript writing, manuscript review
Dr.Naeem Kasuri: Data collection, data analysis, manuscript writing, manuscript review