PREVALENCE AND RISK FACTORS FOR DIABETIC PERIPHERAL NEUROPATHY AMONG TYPE 2 DIABETES MELLITUS PATIENTS.

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Article received on:
12/10/2019
Accepted for publication:
25/01/2020

ABSTRACT… Objectives: To determine the prevalence of diabetic peripheral neuropathy (DPN) and associated risk factors among patients with type 2 diabetes mellitus (T2DM). **Study Design:** Cross Sectional Study. **Setting:** Outpatient Department Combined Military Hospital, Abbottabad. **Period:** From Jan 2017 to May 2017. **Material & Methods:** A total of 270 patients with T2DM and age greater than 30 were included in the study. Peripheral diabetic neuropathy was assessed by using Neuropathy Symptoms Score (NSS) and Neuropathy Disability Score (NDS). Data was collected by using a self structured questionnaire and analyzed by using SPSS software version 20. **Results:** Majority (60%) of patients were male; male to female ratio being 1:1.5. Mean age was 62.26 ± 11.38 years and the most frequent age group was 60-69 years (30.37% of patients). Overall prevalence of DPN was 36.7 % (n=99). Gender, age, educational status, duration of diabetes, HbA1c level, hypertension and mode of treatment were found to be significantly associated with DPN. **Conclusion:** Diabetic peripheral neuropathy is common entity seen in 36.7% patients with type 2 diabetes and is associated with several demographic and clinical factors.

Key words: Complications, Diabetic Peripheral Neuropathy, Risk Factors, Type 2 Diabetes.

INTRODUCTION

Over the past few years, there has been a shift in the global burden of disease from infectious diseases to non-communicable diseases. The current diabetes epidemic has emerged as one of the biggest epidemic and the world can no longer underestimate its rise.[1] Initially, diabetes was confined to developed countries; however recent data has revealed that the prevalence is very high in developing countries as well. Non-communicable diseases including diabetes put significant strain on the economy of developing countries. The worldwide prevalence of diabetes has been reported to be 2.8% and it may rise to 4.4% by year 2030.[2] In Pakistan, the disease burden has dramatically increased in the last few years. Current rate of diabetes in Pakistan is 11.8%. As per International Diabetic Federation's (IDF) 2015 report, about 7 million people have diabetes in Pakistan.[3]

Diabetic neuropathy is one of the complications of diabetes[4] affecting up to 50% of the patients.[5] In literature, prevalence of diabetic neuropathies varies from 7 to 80%.[6] Diabetic peripheral neuropathy (DPN), also known as chronic peripheral sensorimotor symmetrical neuropathy, is the most common form accounting for about 75% of all the neuropathies.[7] About 20-50% of the diabetic patients develop DPN over time.[8] DPN is presence of signs and symptoms of peripheral nerve dysfunction in diabetics in the absence of any other contributing factors.[9] DPN manifest as lack of sensation in the toes which eventually involve the foot and the leg, causing numbness and pain. It hinders patient's ability to recognize stimuli and even obvious foot ulcers. Foot ulcers in diabetics are mostly neuropathic in origin. Foot ulcerations are followed by amputations in about 85% of the cases.[10] Neuropathies account for disability in 44% type 1 diabetes patients

and restricted daily activities in 74% with type 2 diabetes.[11]

It has been observed that even under strict glycemic control, there is substantially higher incidence of DPN, supporting the role of other risk factors in the development of DPN. Glycemic control, duration of hyperglycemia, smoking, hypertension, dyslipidemia and a high body mass index are recognized as risk factors.[12] Also, differences in ethnicity and environmental factors are other proposed mechanisms for the observed variation in rate of DPN in different populations and regions. Keeping this in mind we conducted a study at our setting that aimed at determining the prevalence of neuropathies and associated risk factors.

MATERIAL & METHODS
This cross-sectional study was conducted at the outpatient department of Combined Military Hospital, Abbottabad from Jan 2107 to May 2017, over a period of 5 months. A total of 270 patients who attended outpatient department for routine visits were included in the study after taking verbal consent. All patients were selected by non-probability convenience sampling technique. Inclusion criteria included age greater than 30 years and a known case of T2DM, diagnosed according to WHO criteria (fasting plasma glucose ≥7.0 mmol/l or OGTT ≥ 11.1 mmol/l or HbA1c ≥6.5%). While patients with known cases of vitamin B_{12} deficiency, alcoholism, drug-abuse, hypothyroidism, paraneoplastic disorders, Parkinsonism, rheumatic disease, cerebral vascular disease, uremia, and acute or chronic musculoskeletal disorders were excluded. A structured questionnaire containing information regarding age, gender, BMI, socioeconomic status, smoking, hypertension, hyperlipidemia, thyroid disease, cardiovascular disease, family history of diabetes and hypertension, type and duration of diabetes, mode of treatment and glycemic control was used. Investigations like HbA1c, lipid profile, thyroid profile, renal function test and echocardiogram were carried out. Hypertension was considered if systolic blood pressure was greater than 160mmHg and diastolic greater than 95mmHg. Hypercholesterolemia

was defined as cholesterol level greater than 200mgdl.

Neuropathy Symptom Score (NSS) and Neuropathy Disability Score (NDS) were used to assess peripheral neuropathies. NSS contains five questions with assigned scores regarding presence of symptoms like numbness, cramps and fatigue, their anatomic location, presence of associated factors like nocturnal exacerbation, interference with sleep and relief with walking or standing. The maximum score on NSS is 9. An NSS score of 3-4 is considered mild, 5-6 moderate, and 7-9 severe. NDS consists of four clinical tests including Achilles tendon reflex, vibration perception, thermal sensation and pin prick sensation. Maximum score on NDS is 10. Total NDS score of 3-5 is considered mild disability, 6-8 moderate disability, and 9-10 severe disability. The criterion for the diagnosis of DPN was presence of at least moderate disability, either alone or with symptoms, or presence of at least mild disability with presence of at least moderate symptoms.[13] Data were entered, coded and analyzed in SPSS software version 21. Unpaired, two tailed t test was used to compare groups of patients with and without DPN in terms of age, duration of DM, HbA1c, and BMI. Chi square was used to determine significance of differences in groups for gender, educational status, family history of DM, hypertension, smoking, and mode of treatment of DM. Chi square and Fisher exact were also used for differences in groups for prevalence of DM complications other than DPN. P-values less than or equal to 0.05 were considered statistically significant.

RESULTS
A total of 270 patients were included in our study, out of which 162 (60%) were male while remaining 108 (40%) were female, with male to female ratio of 1:1.5. Mean age was 62.26±11.38 years with 82 (30.37%) patients being in age group of 60-69 years. Mean duration of diabetes was 8.96±3.55 years, mean HbA1c value being 6.30±0.68. A family history of diabetes was present in 153 (56.7%) patients. Overall incidence of DPN in our study was found to be 36.7% (n=99) while mean values of NSS and NDS were 3.73±2.06 (0-9)

and 5.11±2.71 (0-10), respectively.

Table-I. Shows baseline characteristics of patients with DPN and without DPN.

Table-I shows that prevalence of DPN was higher among males (54.54%) than among females (p=0.2). In addition, it was observed that patients with DPN were older compared to the patients who did not have DPN (p<0.001). Level of education was also found to be significantly associated with development of DPN and DPN was more commonly observed in patients with poor educational status (p<0.001). Most of the patients who had DPN were either illiterate (36.84%) or had matric or lower level of education (57.89%). A longer duration of diabetes was associated with an increased risk of DPN (p<0.001). Patients with DPN showed significantly poorer control of diabetes (HbA1c=6.89±0.54) (p<0.001). Presence of hypertension and use of

insulin, or insulin and oral hypoglycemic drugs to control hyperglycemia were also found to be significantly associated with DPN (p<0.001 for both). Gender, educational status, duration of diabetes, glycaemic control, hypertension, and mode of treatment of DM were found to be significantly associated with DPN while family history of DM and history of smoking were not Major complications of diabetes other than DPN were also prevalent among the study population, most frequent being diabetic eye disease, which was present in 108 (40%) patients, followed by diabetic foot ulcer which was present in 90 (33.3%) patients, and cardiovascular disease which was present in 72 (26.7%) patients. Only 9 (3.3%) patients had history of amputation. It was also observed that prevalence of these complications was significantly higher among patients who had peripheral neuropathy. Table-II shows prevalence of other complications among patients.

S. No.	Characteristics	DPN present (n=99)	DPN Absent (n=171)	P-Value
1	**Gender** Male Female	54 (54.54%) 45 (45.45%)	108(63.15%) 63 (36.84%)	0.2
2	Age (years ±SD)	74.36±9.7.41	55.26±6.24	<0.001
3	**Educational status** Illiterate Matric and below Intermediate Graduation and above	43 (43.43%) 35 (35.35%) 16 (16.16%) 5 (5.05%)	63 (36.84%) 99 (57.89%) 9 (5.2%) 0	<0.001
4	Duration of DM (years ±SD)	12.81±1.59	6.73±2.20	<0.001
5	HbA1c	6.89±0.54	5.96±0.49	<0.001
5	**Family Hx of DM** Yes No	63 (63.63%) 36 (36.36%)	90 (52.63%) 81 (47.36%)	0.08
6	**Hypertension** Yes No	72 (72.72%) 27 (27.27%)	72 (42.10%) 99 (57.89%)	<0.001
7	BMI (kg/m² ±SD)	25.09±2.09	24.88±2.30	0.439
8	**Smoking Hx** Yes No	18 (18.18%) 81 (81.81%)	18 (10.52%) 153 (89.48%)	0.073
9	**Mode of treatment** Oral medication Insulin only Combination of oral and insulin	9 (9.09%) 42 (42.42%) 48 (48.48%)	131 (76.60%) 40 (23.39%) 0	<0.001

Table-I. Baseline characteristics of patients.

S. No	Complications	DPN Present	DPN Absent	P-Value
1	Eye problems	72	36	p<0.001
2	Diabetic foot ulcer	63	27	p<0.001
3	Cardiovascular disease	45	27	p<0.001
4	Amputation	9	0	p<0.001

Table-II. Prevalence of other complications.

DISCUSSION

T2DM has emerged as one of the major public health challenges in the 21st century. In our society, the rapidly growing diabetes epidemic and its complications put a heavy toll on health and economic systems. DPN is a common complication of diabetes, affecting more than half of the patients during their lifetime.[14] Prevalence of DPN varies among different populations and in different studies. This discrepancy is attributed to differences in populations studied and diagnostic tools used. Different diagnostic tests and examinations are used for DPN in different studies. We used NSS and NDS to determine the prevalence of DPN. These instruments are easy, simple, reproducible and sensitive. According to Rochester Diabetic Neuropathy Study Group, NSS and NDS are very sensitive for early diagnosis of DPN and have comparable results to that of electrophysiological examination.[15]

Overall incidence of DPN in our study was 36.7%. Since country-wide data on the prevalence of DPN in Pakistan is not available and a national average for prevalence cannot be calculated, it is not possible to compare our results with overall national prevalence. Some recent studies have reported prevalence at certain centres and institutions. A 2014 cross-sectional survey conducted at the Diabetes Management Centre, Services Hospital, Lahore included 250 patients of either gender, aged 16–60 and at least 5 years duration of diabetes with HbA1C between 6 and 8. DPN was present in 187 (74.8%).[16] Our observed rate of DPN was much lower by comparison. In this study, higher DPN rates were observed for patients with longer duration of diabetes although statistical significance was not reported. This finding is consistent with our finding that patients with longer duration of diabetes were significantly more likely to have DPN.

Two recent studies looked at prevalence of DPN among recently diagnosed cases of type 2 diabetes in Pakistan. A study carried out at the diabetes clinic of Sheikh Zayed Postgraduate Medical Institute, Lahore included male and female patients, with age ranging from 30 to 70 years. Patients were diagnosed with T2DM within 6 months of enrollment. Of the 113 patients, 73 (64.6%) had DPN[17] and the rate was slightly higher (68.5%) for the subgroup of patients with poor glycaemic control. Although our overall observed rate of DPN was lower, we also found that DPN rates were higher among patients with poor glycaemic control. Another study, conducted at the Department of Neurology, Civil Hospital and Dow University of Health Sciences, Karachi included patients of either gender aged between 30 and 60 years, who were newly diagnosed (within four weeks of presentation) with diabetes mellitus type 2. Out of 107 patients, DPN was present in 35 (32.7%) patients at the time of presentation. Our observed incidence of DPN was close to the prevalence observed in this study, however, our patient population, on average, exhibited a much longer duration of diabetes.[18]

Our DPN rate is comparable to two important European studies using the same instruments for diagnosis of DPN. DPN rates reported in these studies were 32.1% with mean duration of diabetes 9.7 years, and 35.4% with mean duration of diabetes 8.52±7.13 years.[19,20] However our rate is higher than the rate observed by Morkrid et al using similar diagnostic tool. He found a prevalence of 19.7% with mean duration of diabetes 7.0 + 1.8 years.

In our study, a higher proportion of males than females were found to be affected with DPN a finding similar to the findings reported by Gogia et al.[21] Age is one of the most important determinants

for the development of DPN. We found that DPN was more prevalent among older patients. Gogia et al[21] and Bansal et al[22] have reported similar findings. In our study there is positive linear trend between duration of diabetes and occurrence of DPN. This trend has been observed in several other studies.[21,22,23] HbA1c levels, mode of treatment and hypertension are other associated risk factors identified in our study which have also been reported by Yang et al[24] and Dong et al.[25]

Our study has some limitations. Since the study was conducted at a single centre and the sample size was relatively small, it might not be representative of the general population. There is a need for multicentre trials to better estimate the prevalence of DPN at the population level. There is also a need to establish standardized diagnostic criteria to define and categorize DPN.

CONCLUSION
Diabetic peripheral neuropathy is common entity seen in 36.7% patients with type 2 diabetes. Several factors are associated with development of DPN including age, gender, education level of the patients, duration of diabetes, glycaemic control and presence of co-morbid conditions like hypertension. There should be a continuous process of evaluation and imparting education which will not only improve practice but also patient care as a whole.

Conflict of Interest
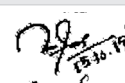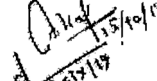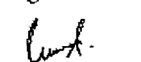This study has no conflict of interest to declare by any author.
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4	Shahbaz Khan	Literature search, Data analysis, Interpretaion.	
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