

Study of prevalence and determinants of peripheral neuropathy in patients with type 2 diabetes mellitus

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Abstract

Background: India is witnessing a depressing situation due to escalating incidence and prevalence of type 2 diabetes mellitus (T2DM) and its inevitable outcomes of cardiovascular diseases (CVD), diabetic neuropathy, nephropathy and retinopathy. Present study was aimed to investigate peripheral neuropathy in adult patients with type 2 diabetes. **Material and Methods:** Present study was hospital based, prospective, observational study conducted in subjects recruited from the diabetes OPD of both gender ≥ 30 years, known case of type 2 diabetes mellitus. The screening for DPN was conducted using the Michigan Neuropathy Screening Instrument (MNSI). **Results:** In present study, 256 subjects satisfying study criteria were considered for study. Most of patients were from 51-65 years age group (39.8%) followed by 31-50 years age group (37.1%). Male subjects (54.3%) were more than females (45.7%). Mean duration of type 2 diabetes mellitus was 10.6 ± 6.3 years. Mean HbA1c was $9.3 \pm 2.8\%$ and 65.6% had HbA1c $\geq 7\%$. Common high risk factors were hypertension (52.3%), alcoholic > 60 mg/day (30.5%), BMI $> 30\text{kg/m}^2$ (26.6%), smoking habits > 1 pack/day (18.0%), history of peripheral artery disease (12.5%) and history of prior ulcer (12.1%). Prevalence of peripheral neuropathy in subjects with type 2 diabetes mellitus in present study was 35.2%, calculated as per reduced perception/absent monofilament test. Vibration perception test was absent in 22.7% subjects and ankle reflex was absent in 13.3% subjects. Age, duration of diabetes, fasting blood sugar, BMI, HbA1c $\geq 7\%$ and alcoholic (> 60 mg/day) were statistically significant in subjects of type 2 diabetes mellitus with peripheral neuropathy and difference was statistically significant. **Conclusion:** Diabetic peripheral neuropathy was significantly and positively associated with age, duration of diabetes, fasting blood sugar, BMI, HbA1c $\geq 7\%$ and alcoholic (> 60 mg/day). Regular screening of patients with diabetes mellitus for peripheral neuropathy may be recommended for early diagnosis and treatment.

Keywords: Type 2 diabetes; Peripheral neuropathy, prevalence, risk factors

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INTRODUCTION

Diabetes Mellitus is a noncommunicable disease having predominant public health concern, affecting millions of people worldwide. According to International Diabetes Federation report, 415 million people worldwide have this disease and India harbors 69.1 million, the second highest number of diabetics in the world. Type 2 Diabetes mellitus (T2DM) is the most prevalent form of diabetes.¹ India is witnessing a depressing situation due to escalating incidence and prevalence of type 2 diabetes mellitus (T2DM) and its inevitable outcomes of cardiovascular

diseases (CVD), diabetic neuropathy, nephropathy and retinopathy.² The consequences of diabetic peripheral neuropathy, development of foot ulcers, may lead to lower limb amputation, neuropathic pain and decreased sensation can contribute impaired quality of life and restrictions in activities of daily living.^{3,4} In persons with diabetes mellitus, the annual population-based incidence of foot ulcer ranges from 1-4.1%, and the prevalence ranges from 4-10%, which suggests that the lifetime incidence may be as high as 25%.⁵ The early identification of diabetes with peripheral neuropathy and its associated factors is the key for reducing further complications and for providing baseline information to initiate appropriate interventions. Present study was aimed to investigate peripheral neuropathy in adult patients with type 2 diabetes.

MATERIAL AND METHODS

Present study was hospital based, prospective, observational study conducted in department of physiology with help from department of general medicine at Sri Manakula Vinayagar Medical College and Hospital, Puducherry, India. Present study was conducted over 6 month's duration from January 2016 to June 2016. Study was approved by institutional ethical committee.

Inclusion criteria

- Subjects recruited from the diabetes Out Patient Department (OPD), of both gender, ≥ 30 years, known case of type 2 diabetes mellitus

Exclusion criteria

- Subjects with type I diabetes mellitus, h/o cerebro-vascular accident, Hansen's disease.
- Subjects not willing to participate

The screening was conducted after obtaining a written informed consent from the participants. The screening consists of demographic, clinical and lifestyle (gender, age, race, marital status, education, type of DM, year of diagnosis of diabetes, presence of hypertension, insulin use, glycohemoglobin, dyslipidemia, previous ulcer, obesity, smoking or drinking). The screening for DPN was conducted using the Michigan Neuropathy Screening Instrument (MNSI). The MNSI is a validated tool for the screening of DPN.⁶ The MNSI includes two parts, the first part is related to patient's perception of

symptoms in relation to DPN (in form of questionnaire of 12 questions, score of ≥ 7 was taken as positive for the DPN) and the second part consists of a set of examinations done to detect the presence of DPN among the patients.

The examinations include,

- vibration sensation test using a 128 Hz tuning fork,
- elicitation of muscle jerk reflex at the ankle joint and
- monofilament testing.

All the examinations were conducted under supervision of Department of general medicine. After examining the patient's both extremities, each component is given a score of 0 (finding is present) and 1 (abnormality present). After summing up all the components if the overall score was found to be ≥ 2.5 , then it was considered to be positive for the presence of DPN. Data was collected and compiled using Microsoft Excel. The collected information was entered and analysed using SPSS version 23. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi-square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant.

RESULTS

In present study, 256 subjects satisfying study criteria were considered for study. Most of patients were from 51-65 years age group (39.8 %) followed by 31-50 years age group (37.1 %). Mean age was 56.8 ± 10.4 years. Male subjects (54.3 %) were more than females (45.7 %). Mean age at diagnosis of type 2 diabetes mellitus was 47.6 ± 13.2 years. Mean duration of type 2 diabetes mellitus was 10.6 ± 6.3 years. Other variable were mean BMI as 25.4 ± 7.3 kg/m², 18% subjects were using insulin. Mean fasting and Postprandial blood sugar levels were 153.3 ± 84.1 mg/dl and 210.4 ± 86.3 mg/dl respectively. Mean HbA1c was 9.3 ± 2.8 % and 65.6 % had HbA1c ≥ 7 %. Common high risk factors were hypertension (52.3 %), alcoholic > 60 mg/day (30.5 %), BMI > 30kg/m² (26.6 %), smoking habits >1 pack/day (18.0 %), history of peripheral artery disease (12.5 %) and history of prior ulcer (12.1 %).

Table 1: Baseline characteristics of the study population

Variable	Number of subjects (n=256)	Percentage
Age (years)		
31 – 50	95	37.1
51 – 65	102	39.8
>65	59	23.0
Age (years)	56.8 ± 10.4	
Gender		
Male	139	54.3
Female	117	45.7

Age at diagnosis (years)	47.6 ± 13.2	
DM diagnosis time (mean ± standard deviation)	10.6 ± 6.3	
BMI (kg/m ²)	25.4 ± 7.3	
Fasting blood sugar (mg/dl)	153.3 ± 84.1	
Postprandial blood sugar (mg/dl)	210.4 ± 86.3	
Insulin using now	46	18.0
Glycohemoglobin/ HbA1c (%)	9.3 ± 2.8	
≥ 7	168	65.6
< 7	88	34.4
High risk factors		0.0
Hypertension	134	52.3
Alcoholic (> 60 mg/day)	78	30.5
Obesity (BMI > 30kg/m ²)	68	26.6
Smoking habits (>1 pack/day)	46	18.0
History of Peripheral Artery Disease	32	12.5
History of Prior ulcer	31	12.1

Prevalence of peripheral neuropathy in subjects with type 2 diabetes mellitus in present study was 35.2 %, calculated as per reduced perception/absent monofilament test. Vibration perception test was absent in 22.7 % subjects and ankle reflex was absent in 13.3 % subjects.

Table 2: Distribution according to the monofilament test, ankle reflex and vibration perception test

Variable	Number of subjects (n=256)	Percentage
Monofilament test		
Normal (10)	166	64.8
Reduced (1-7)response	88	34.4
Absent (0)	2	0.8
Vibration perception test		0.0
Present	198	77.3
Absent	58	22.7
Ankle reflex		0.0
Present	222	86.7
Absent	34	13.3

Age, duration of diabetes, fasting blood sugar, BMI, HbA1c ≥ 7 % and alcoholic (> 60 mg/day) were statistically significant in subjects of type 2 diabetes mellitus with peripheral neuropathy and difference was statistically significant.

Table 3: Significant variables between DPN present and absent subjects

Variables	DPN Present	DPN Absent	p-value
	No. of subjects (%)/(Mean ± SD)	No. of subjects (%)/(Mean ± SD)	
Age (years)	59.65 ± 11.56	54.27 ± 10.23	<0.001
Duration of Diabetes (years)	8.55 ± 7.67	6.34 ± 4.21	<0.001
Fasting blood sugar (mg/dl)	192.29 ± 52.66	149.88 ± 51.22	<0.001
BMI (kg/sq.m)	27.56 ± 4.17	25.02 ± 3.37	<0.001
Glycohemoglobin/ HbA1c (%)	9.54 ± 3.32	6.71 ± 2.66	<0.001
Alcoholic (> 60 mg/day)	46 (18.0 %)	32 (12.5 %)	<0.001

DISCUSSION

As a cost of urbanization, the overall status of diabetes according to IDF estimates in 2017 showed that there are now 425 million adults with diabetes and 352 million adults with impaired glucose tolerance worldwide.⁷ Diabetic peripheral neuropathy is thought to be caused by nerve dysfunction and cell death that results from oxidative stress and inflammation mainly due to hyperglycemia, dyslipidemia, and insulin resistance commonly noted in diabetic patients.⁸ Patients with diabetic peripheral neuropathy who are at the highest risk for developing foot

ulcers that lead to amputation include those with a prior history of foot ulcers, a structural foot deformity, peripheral artery disease, visual impairment, diabetic nephropathy, poor glycemic control, and smoking.⁹ There are many tools for screening DPN like Diabetic neuropathy symptom score, Neuropathy disability score, Neuropathy symptom score, Toronto clinical scoring system and Michigan Neuropathy Screening Instrument (MNSI). MNSI has been used in this study which has a sensitivity of 80% and specificity of 95%.¹⁰ MNSI has got a kappa value of 0.588.¹¹ Prevalence of DPN in other studies

conducted elsewhere showed a lot of variation, ranging from 13% to 75%.^{12,13,14} The difference in prevalence of DPN across the studies can be attributed to differences in diabetes duration, study designs, type of study population included and different types of scales used to assess the magnitude of DPN in different study settings. Nonetheless, the high prevalence of DPN in our study highlights the importance of proper foot care and adequate blood sugar control among diabetics. Typically, neuropathic symptoms range from severe painful positive symptoms such as burning or blazing sensations, stabbing and acute pain, uncomfortable sensations of temperature, paresthesia and hyperesthesia; the mild symptoms or “negative”, such as decreased pain sensation, fatigue and numbness.¹⁵ Symptoms alternate throughout the day and are extremely uncomfortable and painful at night. Smoking causes atherosclerosis, elevates blood pressure, and causes nerve injury due to inflammation, which collectively leads to impaired nerve functioning. Obesity, sedentary life-style causes insulin resistance which promotes low-grade inflammation. This inflammation influences endothelial dysfunction and micro-vascular complications.¹⁶ In a cross-sectional study of 1003 patients with type 2 diabetes, overall prevalence of DPN based on MNSI was 39.5%. The most frequently reported symptoms were numbness (32.3%) and pain with walking (29.7%), while the least reported symptoms were the history of amputation (1.3%) and loss of sensation in legs/feet while walking (3.8%). Logistic regression analysis revealed that unemployment, cardiovascular disease, dyslipidemia, diabetic retinopathy and long-standing DM (diabetes of ≥ 5 years) were significantly associated with DPN.¹⁷ Darivemula S *et al.*¹⁸ studied 336 patients from Andhra Pradesh region, 202 (60.1%) were male and 134 (39.9%) were female. The prevalence of the DPN was 39.3% among them 28.9% in males and 10.4% in females, respectively. The other determinants of the participants, 264 (78.6%) had the Glycated hemoglobin (HbA1c) >7 , 205 (61%) had a burning foot sensation, 124 (36.9%) of them were had numbness of the foot, almost 50% of them had pricking sensation in the foot and more than one-third (130) of them had callosity over foot. The study showed the severity of DPN was significantly associated with age, sex, duration of diabetes, HbA1c value, hypertension, and body mass index. Similar findings were noted in present study. Mathiyalagen P *et al.*,¹⁹ conducted a cross-sectional study among 421 type 2 DM patients, prevalence of DPN was 31.1%. The mean age, duration of diabetes, and duration of foot symptoms were 57.91 ± 10.61 , 7.00 ± 6.23 , 5.56 ± 5.26 years. Smoking, mean duration of diabetes > 5 years, hyperglycemic status (> 200 mg/dl) and unemployment were found to be statistically significant determinants of DPN on binary logistic regression analysis. Early

diagnosis and recognition of at-risk individuals are cornerstones for intervention strategies to prevent DPN-associated complications.²⁰ The American Diabetes Association (ADA) recommends that all patients should be assessed for DPN starting at diagnosis of T2D and 5 years after the diagnosis of T1D, followed by annual evaluations thereafter.²¹ Regular and comprehensive foot examination, patient education on foot care practices such as simple hygienic practices, provision of appropriate footwear, and prompt treatment of minor injuries and a multidisciplinary team approach can reduce the ulcer occurrence by 50% and amputations by up to 85%.²² The limitations of present study were hospital based study, lack of nerve conduction velocity (NCV) studies which is the definite tool for diagnosing neuropathy, lack of etiology determination of DPN (e.g., vitamin B12 or folic acid deficiency) and study of potential confounding factors.

CONCLUSION

Diabetic peripheral neuropathy was significantly and positively associated with age, duration of diabetes, fasting blood sugar, BMI, HbA1c ≥ 7 % and alcoholic (> 60 mg/day). Regular screening of patients with diabetes mellitus for peripheral neuropathy may be recommended for early diagnosis and treatment.

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