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Prevalence and risk factors of development of peripheral diabetic neuropathy in type 2 diabetes mellitus in a tertiary care setting

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ABSTRACT

Aims/Introduction: The study was carried out to assess the prevalence of diabetic peripheral neuropathy (DPN), compare the prevalence between known diabetes mellitus (KDM) and newly detected diabetes mellitus (NDDM), identify risk factors associated, its prevalence pattern and to assess if any sex-specific differences are present.

Materials and Methods: A cross-sectional study was carried out in a tertiary care hospital. Patients with duration of diabetes ≤6 months were considered to be NDDM. DPN was diagnosed by the combination of more than one abnormal result of 10-g monofilament, pinprick sensations and ankle reflexes, and categorized according to the severity level using vibration perception threshold. The study included 1,637 KDM and 369 NDDM patients.

Results: A total of 586 participants were found to have DPN, accounting for 29.2% (95% confidence interval [CI] 27.2–31.2) prevalence. The higher prevalence was observed in KDM compared with NDDM 33.7% (95% CI 31.42–36.01) vs 9.2% (95% CI 6.3–12.2; $P < 0.001$). Prevalence of mild, moderate, and severe neuropathies was 8.06, 14.55 and 6.63%, respectively. Regression analysis showed age ($P < 0.001$), duration of diabetes ($P < 0.001$), dyslipidemia ($P = 0.03$), glycated hemoglobin ($P < 0.001$), the presence of other microvascular complications ($P < 0.001$), macrovascular complications ($P = 0.003$) and alcoholic status ($P < 0.033$) to be associated. No sex-specific differences were observed in the mean age at diagnosis of diabetes, mean age at the diagnosis of neuropathy, and duration taken for the DPN development among females and males.

Conclusions: The study showed a high prevalence (29.2%) of DPN among north Indian type 2 diabetes mellitus patients. Thus, timely screening with earlier detection and intervention would be useful in preventing the progression of neuropathy.

INTRODUCTION

With 371 million people diagnosed with diabetes mellitus worldwide and a prevalence of 8.3% as per the Diabetes Atlas 2012, diabetes mellitus has become a global burden[1]. This pandemic mostly relates to type 2 diabetes mellitus, which remains asymptomatic in many patients for a prolonged duration, and is diagnosed only with the emergence of associated complications[2]. Diabetic peripheral neuropathy (DPN) is a well-known microvascular complication of type 2 diabetes mellitus attributed to chronic hyperglycemia, and is defined as the presence of peripheral nerve dysfunction in diabetics after exclusion of other causes[3–6]. DPN leads to further infections, increasing the risk of foot ulcers and non-traumatic amputations. Estimates of foot infections in type 2 diabetes mellitus range from a lifetime risk of 4–7% annually[7,8].

Approximately 40–50% of the patients developing DPN further develop painful DPN[9]. Neuropathy and neuropathic pain

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are among the strongest determinants of reduced health-related quality of life in patients with type 2 diabetes mellitus. Also, neuropathy management including adequate podiatric care in patients with type 2 diabetes mellitus adds on to the economic burden of the national health system. It has been reported that excess healthcare costs attributed to the management of DPN can lie between $1,600–7,000, and painful DPN management can increase the cost of treatment up to threefold. Apart from the direct costs involved, DPN can also lead to work absence, change in employment and disability[10].

To date, the majority of studies on the prevalence and associated determinants of DPN are carried out in Western countries. Few data are available in Asian populations, especially north Indian populations. Although few population-based studies are carried out in southern India,[11–13] ethnic, cultural, anthropometric and weather differences makes the north Indian population a distinct entity, and exposes them to a different risk profile for the development of type 2 diabetes mellitus.

Therefore, we set out to accomplish several goals in the present study. First, we calculated the estimates of the prevalence of DPN and the risk factors associated with DPN in a north Indian population diagnosed with type 2 diabetes mellitus. Second, we evaluated the relationship between DPN and other chronic diabetic complications. Third, we also assessed the prevalence and predictors of progression of DPN among the established and newly detected type 2 diabetes mellitus patients along with sex-specific differences in DPN development.

MATERIALS AND METHODS

The present cross-sectional epidemiological study was carried out in an outpatient setting of an endocrinology clinic of a public tertiary care hospital in north India. Consecutive patients were recruited by screening patient cards meeting the inclusion criteria. The study was initiated after approval by the Institutes Ethical Review Committee, PGIMER, Chandigarh, India.

Selection of Participants

Patients of either sex diagnosed with type 2 diabetes mellitus of any duration, established as per American Diabetes Association (ADA) guidelines (random blood sugar >200 mg/dL or fasting blood sugar >126 mg/dL) and willing to participate were included in the study. They were further classified into known diabetes mellitus (KDM) and newly detected diabetes mellitus (NDDM) based on the duration of diabetes. Patients with the diagnosis of type 2 diabetes mellitus of less than 6 months' duration were considered to be NDDM and KDM otherwise. Patients having type 1 diabetes, gestational diabetes and maturity onset diabetes of the young were excluded from the study.

Data Collection

Physicians were requested to report the clinical and biochemical data not exceeding 6 months before the observation. The information regarding demographics (age, sex), socioeconomic and lifestyle characteristics (smoking, alcohol consumption) were collected by interviewing the participant. Biochemical parameters were derived from the latest laboratory investigation reports documented in the clinical records. Socioeconomic status was assessed using the modified Kuppuswamy's scale, which considers the education qualification, occupation of the family head and family income per month of the participant. All the relevant data were collected in a predesigned paper case record form with prior consent of the participant.

Clinical and Biochemical Measurements

Anthropometric measurements including weight, height (using stadiometer), body mass index (BMI; kg/m^2) and waist circumference (using inelastic and flexible tape at the midpoint between the lower margin of the least palpable rib and top of the iliac crest nearest to 0.1 cm) were carried out at the time of recruitment. Clinical systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels, serum lipids, blood glucose and glycated hemoglobin (HbA1c), and hepatic and renal function levels were extracted from available clinical records (in the previous 6 months).

Blood pressure of the participants was measured at the time of recruitment in the sitting position in the right arm to the nearest 2 mmHg with a mercury sphygmomanometer (Diamond Deluxe BP apparatus, BP Instruments, Pune, India), and the participants were considered to be hypertensive if were taking antihypertensive medication (as documented in clinic records) or SBP ≥140 mmHg or DBP ≥90 mmHg. HbA1c was also measured using the Variant machine (Bio-Rad Laboratories, Hercules, CA, USA). Proteinuria according to spot urine testing by sulfosalicylic acid technique was diagnosed if the estimated 24 h protein excretion was ≥500 mg/day.

Assessment of Neuropathy

Neuropathy was assessed using 10-g monofilament, pinprick sensations, ankle reflexes and vibration perception threshold (VPT) test. The 10-g Vonfrey monofilament was placed perpendicular to the skin and pressure was applied until the filament just buckled with a contact time of 2 s. Inability to perceive the sensation at any one site was considered abnormal. In addition, ankle reflexes were also assessed with a percussion hammer, and recorded as either present or absent.

Initially, each diabetic patient was confirmed by the physician to have DPN if diagnosed with one or more abnormal finding of 10-g monofilament, pinprick sensations and ankle reflexes. Thereafter, the patient underwent VPT test to categorize them according to the severity level of DPN.

Quantification of DPN was assessed by VPT using a Biothesiometer (Dhansai Laboratories, Mumbai, India) in a standardized manner by a single observer for all the participants. VPT was then measured at five different locations on the feet (distal plantar surface, meta tarsals) of both legs. If the great toe was affected by ulcer, VPT was measured at the base of the first, third or fifth metatarsals. The voltage was slowly increased at the rate of 1 mV/s, and the VPT value was defined as the volt-

age level when the participant indicated that he or she first felt the vibration sense. The mean value of five measurements of both legs were calculated and considered for analysis, and accordingly the patients were categorized into the grades of DPN. In the participants with DPN diagnosis established earlier, the year of neuropathy diagnosis was taken from the patients' previous records[14].

A cut-off value of 20 mV was considered for the presence of DPN along with three grades of mild (20–24 mV), moderate (25–39 mV) and severe (>39 mV) based on VPT score. The present cut-off value of 20 mV of VPT among the Indian population was found to have better sensitivity compared with Neuropathy Disability Scores (NDS) taken as the gold standard[15].

Assessment of Retinopathy

The diagnosis of diabetic retinopathy was made by an ophthalmologic examination that included fundoscopy or retinal photography and measurement of visual acuity, carried out by an ophthalmologist.

Assessment of Nephropathy

The diagnosis of nephropathy was confirmed from the clinical records (if already documented) or if estimated 24-h protein excretion was ≥500 mg/day.

Statistical Analysis

Data are presented as the mean with standard deviation (SD), or median with interquartile range (IQR) and numbers with percentages. Demographic data were analyzed using either two-sample independent Student's *t*-test, Mann–Whitney *U*-test or χ^2-test. Multivariate logistic regression was used to estimate odds ratios (OR) for the presence of neuropathy with 95% confidence interval (CI). The duration taken for the development of DPN was calculated by subtracting the age at diagnosis of type 2 diabetes mellitus from the age at diagnosis of DPN. Kaplan–Meier survival curves were plotted to assess the time taken for neuropathy development and compared using the log–rank test. $P < 0.05$ was taken as significant. All the analyses were carried out using SPSS version 14 (SPSS Inc., Chicago, IL, USA).

RESULTS

A total of 2,006 patients with diabetes including 989 (49.3%) male patients and 1,017 (50.7%) female patients were recruited into the study. Among the study cohort, 369 (18.4%) patients were NDDM with duration of diabetes <6 months and the remaining 1,637 (81.6%) patients were KDM. Overall, 586 patients were found to have DPN accounting for 29.2% (27.2–31.2). The prevalence of neuropathy among males and females were 29.1% (26.2–31.9) and 29.3% (26.5–32.1; $P = 0.922$), respectively (data not shown). The prevalence was found to be significantly higher ($P < 0.001$) among KDM patients (33.7%, 31.4–36.0) as compared with NDDM patients (9.2%, 6.2–12.3; Table 1).

Depending on VPT scores, the distribution of mild, moderate, and severe neuropathies were found to be 8.1% (95% CI 6.7–10.2), 14.5% (95% CI 12.6–16.4) and 6.6% (95% CI 4.4–8.2), respectively. More than 25% of patients with DPN fell under the moderate-to-severe category in patients with KDM, whereas 6.26% (23) of NDDM patients with DPN had mild neuropathy, suggesting the fact that prolonged duration of diabetes increases the prevalence as well as severity of DPN (Table 1).

The mean age of patients (57.1 [9.7] vs 52.5 [10.4], $P < 0.001$) and duration of diabetes (10.8 [7.5] vs 6.6 [6.9], $P < 0.001$) of patients with DPN were found to be significantly higher than patients without DPN. Among the DPN patients, there was a higher percentage of alcoholics ($P = 0.02$), higher percentage of hypertension ($P = 0.003$) than the patients without DPN. However, the two groups were similar with respect to sex distribution ($P = 0.92$), BMI ($P = 0.61$), waist circumference ($P = 0.4$), HbA1c ($P = 0.3$) and smoking status ($P = 0.57$). Patients with DPN belonged more to the lower and middle class ($P < 0.001$) according to Kuppuswamy's Socioeconomic Status Scale. DPN patients had a lower percentage of dyslipidemia ($P = 0.02$) than the patients without DPN (Table 2).

The prevalence of other microvascular complications, such as retinopathy (41.8 vs 18.3%, $P < 0.0001$) and nephropathy (20.9 vs 3.8%, $P < 0.001$), were higher in those with DPN compared with those without it (Table 2).

Figure 1 shows the age-wise prevalence of neuropathy. There was a positive linear trend in the prevalence of neuropathy with increase in age ($R^2 = 0.971$, $P = 0.002$). The odds of developing neuropathy in relation to duration of diabetes is shown in Figure 2. A similar positive linear trend ($R^2 = 0.819$, $P = 0.095$) showing a progressive increase in risk for neuropathy

Table 1 | Diabetic peripheral neuropathy prevalence in study cohort

Group	Severity of neuropathy* *n* (%), [95% CI]			
	Overall neuropathy	Mild neuropathy	Moderate neuropathy	Severe neuropathy
Total (*n* = 2,006)	586 (29.2) [27.2–31.2]	(161) (8.06) [6.7–10.2]	(292) (14.55) [12.6–16.4]	(133) (6.63) [4.4–8.2]
KDM (*n* = 1,637)	552 (33.7) (31.4–36.0)	132 (8.06) [5.7–10.5]	285 (17.4) [15.1–19.8]	135 (8.3) [5.9–10.7]
NDDM† (*n* = 369)	34 (9.2) [6.3–12.2]	23 (6.2) [3.3–9.1]	11 (2.98) [0.2–5.9]	–

*Severity assessed according to vibration perception threshold test scores in to three grades, mild (20 – 24 mV), moderate (25–39 mV) and severe (>39 mV). †Newly detected diabetes mellitus is considered as <6 months of duration of diabetes. DPN, Diabetic Peripheral Neuropathy; CI, confidence interval; KDM, Known diabetes mellitus; NDDM, Newly detected diabetes mellitus.

Table 2 | Clinical, biochemical and socioeconomic characteristics of the study participants

Variables	DPN Present (n = 586)	DPN Absent (n = 1420)	P-value
Age (years)*	57.1 (9.7)	52.5 (10.4)	<0.001†
Duration of diabetes (years)	10.8 (7.5)	6.6 (6.9)	<0.001‡
Male, n (%)	288 (49.4)	701 (49.4)	0.92§
Female, n (%)	298 (51.9)	719 (51.6)	
BMI (kg/m^2)	26.9 (4.5)	27.1 (4.7)	0.61†
Waist circumference (cm)	95.2 (12.6)	94.6 (12.4)	0.4†
HbA1c	8.8 (2.3)	8.6 (2.2)	0.3†
Smoking, n (%)	73 (12.4)	190 (13.3)	0.57§
Alcohol, n (%)	146 (24.9)	289 (20.3)	0.024§
Socioeconomic status¶			
Upper, n (%)	60 (10.2)	230 (16.1)	<0.001§
Upper middle, n (%)	130 (22.1)	412 (29.0)	
Lower middle, n (%)	95 (16.2)	255 (17.9)	
Upper lower, n (%)	33 (5.6)	148 (10.4)	
Lower, n (%)	284 (48.4)	376 (26.4)	
Hypertension n (%)	227 (38.7)	453 (31.9)	0.003§
TC (mg/dL)	179 (51.3)	190.5 (54.2)	0.006†
LDL-C (mg/dL)	92 (46.6)	108.1 (39.9)	<0.001†
HDL-C (mg/dL)	62.1 (39.6)	45.4 (15.3)	<0.001†
TG (mg/dL)	163.8 (96.9)	174 (85.5)	0.15†
Dyslipidemia, n (%)**	8 (0.8)	44 (3.1)	0.02§
Retinopathy, n (%)	245 (41.8)	260 (18.3)	<0.001§
Nephropathy, n (%)	123 (20.9)	54 (3.8)	<0.001§

*Age at the time of recruitment. †Analyzed using unpaired t-test. ‡Analyzed using Mann–Whitney U-test. §Analyzed using χ^2-test. ¶Socioeconomic status was assessed using Kuppuswamy's Socioeconomic Status Scale. **Dyslipidemia is considered as total cholesterol (TC) >200 mg/dL, high-density lipoprotein cholesterol (HDL-C) ≤60 mg/dL, low-density lipoprotein cholesterol (LDL-C) >100 mg/dL, triglycerides (TG) >150 mg/dL. BMI, body mass index; HbA1c, glycated hemoglobin.

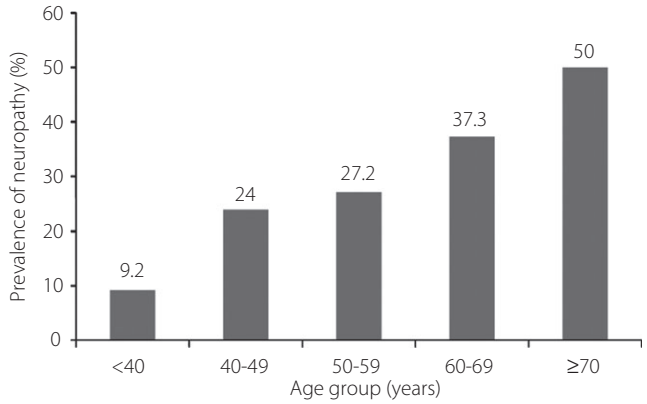

Figure 1 | Prevalence of neuropathy according to Age groups.

with an increasing duration of diabetes was observed. The odds of developing neuropathy in patients who had diabetes for >15 years duration was 8.03 (95% CI 5.96–10.8, $P < 0.001$) compared with duration <5 years was observed.

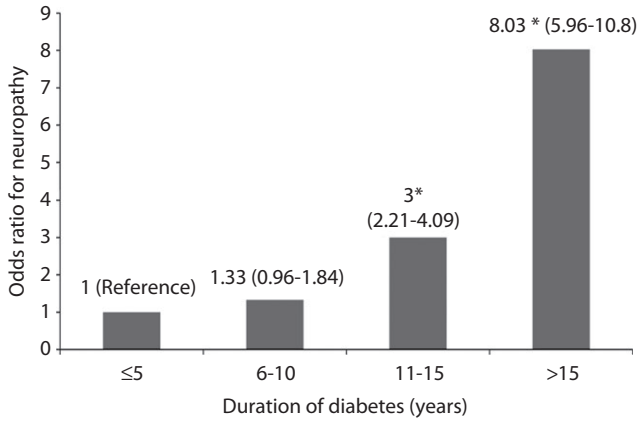

Figure 2 | Risk of neuropathy according to the duration of diabetes. Values shown in parenthesis are 95% confidence intervals. *$P < 0.001$ compared with reference.

Risk Factors of DPN

Results of multivariate logistic regression are shown in Table 3. The age (continuous variable) of the participants showed a positive association (OR 1.02, 95% CI 1.01–1.03, $P < 0.001$). Longer duration of diabetes (OR 1.044, 95% CI 1.02–1.06, $P < 0.001$) and the presence of other microvascular complications (either nephropathy or retinopathy or both), (OR 3.45, 95% CI 2.65–4.5, $P < 0.001$) were found to be significantly associated with the presence of DPN. Females were found to have a threefold (OR 3.15, 95% CI 1.57–6.31, $P < 0.001$) higher risk for the development of DPN than males. However, the presence of macrovascular complications ($P = 0.17$), hypertension ($P = 0.12$), alcohol use ($P = 0.53$), smoking ($P = 0.57$) and higher HbA1c levels ($P = 0.65$) were the other variables found to be non-significantly associated with DPN. Dyslipidemia was inversely associated with DPN (OR 0.43, 95% CI 0.20–0.92, $P = 0.03$), this could be as a result of early intervention of antihyperlipidemics among diabetics.

Sex Difference

Table 4 compares the mean age at diagnosis of diabetes (46.03 vs 46.05 years, $P = 0.948$), mean age at the diagnosis of neuropathy (51.47 vs 52.35 years, $P = 0.269$) and duration taken for the DPN development (5.51 vs 5.87 years, $P = 0.25$) among females ($n = 1017$) and males ($n = 989$), respectively. No sex-specific differences were observed in either of the variables considered for comparison. Kaplan–Meier analysis (Figure 3) of a subgroup of participants having neuropathy based on sex was drawn to support the earlier results of no significant difference between males and females in duration from the initial diagnosis of diabetes to the development of neuropathy ($P = 0.54$).

DISCUSSION

According to recent statistics published by the International Diabetes Federation of Diabetes Atlas, India having 63 million

Table 3 | Risk factors for diabetic peripheral neuropathy in multivariate logistic regression

Variables	Odds ratio (95% CI)	*P*-value
Age*	1.03 (1.01–1.04)	<0.001
Duration of diabetes	1.04 (1.03–1.06)	<0.001
Sex		
Male	1 (Ref.)	
Female	1.14 (0.84–1.5)	0.423
Smoking		
Non-smoker	1 (Ref.)	
Smoker	0.71 (0.47–1.06)	0.096
Alcohol		
Non-drinker	1 (Ref.)	
Drinker	1.46 (1.03–2.07)	0.033
Hypertension		
Absent	1 (Ref.)	
Present	2.02 (1.56–2.61)	<0.001
HbA1c		
<6.5%	1 (Ref.)	
>6.5%	1.03 (0.97–1.09)	<0.001
Body mass index		
<25 kg/m^2	1 (Ref.)	
>25 kg/m^2	1.01 (0.98–1.03)	0.364
Dyslipidemia†		
Absent	1 (Ref.)	
Present	0. 43 (0.2–0.92)	0.03
Macrovascular complications‡		
Absent	1 (Ref.)	
Present	1.6 (1.18–2.19)	<0.01
Microvascular complications§		
Absent	1 (Ref.)	
Present	3.45 (2.65–4.5)	<0.001

*Age at the time of recruitment. †Dyslipidemia is considered as total cholesterol >200 mg/dL, high-density lipoprotein cholesterol ≤60 mg/dL, low-density lipoprotein cholesterol >100 mg/dL, triglycerides >150 mg/dL. ‡Macrovascular complications include coronary artery disease, peripheral arterial disease and cerebrovascular accident. §Microvascular complications include neuropathy, nephropathy and retinopathy. CI, confidence interval; HbA1c, glycated hemoglobin; Ref., reference category.

Table 4 | Sex differences in the age at diagnosis of type 2 diabetes mellitus and time gap for diabetic peripheral neuropathy development

	Women	Men	*P*-value
Age at diagnosis of diabetes mellitus (years)	46 (10.3)	46.1 (10.8)	0.94
Age at diagnosis of DPN (years)	51.5 (9.6)	52.3 (9.6)	0.27
Time gap between diagnosis of diabetes mellitus and DPN	5.5 (3.6)	5.9 (4.0)	0.25

Data presented as mean (standard deviation). DPN, diabetic peripheral neuropathy.

people with diabetes accounts for 17% of the total diabetic population[1]. This is the first prospective, cross-sectional study carried out in a public tertiary care set-up in a north Indian

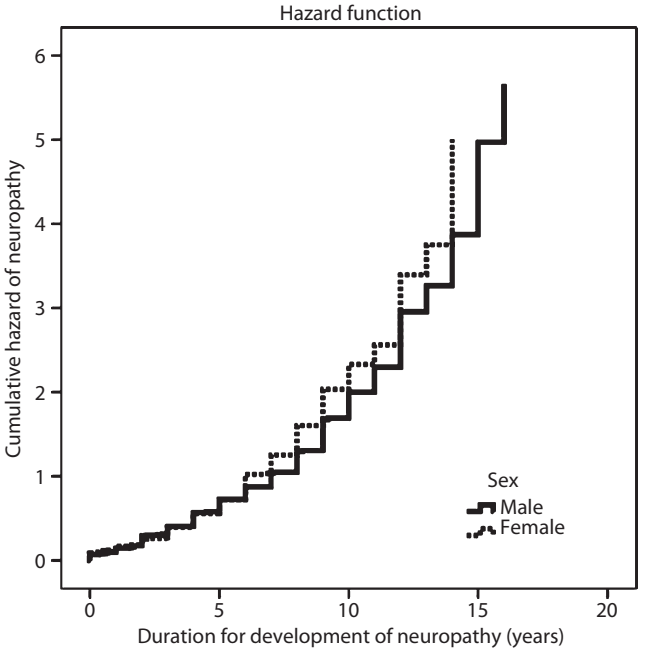

Figure 3 | Kaplan–Meier curves for the period from diagnosis of type 2 diabetes mellitus to the establishment of diabetic peripheral neuropathy in men and women.

population for the assessment of DPN prevalence and its risk factors among patients with type 2 diabetes mellitus. The prevalence of DPN was found to be 29.1% in the present study. The estimates of DPN prevalence vary widely from 9.6 to 78% in different populations[11–13,16–27]. This could be attributed to different types of diabetes (e.g. type 1 and type 2 diabetes), genetic predisposition, age of onset of diabetes, existing healthcare facilities, sample selection, different diagnostic criteria used (pin-prick perception, clinical signs and symptoms, and quantitative sensory tests or electrodiagnostic tests)[16,28–31].

The present study is one of the few studies reporting DPN prevalence (considered to be a long-term microvascular complication) among KDM and NDDM patients[11–13]. We found DPN prevalence in NDDM to be 9.1%. This is much lower than reports from other studies in Indian patients by Pradeepa *et al.*[12] (19.5%) and Rani *et al.*[11] (14.4%), respectively. The lower prevalence in the present study could possibly be because of a different study set-up (tertiary care vs community based), increased knowledge and awareness of diabetes and its complications in recent times leading to earlier type 2 diabetes mellitus diagnosis and control of its complications. The present study was in line with that of Raman *et al.*[13], which was carried out in a similar clinical set-up including 248 NDDM patients reporting DPN prevalence to be 10.5%.

A comparatively higher DPN prevalence of 33.7%, accounting for one-third recruited participants, was observed in KDM patients, thus, imposing a need of early detection and control of diabetes to prevent the emergence of long-term microvascular complications.

In a prospective follow-up study of 1-year duration carried out to examine the ability of VPT to predict the development of diabetic foot ulceration, it was found that among diabetic patients with a VPT score of >25 mV, 19.8% had the incidence of foot ulceration. This proportion increased with longer duration of diabetes[16]. Applying the results of the aforementioned study in the present study participants, it was shown that 19.7% of participants fell under the moderate and severe neuropathy categories, and were at greater risk of foot ulcers and amputations in the near future. The majority (77%) of the participants with DPN in the KDM group belonged to the moderate and severe categories, showing that longer duration of diabetes is not only a risk factor, but also a determinant of severity of DPN.

The present study found a significant ($P = 0.009$) positive linear trend between duration of diabetes and the odds of DPN, which was observed similarly in another prevalence study by Pradeepa *et al.*[12] In a cross-sectional study by Davies *et al.*[32], an increasing prevalence of DPN was associated with an increase in the risk of painful DPN (PDPN). Thus, earlier screening is also required for preventing or delaying PDPN.

The present study also showned another interesting fact, that more than two-thirds of participants with DPN in the present study cohort of type 2 diabetes mellitus belonged to a lower socioeconomic class. This represents a lack of healthcare awareness of and facilities for diabetes and its complications in the developing world, which bears the maximum burden of diabetes. Similar results were also observed in study carried out by Kamenov *et al.*[33] in the developing country of Bulgaria.

Increasing age, longer duration of diabetes, dyslipidemia and the presence of other microvascular complications were found to be significantly associated with DPN in the present study. Many studies have shown age as a risk factor[11–13,17,18,21,23,24,27,30], whereas few studies have shown no association[26]. Sex-specific predisposition to DPN has been observed with female preponderance in a study by Katulanda *et al.*[19], with males being at higher risk in the Diabetes Control and Complications Trial (DCCT)[34]. However, the present study neither showed any sex predisposition nor any time-gap difference among males and females for DPN development. There was a significant association with neuropathy similar to earlier studies[12,17,18,20,21,25]. The present observation was supported by Gregersen *et al.*[35], who reported no sex difference. However, in retrospective studies carried out by Aaberg *et al.*[36] and Kamenov *et al.*[33], sex differences were observed in the onset of diabetic neuropathy, with males developing earlier than females with the explanation of sex differences in lifestyle with men's lifestyles being more hazardous (stressful jobs, smoking habits, alcohol and drug use, lower compliance with treatment) than women's. Androgens (testosterone, dihydrotestosterone) have specific neuroprotective effects on the central and peripheral nervous system, the depletion of which usually occurs in diabetes mellitus condition[33,36].

Longer duration of diabetes was identified as a risk factor in the present study, in accordance with many of the neuropathy prevalence studies carried out across the world[11,12,16,18,20,23–26]. The present has accounted for lipid profile as a whole and tested for its association. Existing literature proved dyslipidemia as a risk factor associated with DPN, along with higher TG levels[19], higher high-density lipoprotein cholesterol[37] and low high-density lipoprotein cholesterol levels[20]. Early intervention of antihyperlipidemic agents and better management among DPN patients could be a few of the reasons for the discrepancies in lipid profiles showing that DPN patients having better lipid profiles than non-DPN subjects[11,19,21,25].

The presence of other microvascular complications, such as nephropathy or retinopathy acting as a risk factor for DPN, shows that these complications go hand-in-hand in diabetic patients. The present study found retinopathy to be strongly associated than nephropathy, as shown in earlier studies[6,13,15,19].

The significance of the present study was that it is one of the large prospective population studies carried out at a tertiary care endocrinology clinic. The specific diagnosis of DPN was established by an endocrinologist with the use of multiple tests. A sample size of 2,006 was considered to be adequate for estimating the prevalence and risk factors of DPN. The chance of over- and underestimation were possible in previous studies as a result of the use of only VPT or diabetes neuropathic score. The present study used standard ADA criteria for diagnosing DPN, which includes using 10-g monofilament along with pin prick, VPT test and tendon reflex. Therefore, the prevalence estimate was considered to be accurate. Modifiable risk factors found significant in the present study were alcohol use, hypertension and high levels of HbA1c. Optimal glycemic control, in particular, achieving HbA1c <7% with effective management of hypertension, will be an effective strategy to reduce the emergence of diabetes-related complications. The limitations of the study were that no inferences on cause and effect can be drawn as a result of the cross-sectional study design.

The present study found DPN to be highly prevalent as compared with other microvascular complications, especially in KDM patients. As PDPN can set in with prolonged duration of neuropathy along with foot ulcers and amputations, earlier detection with proper screening and pertinent foot care education would be constructive. The present study used standard ADA criteria for diagnosing DPN, so the prevalence estimate will be accurate. No sex differences were observed in the development of DPN, with equal likelihood for males and females. The present study is unique in the sense that it estimated the prevalence rates of neuropathy, severity wise, modifiable risk factors and sex difference. These finding are clinically relevant, and could inspire resource mobilization for diagnosis and treatment of diabetes and its complications. Further studies including a larger sample size should be carried out to assess the sex difference in the development of DPN.

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