

Prevalence and Risk Factors for Peripheral Neuropathy among Type 2 Diabetes Mellitus Patients at a Tertiary Care Hospital in Coastal Karnataka

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Abstract

Context and Objective: In view of the growing burden of type 2 diabetes mellitus (T2DM) globally and associated microvascular and macrovascular complications, the study was done to assess the prevalence and risk factors for diabetic neuropathy among T2DM patients attending a tertiary care hospital. **Subjects and Methods:** T2DM patients' ≥ 30 years of both gender, presenting to the Medicine Department at a tertiary care hospital were included in the study. Diabetic Neuropathy Symptom (DNS) questionnaire to assess symptoms and Diabetic Neuropathy Examination (DNE) scoring to assess clinical signs were used. **Results:** A total of 273 patients were included. The mean age was 57.8 ± 11.5 years. The male to female distribution was 75% (202) and 25% (71), respectively. According to DNS instrument, 41.4% patients scored positive for the presence of neuropathy while only 24.5% had neuropathy according to DNE score. The proportion of males affected by neuropathy was more than females. 43.1% males had a positive DNS score while only 27.2% of them had a positive DNE score. Duration of the disease was positively correlated with neuropathy. Neuropathy was more prevalent among people who had higher systolic and diastolic blood pressure as per DNS and DNE instruments. **Conclusions:** The present study identified a higher proportion of males to be affected by neuropathy. Hence, more detailed evaluation must be accorded to elderly male diabetic patients with longer duration of the disease. Lifestyle modifications and watchful screening need to be incorporated as part of routine patient health education during follow-up clinic visits.

Keywords: Diabetic Neuropathy Examination, Diabetic Neuropathy Symptom, peripheral neuropathy, prevalence, risk factors, type 2 diabetes mellitus

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is one of the most common chronic diseases across the world and number of diabetic patients is on the rise. In 2011, there were 366 million people with diabetes globally, and this is expected to rise to 552 million by 2030.^[1] According to the ICMR – INDIAB study, there are 62.4 million people living with diabetes in India. T2DM is a progressive disease and hampers the quality of life of the patients due to micro and macrovascular complications.^[2]

Lower extremity disease, including peripheral neuropathy, foot ulceration, peripheral arterial disease, or lower extremity amputation, is twice as common in diabetic persons compared with nondiabetic persons and it affects 30% of diabetic persons who are older than 40 years. In persons with diabetes mellitus, the annual population-based incidence of foot ulcer ranges from 1.0% to 4.1%, and the prevalence ranges from 4% to

10%, which suggests that the lifetime incidence may be as high as 25%.^[3]

Screening and early identification of neuropathy offer a crucial opportunity for the patient with diabetes to actively modulate the course of suboptimal glycemic control to currently recommended targets and to implement improved foot care before the onset of significant morbidity. Clinical trial evidence for the efficacy of screening strategies has demonstrated reduced incidence of amputation and ulceration, and screening for neuropathy is recommended in clinical practice guidelines.^[4]

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Most of the available modalities have been evaluated in developed countries where foot care practices are widely followed. Contrary to it, in developing countries, barefoot walking is still prevalent, and foot care practices are hardly followed.^[5]

With this background in mind, the current study was designed to assess the prevalence and risk factors for diabetic neuropathy among hospital attendees.

SUBJECTS AND METHODS

A cross-sectional study among T2DM patients of either gender, presenting to the medicine department (both outpatients and inpatients) at a tertiary care hospital were recruited over a period of 2 months. Patients ≥ 30 years of both gender diagnosed with T2DM at least since 2 years, willing to participate, and attending the medicine department OPD or admitted in medicine wards at the tertiary care referral hospital were included. Patients of T2DM having severe comorbidities such as stroke and chronic renal diseases, at time of recruitment into the study, patients who had come to the hospital due to other illness and referred to the medicine OPD only for a consultation and pregnant females were excluded from the study.

Sample size

Assuming the prevalence of diabetic neuropathy to be 33%^[6] and accounting for alpha error of 5% at 20% relative precision and 10% nonresponse rate, using the formula $4pq/d^2$, the sample size was calculated to be 273.

Methodology

The Institutional Ethical Committee clearance (IEC 113/2015) was obtained before the initiation of the study. Written informed consent was obtained from all the study participants. Information pertaining to sociodemographic characteristics, anthropometric measurements, and blood pressure (BP) was collected by personal interviews using a predesigned questionnaire. Additional details about investigations, complications was obtained from patient records. BP was measured for all participants in the study using a standardized mercury sphygmomanometer in the right arm in the sitting posture. If the recorded BP was $\geq 140/90$ mm of Hg, repeat BP reading was taken after five minutes.

Peripheral neuropathy was assessed using Diabetic Neuropathy Symptom (DNS) questionnaire^[7] and Diabetic Neuropathy Examination (DNE) score.^[8]

All participants were questioned regarding the presence of symptoms, either positive or negative suggesting the presence of neuropathy. The questionnaire - DNS score was used. Patients were asked if they have unsteadiness in walking, burning, aching pain, tenderness, pricking sensations, and numbness of their legs or feet. The questions were answered “yes” (positive: 1 point) if a symptom occurred more times a week during the last 2 weeks or “no” (negative: No point) if it did not. Maximum score: Four points; 0 points - polyneuropathy absent; 1–4 points - polyneuropathy present.^[7]

A neurological examination was carried out, and the neurological signs were scored following a DNE score. The DNE score consists of eight items, two testing muscle strength, one a tendon reflex, and five sensations. The maximum score is 16. A score of >3 points is considered abnormal.^[8]

Anthropometric variables

All the variables were measured according to the WHO guidelines and quality control were maintained during collection of data.^[9] All the measurements were taken over light clothing. Weight was measured by the mechanical weighing scale in kilograms to the nearest 0.5 kg, without footwear with the scale being placed on a flat firm surface. Height was measured by a measuring tape against a flat vertical surface and recorded in centimeters, to the nearest 0.1 cm.

Statistical analysis used

Data were entered and analyzed using Statistical Package for Social Sciences version 15 (Chicago, SPSS Inc.). The results were summarized as percentages and proportions. Chi-square test was used for univariate analysis. $P < 0.05$ was considered statistically significant.

RESULTS

A total of 273 patients were included. Baseline characteristics of the study group are described in Table 1. The mean age was 57.8 ± 11.5 years, (range 30–89 years). The male to female distribution was 75% (202) and 25% (71), respectively. The mean duration of diabetes mellitus was 8.3 ± 6.7 years, (range 2–35 years) with the mean age at diagnosis being 49.7 ± 11.2 years (range 24–80 years). Nearly 43.1% males had agriculture-based occupation and 88.7% females were homemakers. Fifty-six percent were employed, 12.8% were unemployed, 8.1% were retired, and 23.1% were homemakers. 9.5% patients were illiterate, 29.4% were educated up to 5th standard, 48.8% were educated up to 12th standard, while 12.3% were graduates. Most of the

Table 1: Baseline characteristics of the study population (n=273)

Baseline characteristics	Mean \pm SD
Age (years)	57.8 \pm 11.5
Duration of DM (years)	8.3 \pm 6.7
Age at diagnosis (years)	49.7 \pm 11.2
BMI (kg/m ²)	24.7 \pm 4.3
Systolic BP (mm Hg)	128.4 \pm 12.6
Diastolic BP (mm Hg)	78.3 \pm 15.3
Fasting blood sugar (mg/dl)	185.3 \pm 84.1
Postprandial blood sugar (mg/dl)	252.0 \pm 106.3
HbA1c (%)	9.2 \pm 2.6
Total cholesterol (mg/dl)	158.7 \pm 52.6
Triglycerides (mg/dl)	163 \pm 113.9
High-density lipoprotein (mg/dl)	34.6 \pm 15.4
Low-density lipoprotein (mg/dl)	93.7 \pm 42.8

SD: Standard deviation, HbA1c: Glycated hemoglobin, DM: Diabetes mellitus, BMI: Body mass index, BP: Blood pressure

patients (45.4%) were taking oral hypoglycemic agents, 26% were on insulin, and 28.5% were on both insulin as well as oral hypoglycemic agents. According to DNS instrument, 41.4% patients scored positive for the presence of neuropathy while only 24.5% had neuropathy according to DNE score, as described in Table 2. Age and gender comparison with peripheral neuropathy is shown in Table 3. Most of the patients belonged to the age group of 60–69 years. Peripheral neuropathy identified by DNS was more as compared to DNE.

Table 2: Presence of peripheral neuropathy among diabetic patients by Diabetic Neuropathy Symptom and Diabetic Neuropathy Examination tools (n=273)

Tools	Neuropathy present, n (%)	Neuropathy absent, n (%)
DNS Questionnaire	113 (41.4)	160 (58.6)
DNE score	67 (24.5)	206 (75.5)

DNS: Diabetic Neuropathy Symptom, DNE: Diabetic Neuropathy Examination

The proportion of individuals affected by neuropathy increased with advancing age, assessed either by DNS or DNE, and this association was found to be statistically significant by Chi-square test ($P < 0.05$). The proportion of males affected by neuropathy was more than females. 43.1% males had a positive DNS score while only 27.2% of them had a positive DNE score.

The disease parameters associated with the presence of peripheral neuropathy have been elaborated in Table 4. Among the people who had neuropathy, nearly half of the patients had been diagnosed between 40 and 49 years of age. Neuropathy assessed by DNS tool was more (53.8%) among individuals who had been diagnosed with diabetes before the age of 30 years.

Longer the duration of the disease, the possibility of the presence of neuropathy was more, especially when screened with the DNS tool, where the proportion of individuals ranged from 18.5% to 100% when the duration of disease ranged from

Table 3: Comparison of age and gender parameters with peripheral neuropathy among diabetics (n=273)

Variables	DNS			DNE		
	Total (n)	Neuropathy present, n (%)	Neuropathy absent, n (%)	Total (n)	Neuropathy present, n (%)	Neuropathy absent, n (%)
Age group (years)						
30-39	19	4 (21.1)	15 (78.9)	19	3 (15.8)	16 (84.2)
40-49	41	13 (31.7)	28 (68.3)	41	6 (14.6)	35 (85.4)
50-59	78	30 (38.5)	48 (61.5)	78	14 (17.9)	64 (82.1)
60-69	97	44 (45.4)	53 (54.6)	97	30 (30.9)	67 (69.1)
≥70	38	22 (57.9)	16 (42.1)	38	14 (36.8)	24 (63.2)
Gender						
Male	202	87 (43.1)	115 (56.9)	202	55 (27.2)	147 (72.8)
Female	71	26 (36.6)	45 (63.4)	71	12 (16.9)	59 (83.1)

DNS: Diabetic Neuropathy Symptom, DNE: Diabetic Neuropathy Examination

Table 4: Comparison of disease characteristics with peripheral neuropathy (n=273)

Disease characteristics	DNS			DNE		
	Total (n)	Neuropathy present, n (%)	Neuropathy absent, n (%)	Total (n)	Neuropathy present, n (%)	Neuropathy absent, n (%)
Age at diagnosis (n=273)						
<30	13	7 (53.8)	6 (46.2)	13	3 (23.1)	10 (76.9)
30-39	36	16 (44.4)	20 (55.6)	36	11 (30.6)	25 (69.4)
40-49	83	41 (49.4)	42 (50.6)	83	24 (28.9)	59 (71.1)
50-59	83	29 (34.9)	54 (65.1)	83	18 (21.7)	65 (78.3)
≥60	58	20 (34.5)	38 (65.5)	58	11 (19.0)	47 (81.0)
Duration of disease and treatment (n=273)						
≤5	124	23 (18.5)	101 (81.5)	124	13 (10.5)	111 (89.5)
6-10	74	30 (40.5)	44 (59.5)	74	13 (17.6)	61 (82.4)
11-15	40	28 (70.0)	12 (30.0)	40	21 (52.5)	19 (47.5)
16-20	25	22 (88.0)	3 (12.0)	25	14 (56.0)	11 (44.0)
>20	10	10 (100.0)	0	10	6 (60.0)	4 (40.0)
Current fasting blood sugar (mg/dl) (n=252)						
<125	58	28 (48.3)	30 (51.7)	58	18 (31.0)	40 (69.0)
≥126	194	78 (40.2)	116 (59.8)	194	44 (22.7)	150 (77.3)

DNS: Diabetic Neuropathy Symptom, DNE: Diabetic Neuropathy Examination

<5 years to >20 years. The association between duration of disease and presence of neuropathy by both DNS and DNE was found to be statistically significant ($P < 0.05$). Surprisingly, well-controlled diabetes status as assessed by fasting blood sugar (FBS) examination had higher proportion of individuals affected by neuropathy.

More number of individuals in the normal body mass index (BMI) category and obese category (43% each) had neuropathy as per DNS, in contrast to marginally higher proportion of patients in the overweight category (26%) who had neuropathy as assessed by DNE tool, as shown in Table 5. Neuropathy was more prevalent among people who had higher systolic and diastolic BP, as per DNS and DNE instruments.

DISCUSSION

Diagnosis of diabetic neuropathy is done through many methods including neurological examination and electrophysiology to detect and evaluate the disease at its earliest stage. However, the role of traditional methods and parameters for diagnosis, as a prognostic factor of diabetic neuropathy, is a matter of on-going debate. Early detection or diagnosis of neuropathy enables the clinician to give appropriate drugs to control it or at least retard its progress. It is also important to educate the patient to take care of his illness vigilantly. Neuropathy is a debilitating and crippling problem if not controlled at an early stage.^[10,11]

The study involved the assessment of symptoms and signs for the diagnosis of peripheral neuropathy. Since peripheral sensory neuropathy is a pivotal element in the causal pathway to both foot ulceration and amputation, selecting a quick, inexpensive, and accurate instrument to evaluate the high-risk patient is essential to make decisions.^[8]

In the present study, peripheral neuropathy assessed using DNS questionnaire and DNE score was 41.4% and 24.5%, respectively. There is a disparity because the symptom score

is more sensitive as it has a cutoff value of one as in the study done by Meijer *et al.*^[12] In the study done by Meijer *et al.*,^[12] the odds ratios for the DNS and DNE scores with other tests such as nerve conduction studies were high. Hence, these abnormal DNS and DNE scores could be used for peripheral neuropathy screening as confirmed by findings of Asad *et al.*^[13,14]

Chennai Urban Rural Epidemiology study^[15] identified the prevalence of neuropathy to be 26%; the outpatient setting of an endocrinology clinic of a public tertiary care hospital in north India identified 29.2% prevalence of neuropathy,^[16] however, this study shows a high number of people having neuropathy because a tertiary care hospital caters to referred patients who are more symptomatic and tend to have more complications, comparable to the findings from Chandigarh.^[17]

The proportion of males affected by neuropathy was more than females, in the present study contrary to findings by Bansal *et al.*,^[16] who reported that there were no sex-specific differences. Neuropathy was more prevalent in the advanced age groups and among those with longer duration of the disease. Our study findings were similar to those reported from other parts of India and abroad.^[6,16,18-20]

Studies have correlated the severity of diabetic peripheral neuropathy to total hyperglycemia exposure.^[21,22] However, in the present study, we used fasting plasma glucose to assess the glycemic control due to unavailability of glycated Hb values for all patients. Neuropathy was found to be more prevalent among the people with FBS <125 mg/dl in the present study in contrast to the study by Dyck *et al.*^[21]

Most of the patients who were symptomatic had normal BMI, and there was no significant association between BMI and presence of diabetic peripheral neuropathy. These findings concurred with other studies^[16,23] wherein anthropometric variables were not identified as risk factors.

Table 5: Association between body mass index, current blood pressure, and presence of neuropathy among diabetic patients (n=273)

Variables	DNS			DNE		
	Total (n)	Neuropathy present, n (%)	Neuropathy absent, n (%)	Total (n)	Neuropathy present, n (%)	Neuropathy absent, n (%)
BMI (kg/m ²)						
<18.5	14	5 (35.7)	9 (64.3)	14	3 (21.4)	11 (78.6)
18.5-24.9	140	61 (43.6)	79 (56.4)	140	35 (25.0)	105 (75.0)
25-29.9	96	37 (38.5)	59 (61.5)	96	25 (26.0)	71 (74.0)
≥30	23	10 (43.5)	13 (56.5)	23	4 (17.4)	19 (82.6)
Systolic BP (mm Hg)						
<140	200	77 (38.5)	123 (61.5)	200	43 (21.5)	157 (78.5)
≥140	73	36 (49.3)	37 (50.7)	73	24 (32.9)	49 (67.1)
Diastolic BP (mm Hg)						
<90	194	78 (40.2)	116 (59.8)	194	44 (22.7)	150 (77.3)
≥90	79	35 (44.3)	44 (55.7)	79	23 (29.1)	56 (70.9)

DNS: Diabetic Neuropathy Symptom, DNE: Diabetic Neuropathy Examination, BMI: Body mass index, BP: Blood pressure

Nearly, half of the study patients with BP \geq 140/90 mm of Hg had neuropathy as per the DNS tool. This could be due to common nonmodifiable risk factors such as age. However, a study conducted by Booya *et al.*^[18] and Mørkrid *et al.*^[20] showed no significant relationship between distal symmetric sensory/motor polyneuropathy and BP levels, while a study from Imphal^[19] identified contribution of systolic BP to diabetic neuropathy.

DNS and DNE testing is fast and easy to perform in clinical practice and is useful to detect neuropathy early. A limitation of DNE is that, it does not take into account loss of temperature sensation, and hence, small fiber neuropathy could be missed by this technique. Since DNS and DNE are subjective and depend on the subject's cooperation and response, it has to be used along with other investigations such as vibration perception threshold to arrive at a diagnosis. Incomplete data in patient files were another limitation.

Duration of the disease was significantly associated with the presence of neuropathy. Hence, primary prevention through lifestyle modifications which delay the onset of disease not only diabetes but also other comorbidities such as hypertension should be made as an essential component of everyday practice.

CONCLUSIONS

More than 40% of the diabetic patients had peripheral neuropathy as per the DNS tool. Advancing age, male gender, younger age at diagnosis, longer duration of diabetes, and individuals with higher current BP values were found to have a higher proportion of neuropathy. Only advancing age and longer duration of the disease were found to be significantly associated with the presence of neuropathy. The DNS-score is a sensitive, validated symptom score, fast and easy to perform in clinical practice, for screening peripheral neuropathy among diabetics.

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Conflicts of interest

There are no conflicts of interest.

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