Original Article

Prevalence of Neuropathy in Type 2 Diabetic Patients Attending a Diabetes Centre in South India

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Abstract

- **Objective : The aim of this study was to determine the prevalence and risk factors for neuropathy among South Indian type 2 diabetic patients attending a diabetes centre.**
- **Methods : One thousand consecutive type 2 diabetic patients attending a diabetes centre in South India were recruited for the study. Biothesiometry studies were performed by a single observer using a biothesiometer. Neuropathy was diagnosed if the vibratory threshold of the great toe exceeded twenty five.**
- **Results : Overall, 19.1% of the patients had evidence of neuropathy. The prevalence of neuropathy increased with increase in age ($p < 0.001$) and duration of diabetes ($p < 0.001$). Multiple logistic regression analysis revealed age (OR-3.2, 95% confidence interval - 2.7-4.1, $p < 0.001$) and duration of diabetes (OR - 1.4, 95% confidence interval - 1.2-6.4, $p = 0.001$) as the risk factors for neuropathy.**
- **Conclusion : The overall prevalence of neuropathy in this South Indian type 2 diabetic subjects is 19.1% and age and duration of diabetes are the risk factors for neuropathy. (J Assoc Physicians India 2002;50:546-550)**

Introduction

Type 2 diabetes mellitus in India has certain differences compared to Europeans. The prevalence is high,[1] onset of diabetes is at a younger age,[2] genetic factors appear to be stronger[3] and obesity is less common.[4] A recent WHO report indicates that India already has the largest number of diabetic patients in any given country[5] and this is believed to increase further in the years to come.[6] Studies on complications of diabetes in India are hence of great interest. We have earlier reported on the prevalence of retinopathy,[7] ischaemic heart disease,[8] peripheral vascular disease[9] and autonomic neuropathy[10] in type 2 diabetic patients seen at our centre in Southern India. In this paper, we report on the prevalence of peripheral neuropathy using biothesiometry.

Material and Methods

The study group comprised of 1000 consecutive type 2 patients attending the MV Diabetes Specialities Centre, a specialized diabetes centre in South India. The diagnosis of diabetes and the classification as type 2 diabetes were based on the criteria laid down by the WHO study report group.[11]

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A detailed clinical history was taken using a structured questionnaire in all patients which included the age and duration of diabetes. In all the study patients a complete clinical workup was done including height and weight and body mass index (BMI) was calculated using the formula : weight in kilograms divided by height in meters squared. Blood pressure was recorded in the sitting position in the right arm with a mercury sphygmomanometer (Diamond Deluxe BP apparatus, Pune, India). Biochemical studies were done on Corning Express Plus Auto Analyser (Corning, Medfield, MA, USA) using kits supplied by Boehringer Mannhiem, Mannhiem, Germany. Fasting glucose (glucose oxidase), serum cholesterol (CHOD-PAP), serum triglycerides (GPO-PAP), and serum creatinine (modified kinetic method of Jaffe) were estimated in all patients. High density cholesterol (HDL) was estimated by CHOD-PAP method after precipitating low-density lipoprotein and chylomicron fractions by the addition of phosphotungstic acid in the presence of magnesium ions.

Glycosylated hemoglobin (HbA_1c) was estimated by high-pressure liquid chromatography using the variant machine (Bio Rad, Hercules, CA, USA).

All patients had a resting 12 lead computerised electrocardiogram. Peripheral arterial Doppler studies were done using a hand held recording device (Kody Vaslab, Madras) and the ankle/brachial index was calculated. The ocular fundi were examined by a trained retinal specialist after complete dilatation of the pupils using both direct and indirect ophthalmoscopy.

The following definitions were used for diagnosis of various complications :

Ischaemic heart disease was considered to be present when either myocardial ischaemia or infarction was present.

Myocardial ischaemia was diagnosed if there was history of classical chest pain with unequivocal ECG changes suggestive of ischaemia, but no evidence of infarction.

Myocardial infarction was diagnosed on the basis of a definite history of myocardial infarction or unequivocal changes on ECG suggestive of a recent or past myocardial infarction.

Peripheral vascular disease (PVD) was diagnosed if the ankle/branchial index was less than 0.9.

Nephropathy was defined as persistent proteinuria of ≥ 500 mg/dl assessed by the sulphosalicylic acid method,[12] in the absence of urinary tract infection.

Retinopathy when present was classified into :

Non-proliferative diabetic retinopathy (NPDR) which was diagnosed when microaneurysms, dot haemorrhages or exudates were seen in the retina, in the absence of new vessels.

Non-proliferative diabetic retinopathy with maculopathy was diagnosed when signs of retinal thickening and/or exudates within 500 microns of the fovea were seen in addition to the lesions seen in NPDR.

Proliferative diabetic retinopathy (PDR) was diagnosed when new vessels on the disc or elsewhere or advanced diabetic eye disease with vitreous haemorrhages and/or retinal detachment.

Neuropathy Assessment

Neuropathy was assessed using biothesiometer (Biomedical Instrument Co., Newbury, Ohio, USA), by measuring vibratory perception threshold (VPT) on the great toes. VPT's were measured in a standardised fashion by one observer. Subjects were initially requested to remove their shoes and socks and lie supine on a couch for at least five minutes before the measurements were made. The foot was kept warm during the measurement and as the room was air-conditioned, the temperature of the room was around 25°C. The biothesiometer factor, which vibrates at 100 Hz with an amplitude proportional to the square of the applied voltage was applied perpendicular to the test site with a constant and firm pressure. Subjects were initially familiarised with the sensation by holding the tactor against the distal palmar surface. VPT was then measured at the distal plantar surface of the right great toe. The voltage was slowly increased at the rate of 1 v/s and the VPT was defined as the moment when the subject indicated he/she first felt the vibration. The voltage at which this occurred was recorded. Three further cycles of readings at each site were performed and recorded. Neuropathy was diagnosed if the VPT of the great toe exceeded ≥ 25V.[13,14]

Statistical Analysis

Analyses were performed using SPSS Program (Version 4.0.1) on an IBM PC compatible computer. Chi-squared tests were used to compare frequencies and t-tests were used to compare means. Multiple logistic regression analysis was done to look for risk factors associated with peripheral neuropathy. The dependent variable was diabetic neuropathy. Independent variables were : sex, age, height, duration of diabetes, systolid BP, diastolic BP, fasting plasma glucose, HbA1c, serum cholesterol and serum triglycerides.

Results

Overall, 19.1% of the study population had evidence of neuropathy. There was no significant difference in the prevalence of neuropathy between males (18.2%) and females (20.9%).

Table 1 shows the clinical and biochemical characteristics of the neuropathy and the non-neuropathy groups. The neuropathy subjects were older ($p < 0.01$) and had longer duration of diabetes (p value < 0.001) and higher BMI ($p < 0.001$) compared to subjects without neuropathy. Systolic blood pressure was also significantly higher in the neuropathy group ($p < 0.001$). However the triglycerides levels were higher in the non-neuropathy group. More subjects with neuropathy were on insulin compared to the non-neuropathy group ($p < 0.001$).

Table 1 : Clinical and biochemical characteristics of the neuropathy and the non-neuropathy groups

Parameters	Non-neuropathy group (n=809)	Neuropathy group (n=191)	p Value
Age (years)	49 ± 9	62 ± 8	< 0.001
Duration of diabetes (yrs)	6 ± 6	12 ± 8	< 0.001
Body mass index (Kg/m^2)	23.1 ± 3.9	24.3 ± 3.9	< 0.001
Systolic BP (mmHg)	134 ± 14	141 ± 17	< 0.001
Diastolic BP (mmHg)	83 ± 8	84 ± 9	NS
Fasting plasma glucose (mmol/L)	11.0 ± 4.2	11.6 ± 4.8	NS
HbA_{1c} (%)	9.7 ± 2.4	9.6 ± 2.4	NS
Serum cholesterol (mmol/L)	5.5 ± 1.1	5.4 ± 1.4	NS
Serum triglycerides (mmol/L)	2.2 ± 1.6	1.9 ± 1.1	< 0.01
HDL cholesterol (mmol/L)	1.1 ± 0.3	1.1 ± 0.3	NS
Insulin treatment n (%)	307 (38%)	138 (73%)	< 0.001

Fig. 1 shows the prevalence of neuropathy in relation to the duration of diabetes. 7.9% of patients with duration of diabetes ≤ 5 years had neuropathy which increased to 54.2% in those with over 20 years duration (trend chi square, 120, $p < 0.001$).

Fig. 2 shows the relationship between the age of the patients and the prevalence of neuropathy. There is a linear increase in the prevalence of neuropathy with age (trend chi

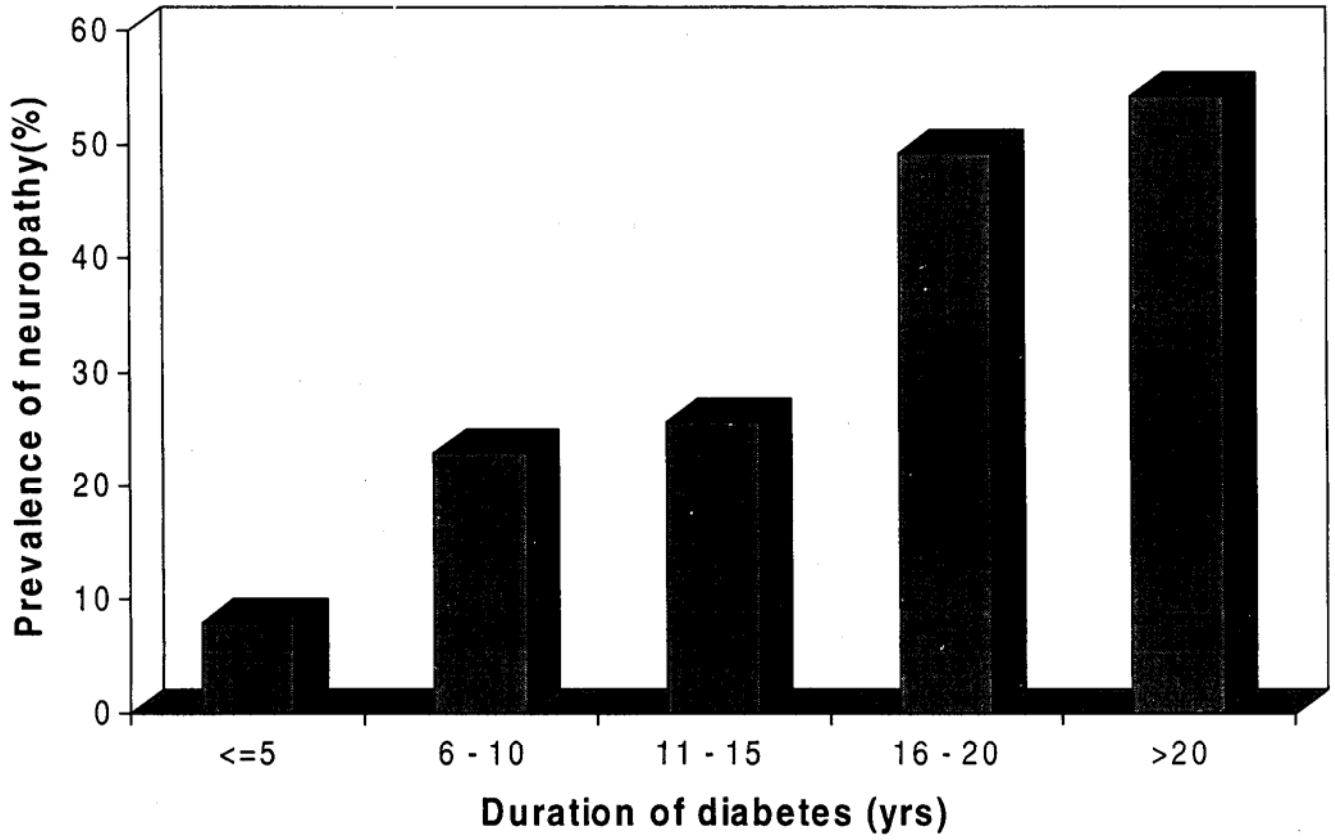

Fig. 1 : Prevalence of neuropathy according to the duration of diabetes, trend chi square = 120, p < 0.001.

square, 250, p < 0.001).

Results of multiple logistic regression analysis using neuropathy as the dependent variable. Age (OR - 3.2, 95% confidence interval, 2.7-4.1, p < 0.001) and duration of diabetes (OR - 1.4, 95% confidence interval, 1.2-6.4, p = 0.001) were the risk factors for neuropathy.

Table 2 shows the prevalence of other complications in patients with neuropathy. Prevalence of virtually all complications were higher in the neuropathy group.

Table 2 : Prevalece of other diabetic complications in patients with and without peripheral neuropathy

Parameter	Non-neuropathy (n=809)	Neuropathy (n=191)	P value
Ischaemic heart disease			
Myocardial ischaemia	50 (6.2)	24 (12.5)	0.002
Myocardial infarction	29 (3.6)	24 (12.5)	< 0.001
Retinopathy			
NPDR	95 (11.7)	40 (20.9)	< 0.001
NPDR with maculopathy	60 (7.4)	31 (16.2)	< 0.001
PDR	17 (2.1)	20 (10.5)	< 0.001
PVD	19 (2.4)	34 (17.8)	< 0.001
Proteinuria	61 (7.5)	47 (24.6)	< 0.001

NPDR - Non-proliferative diabetic retinopathy;
PDR - Proliferative diabetic retinopathy; PVD - Peripheral vascular disease; Percentages in parentheses.

Discussion

This paper reports on the prevalence of peripheral neuropathy in a large group of consecutive South Indian type 2 diabetes attending a diabetic centre, who were screened for neuropathy using biothesiometry, irrespective of symptoms of neuropathy or the duration of diabetes. To our knowledge, this is the first report of a biothesiometer based assessment of the prevalence of peripheral neuropathy in Indian type 2 diabetic patients. The overall prevalence of neuropathy in our study appears to be lower than that reported in Europeans although this could be attributed to a lower mean duration of diabetes in our patients. Young *et al*,[15] in a multicentre study conducted at 118 clinics in UK involving 6487 type 2 diabetics, using vibration perception thresholds reported neuropathy in 32.1% of patients. They also

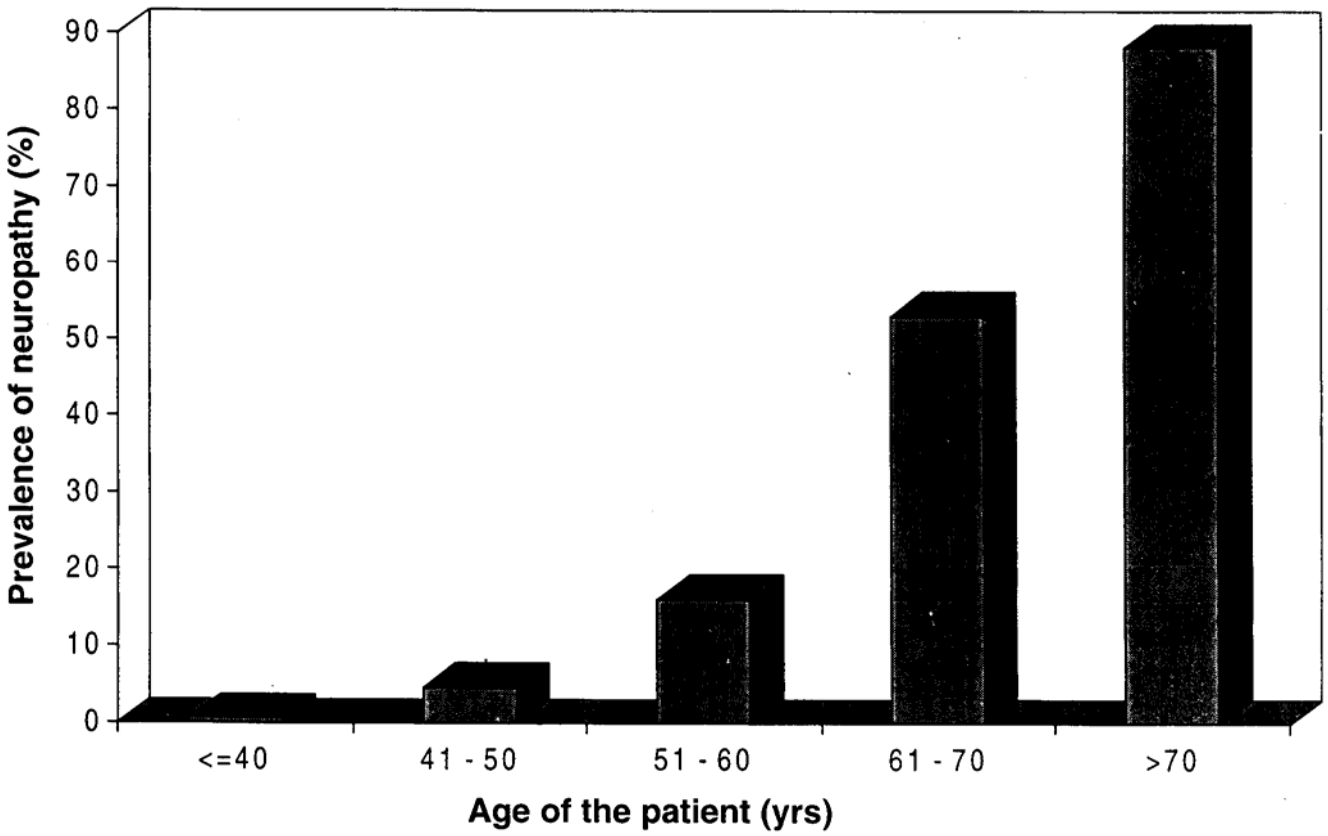

Fig. 2 : Prevalence of neuropathy according to the age of the patients, trend chi square = 250, $p < 0.001$.

showed an association between neuropathy and age and duration of diabetes.

Studies from Sri Lanka[16] show a high prevalence of neuropathy at the time of diagnosis (9.8%) and a significantly higher prevalence with increasing duration of disease and advancing age. Our study showed that 5.4% of the diabetics had neuropathy at the time of diagnosis. The difference could be explained either by a later diagnosis of the patients in Srilanka or an earlier referral to our centre as ours is a private centre.

Using vibration sensation, Nielsen *et al*[17] reported neuropathy in 38% of Saudi Arabian patients while Cheng *et al*[18] found neuropathy in 33.9% of a group of Taiwanese patients. The prevalence of neuropathy among Africans is also considerably higher than that obtained in our study.[19] The wide variation in prevalence rates could probably be attributed to differences in the population studied, duration of diabetes or the severity of hyperglycemia in different studies.

The results of the multiple logistic regression analyses revealed that age and duration of diabetes showed an association with peripheral neuropathy. This study confirms that the most important risk factors for neuropathy are the same as reported in Europeans. It is also of interest that all the diabetic complications like nephropathy, retinopathy, peripheral vascular disease and ischaemic heart disease were more common in the neuropathy group. The greater duration of diabetes and the older age of the patients in the neuropathy group could possibly explain this.

Although biothesiometry is a useful clinical tool for screening for neuropathy, its sensitivity is probably much lower than performing nerve conduction studies for diagnosing neuropathy. However, it is extremely different to perform nerve conduction studies for screening large number of patients. Another limitation to biothesiometry is that it is observer dependent as a subjective assessment is made based on the patient's response. Even given these limitations, it is still a

widely used screening test for a quick assessment of neuropathy in a busy outpatient clinic or in a field setting. Moreover, the few population studies that have been done, have mostly used biothesiometry.[20] Finally, biothesiometry is a good predictor of future foot ulceration. Being a clinic based study, it is difficult to exclude referral bias affecting the results. However, our centre caters about 15% of the known diabetic population of Chennai. Moreover ongoing epidemiological study has shown that the patient profile of our centre is not very different from the population.

In summary, we report that using biothesiometry, 19.1% of this diabetic clinic population in Southern India had neuropathy. Given the large number of diabetic patients in India, (19 million in 1995 which is expected to rise to 57 million in 2025),[5] this underscores the need for tight control of diabetes to prevent diabetic foot problems in the future.

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