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Original Research Paper

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A STUDY OF PREVALENCE AND ASSOCIATION OF PERIPHERAL NEUROPATHY IN PATIENTS WITH NEWLY DIAGNOSED TYPE 2 DIABETES MELLITUS IN A URBAN LOCALITY OF RAIPUR DISTRICT

Dr Shuddhodhan B Gaikwad — Asst Professor , Department of General Medicine , Raipur Institute of Medical Sciences, Raipur , CG , India

Dr. Jaiwant P Sachdev* — Asst Professor,Department of General Medicine,Raipur Institute of Medical Sciences, Raipur , CG , India*Corresponding Author

ABSTRACT

INTRODUCTION: Diabetes is one of the commonest non-communicable disease in India with its onset almost a decade earlier as compared to developed countries. Diabetic peripheral neuropathy (DPN) predisposes to foot ulceration and gangrene. Studies among recent onset patients with type 2 diabetes mellitus (T2DM) are very few. We studied the prevalence and risk factors of DPN in patients with newly diagnosed T2DM.

METHOD: We studied 195 consecutive patients over age 30 with a duration of diabetes ≤6 months. All underwent a clinical and biochemical evaluation and were screened for DPN using Neuropathy Symptom Score (NSS) and Neuropathy Disability Score (NDS) as well as the vibration perception threshold using a biothesiometer.

RESULTS: The overall prevalence of DPN was 29.% . PN among control was 10.7% . The prevalence of DPN showed an increasing trend with age . Abnormal vibration perception threshold was present in 43.% of cases and had a significant correlation with NDS . Abnormal monofilament testing was present in 6.1% of cases. A regression analysis showed that DPN was independently associated with age and duration of diabetes prior to presentation but not with body mass index, plasma glucose, or HbA1c.

CONCLUSION: Study showed high prevalence of PN in recently diagnosed patients with T2DM, which was independently associated with age and duration of symptoms of diabetes prior to the diagnosis. Screening for DPN at diagnosis of diabetes is warranted, especially among older subjects.

KEYWORDS : Diabetic peripheral neuropathy, newly diagnosed, type 2 diabetes mellitus, vibration perception threshold

INTRODUCTION

India has one of the highest prevalence of type 2 diabetes mellitus (T2DM) in the world.[1] It is estimated that by the year 2030 there are will be nearly 80 million Indians with T2DM in the country.[2,3] The disease constitutes a substantial burden for both the patient and health care system, mainly due to macrovascular and microvascular complications.[1,2] In contrast to patients in industrialized countries, Indians with T2DM have an earlier age at onset of the disease and fewer resources for achieving optimal metabolic control, potentially predisposing them to a higher prevalence of complications.[4,5,6]

The prevalence of diabetic peripheral neuropathy (DPN) varies greatly in different studies, ranging from 8% to 59%.[7,8,9,10] DPN significantly increases the risk of complications such as foot infections, deformities, gangrene, and amputations.[11] In India, the adverse effects of peripheral neuropathy (PN) are compounded by poor foot hygiene, improper foot wear, and frequent bare foot walking. In such circumstances, complications of foot infections and gangrene are a common cause of hospital admissions.[1,12]

T2DM is characterized by a long asymptomatic phase (ranging from 4 to 7 years) between the actual onset of hyperglycemia and clinical diagnosis which may explain the relatively high prevalence of microvascular complications in newly diagnosed patients with T2DM.[13]The prevalence of DPN at diagnosis of type2DM ranges from 10% to 48%, depending upon the population studied and method used to evaluate neuropathy. [14,15,16] In view of the poor awareness and lack of regular screening programs, the initial presentation to the physician is frequently delayed. This may predispose to an increased rate of microvascular complications at onset. Ethnic differences in the prevalence of various diabetes-related complications have also been documented.[17]

There is a paucity of reports on DPN in Indians. In a study comparing European and south Asian subjects with T2DM in United Kingdom, the prevalence was lower in the latter. However, in surveys in Indian patients, the prevalence has ranged from 26% to 31%. [18,19]In these studies, no controls were studied. Since PN is present in a significant proportion of healthy individuals, especially among the elderly, this fact needs to be taken into account before ascribing the PN to hyperglycemia.[11,20,21] The present study was planned to determine the prevalence and risk factors for DPN in newly diagnosed Indian patients with T2DM and age-matched controls.

METHEDOLOGY

After local ethical committee approval a community-based study was planned. The study area was near the Urban Health Centre of the Institute. Over a period of 8 months , we studied 195 consecutive patients with newly diagnosed T2DM (mean age 47.6 ± 10.2 years, 59.0 % males). Inclusion criteria included age ≥30 years and duration of diabetes ≤6 months at the time of presentation. Patients with acute illness or chronic diseases such as leprosy, those with disability, pregnant women, and patients taking medications known to impair nerve function were excluded from the study. Seventy-five healthy subjects (age 45.9 ± 9.9 years, 72% males) with normal fasting glucose levels, matched for age and sex with the patients, served as controls. The protocol was approved by the institutional ethics committee. Informed written consent was obtained from all subjects.

All participants underwent a standardized clinical evaluation. Height was measured using a stadiometer, while weight was recorded with a weighing machine with a beam balance. Waist and hip circumference were measured and mean of two readings was taken for calculating the waist - hip ratio (WHR). All testing was performed by a single observer (HG). Tests were performed in a random sequence among different patients. Patients were screened for DPN using the Neuropathy Symptom Score (NSS) and Neuropathy Disability Score (NDS), as previously described. [7] In short, for NSS, symptoms like burning, tingling, numbness, fatigue, cramping, and aching with their worsening and relieving factors were taken into account. Depending upon the severity, a point of 0 to 2 was given and NSS was classified into mild

(score 3-4), moderate (score 5-6), and severe (score 7-9). For NDS, pain, temperature, vibration (by biothesiometer) perception and ankle reflexes were tested and score of 0 to 2 were given depending upon normal, diminished or absent signs. NDS was categorized into mild (score 3-5), moderate (score 6-8), or severe (score 9-10). DPN was diagnosed if moderate-severe signs with or without symptoms or mild signs with moderate-severe symptoms were present. The NSS and NDS have been previously been validated against electro-diagnostic studies.[22]

VIBRATION PERCEPTION THRESHOLD (VPT)

This was measured using a biothesiometer (Dhansai Lab, Mumbai, India). The biothesiometer tractor, which vibrates at 100 Hz, was applied at the distal plantar surface of the great toe (right and left). Three cycles of readings at each site (right and left great toe) were performed. If the best value was >9 mV in any great toe it was considered abnormal. This value was derived from the VPT value 2SD above the mean for 35 healthy controls of age 30-50 years. [23] A 128-Hz tuning fork was used to examine vibration perception at the dorsum of the interphalangeal joint of the right hallux. The vibrating tuning fork was put on the interphalangeal joint and when nothing was felt, the score was 2 points. When something was felt, the still vibrating tuning fork was immediately placed at the dorsal wrist. When it was felt the same at that location the score was 0 points, when it felt stronger the score was 1 point. [24] Monofilament testing: This was done with Semmes - Weinstein monofilament of 5.07/10 g was performed three times at each site (dorsal between base digit 1-2; ventral digit 1, 3, 5; meta-tarsal heads 1, 3, 5; medial and lateral mid-foot; heel). If the patient missed more than once at one site it was considered as abnormal at that site. If a subject did not perceive the filament at 2 or more of the 10 sites, the test was reported as abnormal.[25]

SCREENING FOR ALBUMINURIA

Nephropathy was tested in 178/195 patients. A urine sample was screened for urine albumin using a dipstick (Uristix, Siemens, Vadodara, India). If positive, 24 h urine albumin was measured and macroalbuminuria was defined as a value >300 mg. If the dipstick was negative, timed overnight urine specimens or by morning albumin/creatinine ratio were measured. If first sample was suggestive of microal buminuria, two more urine specimens were collected. Microalbuminuria was diagnosed if at least 2 of the 3 samples had overnight microalbumin concentration of 20-200 µg/min or urine microalbumin/creatinine ratio of 30-300 µg/mg creatinine.

STATISTICS

The Student's *t*-test was used for comparison of continuous variables if found to be normally distributed while chi-square test was used to compare categorical variables. Variables associated with PN were tested using univariate logistic regression analysis. Variables shown to have a significant association by this analysis were tested by multivariate logistic regression to determine the variables independently associated with PN. A P value <0.05 was considered significant. Statistical analyses were performed using the SPSS software package (version 20.0; SPSS Inc., Chicago, IL, USA).

RESULTS

Patients had mean duration of symptoms of diabetes 5.9 months (range 0-60 months) before diagnosis. They presented to our hospital within 2.3 months (range 0-6 months) of diagnosis. At the time of presentation, patients had a poor glycemic control (mean plasma glucose 321.0 ± 100.2 mg%, mean HbA1c 9.1 ± 2.4%).

By NSS and NDS criteria, the prevalence of DPN was 29.2% . The prevalence was similar in males (26.1%) and females (33.8%). An abnormal NDS was present in 44.5%, ulceration.[25] The prevalence of impaired monofilament sensation was 6%, considerably lower than that of DPN. This low frequency may be reflective of the fact that the10-g (5.07) monofilament testing is appropriate for the clinical assessment of risk for foot ulceration [25] but not a sensitive means to detect prevalence of neuropathy. In the latter case, a monofilament of 1 g or less may be more appropriate.[28]

Previous studies have identified several risk factors for DPN such as age, poor glycemic control, increasing duration of diabetes, gender, height, body mass index, retinopathy, hypertension, smoking, and alcohol consumption. [14,15,16,18] In the current study, age at diagnosis and duration of symptoms of diabetes prior to diagnosis were independent risk factors for DPN. For each decade increase in age, the prevalence of DPN increased significantly (trend chi-square 11.8, $P = 0.001$), and after the age of 60 years the frequency of DPN was 1.7-fold greater than those aged less than 60 years. Since elderly patients have other risk factors for foot ulcerations, such as vision abnormalities and vascular involvement, neuropathy screening assumes an even greater importance in this age group. The prevalence of DPN increased with longer prediabetic period, as reflected by duration of symptoms attributable to diabetes. [29] While some earlier studies have also reported similar findings, [30] these have not been confirmed by others. [31,32] We could not demonstrate any association between HbA1c, but this may be partly due to the fact that 65% of patients were already on treatment at the time of examination. Another proposed possibility is that any elevated glucose beyond a threshold will predispose to DPN.[33,34]

We noted a prevalence of albuminuria of 7.9% among newly diagnosed T2DM. However, we found no association of DPN with albuminuria, which may be due to low prevalence of albuminuria noted in this study. Alternatively, there are differences in the pathogenesis of the two complications. In previous studies, the association of DPN with albuminuria has been variably present.[16,35]

The prevalence of DPN depends on the criteria and methods used. After a simple clinical test such as VPT, 43% of subjects had an increased threshold suggestive of PN. Among the patients with DPN, 60% had absent or decreased ankle jerks, 78% had abnormal VPT, 76% had reduced pain sensation, and 76% had reduced temperature sensation (not shown in results). Thus a good clinical examination is a sensitive measure to diagnose PN and other studies have also suggested neuropathy scoring to be simple, inexpensive, easy, and sensitive method for PN detection.

DISCUSSION

In various Caucasian populations, the prevalence of DPN in newly diagnosed T2DM varies widely from 10% to 48%. This may be due to different methodologies employed for detection of neuropathy as well as variability in patient ages and time elapsed before diagnosis. However, ethnic differences in DPN may also be relevant. [17] Interestingly, it has been previously reported that both DPN and foot ulcers are lower in Indians compared with European Caucasians. In the current study, 30% of patients had DPN, based on the NSS and NDS criteria. Two earlier studies in Indians have reported on the prevalence of DPN in newly diagnosed T2DM of 19.5% and 29.0%. In the latter study, the prevalence of DPN was measured by NSS and NDS in 100 newly diagnosed T2DM. [27] In a community-based study from Chennai, south India, Pradeepa *et al*. measured the prevalence of DPN using VPT by biothesiometer. The prevalence in newly diagnosed patients was 19.5% and 27.8% in those with known diabetes. [18] However, the frequency of DPN in the subjects without diabetes was not studied.

Since PN is found in a proportion of healthy individuals,

especially in the elderly, comparison with a matched control group is essential. We noted PN in 10.7% of age- and sex-matched control subjects, which increased with advancing age. This fact should be taken into account when assessing PN in patients with diabetes.

Monofilament sensation is a measure of protective sensations in the foot and is strongly associated with risk of foot ulceration. [25] The prevalence of impaired monofilament sensation was 6%, considerably lower than that of DPN. This low frequency may be reflective of the fact that the10-g (5.07) monofilament testing is appropriate for the clinical assessment of risk for foot ulceration [25] but not a sensitive means to detect prevalence of neuropathy. In the latter case, a monofilament of 1 g or less may be more appropriate.[28]

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CONCLUSION:

we detected a high prevalence of PN in recently diagnosed patients with T2DM. The neuropathy was independently associated with age and duration of symptoms of diabetes prior to the diagnosis. Screening for DPN using simple clinical examination is cost-effective means to prevent foot ulceration and infections in Indian patients with T2DM.

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