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### Efficacy of Simple Bed Side Methods in Diagnosing Peripheral Neuropathy in Diabetic Patients in Comparison with Vibration Perception Threshold

Upneet Bedi\* and Gaurav Mittal

Department of Medicine, Department of Physiology, Punjab Institute of Medical Sciences Hospital and Medical College, Jalandhar, Punjab.

#### ABSTRACT

Diabetic neuropathy is among the most common disorders of the peripheral nerves, also among one of the least treatable. Screening and early diagnosis of neuropathy helps the patients with diabetes to actively have glycaemic control before the onset of complications. The present study was aimed to evaluate the usefulness of simple bed side methods like Diabetic Neuropathy Symptom (DNS) score, 10-g Semmes-Weinstein monofilament testing, vibration testing by 128 Hz tuning fork and ankle reflex testing in diagnosing neuropathy in diabetic patients in comparison with measuring vibration perception threshold (VPT) with a biothesiometer. The study was carried out at the medicine outpatient department of Punjab institute of medical sciences hospital and medical college Jalandhar. A total number of 106 T2DM patients aged above 30yr were taken. The study included information about socio-demographic characteristics and other parameters like height, weight, BMI, waist circumference, BP, fasting blood sugar, lipid profile and physical activity. The prevalence of peripheral neuropathy was 36.79 per cent with VPT. When compared with VPT, DNS score was most sensitive (53.6%) and specific (55.17%). The tuning fork, monofilament and ankle reflex tests had lower sensitivity (51.14%, 48% and 47.18%). There was significant correlation between the VPT score and the DNS score ( $r = 0.84$ ,  $P < 0.01$ ), tuning fork testing ( $r = 0.94$ ;  $P < 0.01$ ), monofilament testing ( $r = 0.9$ ;  $P < 0.01$ ) and ankle reflex ( $r = 0.76$ ,  $P < 0.01$ ). Therefore it can be concluded that these simple bed side tests are useful in clinical practice.

**Keywords:** diabetes, VPT, peripheral neuropathy,

*\*Corresponding author*



## INTRODUCTION

Diabetes is increasing in epidemic proportions in India and worldwide. India, the world's second most populous country, now has more people with type 2 diabetes (more than 50 million), than any other nation. The problem has been well documented in a battery of recent papers [1-7].

Diabetic neuropathies are one of the most common, yet least understood and often ignored chronic complications of diabetes [8]. Diabetic patients may develop mononeuropathies or polyneuropathy, or a combination of both. Peripheral neuropathy and foot ulceration is twice as common in diabetic persons compared with non-diabetic persons and it affects 30 per cent of diabetics who are older than 40 yr. In persons with diabetes mellitus, the annual population-based incidence of foot ulcer ranges from 1.0 to 4.1 per cent and the prevalence ranges from 4 to 10 per cent, this suggests that the lifetime incidence may be as high as 25 per cent [9]. Two studies reported a median prevalence of about 32% in both Type 1 and Type 2 diabetic subjects [10,11]. Therefore there is a requirement to implement simple bed-side methods for its early recognition.

Screening and early identification of neuropathy helps to modify the course of glycemic control to currently recommended targets and to follow better foot care before the onset of significant morbidity. Reduced incidence of amputation and ulceration is seen after proper screening strategies and screening for neuropathy is recommended in clinical practice guidelines [12].

There can be alteration in the cutaneous morphology in India where barefoot walking is still common and foot care practices are hardly followed [13] which can influence the outcome of commonly used tools to identify neuropathy like the Diabetic Neuropathy Symptom (DNS) Score, 10-g Semmes-Weinstein monofilament testing, vibration testing by 128 Hz tuning fork and ankle reflex. Therefore, this study was planned to evaluate the usefulness of the above modalities with the standard well validated screening method of measuring vibration perception threshold (VPT) with a biothesiometer in a population where foot care practices are scantily followed.

## METHODS

Present study was planned to evaluate the usefulness of simple bed side methods like Diabetic Neuropathy Symptom score, 10-g Semmes-Weinstein monofilament testing, vibration testing by 128 Hz tuning fork and ankle reflex testing in diagnosing neuropathy in diabetic patients in comparison with measuring vibration perception threshold with a biothesiometer.

The study was conducted in the Punjab Institute of Medical Sciences, Jalandhar (Punjab). Total of 106 patients who were suffering from diabetes mellitus according to the American Diabetes Association (ADA) criteria [12] and who had at least two visits in the last six months were included consecutively in the study. Institutional ethics committee approved the

study protocol. These patients were from both rural and urban population and were attending medical outpatient department (OPD) regularly. Patients who had history of chronic alcohol intake or who were anemic were excluded from the study. An informed written consent was obtained from the study participants. Detailed history regarding the type, duration and treatment of diabetes was recorded. Symptoms of diabetic neuropathy were scored with the Diabetic Neuropathy Symptom (DNS) score [14] and a score  $\geq 1$  was considered significant. Vibration perception threshold (VPT) was measured with a biothesiometer in a standardized fashion by a single observer. The biothesiometer probe, which vibrates at 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 familiarized with the sensation by holding the probe against the distal palmar surface of hand. VPT was then measured at the distal plantar surface of great toe of both the legs. If 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/sec and the VPT value was defined as the voltage level when the subject indicated that he or she first felt the vibration sense. The mean of three records was taken and neuropathy was diagnosed if the VPT was  $\geq 25$ mV [15]. Evaluation for peripheral neuropathy was done using 10 g Semmes-Weinstein monofilament. The filament was placed perpendicular to the skin and pressure was applied until the filament just buckles with a contact time of 2 sec. The patient was prevented from seeing if and where the examiner applied the filament. Monofilament was applied to the plantar surface of great toe and base of first, third, and fifth metatarsals of both foot. Areas affected by ulceration or thick callus formation were omitted. The patient was asked to say whether he could feel the pressure applied (yes/no) and in which foot it was applied (right/left foot). Inability to perceive the sensation at any one site was considered abnormal. Assessment of vibration sensation was done with a 128 Hz tuning fork applied at the distal plantar surface of big toe of both legs. The response was considered abnormal when the patient loses vibratory sensation while the examiner still perceived it. Ankle reflex was assessed with a tendon hammer and recorded as either present or absent.

### Statistical Analysis

Data generated from study was analyzed according to standard statistical methods.  $P < 0.05$  was considered as statistically significant.

### RESULTS

A total of 106 patients who were suffering from Type-2 Diabetes Mellitus, were included in the study. Baseline characteristics of the study group showed that the mean age was  $54.99 \pm 11.08$  years, (range 26 - 85 yr) with gender distribution (M:F :: 1.08:1.0). The mean duration of diabetes mellitus was  $8.57 \pm 7.79$  years. Mean body mass index was  $28.3 \pm 4.14$  and mean waist circumference was  $96.7 \pm 9$ , (Table 1).

**Table 1: Characteristics of the study population (n= 106)**

	Mean±S.D
<b>Age</b>	54.99 ± 11.08
<b>Sex(M:F)</b>	48:58:00
<b>Duration(yr.)</b>	8.57 ± 7.79
<b>BMI</b>	28.3 ± 4.14
<b>WC</b>	96.7 ± 9
<b>SBP</b>	137 ± 21
<b>DBP</b>	85 ± 11
<b>FPG</b>	150 ± 51
<b>PPPG</b>	221.8 ± 83.05
<b>TC</b>	190 ± 44
<b>TG</b>	199 ± 77
<b>LDL</b>	107 ± 36
<b>HDL</b>	42.88 ± 5.95

On evaluation for neuropathy with biothesiometer showed a VPT score  $\geq 25$  mV in 39 patients, thus showing a prevalence of peripheral neuropathy of 36.79 per cent in the study population. On evaluating for the symptoms of neuropathy with the DNS questionnaire, 59 (55.66%) patients were having a score of zero which indicated that they did not have symptoms of neuropathy, 13 (12.26%) had a DNS score of one, 13 (12.26%) had a score of two, 15 (14.15%) had a score of three and 6 (5.66%) had the maximum score of four thus, 47 (44.34%) were having significant DNS score indicating that the vast majority of patients with diabetic neuropathy were symptomatic.. Using the other testing modalities, neuropathy was found in 42 (39.62%) with tuning fork testing and in 36 (33.96%) patients with monofilament testing. The ankle reflex was absent in 31 (29.24%) patients.

When the sensitivity, specificity and positive predictive value of each diagnostic modality was compared with biothesiometry which is taken as the gold standard, DNS score and tuning fork testing were more sensitive and specific (53.6% and 55.17%) ,(51.14 and 51.85%) respectively of all the diagnostic tests while positive predictive value was highest for ankle reflex (70.75%). Though the DNS score was most sensitive it had poor positive predictive value, (Table 2).

**Table 2: Diagnostic accuracy of different tests compared to Vibration**

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
<b>DNS Score</b>	53.6	55.17	54.72	45.28	54.24
<b>Tuning Fork</b>	51.14	51.85	60.38	39.62	51.41
<b>Monofilament</b>	48.9	48	66.04	33.96	48.58
<b>Ankle Reflex</b>	47.18	44.28	70.75	29.24	46.23

Correlation between VPT score and other diagnostic modalities showed that there was high degree of significant correlation between the VPT score and the DNS score ( $r = 0.84, P < 0.01$ ), tuning fork testing ( $r = 0.94; P < 0.01$ ), monofilament testing ( $r = 0.9; P < 0.01$ ) and ankle reflex ( $r = 0.76, P < 0.01$ ) (Table 3).

**Table 3: Correlations between VPT score and Tuning Fork, monofilament**

	DNS Score	Tuning Fork	Monofilament	Ankle Reflex
<b>VPT Score Corr.Coeff.</b>	0.84	0.94	0.9	0.76
<b>P(2-tailed)</b>	<0.01	<0.01	<0.01	<0.01

### DISCUSSION

The present study has used VPT of >25mv as the standard for the diagnosis of neuropathy and the prevalence of neuropathy was 36.79 per cent. The use of VPT for the diagnosis of neuropathy has been studied by clinical studies with a sensitivity and specificity of 87% and 51% respectively [16]. In another study the vibration perception threshold showed a steady increase in specificity with a little change in sensitivity until 25V above which there was a significant decrease in sensitivity [17]. VPT of more than 25 mv had a sensitivity of 83% and specificity of 63 % and a positive and negative likelihood ratio of 2.2 and 0.27 for predicting foot ulceration over 4 years [18]. Vibratory threshold has been demonstrated to detect subclinical neuropathy [19]. VPT is most specific and the results of VPT are comparable to the nerve conduction studies in diagnosing diabetic polyneuropathy [20].

Determination of VPT has the advantage of being a simple and unobtrusive method to detect diabetic neuropathy. An accurate instrument to evaluate the patients who are at high risk for the development of peripheral sensory neuropathy is important. Apart from VPT , we also assessed monofilament , tuning fork , ankle reflex and DNS score for evaluation of peripheral neuropathy.

The present study showed sensitivity 48.9% and specificity of 48% for monofilament sensation for the diagnosis of neuropathy .There was high degree of significant correlation between VPT and monofilament with correlation coefficient of 0.9 and p value<0.01. Clinically significant large fibre neuropathy is associated with inability to perceive the 10 gm of force which a 5.07 monofilament applies. Several case studies have been reported with variable sensitivity and specificity for monofilament sensation upto 100% and 87% respectively [21]. However another study has shown sensitivity and specificity of 77% and 96% [22]. The filament has been demonstrated to be more sensitive 100% but less specific 77.7% in identifying patients who have foot ulcers compared to biothesiometry which is less sensitive 78.6% and more specific 93.4% [23].

The present study showed a sensitivity and specificity of 51.14% and 51.85% for tuning fork for the diagnosis of neuropathy. There was a highly significant correlation between VPT and tuning fork with correlation coefficient value 0.94 and p value of <0.01.The 128 Hz tuning

fork provides an easy and inexpensive test of vibratory sensation. The sensitivity and specificity of vibration testing for peripheral neuropathy has been estimated to be 53% and 99% respectively<sup>[22]</sup> and 83% and 68% [21].

In present study, ankle reflex was also used for assessing peripheral neuropathy. Ankle reflex had sensitivity and specificity of 47.18% and 44.28% for the diagnosis of peripheral neuropathy and positive predictive value of 70.75% as compared to biothesiometry. There was a highly significant correlation with correlation coefficient of 0.76 and p value of <0.01. One study showed the sensitivity and specificity of 75% and 89% respectively.<sup>[21]</sup> The combination of monofilament test and ankle reflex had a sensitivity of 92%, specificity of 63%, PPV of 63% and NPV of 92%.<sup>[21]</sup> As the age increases, there is increase in the prevalence of absent ankle reflex, which is shown by one of the study of 1074 normal adults in which the proportion of subjects with absent ankle reflex increased rapidly from 5% at 40 to 50 years of age to 80% at 90 to 100 years of age [24].

The DNS score is the most widely used and accepted scoring system for diabetic neuropathy. In the present study, the DNS score had sensitivity of 53.6% and specificity of 55.17% respectively and it was well correlated with VPT with correlation coefficient of 0.84 and p value of <0.01. In another study, correlation coefficient between DNS score and VPT was 0.73 and p<0.001 [25]. Similar strong correlation has been documented between DNS score and electrodiagnostic investigations by Meijer et al [26].

## CONCLUSION

In conclusion the good correlation of VPT score with DNS score, tuning fork testing, monofilament testing and ankle reflex testing shows that these simple bed side tests are very useful in diagnosis of peripheral neuropathy in diabetic patients in clinical practice.

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