

ABSTRACT This study aims to find out the proportion of Diabetic Peripheral Neuropathy(DPN) in patients with diabetes attending the Community Based Rehabilitation(CBR) Unit and to find if there is any association between Vibration Perception Threshold(VPT) and Nerve Conduction Study(NCS) in Lower limbs. Patients with Diabetes were assessed using a Proforma and Proportion of patients with DPN is found out by measuring VPT using Biothesiometer and compared with NCS parameters. Out of 127 patients,109 were found to have DPN and on evaluating with NCS 113 patients tested positive for neuropathy. On checking for association of VPT and NCS parameters, significance was seen between Tibial Nerve Latency, Tibial Amplitude and F wave Latency and severity of VPT loss but diagnostic accuracy of Biothesiometry with NCS showed poor agreement. The prevalence of DPN was very high in patients visiting the CBR Unitand steps for early identification and complication prevention need to be taken.

KEYWORDS: diabetic polyneuropathy, nerve conduction study, Biothesiometry, Vibration Perception Threshold

INTRODUCTION

Diabetes Mellitus is a metabolic disorder, resulting from the defect in Insulin secretion, action or both and Diabetic Peripheral Neuropathy (DPN) is one of the most common complications in both Type I and Type II diabetes. It is estimated that disease burden of diabetes will reach around 60 million in 20301. Diabetic Peripheral Neuropathy affects almost half of people with diabetes causing considerable morbidity and mortality and huge economic burden and accounts for 50-75% of Non-Traumatic amputations2. The Toronto Diabetic Neuropathy Expert Group defined DPN as symmetrical length dependent sensorimotor neuropathy attributable to metabolic and microvascular changes3. The loss of small fiber mediated sensations results in alteration of thermal and pain perception and large fiber mediated loss results in touch and vibration perception difficulty. More than 50% of DPN patients are asymptomatic and hence diabetic neuropathy is grossly under diagnosed and untreated. This is in part due to the variability of diagnostic criteria, lack of standardised methodologies for diagnosis. The Diabetes Control and Complications Trial (DCCT) concluded that the long standing hyperglycemia is the main cause in the development of diabetic neuropathy and early onset may occur with exposure of peripheral nerves to hyperglycemia. Hence early detection of diabetic peripheral neuropathy will help in delaying or even stalling its progress. One of the proposed classifications of Diabetic Peripheral Neuropathy by Thomas 4 divides it into Small Fiber Neuropathy Large Fiber Neuropathy Proximal Motor Neuropathy Acute Mononeuropathies

Entrapment Neuropathy

It is to be noted that different forms of neuropathy can coexist in a patient.

The Vibration Perception Threshold of a patient can be measured by the use of a Biothesiometer which is one of the simplest method of detecting large fiber dysfunction. There have been studies which claim that there is no correlation between either vibration threshold or thermal threshold5. The Vibration Perception Threshold is easy to measure and can be done in the field at minimal cost and for large number of patients in limited time. This is especially important in developing countries like India as the disease burden is high and due to poor foot hygiene, improper footwear and barefoot walking results in chronic infected ulcers and subsequent amputations.

Nerve Conduction Study(NCS) serves as the gold standard test in detection of subclinical neuropathy6, 7. Their use is recommended for qualitative confirmation of DPN in clinical practice8. However widespread access to NCS in India is difficult as it is available only in Teritiary care setup and may not be helpful in determining the DPN status in the large majority of diabetic patients in the rural population of India. Here our current study assumes importance to find out the proportion of patients with DPN among diabetic patients using Biothesiometry and to find if there is any association between the VPT measurements using a Biothesiometer and Nerve Conduction Study.

METHODOLOGY

The objective was to study the proportion of DPN among patients with diabetes attending the CBR unit, Department of Physical Medicine & Rehabilitation, Government Medical College, Thiruvananthapuram and to find out if there is any association between Vibration Perception Threshold(VPT) using a Biothesiometer and Nerve Conduction Study in lower limb. The Study design was Cross Sectional and duration was 6 months from the date of Human Ethics Committee approval.

The Inclusion Criteria was patients with Type 2 Diabetes attending the CBR unit above the age of 40 yrs. The exclusion criteria was those who have family history of inherited neuropathy, history of occupational or environmental exposure to heavy metal, history of lumbar or cervical radiculopathy, use of medications which could cause polyneuropathy, seriously ill patients, bilateral lower limb amputees, those who do not give consent for the study. Sample size was calculated as 110 patients.

$$n = \frac{p x q x (z_{1-\alpha/2})^2}{d^2}$$
$$z_{1-\alpha/2} = 1.96$$
$$p = 50 \%$$
$$q = 100 - p$$
$$d - absolute precision$$

The Methodology was to assess patients using a proforma and find out the proportion of patients with DPN by measuring VPT using Biothesiometer following which the patients are classified into four groups (without neuropathy-values less than 13 Volts, Mild Neuropathy-Between 13-19 Volts, Moderate Neuropathy-Between 20-25 Volts, Severe Neuropathy-Above 25 Volts). Nerve Conduction studies were performed on bilateral tibial nerves in lower limbs for motor neuropathy and Sural nerve in lower limb for sensory neuropathy with surface recording using standardized technique. The following parameter on Nerve Conduction Study were evaluated: 1) Onset Motor Latency 2) Compound Muscle Action Potential 3) F wave Latency 4) Sural sensory latency 5) Sensory Nerve Action Potential. Based on the results of the above parameters, the diagnosis of diabetic neuropathy is made. Accordingly, sensory neuropathy is defined if any one of the findings are present in sural nerve, i.e. prolonged sensory latency (>4.4 ms), reduced SNAP Amplitude (<6 microvolts). Motor Neuropathy is defined if any one or more of the findings are present in tibial nerve i.e prolonged onset latency (>5.8 ms), reduced CMAP (<8 mV), prolonged F wave Latency (>51 ms). The values obtained from NCS are compared with VPT values in the different groups to find out if any association could be established.

The tools used during the study was a Semi-structured questionnaire, Biothesiometer and Natus EMG/NCS machine. Data was entered into excel sheet and statistical analysis was done with SPSS version 16.0. categorical variables were expressed as proportion and association was tested using Chi square test. P value <0.05 was considered as significant. Quantitative variables was expressed in Mean and SD. Informed consent was taken from relatives and parents and confidentiality was ensured and maintained throughout the study. The study was done after Institutional Scientific Committee & Human Ethics Committee clearance (HEC No 02/16/2018/MCT dated 19/01/2018

RESULTS

The Vibration Perception threshold and Nerve Conduction study of 127 patients with diabetes were assessed during the period of the study. The mean age of the study population was 57.4 years with standard deviation of 7.82 years, of these 49 were males and 78 subjects were females. (TABLE 1).On testing with Biothesiometer out of the 127 study subjects, 109 tested positive for DPN and 41 had mild, 18 moderate and 50 showed severe Vibration Perception Threshold loss (FIGURE 1).

TABLE 1

NCS	Normal	Mild	Moderate	Severe	
Yes	13 (11.5)	34 (30.1)	18	48 (42.5)	
		(15.9)			
No	5 (35.7)	5 (35.7) 7 (50)		2 (14.3)	
	0.0 50.0 10.0 0.0	Be 40.0 30.0 10.0 0.0 holna hud hoderae seere			

FIGURE 1

These patients when checked using NCS, 113 patients showed evidence of DPN in any one of the tested parameters. That was 89% of the patients with diabetes visiting the CBR unit and when the different NCS parameters were considered 93 showed increased Sural latency followed by 75 showing decreased Tibial amplitude, 68 patients had prolonged F wave latency, 41 patients showed decreased sural amplitude and only 36 patients showed prolonged Tibial latency. (TABLE 2).

TABLE 2.

Age	Count	Percent
40-49	29	22.8
50-59	39	30.7
60-69	48	37.8
>=70	11	8.7
Mean+/- SD	57.4 -	+/- 7.8

On comparison of VPT values and NCS Parameters, there was significant association especially in the higher categories of VPT loss(TABLE 3). NCSNormalMildModerateSevereYes13 (11.5)34 (30.1)18

(15.9)48 (42.5)No5 (35.7)7 (50)0 (0)2 (14.3)c2 11.43** p 0.010

TABLE 3.

NCS Parameters	Count	Percent
Sural latency	93	73.2
Sural amplitude	41	32.3
Tibial nerve latency	36	28.3
Tibial amplitude	75	59.1
F wave	68	53.5

When each NCS variable was individually compared with the VPT loss groups, there was significance seen with Tibial Nerve Latency, Amplitude and F wave latency values(TABLE 4 & FIGURE 2)

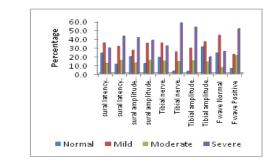


TABLE 4.

		Normal	Mild	Moderate	Severe	χ ²	p
Sural	Normal	8 (23.5)	12 (35.3)	4 (11.8)	10 (29.4)	4.36	0.225
latency	Positive	10 (10.8)	29 (31.2)	14 (15.1)	40 (43)	4.30	0.225
Sural	Positive	8 (19.5)	11 (26.8)	5 (12.2)	17 (41.5)	2.01	0.570
amplitude	Normal	10 (11.6)	30 (34.9)	13 (15.1)	33 (38.4)	2.01	0.570
Tibial	Normal	17 (18.7)	32 (35.2)	13 (14.3)	29 (31.9)		
nerve	Positive	1 (2.8)	9 (25)	5 (13.9)	21 (58.3)	10.02	0.018
latency						•	
Tibial	Positive	2 (2.7)	22 (29.3)	11 (14.7)	40 (53.3)		
amplitude	Normal	16 (30.8)	19 (36.5)	7 (13.5)	10 (19.2)	26.71	p<0.01
Europe	Normal	14 (23.7)	26 (44.1)	4 (6.8)	15 (25.4)	31.53	a (0.01
Fwave	Positive	4 (5.9)	15 (22.1)	14 (20.6)	35 (51.5)	21.53	p<0.01

However while checking the diagnostic accuracy of VPT loss against NCS values, there was poor agreement as 13 patients came as false negatives and although there was high sensitivity (88.5%), the specificity was very low (35.7%)(TABLE 5 & FIGURE 3).

TABLE 5.

Biothesiometry	NCS			
value	Yes	No	Total	
Yes	100	9.0	109	
No	13	5.0	18	
Total	113	14.0	127	

VOLUME-9, ISSUE-4, APRIL -2020 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

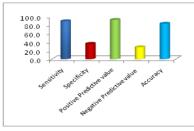


FIGURE 3.

DISCUSSION

In this study out of the 127 patients who participated, 109 patients(85.9%) were found to have decreased VPT and were diagnosed to have DPN which is much higher than the predicted lifetime prevalence of 50% by many studies9. In another study10 done in India using Biothesiometer, it was found that the prevalence of clinical neuropathy among patients with diabetes was 73.2% when Abnormal VPT was taken as above 15 Volts. The higher prevalence in our study may be due to the fact that the patients who were visiting the CBR Unit were already seen and screened from a Primary Health Centre. Another reason is that the abnormal value for VPT was taken as above 13 Volts. In a study11 done by Heung Young Jin and Tae Sun Park, it was found that the prevalence of DPN on 4 year follow up on using various parameters of NCS was 85% which corresponds to the 89% that was observed in the present study. This goes on to show that the prevalence of DPN is very high and all patients visiting CBR unit should be advised regarding proper foot care measures and given protective footwear.

When VPT values were compared with the parameters assessed in NCS it was found that Tibial Nerve Latency, Amplitude and F wave Latency was having significant association but the diagnostic accuracy of Biothesiometer was found to be poor compared to NCS parameters as there were false negatives. Hence on the basis of the results obtained, it was shown that Vibration Perception Threshold Measurement using Biothesiometer as a screening tool for DPT is not ideal. However in situations where patients with diabetes does not have access to Institutionalised Rehabilitation and Nerve Conduction Study facilities, it helps to find out the large majority of the population which is at risk for further complications. These findings are similar to an earlier study12 which stated that although VPT is an effective tool for detecting foot at risk for complications, there was no statistically significant association between NCS and VPT checked by Biothesiometer. This is because Diabetes causes a wide variety of neuropathy namely Motor, Sensory, Sensorimotor, Autonomic and the neuropathy caused is not uniform to all nerves. A similar study done by Perkins et al13 found agreement of VPT measurement with Neurothesiometer and Sural Nerve Amplitude measurement but in this study although the detection rates with regard to sural Nerve latency was high, there was no significance in comparison with VPT values.

CONCLUSION

The study concluded that the prevalence of DPN among patients with diabetes visiting a CBR unit in Kerala was very high and steps like frequent screening camps, patient sensitization, and protective footwear should be taken for prevention of future complications. It was also observed that Biothesiometer is not a good screening tool but may be used to find out the large majority of foot at risk population especially in the rural population which do not have access to NCS

REFERENCES:

 Yach, D., Stuckler, D. & Brownell, K. Epidemiologic and economic consequences of the global epidemics of obesity and diabetes. Nat Med 12, 62–66 (2006). https://doi.org/10.1038/nm0106-62

- [2]. Holzer SE, Camerota A, Martens L, Cuerdon T, Crystal P, Zagari M: Costs and duration of care for lower extremity ulcers in patients with diabetes. ClinTher 20:169-181. 1998
- [3]. Tesfaye S, Boulton AJ, Dyck PJ, Freeman R, Horowitz M, Kempler P, Lauria G, Malik RA, Spallone V, Vinik A, Bernardi L, Valensi P. Diabetic neuropathies: update on definitions, diagnostic criteria, estimation of severity, and treatments. Diabetes Care 33:2285-2293, 2010
- [4]. Thomas PK: Classification, differential diagnosis, and staging of diabetic peripheral neuropathy. Diabetes 46 Suppl 2:S54-S57, 1997
- [5]. Gelber DA, Pfeifer MA, Broadstone VL et al. Components of variance for vibratory and thermal threshold testing in normal and diabetic subjects. J Diabetes Complication 1995;9:170-176.
- [6]. H. Dorchy, P. Noel, M. Kruger et al, Peroneal Motor Nerve Conduction velocity in diabetic children and adolescents. European Journal of Pediatricsvol 144, no 4:310-315,1985
- [7] Perkins BA, Olaleye D, Zinman B, Bril V. Simple screening tests for peripheral neuropathy in the diabetes clinic. Diabetes Care. 2001;24(2):250-256
- [8]. Boulton AJ, Vinik AI, Arezzo JC, Bril V, Feldman EL, Freeman R, Malik RA, Maser RE, Sosenko JM, Ziegler D; American Diabetic Association. Diabetic neuropathies: a statement by the American Diabetes Association. Diabetes Care. 2005;28(4):956-962
- [9]. Tesfaye S, Boulton AJ, Dyck PJ, et al. Diabetic neuropathies: update on definitions, diagnostic criteria, estimation of severity, and treatments [published correction appears in Diabetes Care. 2010 Dec;33(12):2725]. Diabetes Care. 2010;33(10):2285–2293. doi:10.2337/dc10-1303
- [10]. BMK Aruna, R. Haragopal. Role of Biothesiometry in the diagnosis of diabetic neuropathy. Indian Journal of Clinical Anatomy and Physiology, July-Sept, 2017;4(3):329-331. DOI: 10.18231/2394-2126.2017.0083
- [11] Jin HY, Park TS. Can nerve conduction studies detect earlier and predict clinical diabetic neuropathy? J Diabetes Investig. 2015;6(1):18–20. doi:10.1111/jdi.12236
- [12]. Dr Amit Shah, Dr Dhruvin Shah. A STUDY TO COMPARE DETECTION OF PERIPHERAL NEUROPATHY IN TYPE 2 DIABETES USING NERVE CONDUCTYION VELOCITY AND BIOTHESIOMETRY. Indian Journal of Research. Vol-7, Issue-2, Feb 2018, Print ISSN No 2250-1991
- [13]. Comparison of vibration perception thresholds obtained with the Neurothesiometer and the CASE IV and relationship to nerve conduction studies. Vera Bril, B. A. Perkins Diabet Med. 2002 Aug; 19(8):661–666.