Original Article

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Applicability of Toronto Clinical Neuropathy Scoring and its Correlation with Diabetic Peripheral Neuropathy: A Prospective Cross-sectional Study

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ABSTRACT

Introduction: Diabetes is a non-communicable metabolic disorder which is associated with numerous vascular and non-vascular complications. Neuropathy is one of the most important complications which, if not recognized and treated early may result in significant disability and poor quality of life. In a resource poor setting like India, where diagnostic modalities like Nerve Conduction Study (NCS) are expensive for early diagnosis, the present study aimed to evaluate the effectiveness of a simple bed side assessment test, the Toronto Clinical Neuropathy Scoring (TCNS) system in diagnosing Diabetic Peripheral Neuropathy (DPN).

Aim: The primary objective was to determine the applicability of Toronto clinical scoring system in DPN diagnosed by NCS in the South Indian population. The secondary objective was to evaluate the correlation between duration of Diabetes Mellitus (DM), HbA1C, diabetic retinopathy and neuropathy with severity of diabetic neuropathy as determined by the TCNS.

Materials and Methods: In a prospective cross-sectional study, conducted over a period of 12 months from June 2015 to May 2016 at a tertiary care institute in semi-urban South India, 50 diabetic patients with symptomatic neuropathy were included. All patients were subjected to TCNS and the results were compared with neuropathy confirmed by NCS. Categorical variables were expressed as percentage or proportions. Comparison of normally and abnormally distributed continuous variables were done by independent sample t-test and Mann – Whitney U test respectively. Categorical variables were compared using Chi-square test or Fisher's exact test. A p-value less than 0.05 was considered statistically significant.

Results: The presence of neuropathy by TCNS was confirmed in all cases by NCS. Further the severity of neuropathy as assessed by TCNS was found to correlate well with duration of diabetes, and the presence of diabetic retinopathy and nephropathy. Presence of foot weakness, ataxia and upper limb symptoms also had direct correlation with severity of diabetic neuropathy.

Conclusion: TCNS is a sensitive scoring system used to diagnose diabetic neuropathy and can be used as an inexpensive bedside screening tool.

Keywords: Diabetes mellitus, Nerve conduction study, Neuropathy, Toronto clinical scoring system

INTRODUCTION

Diabetes is a non-communicable metabolic disorder with an estimated prevalence of 382 million worldwide and 65 million in India, which is predicted to increase to 100 million by 2030 [1]. Diabetes is well known to cause both vascular (micro and macrovascular) and non vascular complications. Neuropathy is one of the most frequently encountered microvascular complications and along with peripheral vascular disease; it is one of the leading causes of non-traumatic lower limb amputation [2].

The prevalence of diabetic neuropathy in the Indian population ranges from 19.1% [3] to 29.2% [4]. Distal symmetrical neuropathy is the most common form of diabetic neuropathy, and its prevalence has been reported to be as high as 50 to 75% among type 2 DM patients [5,6]. The gold standard of diagnosis of peripheral neuropathy has been the NCS. However, it is cumbersome and expensive and not widely available [7]. Therefore, a clinical scoring system which can be easily performed and that correlates well with NCS, is needed in resource poor settings like India. Several scoring systems have been introduced for diagnosis and classification of DPN, and include the TCNS and its modified score (mTCNS), Michigan Neuropathy Screening Instrument (MNSI), Neuropathy Impairment Score (NIS) among others [7,8].

In India, the commonly used tests are the Semmes-Weinstein Monofilament test (SWM), Vibration Perception Test (VPT), Neuropathy Symptom Score (NSS) and Neuropathy Disability Score (NDS) [9-11]. The sensitivity and specificity of these scores have been compared by Mythili A et al., and the VPT was found to have the best sensitivity of 86% and specificity of 76%. The TCNS, introduced by Bril V and Perkins B, has been evaluated in several studies from Canada and the United States, and has been found to have a significant correlation with sural nerve myelinated fiber density in patients with diabetic neuropathy [12]. However, this score has not been validated in the Indian population. The present study evaluated the applicability of TCNS in diagnosing DPN in South Indian population. The primary aim of the present study was to evaluate the applicability of TCNS in South Indian diabetic patients with peripheral neuropathy and to establish its correlation with NCS. The secondary objectives included correlation of the severity of DPN with the duration of diabetes, diabetic control (as assessed by HbA1C) and with other microvascular complications.

MATERIALS AND METHODS

Study Design

This was a prospective observational study carried out in the medicine wards of a tertiary care university teaching hospital in semi-urban Southern India over a period of 12 months (June 2015 to May 2016). The study included all patients above the age of 18 years with type 1 or type 2 Diabetes with symptoms suggestive of peripheral neuropathy. Patients with neuropathy due to causes other than diabetes and those who refused informed consent were

excluded from the study. Sample size was calculated based on a 19.1% prevalence of neuropathy in diabetes in South India [3], allowing for an error of 10%, and thereby a total of 50 patients were recruited.

Data Collection

After obtaining approval from the Institutional Ethical Committee, patients were recruited in the study based on the inclusion criteria. Informed consent was obtained and the patients were subjected to history and physical examination, including assessment of the TCNS score. They were then evaluated with NCS using RMS EMG EP Mark2 recorder, medicare systems and evaluation of motor function of the median, ulnar, peroneal, and tibial nerves, and sensory function of median, ulnar, radial, and sural nerves were performed. Velocities were documented in meters per second, motor amplitudes in millivolts, and sensory amplitudes in microvolts. A pre-structured proforma was used to record demographic details of the patients. The patient's clinical profile including age, gender, and duration of diabetes, HbA1c and associated microvascular complications were documented.

The individual patient's TCNS score was documented out of a total of 19. Severity of neuropathy was classified based on the score as: no neuropathy (0 to 5), mild neuropathy (6 to 8), moderate (9 to 11) and severe diabetic neuropathy (12 to 19) [Table/Fig-1].

Symptom scores	Reflex scores	Sensory test scores
Foot	Knee reflexes	Pinprick
Pain	Ankle reflexes	Temperature
Numbness		Light touch
Tingling		Vibration
Weakness		Position
Ataxia		
Upper-limb symptoms		

[Table/Fig-1]: Toronto Clinical Neuropathy Scoring System (TCNS) [13]. Sensory testing was performed on the first toe. Symptom scores: present = 1; absent = 0. Reflex scores: absent = 2; reduced = 1, normal = 0. Sensory test score: abnormal = 1. normal = 0. Total scores range from normal = 0 to maximum of 19.

Data Analysis

Continuous variables were assessed for the normality using Shapiro – Wilk's test. If the variables were normally distributed they were expressed as mean±standard deviation, otherwise median (interquartile range). Categorical variables were expressed either as percentage or proportions. Comparison of normally distributed continuous variables was done by independent sample t-test, abnormally distributed continuous variables by Mann-Whitney U test, and categorical variables by either Chi-square test or Fisher's exact test based on the number of observations. Data analysis and validation was carried out by SPSS v.11.0. All p-values less than 0.05 were considered statistically significant.

RESULTS

In our study, the mean age of the study population was 59.9 years (±12.89). The mean duration of diabetes in the study population was 8.40 (±6.09) years. Most of the patients had poorly controlled diabetes with a mean HbA1C of 10.2% (SD± 2.10%). There were four patients (8%) with Type 1 DM. The baseline characteristics of the patients are represented in [Table/Fig-2].

Evaluating for the primary objective, the applicability of TCNS and its correlation with NCS was studied. Out of the total of 50 patients, 49 (98%) were found to have a TCNS score of 6 or more, clinically indicating the presence of neuropathy. The distribution of the signs and symptoms is depicted in [Table/Fig-3]. It was noted that all 50 patients (100%) had foot pain, numbness and tingling. Upper limb symptoms were observed in 41 (82%) patients. On sensory testing, pin prick was diminished in 48 (96%) whereas vibration sense was reduced only in 12(24%). Ankle reflex was reduced in 20 patients (40%) and absent in 30 patients (60%).

The severity of the neuropathy was graded based on the TCNS. Twelve (24%) of patients were diagnosed to have severe DPN [Table/Fig-4] while 20 (40%) and 17 (34%) had moderate and mild neuropathy respectively. Forty eight out of 49 patients who had clinical neuropathy by TCNS were subsequently confirmed by NCS to have peripheral neuropathy (97.9%). One patient who did not have neuropathy by TCNS was found to have neuropathy according to NCS.

On analysis of the secondary objectives, the duration of diabetes correlated well with the severity of diabetic neuropathy. Patients

Clinical Parameter		Total Number of patients N=50 n (%)	Mean
Age (in years)	< 40	4 (8)	59.9±12.89
	41-50	10 (20)	
	51-60	13 (26)	
	61-70	13 (26)	
	>70	10 (20)	
Gender	Male	29 (58)	---
	Female	21 (42)	
HbA1c (%)			10.2±2.10
Duration of diabetes (in years)	<5	21 (42)	8.40 (±6.09)
	5-10	18 (36)	
	>10	11 (22)	
Associated microvascular complications			
Retinopathy	No retinopathy	20 (40)	---
	NPDR	24 (48)	
	PDR	6 (12)	
Nephropathy	No nephropathy	23 (46)	---
	Microalbuminuria	20 (40)	
	Macroalbuminuria	7 (14)	

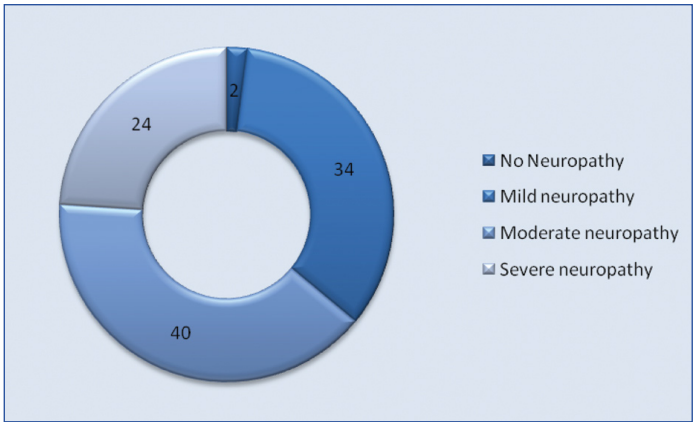
[Table/Fig-2]: Baseline characteristics.

Symptoms	Number of patients (%)	Sensory testing	Number of patients (%)
Foot pain	50 (100)	Pinprick	48 (96)
Foot numbness	50 (100)	Temperature	18 (36)
Foot tingling	50 (100)	Light Touch	42 (84)
Foot weakness	14 (28)	Vibration Sensation	12 (24)
Ataxia	12 (24)	Joint Position	19 (38)
Upper limb symptoms	41 (82)		
Reflex Scores			
Knee reflex Reduced Absent	 20 (40) 13 (26)	Ankle reflex Reduced Absent	 20 (40) 30 (60)

[Table/Fig-3]: Distribution of symptoms and signs of peripheral neuropathy.

who had diabetes for more than five years had either moderate or severe diabetic neuropathy as compared to those with lesser duration of diabetes (<5 years) with p<0.001. However, the severity of neuropathy was not found to have significant association with the degree of glycaemic control (as reflected by HbA1c) p=0.135 [Table/Fig-5].

The severity of other microvascular complications such as retinopathy and nephropathy was compared against the severity of diabetic neuropathy. Among patients with mild diabetic neuropathy only 3 (17.6%) had any evidence of retinopathy, whereas in those patients with moderate to severe neuropathy 22 (68.75%) had Non Proliferative Diabetic Retinopathy (NPDR) and 5 (15.62%) had Proliferative Diabetic Retinopathy (PDR) which was statistically significant p<0.001 [Table/Fig-5]. Similarly, while assessing the presence of co-existing nephropathy in patients with diabetic



[Table/Fig-4]: Distribution of severity of neuropathy as assessed by TCNS in percentage.

Parameter		No DN (%)	Mild DN (%)	Moderate DN (%)	Severe DN (%)	p-value
Duration of diabetes (years)	≤5	1 (4.8)	12 (57.1)	7 (33.3)	1 (4.8)	0.015
	6-10	0	4 (22.2)	6 (33.3)	8 (44.4)	
	>11	0	1 (9.1)	7 (63.6)	3 (27.3)	
HbA1c (%)	<9	1 (7.7)	6 (46.2)	5 (38.5)	1 (7.7)	0.135
	>9	0	11 (29.7)	15 (40.5)	11 (29.7)	
Diabetic retinopathy	No retinopathy 20 (40%)	1(5)	14 (70)	4 (20)	1 (5)	<0.001
	NPDR 24 (48%)	0	2 (8.3)	15 (62.5)	7 (29.2)	
	PDR 6(12%)	0	1 (16.7)	1 (16.7)	4 (66.7)	
Diabetic nephropathy	No nephropathy 23 (46%)	1 (4.3)	15 (65.2)	6 (26.6)	1 (4.3)	<0.001
	Micro-albuminuria 20 (40%)	0	1 (5)	13 (65)	6 (30)	
	Macro-albuminuria 7 (14%)	0	1 (14.3)	1 (14.3)	5 (71.4)	

[Table/Fig-5]: Correlation of severity of neuropathy with risk factors and other microvascular complications.
DN: Diabetic Neuropathy; NPDR: Non Proliferative Diabetic Retinopathy; PDR: Proliferative Diabetic Retinopathy.

neuropathy, only 2 (11.7%) of the patients with mild diabetic neuropathy had evidence of diabetic nephropathy as compared to patients with moderate to severe diabetic neuropathy, 25(78%) of whom had nephropathy (p<0.001).

DISCUSSION

Diabetes is one of the most prevalent metabolic disorders all over the world causing significant morbidity and mortality. A few studies have been done so far on the relationship between TCNS and diabetic neuropathy. Among these, important studies include those done by Bril V et al., [12-14] and Bostani A and Homayuonfar H [15], It is appropriate to compare the present study with their findings.

In the present study mean age was a 59.9±12.89 year which was similar to the above mentioned studies. Out of the total of 50 patients 29 (58%) were males and 21 (42%) females. This is in contrast to Bostani A and Homayuonfar H, in whose study 20% were males and 80% were females [15]. However, other authors such as Bril V et al., have showed distribution among males varying from 61-65% and for females from 35-38%.

When mean duration of diabetes was studied, it was found to be 8.40±6.09 years in this study. This is significantly different from other studies where mean duration of diabetes was more than 11 years. Although, this indicates that patients in current study had relatively shorter duration of diabetes, nevertheless, the duration of diabetes had a statistically significant correlation with the severity of diabetic neuropathy. Similar findings were reported by Ashok S et al., and Gill HK et al., in their research on risk factors associated with diabetic neuropathy [3,4].

The next variable analyzed in the study was the degree of sugar control as determined by mean HbA1C values. The study population had a poorer control of diabetes (mean HbA1C 10.2±2.10%) as opposed to patients of Bril V et al., (mean HbA1C of 8.5±1.7%). But interestingly in this study, the severity of neuropathy had no correlation with their HbA1C. A similar lack of correlation between HbA1C and diabetic neuropathy has been reported by Gill HK et al., who proposed that any level of elevated glucose beyond a particular threshold will predispose to neuropathy, and not necessarily a linear correlation [4,16].

With regards to severity of neuropathy, as assessed by TCNS, out of 50 patients who were included in this study, (1) 2% had no diabetic neuropathy, (17) 34% mild, (20) 40% moderate and (12) 24% had severe diabetic neuropathy. Similar study done by Bril V et al., with 65 patients, 12.3%, 21.5%, 27.7% and 38.5% had no neuropathy, mild neuropathy, moderate neuropathy and severe diabetic neuropathy respectively.

Since neuropathy is known to be associated with other micro-vascular complications such as retinopathy and nephropathy, the current study also analyzed the presence of other co-existing microvacular manifestations. In our study, it was found that among neuropathy patients, 60% had retinopathy and 54% had nephropathy. Comparing this data with a few other studies from India, Bansal D et al., reported a prevalence of 41.8% retinopathy and 20.9% nephropathy among patients with diabetic neuropathy [17]. In the CURES-55 study from Chennai, India the authors report an overall prevalence of 26.1% neuropathy in diabetic patients, with 24.1% of patients having associated retinopathy and 24.8% having nephropathy [18]. Lobo AC et al., reported that the prevalence of retinopathy was 12% and nephropathy was 40%, but this was assessed in patients with a duration of diabetes less than one year [19]. This was markedly different from study done by Bril V et al., where the prevalance of retinopathy was reported as 26% and nephropathy was found to be present only in 2% of patients with neuropathy.

In the present study the severity of retinopathy and nephropathy had a statistically significant correlation with the severity of diabetic neuropathy as assessed using TCNS score (p<0.001). These findings correspond to the results of study done by Weisman A et al., who also reported that the severity of diabetic retinopathy correlated with the severity of diabetic neuropathy [20]. Another study done by Liu F et al., on TCNS in DPN also concluded that severity of diabetic retinopathy and nephropathy went hand in hand with diabetic neuropathy [21].

LIMITATION

The present study had certain limitations, one being that it was a hospital based study and hence the results may not be generalized to the population on a community basis. The differences between patients with type 1 and type 2 diabetes were not compared.

CONCLUSION

From the present study, it can be concluded that, TCNS can be effectively used as a simple bedside screening tool to diagnose the presence of diabetic neuropathy and assess its severity in the Indian population. The duration of diabetes is more likely to have an effect on the severity of neuropathy than glycaemic control. Further, using the severity score of TCNS, the clinician can be alerted to the possibility of other co-existing microvascular complications such as retinopathy and nephropathy.

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