ORIGINAL ARTICLE

PERFORMANCE OF TWO DIFFERENT CLINICAL SCORING SYSTEMS IN DIAGNOSING DISTAL SENSORY POLYNEUROPATHY IN PATIENTS WITH TYPE-2 DIABETES

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Background: Early diagnosis of distal peripheral neuropathy (DSPN) the commonest diabetes complications, helps prevent significant morbidity. Clinical parameters are useful for detection, but subjectivity and lack of operator proficiency often results in inaccuracies. Comparative diagnostic accuracy of Diabetic Neuropathy Symptom (DNS) score and Diabetic Neuropathy Examination (DNE) score in detecting DSPN confirmed by nerve conduction studies (NCS) has not been evaluated. This study compares the performance of these scores in predicting the presence of electro physiologically proven DSPN. The objective of this study was to compare the diagnostic accuracy of DNS and DNE scores in detecting NCS proven DSPN in type-2 diabetics, and to determine the frequency of sub-clinical DSPN among type-2 diabetics. **Methods:** In this cross-sectional study the DNS score and DNE score were determined in 110 diagnosed type-2 diabetic patients. NCS were carried out and amplitudes, velocities and latencies of sensory and motor nerves in lower limb were recorded. **Results:** Comparison between the two clinical diagnostic modalities and NCS using Pearson's chi square test showed a significant association between NCS and DNE scores (*p*-value =.003, specificity 93%). The DNS score performed poorly in comparison (*p*-value=.068, specificity 77%). When the two scores were taken in combination the specificity in diagnosing DSPN was greater (*p*-value=.018, specificity 96%) than either alone. 33% of patients had subclinical neuropathy. **Conclusion:** DNE score alone and in combination with DNS score is reliable in predicting DSPN and is more specific than DNS score in evaluating DSPN. Both tests lack sensitivity. Patients without any evidence of clinical neuropathy manifest abnormalities on NCS.

Keywords: diabetic neuropathy; nerve conduction studies; clinical scoring systems

J Ayub Med Coll Abbottabad 2015;27(1):187–91

INTRODUCTION

Distal peripheral neuropathy (DPN) is amongst the commonest long term complication of diabetes.[1] It has been estimated that 50% of diabetic patients will have neuropathy within 25 years of their disease history.[2] The increased risk of non-traumatic foot amputations and lower extremity disease in diabetics has been attributed to DSPN.[3,4] An early diagnosis helps identify patients at risk before the onset of disabling complications. Despite its common occurrence, DSPN shows considerable variability in prevalence.[5,6] This can be attributed to the differences in definitions of neuropathy and the tests used for evaluation.[5] Although neurological signs and symptoms are recommended diagnostic tools[6,7] subjectivity, lack of reproducibility and proficiency of the examiner leads to inaccuracies[8]. Moreover asymptomatic neuropathy is common, present in up to 50% of cases[9,10], and clinical features do not always correlate with the severity of pathological deficits. Therefore a reliable approach is needed for accurate diagnosis.

Different screening measures and scores to assess clinical symptoms and signs have been described in the past.[11,12] Diabetic Neuropathy Symptom (DNS) score[13] adapted from Neuropathy symptom score (NSS)[6], and Diabetic Neuropathy Examination (DNE) score[14] are validated scoring systems which are accurate, and quick and easy to perform[15]. The relative performance of either scoring system in predicting the presence of DSPN as diagnosed by nerve conduction studies (NCS) has not been evaluated. Nerve conduction studies are an objective and sensitive test for detecting onset and progression of DSPN.[16] Various NC criteria considered accurate for diagnosing peripheral neuropathy have been proposed[17], which are able to detect even sub-clinical cases[18,19]. The present study compared the efficacy of clinical diagnostic scores with NCS and evaluated the sensitivity and specificity of the former in diagnosing DSPN.

MATERIAL AND METHODS

This cross-sectional study was conducted at the Diabetes Management Centre Services Hospital Lahore. The research protocol was registered with the Services Hospital research registry and approved by the ethical review committee of Services Hospital.

Patients with type-2 diabetes coming to the centre were recruited after taking a detailed history. Patients who had evidence of other causes of neuropathy such as alcoholism, liver or renal disease, exposure to toxins, nutritional deficiencies, mal absorptive states or chronic inflammatory diseases were excluded. Patients with endocrine or metabolic disorders resulting in neuropathy or those with a history of cerebrovascular accident or trauma to the examining limb were also excluded. A total of 110 patients who fulfilled the criteria were selected. Informed consent was obtained from all participants, who underwent a comprehensive neurological examination at the centre. Age, gender, duration of diabetes and history of foot ulceration were recorded. Blood glucose levels, serum creatinine, routine biochemical and haematological tests, and glycosylated haemoglobin were measured in all subjects. All 110 patients were evaluated for Diabetic Neuropathy Symptom (DNS) score and Diabetic Neuropathy Examination (DNE) score. Nerve conduction Studies (NCS) were performed on all patients.

All patients were questioned regarding the presence or otherwise of symptoms, either positive or negative indicating the presence of neuropathy. The questionnaire used was the Diabetic Neuropathy Symptom DNS score13 adapted from the Neuropathy Symptom Score (NSS) of Dyck6. The score is based upon the regular occurrence of four different symptoms of DSPN, including tingling, burning, numbness and unsteadiness of gait. The score has a range of 0–4, and a score of ≥1 is considered indicative of DSPN. A version translated in Urdu was developed and tested against the original English version in a pilot study conducted in the department in a population of bilingual patients.

A detailed neurological examination was carried out and the Diabetic neuropathy examination (DNE) score was determined. This is a modification of the Neuropathy Disability Score of Dyck14 and consists of eight items, two testing muscle strength, one a tendon reflex, and five sensory modalities. The score ranges from 0–16, with a score of >3 point considered abnormal.

Nerve Conduction Studies were performed at controlled room temperature (23±2 ºC), using the Nihon Kohden, MEBS 9400 evoked potential measuring system. A simplified nerve conduction studies (NCS) protocol was followed20 in which a minimum of two nerves: (sural and peroneal) and a maximum of three nerves sural (sensory) and peroneal and tibial (motor) were tested. Nerve conduction abnormality was labelled according to the NC criteria for diagnosis of DSPN.17 Criteria included the presence of ≥1 abnormal attribute in ≥2 separate nerves tested. If no abnormal attribute was found, NCS were considered normal. If a response was absent in any of the nerves (sensory or motor), NCS on the contra-lateral nerve were performed. If a Peroneal motor response was absent, test was performed on an ipsilateral tibial motor nerve.

Data were analysed on the SPSS version 17. The diagnostic accuracy of both scores was compared with presence of NCS abnormality and the sensitivity, specificity, negative and positive predictive values were calculated. Pearson chi square test and Fisher exact test were used to compare the difference between the groups. A *p*-value of <.05 was considered significant.

RESULTS

A total of 110 patients with type-2 diabetes were selected from the Diabetes Management Centre (DMC) of Services Hospital Lahore, of which 48 (43.6%) were male. The mean age was 48 years (SD 7.8 years). Mean duration of diabetes was 5.3 years (SD 4.3 years), and mean HbA1c was 8.2% (SD 1.7%). 58% patients had been diagnosed with diabetes for a duration of less than 5 years.

A positive DNS score was recorded in 31% (n=35), while a positive DNE score was recorded in 16.4% patients (n=18). Both scores were positive in only 8 (7.5%) patients. NCS abnormalities were noted in 34.8% of patients (n=38). Among 75 asymptomatic patients, NCS was abnormal in 23 patients (30%) indicating the presence of subclinical DSPN.

Out of the 35 symptomatic patients (positive DNS score), 17 had abnormal NCS while 18 had normal NCS. The sensitivity of the score was 44% and specificity was 73%, with positive predictive value (PPV) of 54% and negative predictive value (NPV) of 65% respectively. A positive DNS score did not show a significant association with NCS (two sided level of significance on Pearson's chi square test: .069). (Table-1)

Amongst the 18 patients with positive DNE score, 12 had abnormal NCS and only 6 patients had normal NCS. The sensitivity of the score was 31% and specificity was 93%, with a PPV of 77% and NPV of 66% (Table-2). Significant association was found between DNE and NCS (two sided level of significance on Pearson’s chi square test: .003). Out of 92 patients with normal DNE score, 28 showed abnormal NCS values (30.4%).

Although only 8 patients had both DNS and DNE scores positive, of these 77% had abnormal NCS. The specifity of both scores together was 96%, with a PPV of 75%, and NPV of 62%. There was significant association with NCS abnormalities (two sided level of significance on Pearson’s chi square test: .018). Among the 102 patients with both scores negative (subclinical neuropathy with regards to both symptoms and signs), 34 (33%) showed NCS abnormalities.

Table-1: A comparative analysis of two clinical diabetic neuropathy scoring systems

Clinical Neuropathy Scoring System		Nerve conduction studies		$\div^2$ 2 sided level of significance	Fisher Exact Test
		Abnormal NCS‡	Normal NCS‡		
DNS*	+	17 (15.5%)	18 (16.4%)	.069	.089
	-	23 (20.9%)	52 (47.3%)		
DNE†	+	12 (10.9%)	6 (5.5%)	.003	.006
	-	28 (25.5%)	64 (58.2%)		
DNS + DNE	+	2 (1.8%)	6 (5.5%)	.018	.026
	-	34 (30.9%)	68 (61.8%)		

*DNS: Diabetic Neuropathy Symptom Score; †DNE: Diabetic neuropathy examination score; NCS: Nerve conduction studies; $\div^2$ Pearsons chi square test

Table-2: Relative performance of the two scores

	DNE†	DNS*	Both together	Either/or
Sensitivity	31%	44%	15%	60%
Specificity	93%	73%	96%	71%
PPV	77%	54%	77%	59%
NPV	66%	65%	62%	72%

*DNS: Diabetic Neuropathy Symptom Score; †DNE: Diabetic neuropathy examination score; PPV: Positive predictive value; NPV: negative predictive value

DISCUSSION

Despite being a common long term complication[1], DSPN is insidious in onset, with a paucity of symptoms[9], often remaining undetected while causing progressive underlying damage. The associated morbidity with its consequent effects on quality of life and entailing economic burden[3,4] renders an early diagnosis imperative. Unfortunately DSPN is not reliably diagnosed and its true prevalence remains uncertain[5,6]. This is attributed to the differences in definition of neuropathy and the diagnostic criteria used[5], which need to be agreed upon in order to achieve diagnostic accuracy.

Expert panels have made recommendations for diagnostic criteria and defined subclinical, possible, probable and confirmed states of neuropathy.[21,2] The presence of any two out of signs, symptoms and tests have been suggested as the minimum criteria for the diagnosis of DSPN by Dyke *et al.*[7] The Diabetic Neuropathy Study Group in Japan have incorporated signs and symptoms in their diagnostic criteria, while maintaining NCS as the gold standard, and reported a sensitivity of 68% and specificity of 74% for their diagnostic criteria in diagnosing DSPN.[22]

The efficacy of DNE and DNS scores in detecting DSPN has been demonstrated by Meiger *et al.*[15] However the two scales are inherently different, as one is a symptom score, while the other relies on eliciting neurological signs, with consequent difference in operator skill level required. The DNS score is a validated tool which has only four items, making it practical for use, with a reportedly high degree of sensitivity and discriminative value.[13] The present study compared the performances of DNS and DNE scores separately and in combination in detecting DSPN proven by NCS. It was noted that in the tested population of Pakistani type-2 diabetic patients, both scores were relatively insensitive in detecting DSPN. Among the two scores DNS showed a higher sensitivity but lower specificity (77%), whereas the DNE score showed a relatively lower sensitivity but a much higher specificity (93%). The specificity of the clinical diagnostic scores increased when performed together (96%). The low sensitivity of the clinical scores can be attributed to common occurrence of asymptomatic DSPN, which may be present in about 50% of diabetic patients, with only 10–20% of patients experiencing troublesome complaints.[10] The low specificity of the DNS score may be attribute to the subjectivity of complaints, which is also contributory towards reduced reliability of symptoms .Moreover symptoms represent small fibre neuropathy which is electro diagnostically silent. Furthermore, the original questionnaire was prone to errors in this population, where bare foot walking is common with no concept of foot care[23] resulting in changes in skin texture and sensitivity, contributing towards the poor performance of the score. An indigenous DNS score could be more sensitive and specific in Pakistani patients who had some difficulty in interpreting the questions in the translated version.

Despite these limitations, a place for a symptom based score in diagnosis of DSPN has been indicated in previous studies (Mythili *et al*[24], Meiger *et al*[13], Yassuda *et al*[22]. In the modified Toronto Clinical Neuropathy Score (mTCNS)[25], symptoms were introduced instead of reflex testing, (as the latter is representative of late-stage abnormalities in the pathophysiology of DSPN), even though no correlation between electrophysiology and symptoms could be demonstrated. Similarly, various trials on diabetic neuropathy have considered symptoms of neuropathy to be reliable outcome measures.[26] On the other hand, many workers have contested the role of symptoms of neuropathy as a reliable diagnostic tool, noting that the absence of symptoms does not equate with absence of neuropathy.[27] This controversy over the utility of neuropathy symptom score was one of the motivations for the present study, which assessed the relative performance of clinical scores based upon symptoms vs signs.

The DNE score used in our study is a validated and sensitive scoring system[14], shown to be an efficient screening tool in view of its cost effectiveness and ease of performance[24]. It has been reported to correlate well with other diagnostic modalities, but with a low sensitivity and without any added advantage with regards to accuracy.[28] In the

present study DNE score showed a higher degree of specificity compared to DNS, and in combination, both scores showed an even higher specificity of 96%. Although earlier studies have correlated these diagnostic scores with NCS[15,29] they focused more on variation in NCS parameters rather than the comparative performance of the two scores[29]. The low positivity of DNE score in the present study can be attributed to the subjectivity involved as well as the proficiency of examiners in accurately evaluating signs and symptoms. In a recent study the comparative performance of physicians using clinical parameters for diagnosis of DSPN showed considerable variability compared to NCS, highlighting the need for improving examiner proficiency.[8] As the DNE score requires careful assessment, adequate training of the operators needs to be ensured.

While diagnostic scoring systems are useful in detecting clinically evident neuropathy, nerve conduction studies have an important place in identification of disease severity and confirmation of diagnosis of DSPN[2,21] and are considered an important component of diagnostic criteria[30,31]. NCS abnormality may be the first objective indication of neuropathy in patients without evident signs and symptoms[2], with various studies highlighting the role of NCS in detecting subclinical neuropathy.[18,19] Some authorities have gone so far as suggesting that annual NCS should be carried out as a routine in diabetic patients.[29] However as this is an expensive and time consuming test, there are limitations to its utility. In practice, NCS may be used as an adjunct to clinical diagnosis and as a means of increasing the reliability of clinical testing.

CONCLUSION

This study presented several interesting findings. A significant proportion of patients had subclinical neuropathy. The clinical diagnostic scores had a maximum sensitivity of 60% in detecting DSPN. Despite this weakness these scores are invaluable, as positive scores had a specificity of up to 96% in diagnosing DSPN in this study. Out of the two scores the DNE was found to be much more valid and had a highly significant association with the gold standard NCS. DNS added to the specificity when taken in conjunction with the DNE score. As the DNS had a somewhat higher sensitivity it might be useful as a screening test.

ACKNOWLEDGEMENTS

The authors wish to express their gratitude to. Dr. Ahsan Numan for conducting NCS and interpreting results.

Funding: The research was not funded by any institution.

Financial disclosure: The authors have no conflict of interest to declare in this research.

AUTHOR CONTRIBUTIONS

KIK designed the study, interpreted results and wrote the manuscript. AN performed NCS and interpreted results. AA helped in performing NCS and participated in data collection, AF interpreted results of the scoring system. SK performed statistical analysis. FM was the team leader. All authors reviewed the final article.

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