Original Article

Diagnostic accuracy of monofilament test to detect diabetic neuropathy

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Abstract

Background
Diabetic peripheral neuropathy (DPN) is a significant independent risk factor for diabetic foot, and an effective screening instrument is required to diagnose DPN early to prevent future ulceration and amputation. This study aims to determine the diagnostic accuracy of monofilament test to detect diabetic peripheral neuropathy.
Methods
This cross-sectional study was conducted in National Academy of Medical Sciences, Bir hospital, Mahabouddha, Kathmandu from February 2016 to January 2017. A total of 96 diabetic patients attending inpatient and outpatient Department were selected. Diabetic peripheral neuropathy was assessed by measurement of loss of protective sensation (LOPS) by monofilament test and compared with vibration perception threshold by standard biothesiometer. The sensitivity, specificity, positive predictive value and negative predictive value of monofilament test were calculated.
Results
The prevalence of diabetic peripheral neuropathy was 26%. The sensitivity, specificity, positive predictive value and negative predictive value of monofilament test were found to be 92.0%, 95.8%, 88.5% and 97.1% respectively. There was strong association between LOPS by monofilament and vibration perception threshold by biothesiometer.
Conclusion
This study showed a strong diagnostic accuracy of monofilament test to detect DPN when compared with biothesiometer. As monofilament test is a cheap, easily available, and portable, it can be used in the periphery where biothesiometer is not available.

INTRODUCTION

Diabetes Mellitus is the most common chronic disease, and is increasing rapidly throughout both the developing and industrialized world, probably as a result of changing life style. [1, 2] According to American Diabetes Association(ADA),the estimated prevalence of diabetes worldwide was around 2.8% in 2000, and is projected to be 4.4% in 2030[3]. The prevalence

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of diabetes in Nepal is 15% among people aged more than 20 years and 19% among people aged 40 years and above.[4] Also, Nepal has the highest prevalence of prediabetes among SAARC countries[5].

Diabetic peripheral neuropathy (DPN) is a significant independent risk factor for diabetic foot, which is a major cause of foot ulcers and lower extremity amputations in patients with diabetes mellitus.[6]Diabetic foot ulcers have a lifelong incidence in patients with diabetes mellitus of approximately 15% and are responsible for more than 50% of non-traumatic lower limb amputations.[7]Chronic hyperglycemia is the root of pathophysiological phenomenon leading to nerve dysfunction in the course of diabetes.[8]The prevalence of diabetic neuropathy is estimated at approximately 30-40% and even 50% several years(20-25 years) after the onset of diabetes.[9]A study in eastern Nepal reported neuropathy as the most common and frequent chronic complication(44.4%)followed by cardiovascular and retinopathy(27.7%), and nephropathy(16.6%) among diabetic patients. [10]Hence, early detection of DPN is very important to prevent diabetic foot.

Biothesiometer is considered as a gold standard for diagnosis of diabetic peripheral neuropathy which employs vibration perception threshold method. [11, 12] It has also demonstrated to detect subclinical neuropathy.[13, 14]Monofilament testing is a cheap, easy to use and portable test for assessing the loss of protective sensation to detect peripheral neuropathy.[15, 16] The 5.07/10g monofilament has been described as the best indicator to determine loss of protective sensation in three prospective studies, the monofilament test identified persons at increased risk of foot ulceration with sensitivity of 66-91%, specificity of 34-86%,positive predictive value of 18-39% and negative predictive value of 94-95%.[11, 17, 18] This study aims to find out the diagnostic accuracy of monofilament test comparing with the standard test to detect DPN.

METHODS

Study settings and patient's inclusion

This was a cross sectional study conducted in National Academy of Medical Sciences (NAMS), Bir hospital, Mahabouddha, Kathmandu from February 2016 to January 2017. Patients diagnosed with diabetes mellitus type 2 visiting Diabetes and Endocrine OPD and Medicine OPD or admitted patients of Bir hospital were included in the study. Known case of hypothyroidism, renal diseases, malignancies, HIV, leprosy, Lumbar spine disorder, Peripheral arterial disease, Vitamin B12 deficiency, Previous history of cardiovascular disorder or other central nervous system disorders, Patients on beta blocker, chemotherapy, or on other medicines to relieve neuropathy, Chronic alcohol consumer and chronic smoker were excluded. Consecutive sampling technique was used.

Sample size

The sample size was calculated using the following formula

$$n=z2p\ (1-p)/d2$$

Where, n=required sample size,

z=statistical value for a level of confidence (for 95% level of confidence, z=1.96)

p=estimated proportion in the population

d=precision or maximum tolerable error

The prevalence of diabetic neuropathy is 44.4% in Nepal [10]. Hence considering z=1.96, p=0.5(proportion of neuropathy 50%),and d=0.1(precision of 10%), total sample size of 96 was estimated.

Intervention details

All the consecutive consenting diabetic patient attending Diabetes and Endocrine OPD and Medicine OPD, Inpatient and Emergency of Bir hospital and fulfilling the criteria were selected for the study after obtaining written informed consent.10-g SWM was shown to the patient and it was applied to the patient's hand first with their eyes open so that their anxiety and fear of a painful prick was removed and the sensation of monofilament was understood. Patient was then instructed to say whether he/she could feel the pressure applied "yes" and in which foot it was applied(right/left foot) every time the monofilament stimulus was perceived. Then with the patient in supine position and with his/her eyes closed the monofilament was placed perpendicular to the skin and pressure was applied until the monofilament just buckled with a contact time of 2 seconds.[19]Monofilament was applied at 10 different site in each foot; the first, third, and fifth digits plantarly; the first, third, and fifth metatarsal heads plantarly;the plantar midfoot medially and laterally; and the plantar heel and the distal first interspaces dorsally[20].The test was repeated three times in each site and the site was considered insensate if there was two "unable to determine" or "incorrect response" for a site. Four or more imperceptible sites in each foot with "yes/no" was considered significant for identifying loss of protective sensation. [20]

Vibration perception threshold was measured in each patient by biothesiometer. The vibrating probe 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. Vibration perception threshold was then measured at the distal plantar surface of great toe of both the legs and then on base of the first, third, fifth metatarsal, plantar midfoot and finally on plantar heel. 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. The mean of six records was taken and neuropathy was diagnosed if the VPT was ≥ 25V.[19]

Data Collection: The data was collected using a structured Performa, which consists of socio-demographic characteristics, personal and medical history and the findings of monofilament and biothesiometer. The data and tests were conducted by the principal investigator.

Statistical analysis: The Data was collected, coded and entered in Excel 2010 and analyzed using Statistical Package for Social Sciences (SPSS) 20.0 version. Descriptive statistics (frequency, percentage, mean, median, and standard deviation) were used to describe the socio-demographic components and other variables. Sensitivity, specificity, positive and negative predictive value were calculated. Chi-square test was used to assess association of DPN with LOPS by monofilament test and absent ankle reflex by biothesiometer. A p-value of 0.05 was used as a cut-off point for the significance of the tests.

Ethical Approval: The study proposal was approved by the Institutional Review Board, NAMS. Data was collected after getting the written informed consent from the patient prior to the study.

RESULTS

A total of 96 patients with either diagnosed or new onset diabetes mellitus were enrolled in this study. The mean age of the participants was 55.3 years (SD 13.1) ranging from 28 to 84 years. The most common age group was more than 60 years followed by 46-60 years. 53.1% were male and 46.9% were female. Most of the participants were diabetes from 1-5 years (55.2%) followed by 6-10 years (Table 1).

Table 1: Age, gender and duration of diabetes of the study participants (n=96)

Variables	Categories	n	%
Age (years)	20-30	1	1.04
	31-45	27	28.12
	46-60	31	32.29
	>60	37	38.54
Gender	Male	51	53.1
	Female	45	46.9
Duration of DM (years)	<1	13	13.5
	1-5	53	55.2
	6-10	19	19.8
	11-15	5	5.2
	16-20	5	5.2
	>20	1	1.1

Table2. Diabetic neuropathy detected by Vibration perception threshold (>25V) by biothesiometer and loss of protective sensation (>4 imperceptible sites) by monofilament test

Diabetic peripheral neuropathy	Right Foot n(%)	Left Foot n (%)
Biothesiometer	23 (24.0)	25 (26.0)
Monofilament	26 (27.1)	26 (27.1)

The prevalence of diabetic neuropathy detected by abnormal VPT via biothesiometer was 26% (24% in right foot and 26% in left foot). Similarly , it was 27.1% (both feet) detected by LOPS via monofilament (Table 2).

Table 3: Cross tabulation of DPN detected by biothesiometer and monofilament

DPN by monofilament (LOPS>4 imperceptible sites)	DPN by biothesiometer n(%) (VPT>25 V)			p–value
	Yes	No	Total	
Yes	23 (92.0)	3 (4.2%)	26	<0.001
No	2 (8.0)	68 (95.8)	70	
Total	25	71	96	

The sensitivity and specificity of monofilament in relation to standard biothesiometer was 92%, and 95.8% respectively. Positive predictive value was 88.5% and negative predictive value 97.1%. These values were statistically significant (p<0.001).

DISCUSSION

This study found the prevalence of diabetic peripheral neuropathy among people with type 2 diabetics attending a tertiary hospital in Kathmandu, Nepal to be 26% using biothesiometer. Similar finding was reported by Ramachandran et al. in India.[21] However, other studies in India reported higher prevalence of peripheral neuropathy of 34.9% and 55.2%[22, 23].The low prevalence in our study compared to this study could be due to short duration of diabetes mellitus in majority (55.2%)of patients enrolled in our study.

Monofilament test detected neuropathy among 27.1% of the study participants, which is similar to study by Jayaprakash et al which showed prevalence of 30.1% [19] and higher prevalence was reported by William H. Herman 37%.[24]. Lesser prevalence was reported in US of 14.8%[25]

The sensitivity, specificity, positive predictive value and negative predictive value of monofilament test compare to biothesiometer in our study was 92%,95.8%,88.5% and 97.1% respectively. Another study by Yuzhe Feng et al using PubMed database searching for articles pertaining to diabetic peripheral neuropathy and Semmes Weinstein monofilament examination had sensitivity ranging from 57-93%, specificity 75-100%, positive predictive value 84-100%, negative predictive value 36-94%. [26] Lesser values were reported by other study of 36%, 92%, 80%, and 61% respectively[27] Although specificity is similar in our study compared to few study ,sensitivity is higher in our study, thereby making monofilament a high sensitive test for screening purpose for diabetic neuropathy in our context. Higher sensitivity in our study could be due to high number of symptomatic diabetic neuropathy patients enrolled.

In our study we found significant association of monofilament test with biothesiometer findings in detecting diabetic polyneuropathy ($p<0.001$). Similar association was reported by other studies conducted by Javed Ahmed Phulpoto et al in pakistan[28] , JiveshMittal [29], P. Jayaprakash et al[19] and Shaffer, S et al [27]

Standard biothesiometer is available only in sophisticated hospitals in major urban cities. Monofilament is cheap, easy to use, portable and does not require electricity or highly trained manpower and it is comparable to biothesiometer to detect diabetic peripheral neuropathy. Use of monofilament can hence be made in majorities of urban as well as rural health care settings to detect early peripheral neuropathy and thus prevent diabetic foot. Further larger studies will be needed to see if monofilament can be used as initial diagnostic tool in circumstances where biothesiometer is not available.

Potential limitation of this study was its small sample size and being tertiary hospital based, the findings could not be generalized to general population who reach to tertiary hospital late in the course of diabetes mellitus. Various risk factors for the development of diabetic neuropathy like microalbuminuria could not be assessed due to unavailability of the test during first visit and lost to follow up of the patients later. Another limitation of the study was the self-reporting of duration of diabetes by the patient without any medical records to verify the duration of diabetes which directly affect the development of neuropathy. Controls were not used to assess neuropathy in healthy individuals which could be another limitation of this study.

CONCLUSION

This study found the prevalence of diabetic peripheral neuropathy among people with type 2 diabetics attending a tertiary hospital in Kathmandu, Nepal to be 26%. This study found excellent diagnostic accuracy of monofilament in detecting diabetic peripheral neuropathy. The good clinical interchangeability between DPN assessment with monofilament test and biothesiometer and high sensitivity with high specificity shows that monofilament may be used to detect diabetic peripheral neuropathy.

REFERENCES

1. Zimmet, P., Type 2 (non-insulin-dependent) diabetes--an epidemiological overview. Diabetologia, 1982. 22(6): p. 399-411.

2. Rathmann, W. and G. Giani, Global Prevalence of Diabetes: Estimates for the Year 2000 and Projections for 2030 Response to Wild et al. Diabetes care, 2004. 27(10): p. 2568-2569.

3. Rathmann, W. and G. Giani, Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care, 2004. 27(10): p. 2568-9; author reply 2569.

4. Singh, D.L. and M.D. Bhattarai, High prevalence of diabetes and impaired fasting glycaemia in urban Nepal. Diabet Med, 2003. 20(2): p. 170-1.

5. White, F. and G. Rafique, Diabetes prevalence and projections in South Asia. Lancet, 2002. 360(9335): p. 804-5.

6. Sumpio, B.E., Foot ulcers. N Engl J Med, 2000. 343(11): p. 787-93.

7. Boulton, A.J., R.S. Kirsner, and L. Vileikyte, Neuropathic diabetic foot ulcers. New England Journal of Medicine, 2004. 351(1): p. 48-55.

8. Greene, D.A., M.J. Stevens, and E.L. Feldman, Diabetic neuropathy: scope of the syndrome. The American journal of medicine, 1999. 107(2): p. 2-8.

9. Pirart, J., Diabetes mellitus and its degenerative complications: a prospective study of 4,400 patients observed between 1947 and 1973. Diabetes care, 1978. 1(3): p. 168-188.

10. Maskey, R., et al., Diabetes mellitus related complications in out-patient clinic of tertiary care hospital. Journal of College of Medical Sciences-Nepal, 2012. 7(2): p. 9-16.

11. Pham, H., et al., Screening techniques to identify people at high risk for diabetic foot ulceration: a prospective multicenter trial. Diabetes Care, 2000. 23(5): p. 606-11.

12. Armstrong, D.G., Loss of protective sensation: a practical evidence-based definition. J Foot Ankle Surg, 1999. 38(1): p. 79-80.

13. Perkins, B.A., et al., Simple screening tests for peripheral neuropathy in the diabetes clinic. Diabetes Care, 2001. 24(2): p. 250-6.

14. Davis, E.A., et al., The use of biothesiometry to detect neuropathy in children and adolescents with IDDM. Diabetes Care, 1997. 20(9): p. 1448-53.

15. Malgrange, D., et al., Screening diabetic patients at risk for foot ulceration. A multi-centre hospital-based study in France. Diabetes & metabolism, 2003. 29(3): p. 261-268.

16. Dros, J., et al., Accuracy of monofilament testing to diagnose peripheral neuropathy: a systematic review. Ann Fam Med, 2009. 7(6): p. 555-8.

17. Boyko, E.J., et al., A prospective study of risk factors for diabetic foot ulcer. The Seattle Diabetic Foot Study. Diabetes Care, 1999. 22(7): p. 1036-42.

18. Rith-Najarian, S.J., T. Stolusky, and D.M. Gohdes, Identifying diabetic patients at high risk for lower-extremity amputation in a primary health care setting. A prospective evaluation of simple screening criteria. Diabetes Care, 1992. 15(10): p. 1386-9.

19. Jayaprakash, P., et al., Validation of bedside methods in evaluation of diabetic peripheral neuropathy. The Indian journal of medical research, 2011. 133(6): p. 645.

20. Wu, S., et al., Clinical examination of the diabetic foot and the identification of the at-risk patient, in The Diabetic Foot. 2006, Springer. p. 201-226.

21. Ramachandran, A., et al., Prevalence of vascular complications and their risk factors in type 2 diabetes. J Assoc Physicians India, 1999. 47(12): p. 1152-6.

22. George, H., et al., Foot care knowledge and practices and the prevalence of peripheral neuropathy among people with diabetes attending a secondary care rural hospital in southern India. Journal of family medicine and primary care, 2013. 2(1): p. 27.

23. Vaz, N.C., et al., Prevalence of diabetic complications in rural Goa, India. Indian journal of community medicine: official publication of Indian Association of Preventive & Social Medicine, 2011. 36(4): p. 283.

24. Herman, W.H. and L. Kennedy, Underdiagnosis of peripheral neuropathy in type 2 diabetes. Diabetes care, 2005. 28(6): p. 1480-1481.

25. Gregg, E.W., et al., Prevalence of lower-extremity disease in the US adult population≥ 40 years of age with and without diabetes: 1999–2000 national health and nutrition examination survey. Diabetes care, 2004. 27(7): p. 1591-1597.

26. Feng, Y., F.J. Schlösser, and B.E. Sumpio, The Semmes Weinstein monofilament examination as a screening tool for diabetic peripheral neuropathy. Journal of vascular surgery, 2009. 50(3): p. 675-682. e1.

27. Shaffer, S., et al., RELIABILITY AND VALIDITY OF SEMMES-WEINSTEIN MONOFILAMENT TESTING IN OLDER COMMUNITY-DWELLING ADULTS. Journal of Geriatric Physical Therapy, 2005. 28(3): p. 112-113.

28. Phulpoto, J.A., K.M. Gurbakhshani, and A. Shaikh, Role of bedside methods in evaluation of diabetic peripheral neuropathy. Rawal Medical Journal, 2012. 37(2): p. 137-141.

29. Mittal, J., et al., A comparative study of various bedside methods in detection of diabetic polyneuropathy in type 2 diabetes patients. JMEDS, 2013. 16: p. 9702-6.