



Asian Journal of **Biochemistry**

ISSN 1815-9923



Academic
Journals Inc.

www.academicjournals.com



Research Article

Diabetic Peripheral Neuropathy: Is it Underdiagnosed?

¹Rizaldy T. Pinzon, ^{1,2}M. Kes and ³Rosa De Lima R. Sanyasi

¹Bethesda Hospital, Yogyakarta, Indonesia

²Duta Wacana Christian University School of Medicine, Yogyakarta, Indonesia

³Panti Rapih Hospital, Yogyakarta, Indonesia

Abstract

Background and Objectives: Diabetic Peripheral Neuropathy (DPN) is a common complication in patients with diabetes mellitus. It often misdiagnosed or underdiagnosed. This study aimed to described the assessment of DPN among clinicians. **Materials and Methods:** A survey conducted at Bethesda Hospital and Panti Rapih Hospital, Yogyakarta, Indonesia. The survey included the questions about gender, duration of clinical practices, the frequency of handling neuropathy case per week, diagnosis of neuropathy, type of instrument or method to make a diagnosis of DPN. **Results:** Most of physicians have already assessed for the presence of neuropathy in diabetic patients routinely. About 88.3% physicians made a diagnosis of DPN through symptoms. No physicians used a monofilament to diagnosed neuropathy. Moreover, more than 90% physicians did not know how to use monofilament as an instrument to diagnose neuropathy. Other instruments such as; questionnaires, nerve conduction study and tuning-fork were also rarely used. **Conclusion:** Most of physicians have already screened for the presence of DPN among diabetic patients. However, the method used is still limited to history taking.

Key words: Diabetes mellitus, neuropathy, screening, diabetic peripheral neuropathy

Citation: Rizaldy T. Pinzon, M. Kes and Rosa De Lima R. Sanyasi, 2020. Diabetic peripheral neuropathy: Is it underdiagnosed? Asian J. Biol. Sci., 13: 168-172.

Corresponding Author: Rosa De Lima Renita Sanyasi, Panti Rapih Hospital, Yogyakarta, Indonesia Tel: +6282138730583

Copyright: © 2020 Rizaldy T. Pinzon *et al.* This is an open access article distributed under the terms of the creative commons attribution License, which permits unrestricted use, distribution and reproduction in any medium, provided the original author and source are credited.

Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Asian countries contribute to more than 60% of the world's diabetic population¹. Diabetes mellitus is common in Indonesia. The prevalence of diabetes mellitus based on diagnosis by physicians in all age in 2018 was 1.5% from all population in Indonesia. Age 55-64 was the peak age of diabetes mellitus (6.3%) and dominated by female (1.8%)².

Diabetic Peripheral Neuropathy (DPN) is a peripheral nerve dysfunction. It is a symmetric sensorimotor disturbance characterized by deficits in tactile sensitivity, vibration sense, lower-limb proprioception and kinesthesia^{3,4}. The DPN is the commonest cause of neuropathy and a common complication which can affect up to 90% of patients with diabetes mellitus^{5,6}. It causes substantial morbidity due to foot ulceration and amputation, gait disturbance and fall-related injury^{6,7}. The DPN lowers quality of life and increases health costs associated with diabetes significantly^{7,8}. Primary care practitioners are expected to better assess for and treat DPN⁹. Unfortunately, DPN is often misdiagnosed or underdiagnosed^{6,7,10,11}. Methods for DPN detection are also underutilized in primary care practice¹².

Based on these findings, it is important to examine the method of doctors in Indonesia to diagnose DPN. The main objective of this study was to describe the assessment of DPN among clinicians. The secondary objective was to identify the type of instrument or method to diagnose DPN.

MATERIALS AND METHODS

A survey performed at Bethesda Hospital and Panti Rapih Hospital, Yogyakarta, Indonesia, from May-June, 2019. The inclusion criteria of subjects were a certified physicians by Indonesian Physicians Association and working as a clinicians in daily practices. Physicians who work as a lecturer and/or researcher, who do not provide a treatment to patients would be excluded in this study. The DPN has been defined by the Toronto Consensus Panel on Diabetic Neuropathy as a "Symmetrical, length-dependent sensorimotor polyneuropathy attributable to metabolic and microvessel alterations as a result of chronic hyperglycemia exposure and cardiovascular risk covariates"¹³.

The data obtained in this study i.e., (i) Gender, (ii) Duration of clinical practices, (iii) The frequency of handling neuropathy case per week, (iv) Diagnosis of neuropathy and (v) Type of instrument or method to make a diagnosis of DPN. Duration of clinical practices classified to <5 years, 5-10 years and >10 years. The frequency of handling neuropathy case classified to no case, 5-10 cases/week, 10-20 cases/week and

>20 cases/week. Type of instrument or method to make a diagnosis of DN differed to using Nerve Conduction Study (NCS), monofilament, questionnaire and symptoms. Range of sensory symptoms in DPN may include: loss of pain sensation, tingling, "pins and needles" sensation, burning, lancinating or shooting pain (electric shocks), allodynia (painful sensation to an inoffensive stimuli), tingling and prickling sensations (paresthesias) or hyperalgesia (increased sensitivity to painful stimuli)¹³.

Other questions i.e., (i) Do you check for the presence of neuropathy in diabetic patients routinely?, (ii) Do you have a monofilament?, (iii) Can you do a monofilament test?, (iv) Do you use an ID pain, Diabetic Neuropathy Symptom (DNS) questionnaire or Diabetic Neuropathy Examination (DNE) score? and (v) Do you use a tuning fork? Each question has a yes or no answer choices. All results stated in percentage.

The NCS is an electrodiagnosis non-invasive test to measure nerve function objectively. Monofilament defined as an instrument to detect peripheral neuropathy by using 10 g Semmes-Weinstein monofilament (SWME)¹⁴. Tuning fork defined as a 128 Hz metal in "Y" shape which is used as vibration test^{15,16}. In the DNS, the patients questioned whether they have unsteadiness in walking, burning, aching pain, tenderness, prickling sensations and numbness of their legs or feet. The answer is "yes" (positive/1 point) if a symptom occurred more times a week during the last 2 weeks or "no" (negative/no point) if it did not. The maximum score is 4 points (0 point indicates the absence of polyneuropathy whereas, 1-4 point(s) indicates the presence of polyneuropathy). The DNE score consists of eight items, i.e., two testing muscle strength, one a tendon reflex and five sensations. The maximum score is 16. A score of >3 points is considered abnormal¹⁷.

RESULTS

There were 60 physicians included in this study. Those physicians consist of 52 general practitioners (86.7%) and 8 neurologist (13.3%). The subjects dominated by male (55%) (Fig. 1). Most of them have already work for less than 5 years (Fig. 2).

On their daily practice, 45% physicians handle <10 neuropathy cases/week, whereas the other 45% handle 10-20 neuropathy cases/week (Fig. 3). The DPN, radiculopathy and entrapment were the most common neuropathy diagnosis (Fig. 4).

Most of physicians (60%) have already assessed for the presence of neuropathy in diabetic patients routinely. About 88.3% physicians made a diagnosis of DPN through

Table 1: Answers of survey

Questions	Answer			
	Yes		No	
	Number	Percentage	Number	Percentage
Do you check for the presence of neuropathy in diabetic patients routinely?	36	60	24	40
Do you have a monofilament?	3	5	57	95
Can you do a monofilament test?	5	8	55	92
Do you use an ID pain, DNS or DNE test?	4	7	56	93
Do you use a tuning-fork?	1	2	59	98

DNS: Diabetic neuropathy symptom, DNE: Diabetic neuropathy examination

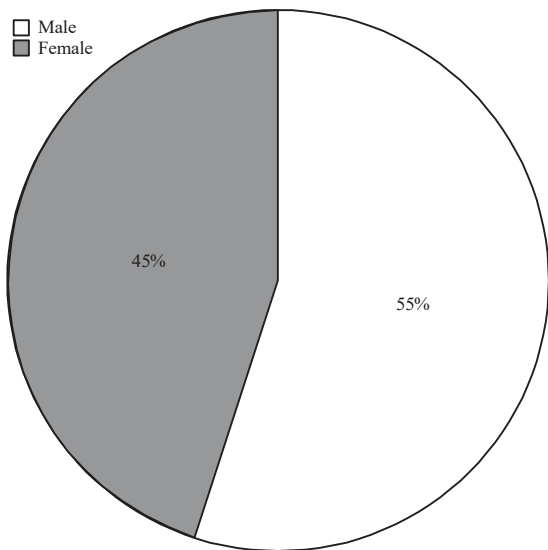


Fig. 1: Physicians gender distribution

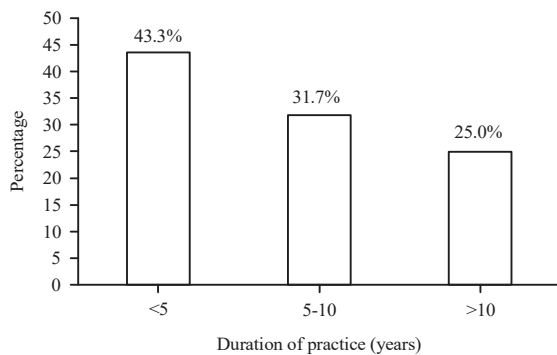


Fig. 2: Physicians duration of practice

symptoms. No physicians used a monofilament to diagnosed neuropathy. Moreover, more than 90% physicians did not know how to use monofilament as an instrument to diagnose neuropathy as shown in Table 1. Other instruments, such as; ID pain, DNS, DNE and tuning-fork were also rarely used as shown in Fig. 5.

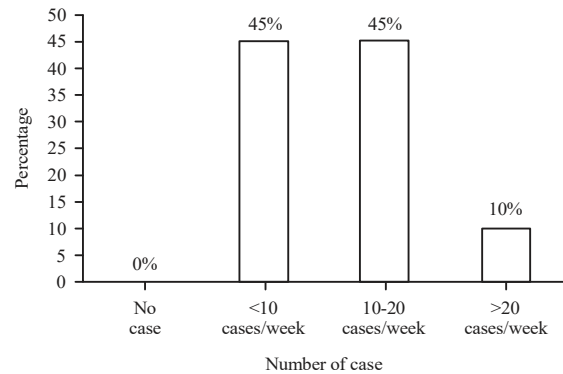


Fig. 3: Number of neuropathy case per week

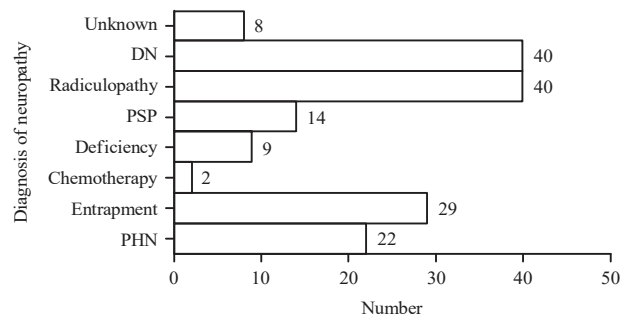


Fig. 4: Variation of neuropathy diagnosis

DN: Diabetic neuropathy, PSP: Post stroke pain, PHN: Post herpetic neuralgia

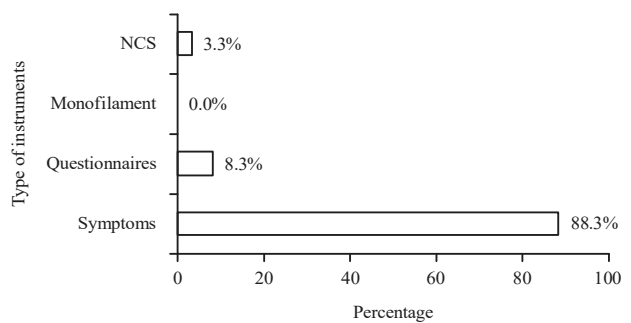


Fig. 5: Type of instrument to detect diabetic peripheral neuropathy

NCS: Nerve conduction study

DISCUSSION

This current study revealed that most of physicians have already assessed for the presence of neuropathy in diabetic patients routinely through patient's symptoms. Diabetes mellitus is a major health problem in Indonesia¹⁸. The DN is the most frequent complication in diabetes mellitus patients in Indonesia (13-78%)¹⁹. It was the fourth leading type of neuropathy from all cases in Indonesia (9.6%)²⁰.

In the present study, the subjects dominated by general practitioners. About 60% from all subjects have already assessed for the presence of DPN in diabetic patients routinely. This number was expected to be higher due to the high prevalence of DPN in Indonesia. Since, Indonesian health care system focused in the primary care, general practitioners play an important role in diagnosis of DPN. General practitioners are expected to increase their skill and knowledge to be able to diagnose DPN precisely. Therefore, the morbidity and mortality caused by DPN can be decreased

Based on the result of this study, 88.3% physicians made a diagnosis of DPN through symptoms such as; loss of pain sensation, tingling, "pins and needles" sensation, burning, lancinating or shooting pain, allodynia, tingling and prickling sensations or hyperalgesia. These typical symptoms of DPN occur symmetrical, distal to proximal, in "stocking-glove" pattern¹⁵. It is sufficient to made DPN diagnosis based on the clinical presentation or the presence of these typical symptoms and may not require additional evaluation or referral^{15,21}. Unfortunately, estimated up to half of patients with DPN may be asymptomatic for a period of time^{15,22}. In this case, further examination using various instruments is important.

In this study, there was no physicians using a monofilament to diagnose DPN. Moreover, 92% physicians did not know how to use monofilament as an instrument to diagnose DPN. Monofilament is a simple, effective and inexpensive device for screening or early detection of DPN even though monofilament is a cheap and easy to use, this instrument is rarely used. This statement supported by previous studies by Baraz *et al.*²³ and Brown *et al.*²⁴. However, a systematic review and meta-analysis concluded that monofilament tests had limited sensitivity for screening DPN²⁵.

From 60 physicians, there was only 1 physician (2%), who use tuning fork as an instrument to detect DPN. The 128 Hz tuning fork is useful to test vibratory sensation^{14,16}. In the study by Sobhy⁹, vibration test is more complex and less feasible for regular use in primary care. The monofilament was shown to be both accurate and feasible to implement in primary care.

The use of both tools will be better because some DPN patients have small myelinated and unmyelinated fibers dysfunction, that convey sensations of light touch, pain and temperature, while other patients may have large fibers dysfunction, that are responsible for vibratory sensation and joint position sense²⁶.

The NCS is a non-invasive electrodiagnostic to measure peripheral nerve function, both motor and sensory nerves. It provides a higher level of specificity and sensitivity. The advantage of NCS compared to other instruments is the objectivity and reliability^{14,21}. However, it required special equipment and only assesses large fiber²¹. It also need a special skill to use NCS. In this study, only 3.3% physicians were used NCS to detect DPN.

Evaluation of neuropathic symptoms and signs using validated questionnaires is better than those that does not²¹. There are many questionnaires to detect DPN such as; ID pain, DNS, DNE, Michigan Neuropathy Screening Instrument (MNSI), Total Symptom Score (TSS), Leeds Assessment of Neuropathic Symptoms and Signs (LANSS), Neuropathic Pain Questionnaire (NPQ) and Toronto Clinical Neuropathy Score (TCNS) etc. These questionnaires are inexpensive, fast and easy to perform in clinical practice to detect DPN early. The limitation of using questionnaires i.e., it is subjective and depend on the subject's cooperation and response. It also has a limited sensitivity and has to be used along with other investigations^{17,21}. In this study, it only 8.3% physicians who use questionnaires to diagnose DPN.

CONCLUSION

Most of physicians have already screened for the presence of DPN among diabetic patients. However, the method used is still limited to history taking. Examination using a validated questionnaire and other tools is required to improve the accuracy of DPN diagnosis. An accurate diagnosis may lead to a proper treatment. Therefore, the morbidity and mortality due to DPN can be reduced. Physicians, especially general practitioners are expected to be more careful in examining patients with diabetes.

SIGNIFICANCE STATEMENT

This study discover the lack of use of instruments that can be beneficial for diagnose DPN in daily practice. This study will help to raise awareness of the physicians to use an instrument to diagnose DPN. The use of standardized instrument such as; monofilament, tuning fork and questionnaires, may improve the accuracy of diagnosis.

REFERENCES

1. Ramachandran, A., C. Snehalatha, A.S. Shetty and A. Nanditha, 2012. Trends in prevalence of diabetes in Asian countries. *World J. Diabetes*, 3: 110-117.
2. Ministry of Health, 2013. Riset Kesehatan Dasar 2013. Ministry of Health Republic of Indonesia, Jakarta.
3. Yoo, M., N. Sharma, M. Pasnoor and P.M. Kluding, 2013. Painful diabetic peripheral neuropathy: Presentations, mechanisms and exercise therapy. *J. Diabetes Metab., Suppl.* 10. 10.4172/2155-6156.S10-005.
4. Cohen, K., N. Shinkazh, J. Frank, I. Israel and C. Fellner, 2015. Pharmacological treatment of diabetic peripheral neuropathy. *Pharmacy Ther.*, 40: 372, 375-388.
5. Cheong, J., K. Alexiadou and S. Devendra, 2017. Absent monofilament sensation in a type 2 diabetic feet. *Lond. J. Primary Care*, 9: 73-76.
6. Iqbal, Z., S. Azmi, R. Yadav, M. Ferdousi and M. Kumar *et al*, 2018. Diabetic peripheral neuropathy: Epidemiology, diagnosis and pharmacotherapy. *Clin. Ther.*, 40: 828-849.
7. Juster-Switlyk, K. and A.G. Smith, 2016. Updates in diabetic peripheral neuropathy. Version 1. *F1000Res.*, Vol. 5: F1000 Faculty Rev-738. 10.12688/f1000research.7898.1.
8. Dobrota, V.D., P. Hrabac, D. Skegro, R. Smiljanic and S. Dobrota *et al*, 2014. The impact of neuropathic pain and other comorbidities on the quality of life in patients with diabetes. *Health Qual. Life Outcomes*, Vol. 12, No. 1. 10.1186/s12955-014-0171-7.
9. Sobhy, T., 2016. The need for improved management of painful diabetic neuropathy in primary care. *Pain Res. Manage.*, Vol. 2016. 10.1155/2016/1974863.
10. Adams, A.S., M.M. Parker, H.H. Moffet, M. Jaffe and D. Schillinger *et al*, 2016. Communication barriers and the clinical recognition of diabetic peripheral neuropathy in a diverse cohort of adults: The DISTANCE study. *J. Health Commun.*, 21: 544-553.
11. Almuhanadi, H., G. Ponirakis, A. Khan and R.A. Malik, 2018. Diabetic neuropathy and painful diabetic neuropathy: Cinderella complications in South East Asia. *J. Pak. Med. Assoc.*, 68: 85-89.
12. Park, J.H. and D.S. Kim, 2018. The necessity of the simple tests for diabetic peripheral neuropathy in type 2 diabetes mellitus patients without neuropathic symptoms in clinical practice. *Diabetes Metab. J.*, 42: 442-446.
13. Tesfaye, S. and D. Selvarajah, 2012. Advances in the epidemiology, pathogenesis and management of diabetic peripheral neuropathy. *Diabetes Metab. Res. Rev.*, 28: 8-14.
14. Yang, Z., Y. Zhang, R. Chen, Y. Huang and L. Ji *et al*, 2018. Simple tests to screen for diabetic peripheral neuropathy. *Cochrane Database Syst. Rev.*, Vol. 2018, No. 7. 10.1002/14651858.CD010975.pub2.
15. Ang, L., N. Cowdin, K. Mizokami-Stout and R. Pop-Busui, 2018. Update on the management of diabetic neuropathy. *Diabetes Spectr.*, 31: 224-233.
16. Jayaprakash, P., A. Bhansali, S. Bhansali, P. Dutta, R. Anantharaman, G. Shanmugasundar and M. Ravikiran, 2011. Validation of bedside methods in evaluation of diabetic peripheral neuropathy. *Indian J. Med. Res.*, 133: 645-649.
17. Gogia, S. and C.R. Rao, 2017. Prevalence and risk factors for peripheral neuropathy among type 2 diabetes mellitus patients at a tertiary care hospital in coastal Karnataka. *Indian J. Endocrinol. Metab.*, 21: 665-669.
18. Ligita, T., K. Wicking, K. Francis, N. Harvey and I. Nurjannah, 2019. How people living with diabetes in Indonesia learn about their disease: A grounded theory study. *PloS One*, Vol. 14, No. 2. 10.1371/journal.pone.0212019.
19. Soewondo, P., A. Ferrario and D.L. Tahapary, 2013. Challenges in diabetes management in Indonesia: A literature review. *Globalization Health*, Vol. 9, No. 1. 10.1186/1744-8603-9-63.
20. Purwata, T.E., H.A. Sadeli, Y. Yuneldi, D. Amir and C. Asnawi *et al*, 2015. Characteristics of neuropathic pain in Indonesia: A hospital based national clinical survey. *Neurol. Asia*, 20: 389-394.
21. Petropoulos, I.N., G. Ponirakis, A. Khan, H. Almuhanadi, H. Gad and R.A. Malik, 2018. Diagnosing diabetic neuropathy: Something old, something new. *Diabetes Metab. J.*, 42: 255-269.
22. Won, J.C. and T.S. Park, 2016. Recent advances in diagnostic strategies for diabetic peripheral neuropathy. *Endocrinol. Metab.*, 31: 230-238.
23. Baraz, S., K. Zarea, H.B. Shahbazian and S.M. Latifi, 2014. Comparison of the accuracy of monofilament testing at various points of feet in peripheral diabetic neuropathy screening. *J. Diabetes Metab. Disord.*, Vol. 13, No. 1. 10.1186/2251-6581-13-19.
24. Brown, J.J., S.L. Pribesh, K.G. Baskette, A.I. Vinik and S.R. Colberg, 2017. A comparison of screening tools for the early detection of peripheral neuropathy in adults with and without type 2 diabetes. *J. Diabetes Res.*, Vol. 2017. 10.1155/2017/1467213.
25. Wang, F., J. Zhang, J. Yu, S. Liu and R. Zhang *et al*, 2017. Diagnostic accuracy of monofilament tests for detecting diabetic peripheral neuropathy: A systematic review and meta-analysis. *J. Diabetes Res.*, Vol. 2017. 10.1155/2017/8787261.
26. Russell, J.W. and L.A. Zilliox, 2014. Diabetic neuropathies. *Peripheral Nervous Syst. Disord.*, 20: 1226-1240.