

# Prevalence and Determinants of Diabetic Peripheral Neuropathy/Foot Syndrome in a rural population of North India

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## Research Article

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# Abstract

**Background** Diabetic peripheral neuropathy (DPN), a common and troublesome complication in patients with type 2 diabetes mellitus (T2DM), contributes to a higher risk of diabetic foot ulcer and lower limb amputation. These situations can negatively impact the quality of life of affected individuals.

**Objectives** The study aimed to assess prevalence of DPN in patients of type 2 DM from rural North India and associated risk factors.

**Methods** A facility based cross sectional study was carried out among type 2 diabetic patients attending NCD clinic of a secondary care hospital in rural North India. A questionnaire which included socio-demographic details, clinical and laboratory parameters, and the Michigan Neuropathy Screening Instrument (MNSI) for detecting peripheral neuropathy, was administered to 100 consecutive patients. Statistical Package for Social Sciences (SPSS) version 25.0 was used for entering and analyzing data. Bivariate analysis was performed for determining the factors significantly associated with presence of DPN.

**Results** The prevalence of DPN was 42.0%. Male gender, advancing age ( $\geq 60$  years), longer duration of diabetes ( $>10$  years), smoking, physical inactivity, obesity, uncontrolled blood pressure, poor A glycaemic control and altered lipid profile were found to be significantly associated with the presence of DPN.

**Conclusion** Prevalence of DPN among type 2 diabetics from rural north India is alarmingly high. There is need of essential screening of all diabetic patients by their primary care provider for early detection of DPN particularly in rural India.

## Introduction

Diabetes mellitus is a major public health problem with rising prevalence worldwide and in the year 2018, approximately 415 million people were known to have diabetes. This estimate is expected to increase to 642 million of the population by 2040 [1]. Further, it is the 6th leading cause of death overall [2], attributing to 5 million deaths globally in 2017. According to recent estimates, 69.2 million people are affected with diabetes in India [1].

Along with the raising prevalence of diabetes, an increase in its complications is also expected. Diabetes along with its complications is expected to result in increasing morbidity, mortality, and health expenditure due to the requirement of specialized care [3].

Diabetic foot is one of the most significant and devastating complication of diabetes and is defined as a group of syndromes in which neuropathy, ischemia and infection lead to tissue breakdown, and possible amputation [4]. Around 15% of diabetic patients will develop foot ulcers in their lifetime and this is known to precede amputation in 85% of the cases [5]. Every 20 seconds a lower limb is lost to diabetes in the world and it is the most common cause of non-traumatic lower limb amputation [6]. It is estimated that

approximately 45,000 lower limbs are amputated every year in India and the vast majority of these are probably preventable [5].

Prevention of diabetic foot ulceration is critical to reduce the associated high morbidity and mortality rates, and the danger of amputation. A number of contributory factors work together to cause foot ulceration in patients with diabetes. These include peripheral neuropathy; mechanical stress and peripheral vascular disease [7]. Since its development, it became imperatively important to diagnose Diabetic Peripheral Neuropathy (DPN) as early as possible in order to prevent amputations, disability and improve the quality of life [8].

Regular comprehensive foot examination, patient education on foot care like simple hygienic practices, provision of appropriate footwear, and prompt treatment of minor injuries and a multi-disciplinary team approach can decrease ulcer occurrence by 50% and amputations by up to 85% [3],[9].

Identification of diabetics with peripheral neuropathy and its associated factors is the key to reduce further complications and to have baseline information to initiate appropriate interventions. There is a dearth of community-based studies particularly from rural settings of India, which assessed the prevalence of diabetic foot and its associated risk factors among diabetics. Hence the present study was planned to find the prevalence of diabetic peripheral neuropathy (DPN) and its associated risk factors in a rural secondary care setting of North India.

## **Research questions**

1. What is the prevalence of peripheral neuropathy (DPN) among diabetics from rural population of North India?
2. What are the modifiable and non-modifiable factors risk factors for development of DPN/ foot syndrome among the rural population of North India?

## **Materials And Methods**

### *Study design & Settings*

This cross-sectional observational study was conducted at Civil Hospital, Naraingarh, a secondary level rural hospital attached to Community Medicine Department of PGIMER, a tertiary care medical & research Institute of North India from October to December 2018. The NCD clinic at the hospital run by resident doctors of Community Medicine under guidance of a faculty receives patients from Naraingarh and its nearby blocks which are rural in nature and caters a population of about 100,000 population. The aim of the hospital is to provide good quality health care that is easily accessible, affordable, and culturally acceptable, and to serve as a model for training post-graduates in community medicine and family medicine. Average general out-patient department (OPD) attendance of the clinic, including new and revisits, is around 100 per day.

### *Study population and Sample size*

All cases of type 2 diabetes as per World Health organization's criteria diagnosed for at least six months of duration constituted the study population. Those with cognitive impairment and obvious disability that could affect the functions of the nervous system affect independent self-care behavior, and those who had undergone amputations of the lower limbs were excluded from the study.

According to a previous study done by George H et al. [10] from Southern India, the prevalence of peripheral neuropathy among people with diabetes was reported to be 47%. Thus, at confidence interval of 95% and 80% power with 10% precision on prevalence of 47%, sample size of 96 subjects was obtained. However, a total of 100 consecutive patients who were eligible and giving consent would be enrolled in the study.

### *Study tools*

All the enrolled patients of type 2 DM were administered a semi-structured questionnaire developed by the investigators. The first part of the questionnaire consisted data on socio-demographic details, history of diabetes mellitus including treatment details and associated risk factors for development of diabetic foot including dietary habits, physical activity, tobacco use and alcohol consumption, anthropometric details (height, weight, waist circumference, BMI), associated co-morbidities such as hypertension and dyslipidemia and laboratory parameters to assess Glycaemic control status such as FBS and HBA1C levels. The second part of the questionnaire assessed peripheral neuropathy by Michigan Neuropathy Screening Instrument (MNSI) [11], a simple and validated screening tool for diabetic peripheral neuropathy (DPN). The MNSI is designed to be used in an outpatient setting by primary care or other providers. It consists of two steps, the history questionnaire, and the physical assessment. The history questionnaire assesses the presence of neuropathic symptoms. This part consists of 15 items, (13) items assessed symptoms of DPN, item number (4) assessed peripheral vascular disease (PVD), and item number (10) assessed general asthenia. The score ranges from 0 to 13 points and a score that is  $\geq 7$  indicates the presence of neuropathic symptoms. The second part of the MNSI is a brief physical examination involving 1) inspection of the feet for deformities, dry skin, hair or nail abnormalities, callous, or infection; 2) semi-quantitative assessment of vibration sensation at the dorsum of the great toe; 3) grading of ankle reflexes; and 4) monofilament testing. Patients screening positive on the clinical portion of the MNSI (greater than or equal to 2.5 points on a 10-point scale) were considered to have peripheral neuropathy and were considered as having high risk feet. The physical assessment was performed by one of the investigators who was trained in performing it.

The subjects found to be having foot problems were classified according to The International Working Group on Diabetic Foot (IWGDF) Risk Classification System.[12] Health education regarding foot care practices was imparted to all subjects. Subjects found to be in category 1 or 2 were managed at the health facility and subjects with category 3 risk were referred to department of endocrinology, PGIMER, Chandigarh.

### *Statistical analysis*

The collected data was tabulated and analyzed using software SPSS (Statistical Package for Social Sciences) V.18.0 for windows. The data was cross checked for data entry errors. Findings were described in terms of proportions and their 95% confidence intervals. Continuous data were summarized using mean, and

standard deviation or median and inter quartile range depending on skewness of data. Chi-square test was applied to find the association and  $p$ -value  $< 0.05$  was considered statistically significant.

### *Ethical considerations*

The study did not involve any potential risks to the participants. The participants were screened for peripheral neuropathy through a non-invasive screening instrument and the screening helped in its timely diagnosis and management so as to prevent patients from developing diabetic foot ulcers and amputation and help in improving their quality of life. The data collected from the participants were kept confidential, and the study protocol was approved from Institute Ethical Committee (IEC), PGIMER, Chandigarh (Vide letter No. PGI/IEC/233/18).

## **Results**

The study included a total of 100 consecutive type 2 diabetic patients aged from 31 to 85 years with a mean age of 59.76 years (SD = 19.82) attending the NCD clinic. More than half (58.0%) of the participants were females, 41.0% were unemployed/retired and 73.0% were found to be physically inactive. The mean BMI of study participants were 33.2 kg/m<sup>2</sup> (SD = 7.63). The mean duration of diabetes was 9.24 years, almost half of participants were having diabetes for more than 10 years and only 34.0% were having controlled diabetes. Microvascular complications in the form of retinopathy and nephropathy were present in 6.0 and 12.0%, respectively. The majority (56.0%) of study subjects were having dyslipidemia and. Moreover, 24.0% and 78.0% were having cardiovascular disease and uncontrolled blood pressure, respectively (Table 1).

### **Table 1- Socio-demographic, clinical & laboratory characteristics of the study participants and their association with presence of DPN(N=100)**

Variables	Neuropathy status			X <sup>2</sup> , p-value
	DPN present(n=42)	DPN Absent(n=58)	Total	
<i>Sex</i>				
Male	24(57.1)	18(42.9)	42(100)	6.82, 0.009*
Female	18(37.9)	40(62.1)	58(100)	
<i>Age (in years)</i>				
<60	16(30.8)	36(69.2)	52(100)	5.62, 0.01*
≥60	26(54.1)	22(45.9)	48(100)	
<i>Marital status</i>				
Married	28 (45.2)	34 (54.8)	62(100)	0.66, 0.41
Unmarried/widowed/divorced/separated	14 (36.8)	24 (63.2)	38(100)	
<i>Education level</i>				
Illiterate	12(57.1)	9(42.9)	21(100)	2.50, 0.11
Literate	30(37.9)	49(62.1)	79(100)	
<i>Employment status</i>				
Unemployed/retired	20(48.8)	21(51.2)	41(100)	1.31, 0.25
Employed	22(37.3)	37(62.7)	59(100)	
<i>Monthly family income (in INR)</i>				
≤10,000	28(46.7)	32(53.3)	60(100)	1.34, 0.24
>10,000	14(35.0)	26(65.0)	40(100)	
<i>Duration of DM (in years)</i>				
≤10	16(27.1)	43(66.1)	59(100)	13.08, 0.0002*
>10	26(63.4)	15(36.6)	41(100)	
<i>Family history of DM</i>				

Present	18(47.4)	20(52.6)	38(100)	0.72, 0.39
Absent	24(38.7)	38(61.3)	62(100)	
<i>Smoking</i>				
Yes	22(61.1)	14(38.9)	36(100)	8.43, 0.003*
No	20(31.3)	44(68.7)	64(100)	
<i>Alcohol intake</i>				
Yes	14(50.0)	14(50.0)	28(100)	1.02, 0.31
No	28(38.8)	44(61.2)	72(100)	
<i>Regular Physical activity</i>				
Present	06(22.2)	21(77.8)	27(100)	5.93, 0.01*
Absent	36(49.3)	37(50.7)	73(100)	
<i>BMI categories</i>				
Normal	04(16.7)	20(83.3)	24(100)	8.32, 0.003*
Overweight/Obese	38(50.0)	38(50.0)	76(100)	
<i>Central Obesity</i>				
Present	34(51.5)	32(48.5)	66(100)	7.21, 0.007*
Absent	08(23.5)	26(76.5)	34(100)	
<i>Blood pressure</i>				
Controlled	06(21.4)	22(78.6)	28(100)	6.75, 0.009*
Uncontrolled	36(50.0)	36(50.0)	72(100)	
<i>Glycaemic control (based on HBA1c)</i>				
Adequate (<7 %)	08(23.5)	26(76.5)	34(100)	7.21, 0.007*
Poor (≥ 7%)	34(51.5)	32(48.5)	66(100)	
<i>Dyslipidemia</i>				
Present	30(53.7)	26(46.3)	56(100)	

Absent	12(27.3)	32(62.7)	44(100)	6.99, 0.008*
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### Prevalence of DPN

The overall prevalence of DPN among study participants based on MNSI score was 42.0% (Table-2). Based on MNSI assessment, 46.0 and 42.0% of study participants had a score of  $\geq 7$  in the history questionnaire and a score of  $\geq 2.5$  in the physical examination section of the MNSI, respectively. Of those detected with DPN on basis of cut off score of 2.5 on physical assessment (42 patients), 97.6% had a score of  $\geq 7$  in the history questionnaire of the MNSI whereas out of 46 patients scoring  $\geq 7$  in the history questionnaire, 89.1% had a score of 2.5 or above on physical assessment.

The history questionnaire of the MNSI assessment showed that most of the participants had at least one symptom of the DPN. The most frequently reported symptoms in DPN patients were numbness and pain with walking which was present in 81.0 and 74.0% of study participants, respectively while, the least reported symptoms were history of one or more toes amputation and loss of sensation in legs/feet while walking which was present in 3.0 and 16.0% of patients, respectively (Table 2).

**Table 2- Scores of the patients based on history and physical assessment by MNSI questionnaire (N=100)**

Scores		Frequency(n)	Percentage (%)
A. Based on History (out of 13)	<7		
	$\geq 7$	54	54.0
		46	<b>46.0</b>
B. Based on Physical assessment (out of 10)	<2.5	58	58.0
	$\geq 2.5$	42	<b>42.0</b>

**Table 3- Responses to MNSI questionnaire in patients with type 2 DM (n =100)**

<b>A. History questionnaire</b>		
<i>Sl. No.</i>	<i>Symptoms</i>	<i>Nos. answering in yes N (%)</i>
1	Are your legs and/or feet numb?	81(81.0)
2	Do you ever have burning pain in your legs/feet?	72(72.0)
3	Are your feet too sensitive to touch?	34(34.0)
4	Do you get muscle cramps in your legs and/or feet?	42(42.0)
5.	Do you have prickling feelings in your legs/feet?	62(62.0)
6.	Does it hurt when the bed covers touch your legs/feet?	25(25.0)
7.	You cannot differentiate hot water from cold water in the tub/shower?	12(12.0)
8.	Have you ever had open sore on your foot?	22(21.0)
9.	Has your doctor ever told you that you have neuropathy?	34(44.0)
10.	Do you feel weak all over most of the time?	46(46.0)
11.	Are your symptoms worse at night?	68(68.0)
12.	Do your legs/feet hurt when you walk?	74(74.0)
13.	You are not able to sense your legs/feet when you walk?	9(9.0)
14.	Is the skin on your legs/feet so dry that it cracks open?	24(24.0)
15.	Have you had an amputation?	2(2.0)
<b>B. Physical assessment</b>		<b>Present in</b>
		<b>Present in</b>

		<b>Right foot N (%)</b>	<b>Left foot N (%)</b>
<b>1.</b>	Abnormal appearance of feet	76(76.0)	76(76.0)
<b>2.</b>	Ulceration	12(12.0)	11(10.0)
<b>3.</b>	Ankle reflexes abnormality	48(48.0)	51(51.0)
<b>4.</b>	Vibration perception abnormality	64(64.0)	64(64.0)
<b>5.</b>	Monofilament test abnormality	62(72.0)	61(71.0)

## Discussion

About 42.0% of diabetic patients were found to be suffering from peripheral neuropathy. This was similar to the findings of other studies on diabetic peripheral neuropathy (DPN) [10],[13-16]. However, this was in contrast to the findings of Kaewput et al.[17] and Perrin et al.[18] in which prevalence ranged from 3.0% to 16.6%. The possible reasons for this variation could be different study settings and different classification used to diagnose DPN in these studies. The prevalence of DPN found in present study was lower as compared to study conducted by Yang Q et al.[19] and Qin L et al.[20] in which prevalence of DPN was close to 71.0% and 80.0% respectively due to the similar reason as they used Neuropathy symptom score (NSS) and Neuropathy disability score (NDS) to assess DPN in their study population. High prevalence of DPN is a matter of concern for clinicians and public health specialists working with diabetic patients as this may lead to ulceration, amputation, life-long disability, and poor quality of life [21]. DPN can also increase the risks of future cardiovascular events and associated mortality [22].

In the present study, it was found that prevalence of DPN was significantly higher among males than females. This was similar to the results of some other studies [15],[17], but different from the findings of Sendi RA et al. [14] who observed no gender difference in DPN prevalence. The higher prevalence of DPN among males could be due to the fact that health seeking behavior among women is poor in most of the developing countries, hence lesser chances of being detected, especially in rural areas.

Being older was found to be significantly associated with DPN. This was in line with the observations of other authors [14],[15],[20]. As age advances, nerve function deteriorates, even in absence of DM. With increasing life expectancy, the population of elderly is bound to increase due to demographic transition and prevalence of non-communicable diseases is also on rise as a result of epidemiological transition happening in India. Their concurrent occurrence complicated by complications of NCDs like diabetes is worrisome.

The prevalence of DPN was also found to be higher among DM patients who were having diabetes for more than 10 years. This was in line with results of previous studies [13],[14],[17],[20]. As the duration of DM increases, the risk of complications advances and this accelerates if the glycemic control is also poor. This

was supported by the findings of the present study in which patients with poor glycemic control were found to have higher prevalence of DPN, similar to findings by other studies [10],[14],[15],[20],[23].

Smoking was also found to be associated with DPN with higher percentage of smokers having DPN compared to non-smokers. This was similar to the findings of study by Van der Velde et al. [23] in which smoking was found to be associated with reduced nerve function. Smoking causes atherosclerosis, elevates blood pressure, and causes nerve injury due to inflammation which collectively leads to impaired nerve functioning.

Uncontrolled blood pressure and dyslipidemia were found to be more prevalent in diabetic patients suffering from DPN. This was similar to findings from other studies [14],[15]. In another study, DPN was found to be associated with elevation of systolic blood pressure and problems in management of hypertension among patients with type 2 DM [24]. This finding needs further exploration as exact mechanism behind co-existence of DPN and uncontrolled blood pressure is still not completely known. The cause-effect studies could help in better understanding of this interaction.

Obesity was another modifiable factor which was found to be associated with DPN in present study. This was in line with findings of other studies conducted globally [15]. DPN originating among DM patients can not solely be attributed to increased blood sugar level, but to complex interplay of increasing age, deranged lipid profile, obesity, and hypertension [25].

## Conclusion

Prevalence of Diabetic peripheral neuropathy (DPN) is alarmingly high among patients with T2DM from rural Northern India. Early detection and appropriate intervention are mandatory among patients with male gender, long standing DM, higher BMI, Central obesity, advancing age, having dyslipidemia, uncontrolled hypertension, and poor glycemic control. There is need of essential screening for early detection for neuropathic complications in patients of type 2 diabetes at primary and secondary level of care

## Declarations

**Compliance with Ethical standards** Approval was sought from the Institutional Ethics Committee of Postgraduate Institute of Medical Sciences & Research before commencement of the study. During the study, informed written consent was taken from all participants after clearly explaining the study objectives in a language known to them. If the participant was unable to read/write, the informed consent was taken from a Legally Authorized representative or next of kin.

*Ethical approval & Informed consent* Prior to the commencement of the study, the study protocol was submitted for approval to the Institutional Ethics Committee (IEC) of Postgraduate Institute of Medical Sciences & Research, Chandigarh. Thereafter, permission was obtained from the Senior Medical Officer of the concerned hospital for conduction of the study. Study objectives were clearly explained to the

participants in a language familiar to them. Anonymity and discretion of the information given by the patients were maintained with utmost care and a written informed consent was obtained from the participants

*Disclosure of potential conflicts of interest* The authors declare that they have no competing interests.

## References

1. Diabetes Atlas. International Diabetes Federation, Brussels. 2017. <https://www.idf.org/e-library/epidemiology-research/diabetes-atlas.html>. Accessed 10 November 2018.
2. Top 10 causes of death. World Health Organization 2017 <http://www.who.int/mediacentre/factsheets/fs310/en/> . Accessed 10 November 2018.
3. Alexiadou K, Doupis J. Management of Diabetic Foot Ulcers. *Diabetes Ther.* 2012; 3:4.
4. Forlee M. What is the diabetic foot? The rising prevalence of diabetes worldwide will mean an increasing prevalence of complications such as those of the extremities. *Continuing Medical Education.* 2010; 28:152–156.
5. Jain AKC, Vishwanath S. Studying major amputations in a developing country using Amit Jain's typing and scoring system for diabetic foot complications - time for standardization of diabetic foot practice. *Int Surg J.* 2015; 2:26–30.
6. The International Working Group on the Diabetic Foot 2017. <http://iwgdf.org/> Accessed 10 November 2018.
7. Katsilambros N, Dounis E, Makrilakis K, Tentolouris N, Tsapogas P. Atlas of the diabetic foot. John Wiley & Sons.
8. Scale DE. Michigan Diabetes Research and Training Center. Online. [https://diabetesresearch.med.umich.edu/Tools\\_SurveyInstruments.php](https://diabetesresearch.med.umich.edu/Tools_SurveyInstruments.php). [Accessed 22 Jan 2018].
9. Bakkar K, Foster A, Houtum WV, Riley P. Diabetes and Foot Care: Time to act. 4<sup>th</sup> Netherlands. 2005.
10. George H, Rakesh PS, Krishna M, Alex R, Abraham VJ, George K, Prasad JH. Foot care knowledge and practices and the prevalence of peripheral neuropathy among people with diabetes attending a secondary care rural hospital in southern India. *J Fam Med Primary Care.* 2013;2(1):27–32.
11. University of Michigan. How to Use the Michigan Neuropathy Screening Instrument. Michigan. [http://diabetesresearch.med.umich.edu/peripherals/profs/documents/svi/MNSI\\_howto.pdf](http://diabetesresearch.med.umich.edu/peripherals/profs/documents/svi/MNSI_howto.pdf). Accessed on [10 November 2018].
12. Bus SA, Netten JJ, Lavery LA, Monteiro-Soares M, Rasmussen A, Jubiz Y, Price PE. IWGDF guidance on the prevention of foot ulcers in at-risk patients with diabetes. *Diabetes Metab Res Rev.* 2016; 32:16–24.
13. Sun J, Wang Y, Zhang X, Zhu S, He H. Prevalence of peripheral neuropathy in patients with diabetes: A systematic review and meta-analysis. *Prim Care Diabetes* [Internet]. 2020; Available from: <https://doi.org/10.1016/j.pcd.2019.12.005>
14. Sendi RA, Mahrus AM, Saeed RM, Mohammed MA, Al-Dubai SAR. Diabetic peripheral neuropathy among Saudi diabetic patients: A multicenter cross-sectional study at primary health care setting. *J Family Med Prim Care.* 2020;9(1):197-201.

15. Braffett BH, Gubitosi-Klug RA, Albers JW, Feldman EL, Martin CL, White NH, et al. Risk factors for diabetic peripheral neuropathy and cardiovascular autonomic neuropathy in the Diabetes Control and Complications Trial/Epidemiology of Diabetes interventions and Complications (DCCT/EDIC) study. 2020;69(5):1000–1010.
16. Shiferaw WS, Akalu TY, Work Y, Aynalem YA. Prevalence of diabetic peripheral neuropathy in Africa: A systematic review and meta-analysis. *BMC Endocr Disord.* 2020;20(1):1–9.
17. Perrin BM, Allen P, Gardner MJ, Chappell A, Phillips B, Massey C, et al. The foot-health of people with diabetes in regional and rural Australia: Baseline results from an observational cohort study. *J Foot Ankle Res.* 2019;12(1):1–9.
18. Kaewput W, Thongprayoon C, Rangsin R, Jindarat S, Narindrarangkura P, Bathini T, et al. The Association between Serum Uric Acid and Peripheral Neuropathy in Patients with Type 2 Diabetes Mellitus: A Multicenter Nationwide CrossSectional Study. *Korean J Fam Med.* 2020;41(3):189–194.
19. Yang Q, Zhang Y, Zeng Q, Yang C, Shi J, Zhang C, et al. Correlation between diabetic peripheral neuropathy and sarcopenia in patients with type 2 diabetes mellitus and diabetic foot disease: A cross-sectional study. *Diabetes, Metab Syndr Obes Targets Ther.* 2020;13:377–86.
20. Qin L, Niu JY, Zhou JY, Zhang QJ, Zhou F, Zhang N, et al. Prevalence and Risk Factors of Diabetic Peripheral Neuropathy in Chinese Communities. *Zhonghua Liu Xing Bing Xue Za Zhi.* 2019;40(12):1578–1584.
21. Pop-Busui R, Boulton AJ, Feldman EL, Bril V, Freeman R, Malik RA, et al. Diabetic neuropathy: a position statement by the American Diabetes Association. *Diabetes Care* 2017;40(1):136-154.
22. Barrett EJ, Liu Z, Khamaisi M, King GL, Klein R, Klein BEK, et al. Diabetic microvascular disease: an endocrine society scientific statement. *J Clin Endocrinol Metab* 2017;102(12):4343-4410.
23. van der Velde JHPM, Koster A, Strotmeyer ES, et al. Cardiometabolic risk factors as determinants of peripheral nerve function: the Maastricht Study. *Diabetologia.* 2020;63(8):1648-1658.
24. Huang L, Zhang Y, Wang Y, Shen X, Yan S. Diabetic Peripheral Neuropathy Is Associated With Elevated Systolic Blood Pressure in Nonhypertensive Adults in the Chinese Han Population With Type 2 Diabetes [published online ahead of print, 2019 Dec 9]. *Can J Diabetes.* 2019;S1499-2671(19)30729-4.
25. Javed S, Hayat T, Menon L, Alam U, Malik RA. Diabetic peripheral neuropathy in people with type 2 diabetes: too little too late. *Diabet Med.* 2020;37(4):573-579.