Analysis of Risk Factors Responsible for Neuropathy in Patients with Type 2 Diabetes Mellitus with Diabetic Foot during the COVID-19 Pandemic

Heri Kristianto

Department of Medical Surgical Nursing, School of Nursing, Faculty of Health Science, Universitas Brawijaya, Malang, Indonesia

Abstract

Background: Neuropathy in diabetic foot is the onset of diabetic foot complications. The COVID-19 pandemic has caused changes in the health service system. The lockdown decision can make it difficult for patients to get medication and consult with health workers due to physical activity restrictions. This research aimed to analyze the factors that contribute to peripheral neuropathy in diabetic foot during the COVID-19 pandemic. **Materials and Methods:** The research is a cross-sectional study with a sample of 122 patients with type 2 diabetes mellitus who participated in the Chronic Disease Management Program at community health centers in Malang, Indonesia, and was selected using a purposive sampling method. Data were analyzed using multivariate linear regression. **Results:** Variables that contributed to the development of neuropathy were ankle-brachial index of the right foot ($\beta = 7.35$, $p = 0.06$), irregular exercise ($\beta = 2.01$, $p = 0.07$), glycated hemoglobin A (HbA1c) ($\beta = 0.97$, $p < 0.001$), and Low-Density Lipoprotein (LDL) ($\beta = 0.02$, $p = 0.06$). Meanwhile, the variables that contributed to reducing neuropathy were ankle-brachial index of the left foot ($\beta = -1.62$, $p = 0.73$) and being female ($\beta = -2.62$, $p = 0.02$). The regression model could explain the variation in the scores of neuropathy in diabetic foot during the COVID-19 pandemic ($R^2 = 20.10\%$). **Conclusion:** The factors that contributed to the incidence of neuropathy in diabetic foot during the COVID-19 pandemic were ankle-brachial index, exercise for diabetes, LDL, HbA1c, and sex.

Keywords: *Ankle brachial index, COVID-19, diabetic neuropathies, exercise, glycated hemoglobin low density lipoprotein*

Introduction

The COVID-19 pandemic has caused changes in the health service system globally, which affects the quality of life for people with Diabetes Mellitus (DM). Indonesia as a developing country is facing various turmoil and problems in health services, especially health services for people with DM, during the COVID-19 pandemic. Various challenges in health care for patients with DM in developing countries, among others, are lack of preventive measures, lower number of patient visits, reduced communication with patients, medication shortages, disruption in routine diabetes care, and unavailability of telehealth services.[1] The lockdown decision can make it difficult for patients to get medication and consult with health workers due to physical activity restrictions.[2,3] It can affect independent efforts to manage blood sugar levels and increase the risk of complications of DM, social isolation, psychological distress, and anxiety.[3-5] One form of complication that occurs is neuropathy in diabetic foot. Social distancing and shielding public health guidelines have impacted the delivery of diabetic foot services.[6]

Neuropathy in diabetic foot is the onset of diabetic foot complications. Neuropathy contributes to the incidence of lesions on the skin of the diabetic foot and even injuries and infections as a result of the activation of proinflammatory mediators, such as interleukin-6, interleukin-10, and tumor necrosis factor-α.[7] Symptoms of neuropathy and sensory dysfunction in the feet are associated with a hypoxemic COVID-19 patient.[8] Therefore, it is necessary to analyze the factors that contribute to neuropathy in diabetic foot

Address for correspondence:
Dr. Heri Kristianto,
Puncak Dieng Eksklusif, Kalisongo, Dau, Malang, East Java, Indonesia.
E-mail: heri.kristianto@ub.ac.id

Access this article online

Website: www.ijnmrjournal.net

DOI: 10.4103/ijnmr.ijnmr_180_21

Quick Response Code:

How to cite this article: Kristianto H. Analysis of risk factors responsible for neuropathy in patients with type 2 diabetes mellitus with diabetic foot during the COVID-19 pandemic. Iranian J Nursing Midwifery Res 2023;28:85-91.

Submitted: 24-Jan-2022. **Revised:** 10-Sep-2022. **Accepted:** 19-Oct-2022. **Published:** 27-Jan-2023.

during the COVID-19 pandemic in order to prevent diabetic foot complications. This research is expected to contribute to the development of nursing service standards for diabetes patients during the COVID-19 pandemic, especially in the development of priorities for assessment types of foot neuropathy during the COVID-19 pandemic. The results of this study can help nurses enforce nursing diagnoses in providing appropriate interventions. This analysis can help develop virtual triage and teleconsultations during the COVID-19 pandemic for people with foot complications in DM. The virtual triage and teleconsultations have become priority targets for foot services during the COVID-19 pandemic.[9] This research aimed to analyze the factors that contribute to peripheral neuropathy in diabetic foot during the COVID-19 pandemic.

Materials and Methods

This research used a cross-sectional design with a sample of 122 patients in 4 community health centers (Pusat Kesehatan Masyarakat: Puskesmas) in Malang, Indonesia, and was conducted from June to September 2020. From March 2020 until this study was conducted, the COVID-19 pandemic had been occurring in Indonesia. The sample size was calculated based on the *d* value 0.05, $Z^{2\alpha}$ value of 1.96, positive proportion of 0.05 (*p*), and risk proportion of 0.95 (*q*). The sample was selected by a purposive sampling method with the inclusion criteria of patients who were members of the Chronic Disease Management Program with no diabetic foot ulcers and brittle toenails. In the data collection process, informed consent was documented by means of telephone and a written consent form. Diabetic foot examinations were scheduled in advance to minimize contact between patients during the COVID-19 pandemic. Single-blind physical measurements and examinations were conducted by licensed nurse practitioners who had received training. COVID-19 screening and Electro-Chemiluminescence Immunoassay (ECLIA) Anti severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) were conducted prior to field research. The instruments used in the research were a patient demographic information assessment form, a digital skin moisture meter (skin detector) (r = 0.92), a nailfold videocapillaroscopy device (Dino-Lite CapillaryScope) (r = 0.91), a digital infrared thermal imager (Hti HT-102) (r = 0.95), a foot vascular Doppler (Vascular Doppler Detector BV-560) (accuracy = 89.57%), and a digital biothesiometer (NeuroScan-LE) (accuracy = 84%).[10-15]

The dependent variable was neuropathy scores. Neuropathy scores were measured using the digital biothesiometer (NeuroScan-LE) in the range 0–30 V. The normal categorization was as follows: <10 V was applied to people between 40 and 50 years old and <13 V was applied to those over 50 years old. The use of a biothesiometer test as a diagnostic tool for neuropathy has been recommended in several studies with sensitivity and specificity of 71.4% and 91.2%, respectively, as well as with high accuracy.[16-18]

The independent variables were age, sex, Body Mass Index (BMI), abdominal circumference, blood pressure, HbA1c, lipid profile, ankle-brachial index, moisture status of foot, foot temperature, capillaroscopy score, neuropathy score, diabetes duration, and exercise habit. The age of patients with DM was continuous data, while sex (male/female), diabetes duration (<5/≥5 years), and exercise for diabetes (regularly/irregularly) were dichotomous data. Reference group includes female, duration ≥5 years, and irregularly exercise. Men are at higher risk of developing diabetic neuropathy than women.[19,20] BMI, abdominal circumference, and systolic and diastolic blood pressures were continuous data. BMI was measured by weight (kg) and height (cm). Abdominal circumference was measured with a tape measure (cm). Blood pressure was measured with a sphygmomanometer (mmHg).[21]

HbA1c (%), cholesterol, High-Density Lipoprotein (HDL), and LDL (mg/dl) were continuous data taken during data collection. HbA1c correlates strongly with neuropathic complications in diabetic foot.[22,23] HbA1c and lipid profile examinations were conducted in a certified laboratory in partnership with the Chronic Disease Management Program of the Healthcare and Social Security Agency (Badan Penyelenggaraan Jaminan Sosial: BPJS) in Indonesia. The vascular status of the feet has an influence on the incidence of neuropathy in diabetic foot.[24] The vascular components measured in this study were ankle-brachial index, moisture status of foot skin, foot skin temperature, and capillaroscopy score. The ankle-brachial index of each foot was measured with a foot vascular Doppler (Vascular Doppler Detector BV-560).[25] The foot skin moisture was measured with a digital skin moisture meter, while the foot skin temperature was measured with a digital infrared thermal imager (Hti HT-102) at 5 points on each foot.[26] Capillary measurements were performed with nailfold videocapillaroscopy (Dino-Lite CapillaryScope) on the second toe of each foot.[27] Before the procedure, patients underwent acclimatization for 15–30 min in an examination room with a temperature of 25°C. The patients were provided with education for the examination. For example, the patients were told not to apply foot cream and wash their feet an hour before the examination. Regular exercise can inhibit neuropathy,[28] while diabetes duration contributes to neuropathy in diabetic foot.[29]

Statistical analyses, namely, univariate test on patient characteristics, Pearson's correlation coefficient, independent *t*-test, and multivariate linear regression, were performed using SPSS version 20 (IBM Corp.).

Ethical Considerations

Ethics approval for the research was obtained from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Brawijaya (Reference Number 42/EC/KEPK/02/2020). All respondents have expressed their consent to be involved in this study.

Results

Patient characteristics data based on age, sex, BMI, abdominal circumference, blood pressure, HbA1c, lipid profile, ankle-brachial index, moisture status of foot, foot temperature, capillaroscopy score, score of neuropathy, diabetes duration, and exercise habit are presented in Table 1. Most of the patients involved in this research were female, elderly, and obese, had diabetes duration less than 5 years, did not exercise regularly, and had HbA1c above the normal range, increased cholesterol and HDL, ankle-brachial index within normal range, increased capillaroscopy and neuropathy scores, and decreased foot moisture and temperature.

Bivariate variable selection was conducted to determine which variables met the requirements in modeling by calculating Pearson's correlation coefficient and performing an independent *t*-test. All the variables in Table 2 were analyzed with the results that the variables HbA1c, ankle-brachial index of the right foot and left foot, and sex (p-value < 0.05) were indicated as significant factors in the neuropathy score in diabetic foot during the COVID-19 pandemic.

The multivariate model was used based on the results of the bivariate analysis by selecting variables with p values less than 0.25 as independent variables.[30] The variables that met the requirements under the multivariate modeling were HbA1c (P-value of 0.01), LDL (p-value of 0.24), ankle-brachial index of the right foot and left foot and sex (p-value of 0.01), and exercise habit (p-value of 0.15). Table 2 shows the results of the multivariate analysis after controlling by other variables. The variables LDL, ankle-brachial index of the right foot and the left foot, sex, and exercise habit were retained because they influenced changes in R-squared >10% and beta coefficient. Based on a theoretical study, the variables LDL, ankle-brachial index of the right foot and the left foot, sex, and exercise habit were associated with the incidence of neuropathy in diabetic foot in the COVID-19 pandemic conditions.

The residual variable showed a score of 0.00 ± 0.53; hence, the existence assumption was fulfilled. A Durbin–Watson

Table 1: Patient characteristics based on age, sex, Body Mass Index (BMI), abdominal circumference, blood pressure, HbA1c, lipid profile, ankle-brachial index, moisture status of foot, foot temperature, capillaroscopy score, neuropathy score, diabetes duration, and exercise habit

Characteristics (*n*=122)	Mean (SD)*	Min-Max*	95% CI*
Age (years)	62.90 (8.64)	42-87	61.35-64.45
BMI (kg/m^2)	26.06 (3.06)	19.56-35.38	25.51-26.61
Abdominal circumference (cm)	95.75 (9.15)	66-116	94.11-97.39
Blood pressure (mmHg)			
Systolic	131.64 (13.25)	110-180	129.26-134.02
Diastolic	84.61 (11.28)	50-110	82.59-86.64
Glycated hemoglobin A (HbA1c) (%)	7.50 (1.80)	4.90-12.40	7.20-7.80
Lipid profile (mg/dl)			
Cholesterol	223.91 (47.53)	140-334	215.38-232.42
High-Density Lipoprotein (HDL)	48.92 (10.15)	31-90.70	47.10-50.74
Low-Density Lipoprotein (LDL)	138.08 (48.49)	42.50-238	129.39-146.77
Ankle-brachial index			
Right foot	1.05 (0.15)	0.53-1.38	1.02-1.07
Left foot	1.04 (0.14)	0.63-1.29	1.01-1.06
Moisture status of foot (%)	26.41 (8.42)	10.81-47.15	24.91-27.92
Foot temperature (°C)	22.31 (1.69)	19.48-27.33	22.01-22.61
Capillaroscopy score of foot	12.82 (3.64)	4.50-22.50	12.21-13.44
Neuropathy score (V)	24.19 (5.93)	6-30	23.13-25.26
	Neuropathy score (SD)*	**Min-Max***	**95% CI***
Sex			
Male (32)	26.35 (4.71)	15-30	24.65-28.05
Female (90)	23.65 (5.68)	6-30	22.14-24.72
Diabetes duration (years)			
<5 (58)	24.53 (5.03)	15-30	23.21-25.86
≥5 (64)	24.20 (6.02)	6-30	22.22-25.55
Exercise habit			
Regularly (52)	23.53 (5.69)	6-30	21.34-24.95
Irregularly (70)	24.97 (5.41)	15-30	23.68-26.26

*Descriptive statistic.

Table 2: Bivariate selection and multiple linear regression analysis of the relationship of neuropathy scores to HbA1c, Low-Density Lipoprotein (LDL), ankle-brachial index, sex, and exercise habit during the COVID-19 pandemic

Bivariate (*n*=122)	**Neuropathy score**	**Multiple linear regression**		
		Model	**Neuropathy score**	
	p		**β**	***p***
Age (year)	0.95*	Constant	9.41	0.08
Body mass index (kg/m^2)	0.48*	HbA1C (%)	0.97	0.001
Abdominal circumference (cm)	0.37*	LDL (mg/dl)	0.02	0.06
Blood pressure (mmHg)		Ankle-brachial index		
Systolic	0.75*	Right foot	7.35	0.06
Diastolic	0.44*	Left foot	−1.62	0.73
Glycated hemoglobin A (HbA1c) (%)	0.01*	Sex	−2.62	0.02
Lipid profile (mg/dl)		Exercise habit	2.01	0.07
Cholesterol	0.22*	R^2 (%)	20.10	
High-Density Lipoprotein (HDL)	0.50*			
LDL	0.24*			
Ankle-brachial index				
Right foot	0.01*			
Left foot	0.01*			
Moisture status of foot (%)	0.91*			
Foot temperature (°C)	0.92*			
Capillaroscopy score	0.55*			
Sex	0.01**			
Diabetes Duration (year)	0.73**			
Exercise habit	0.15**			

*Pearson's correlation coefficient; **independent *t*-test

value of 1.82 indicated that the independence assumption was fulfilled (−2 to +2). The ANOVA results showed $p<0.001$ which means that the linearity assumption was fulfilled. The plot results showed that the distribution of dots had a similar pattern to the dots above and below the diagonal line, 0; thus, the assumption of homoscedasticity was fulfilled. The Normal Probability Plot showed that the data spread around the diagonal line and followed the direction of the diagonal line, meaning that the normality assumption was fulfilled [Figure 1]. A variance inflation factor (VIF) in the range from 1.08 to 1.98 indicated no collinearity (VIF <10). Based on the results of the assumption test, it was concluded that the model could be used to predict the condition of diabetic foot neuropathy during the COVID-19 pandemic.

The regression model could explain 20.10% of the variation in neuropathy scores of diabetic foot during the COVID-19 pandemic. The variables that contributed to the development of neuropathy were ankle-brachial index of the right foot, exercise, and HbA1c, while women were 2.62 times less likely to develop neuropathy than men. Any reduction in ankle-brachial index of the left foot was likely to lower the risk of neuropathy in the diabetes population group without arterial disease.

Discussion

Vascular status changes in patients with diabetes greatly contribute to neuropathy in diabetic foot. The incidence of peripheral microvascular and macrovascular complications increases the risk of neuropathy. The vessels in the feet that are often occluded are the tibioperoneal, posterior tibial, and dorsalis pedis arteries.[31] In this research, microvascular changes were indicated by decreases in the mean scores of moisture and temperature of the foot skin, while the mean score of nailfold capillary condition increased. This condition may be a result of the COVID-19 pandemic, which has resulted in decreased activity of patients with diabetes. Therefore, during the COVID-19 pandemic, initiatives to prevent damage to blood vessels in the feet must be taken through increased exercises for diabetic foot, such as exercises for diabetic foot to increase peripheral tissue oxygenation, structured home exercise programs to improve walking performance and physical activity, and electrical stimulation of varying frequencies to increase the maximal walking capacity.[32-34]

An exercise for diabetes is one of the routine programs conducted at community health centers every week. This program is supported by a good cooperation between the Healthcare and Social Security Agency and community health centers as a promotional and preventive effort to prevent complications of DM. This supports the role of nurses as diabetes educators in an effort to increase patient knowledge and skills, change patient behavior, increase patient motivation, improve patient quality of life, and

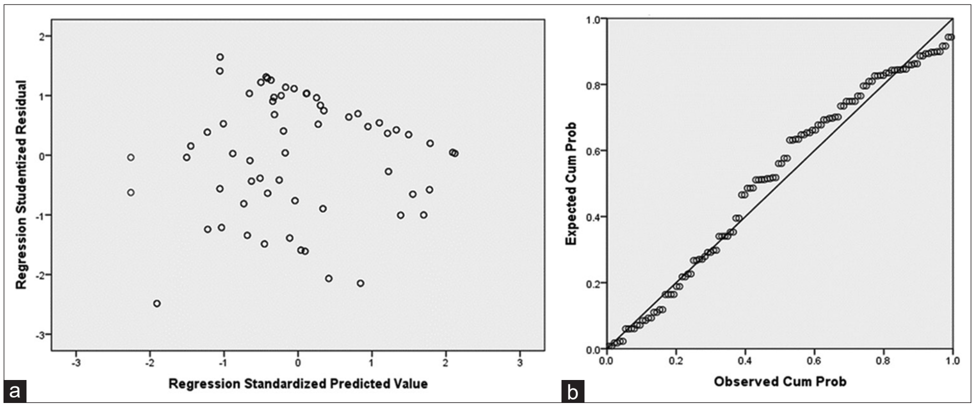

Figure 1: (a) Residual scatter plot and (b) normal probability plot

increase patient involvement in therapy; hence, it has an impact on self-care.[35] During the COVID-19 pandemic, the implementation of this program was halted along with the decision on Large-Scale Social Restrictions in order to minimize crowds at public health centers. The results of some interviews showed that 57.4% of patients with diabetes did not regularly exercise during the COVID-19 pandemic. This had an impact on quality of life and increased the risk of foot complications in patients with diabetes during the COVID-19 pandemic. For patients with DM who receive an insulin therapy, exercises are very useful in preventing neuropathy.[36,37] The recommended forms of exercise include strength exercise, ROM exercise, balance, flexibility, and stretching exercises, circuit training, and gait training.[28] Exercise for diabetes is very beneficial, so it is necessary to increase motivation and appropriate exercise patterns during social distancing in the COVID-19 pandemic. In addition, physical activities also provide benefits in preventing complications of diabetic foot.[38] Education about exercises for diabetes can be developed by uploading videos on various media, allowing patients with diabetes to exercise independently at home during the implementation of the social restriction policy.

The HbA1c examination is a procedure to control DM. Increased levels of HbA1c are potential indicators of diabetic neuropathy.[22,23,39] Based on observations, HbA1c levels increased during the COVID-19 pandemic. Some of the factors that contributed during the COVID-19 pandemic were activity restrictions, difficulty in accessing health services due to restrictions in operating hours, and limited services by health workers. The duration of lockdown is directly proportional to worsening glycemic control and complications of diabetic foot.[40] Therefore, it is necessary to develop telehealth in public health services to control HbA1c. One form of development using innovative team-based care models is the use of telephones and tablets, which are very useful in helping control blood glucose in primary care.[41,42]

Dyslipidemia is a contributing factor to diabetic neuropathy by inducing oxidative stress in the root ganglia sensory neurons.[43,44] This mechanism is also supported by the association of dyslipidemia with the incidence of atherosclerosis, which can cause peripheral vascular disease, which in turn has implications for changes in the ankle-brachial index score and changes in microvascular status of foot, such as moisture, temperature, and capillaries of the foot.[44,45] Based on the results of statistical tests, there was a relationship of ankle-brachial index and LDL level to neuropathy in the multivariate test, although in the bivariate test, there was no relationship of LDL to moisture, temperature, and capilaroscopy. Further research into the microvascular changes associated with changes in humidity, temperature, and capilaroscopy of the feet is needed in order to find a clearer mechanism. The average cholesterol and LDL levels of patients with DM during the COVID-19 pandemic tended to be borderline high, while their HDL levels were still normal. This is a warning for patients with DM that as long as a large-scale social restriction policy is implemented, diet and exercise habits can change and be followed by lifestyle changes. Therefore, it is necessary to conduct educational strategies and efforts as preventive measures in self-management of diabetes during the pandemic by developing an aerobic exercise at home. The aerobic exercise is defined as any form of physical activity that results in an increase in heart rate and respiratory volume to meet the oxygen demand of activated muscles.[46]

Male patients had a higher mean neuropathy score than female patients, indicating that the risk of neuropathy complications during the COVID-19 pandemic was higher in men. The results of this study are consistent with a previous study in India, which found that the prevalence of diabetic peripheral neuropathy was 39.30%, 28.90% in males and 10.40% in females.[47] More men worked at home during the COVID-19 pandemic. Social restriction policies lead to lifestyle changes that have implications for an increased risk of metabolic changes, which is indicated by uncontrolled weight gain.[48] These lifestyle changes include an increase in the consumption of snacks, vegetables, and sugar during periods of lockdown, followed by a decrease in the intensity of physical activity.[49] It can increase the risk of complications of diabetic neuropathy.

The results of the analysis showed that the nursing diagnosis in diabetic foot neuropathy, based on the physiological category according to the Indonesian Nursing Diagnosis Standards (Standar Diagnosis Keperawatan Indonesia: SDKI), during the COVID-19 pandemic is associated with ineffective peripheral perfusion, instability of blood glucose levels, and impaired physical mobility. Ineffective peripheral perfusion is associated with a risk of hyperglycemia, decreased capillary flow, and physical inactivity. Blood glucose level instability is associated with hyperglycemia and hypoglycemia. Impaired physical mobility is associated with diabetic foot neuropathy. Ankle-brachial index, exercise habit, LDL, HbA1c, and sex factors are priority assessment data on diabetic foot neuropathy by nurses in early detection of complications of diabetic foot neuropathy during the COVID-19 pandemic. This study has limitations in explaining the causal relationship; therefore, further research is needed to prove the relationship of neuropathy in diabetic feet to the ankle-brachial index, exercise habit, LDL, HbA1c, and sex variables. Additionally, further research needs to be carried out in the form of nursing interventions under the COVID-19 pandemic conditions. This supports the development of a foot care model during the COVID-19 pandemic with education and self-care as the main priority.[6]

Conclusion

The factors contributing to the development of neuropathy in diabetic feet during the COVID-19 pandemic were ankle-brachial index, exercise habit, LDL, HbA1c, and sex. These factors need special attention during the COVID-19 pandemic without ignoring the possibility of other factors that may influence the incidence of neuropathic complications in diabetic foot.

Acknowledgments

We would like to thank the Primary Health Care in Malang, East Java, Indonesia, for their support in this research (PNBP FKUB TA. 2020: Nomor. 214.41/SK/UN10.F08.06/PN/2020).

Financial support and sponsorship

Research and Community Service Directorate, Department of Nursing, Faculty of Medicine, Universitas Brawijaya.

Conflict of Interest

Nothing to declare.

References

1. Nouhjah S, Jahanfar S. Challenges of diabetes care management in developing countries with a high incidence of COVID-19: A brief report. Diabetes Metab Syndr 2020;14:731-2.
2. Kumar A, Arora A, Sharma P. Effect of lockdown on the glycemic control of diabetes patients. Diabetes Metab Syndr 2020;14:447-8.
3. Rastogi A, Hiteshi P, Bhansali A. Improved glycemic control amongst people with long-standing diabetes during COVID-19 lockdown: A prospective, observational, nested cohort study. Int J Diabetes Dev Ctries 2020;40:476-81.
4. Banerjee M, Chakraborty S, Pal R. Diabetes self-management amid COVID-19 pandemic. Diabetes Metab Syndr 2020;14:351-4.
5. Pal R, Bhadada SK. COVID-19 and diabetes mellitus: An unholy interaction of two pandemics. Diabetes Metab Syndr 2020;14:513-7.
6. Jaly I, Iyengar K, Bahl S, Hughes T, Vaishya R. Redefining diabetic foot disease management service during COVID-19 pandemic. Diabetes Metab Syndr 2020;14:833-8.
7. Papanas N, Papachristou S. COVID-19 and diabetic foot: Will the lamp burn bright? Int J Low Extrem Wounds 2020;19:111.
8. Odriozola A, Ortega L, Martinez L, Odriozola S, Torrens A, Corroleu D, *et al.* Widespread sensory neuropathy in diabetic patients hospitalized with severe COVID-19 infection. Diabetes Res Clin Pract 2021;172:108631.
9. Rastogi A, Hiteshi P, Bhansali AA, Jude EB. Virtual triage and outcomes of diabetic foot complications during Covid-19 pandemic: A retro-prospective, observational cohort study. PLoS One 2021;16:e0251143.
10. Aan de Stegge WB, Mejaiti N, van Netten JJ, Dijkgraaf MGW, van Baal JG, Busch-Westbroek TE, *et al.* The cost-effectiveness and cost-utility of at-home infrared temperature monitoring in reducing the incidence of foot ulcer recurrence in patients with diabetes (DIATEMP): Study protocol for a randomized controlled trial. Trials 2018;19: 520.
11. Clarys P, Barel AO. Measurement of skin surface hydration. In Agache's Measuring the Skin, F. Fanian, P. Humbert, H. Maibach (eds). Vrije Universiteit Brussel. 2017, p. 143-7.
12. Dinsdale G, Moore T, O'Leary N, Tresadern P, Berks M, Roberts C, *et al.* Intra-and inter-observer reliability of nailfold videocapillaroscopy — A possible outcome measure for systemic sclerosis-related microangiopathy. Microvasc Res 2017;112:1-6.
13. Hsu P-C, Liao P-Y, Chang H-H, Chiang JY, Huang Y-C, Lo L-C. Nailfold capillary abnormalities are associated with type 2 diabetes progression and correlated with peripheral neuropathy. Medicine (Baltimore) 2016;95:e5714.
14. Mufti A, Coutts P, Sibbald RG. Validation of commercially available infrared thermometers for measuring skin surface temperature associated with deep and surrounding wound infection. AdvSkin Wound Care 2015;28:11-6.
15. Tomy A, Alexander TA, Joseph P. Accuracy of vibration test and monofilament examination against biothesiometer test for the identification of diabetic peripheral neuropathy among diabetic patients. Int J Innov Res Adv Stud 2021;8:21-5.
16. Latha MM, Yella S. Investigating the use of biothesiometer for detecting the severity of diabetic neuropathy in diabetic type-II patients. J Med Sci Clin Res 2017;5:28806-12.
17. Zografou I, Iliadis F, Sambanis C, Didangelos T. Validation of neuropad in the assessment of peripheral diabetic neuropathy in patients with diabetes mellitus versus the Michigan neuropathy screening instrument, 10 g monofilament application and biothesiometer measurement. Curr Vasc Pharmacol 2020;18:517-22.
18. Saraswathi R. Comparison of standard outpatient screening tools and nerve conduction studies for the diagnosis of diabetic peripheral neuropathy: A pilot study, in physical medicine and rehabilitation.Christian Medical College, Vellore; 2017.
19. Assaad-Khalil SH, Zaki A, Rehim AA, Megallaa MH, Gaber N,

Gamal H, *et al.* Prevalence of diabetic foot disorders and related risk factors among Egyptian subjects with diabetes. Prim Care Diabetes 2015;9:297-303.

20. Salvotelli L, Stoico V, Perrone F, Cacciatori V, Negri C, Brangani C, *et al.* Prevalence of neuropathy in type 2 diabetic patients and its association with other diabetes complications: The verona diabetic foot screening program. J Diabetes Complications 2015;29:1066-70.
21. Roerecke M, Kaczorowski J, Myers MG. Comparing automated office blood pressure readings with other methods of blood pressure measurement for identifying patients with possible hypertension: A systematic review and meta-analysis. JAMA Intern Med 2019;179:351-62.
22. Lai Y-R, Chiu W-C, Huang C-C, Tsai N-W, Wang H-C, Lin W-C, *et al.* HbA1C variability is strongly associated with the severity of peripheral neuropathy in patients with type 2 diabetes. Front Neurosci 2019;13:90.
23. Su J-B, Zhao L-H, Zhang X-L, Cai H-L, Huang H-Y, Xu F, *et al.* HbA1c variability and diabetic peripheral neuropathy in type 2 diabetic patients. Cardiovascu Diabetol 2018;17:47.
24. Eleftheriadou I, Tentolouris A, Grigoropoulou P, Tsilingiris D, Anastasiou I, Kokkinos A, *et al.* The association of diabetic microvascular and macrovascular disease with cutaneous circulation in patients with type 2 diabetes mellitus. J Diabetes Complications 2019;33:165-70.
25. Weller CD, Team V, Ivory JD, Crawford K, Gethin G. ABPI reporting and compression recommendations in global clinical practice guidelines on venous leg ulcer management: A scoping review. Int Wound J 2019;16:406-19.
26. van Doremalen RF, van Netten JJ, van Baal JG, Vollenbroek-Hutten MM, van der Heijden F. Infrared 3D thermography for inflammation detection in diabetic foot disease: A proof of concept. J Diabetes Sci Technol 2020;14:46-54.
27. Maldonado G, Guerrero R, Paredes C, Ríos C. Nailfold capillaroscopy in diabetes mellitus. Microvasc Res 2017;112:41-6.
28. Melese H, Alamer A, Temesgen MH, Kahsay G. Effectiveness of exercise therapy on gait function in diabetic peripheral neuropathy patients: A systematic review of randomized controlled trials. Diabetes Metab Syndr Obes 2020;13:2753-64.
29. Hicks CW, Selvin E. Epidemiology of peripheral neuropathy and lower extremity disease in diabetes. Curr Diab Rep 2019;19:86.
30. Priyo S. Analisis Data Bidang Kesehatan. Penerbit: Raja Grafindo Persada. Jakarta; 2016.
31. Troisi N, Turini F, Chisci E, Ercolini L, Frosini P, Lombardi R, *et al.* Impact of pedal arch patency on tissue loss and time to healing in diabetic patients with foot wounds undergoing infrainguinal endovascular revascularization. Korean J Radiol 2018;19:47-53.
32. Fiogbé E, de Vassimon-Barroso V, de Medeiros Takahashi AC. Exercise training in older adults, what effects on muscle oxygenation? A systematic review. Arch Gerontol Geriatr 2017;71:89-98.
33. Golledge J, Singh T, Alahakoon C, Pinchbeck J, Yip L, Moxon J, *et al.* Meta-analysis of clinical trials examining the benefit of structured home exercise in patients with peripheral artery disease. Br J Surg 2019;106:319-31.
34. Ellul C, Formosa C, Gatt A. Effects of intermittent calf muscle electrical stimulation on walking capacity in claudicants living with type 2 diabetes. J Am Podiatr Med Assoc 2020;110:1-7. doi: 10.7547/17-046.
35. Świątoniowska N, Sarzyńska K, Szymańska-Chabowska A, Jankowska-Polańska B. The role of education in type 2 diabetes treatment. Diabetes Res Clin Pract 2019;151:237-46.
36. Lee EC, Kim MO, Roh GH, Hong SE. Effects of exercise on neuropathy in streptozotocin-induced diabetic rats. Ann Rehabil Med 2017;41:402-12.
37. Jenkins DW, Jenks A. Exercise and diabetes: a narrative review. J Foot Ankle Surg 2017;56:968-74.
38. Matos M, Mendes R, Silva AB, Sousa N. Physical activity and exercise on diabetic foot related outcomes: A systematic review. Diabetes Res Clin Pract 2018;139:81-90.
39. Liu X, Xu Y, An M, Zeng Q. The risk factors for diabetic peripheral neuropathy: A meta-analysis. PLoS One 2019;14:e0212574.
40. Ghosal S, Sinha B, Majumder M, Misra A. Estimation of effects of nationwide lockdown for containing coronavirus infection on worsening of glycosylated haemoglobin and increase in diabetes-related complications: A simulation model using multivariate regression analysis. Diabetes Metab Syndr 2020;14:319-23.
41. Myers A, Presswala L, Bissoonauth A, Gulati N, Zhang M, Izard S, *et al.* Telemedicine for disparity patients with diabetes: The feasibility of utilizing telehealth in the management of uncontrolled type 2 diabetes in black and hispanic disparity patients: A pilot study. J Diabetes Sci Technol 2020;15:1-8.
42. Watkins S, Neubrander J. Primary-care registered nurse telehealth policy implications. J Telemed Telecare 2020;28:1-4.
43. Pai Y-W, Lin C-H, Lee I-T, Chang M-H. Prevalence and biochemical risk factors of diabetic peripheral neuropathy with or without neuropathic pain in Taiwanese adults with type 2 diabetes mellitus. Diabetes Metab Syndr 2018;12:111-6.
44. Savelieff MG, Callaghan BC, Feldman EL. The emerging role of dyslipidemia in diabetic microvascular complications. Curr Opin Endocrinol Diabetes Obes 2020;27:115-23.
45. Shetty V, Jain H, Singh G, Parekh S, Shetty S. Ankle brachial pressure index correlation with diastolic blood pressure, dyslipidemia and anthropometric measurement in patients of essential hypertension. Hypertension 2017;35:39.
46. Wang Y, Xu D. Effects of aerobic exercise on lipids and lipoproteins. Lipids Health Dis 2017;16:132.
47. Darivemula S, Nagoor K, Patan SK, Reddy NB, Deepthi CS, Chittooru CS. Prevalence and its associated determinants of diabetic peripheral neuropathy (DPN) in individuals having type-2 diabetes mellitus in rural South India. Indian J Community Med 2019;44:88-91.
48. Ghosal S, Arora B, Dutta K, Ghosh A, Sinha B, Misra A. Increase in the risk of type 2 diabetes during lockdown for the COVID19 pandemic in India: A cohort analysis. Diabetes Metab Syndr 2020;14:949-52.
49. Ruiz-Roso MB, Knott-Torcal C, Matilla-Escalante DC, Garcimartín A, Sampedro-Nuñez MA, Dávalos A, *et al.* COVID-19 lockdown and changes of the dietary pattern and physical activity habits in a cohort of patients with type 2 diabetes mellitus. Nutrients 2020;12:2327.