



DETERMINANT FACTORS AFFECT NEUROPHATY IN DIABETIC PATIENT

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ABSTRACT

Hyperglycemia conditions will result complications in patients both for cardiovascular and neurological system. The incidence of neuropathy and peripheral arterial disease (PAD) are two things that increase mortality. Loss of protective sensation will reduce the patient's awareness of ulcers so that patients do not receive treatment early. Meanwhile, PAD conditions increase the incidence of ischemia in the distal area, especially in the legs, resulting ulcer. This research aims to look at the factors that contribute to these two conditions. Data collected to 40 respondents with the inclusion criteria who are DM patients which never had an amputation, the relationship and contribution of factors to neuropathy and PAD (were measured by sensation points on sole by monofilament and dorsalis pedis artery palpation) and analyzed with ordinal regression. The results of the study showed that none of the respondents experienced PAD so that bivariate tests could not be carried out. Meanwhile, the results of the bivariate test for neuropathy showed that 3 factors were significantly related to gender ($p=0.038$), duration of illness from DM ($p=0.05$), and foot condition ($p=0.003$). It is found from ordinal regression that foot condition ($\beta= 1.237$; $p= 0.028$; $OR= 1.237$) has significant effect to neuropathy.

Keywords: diabetes mellitus; foot condition; neuropathy; PAD; ulcer

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INTRODUCTION

Diabetes mellitus (DM) occurs due to decreased insulin production and insulin resistance. As a result, there is a decrease in the amount of glucose entering the cells and an increase in glucose in the blood (hyperglycemia) (ADA, 2021a; Harding & Kwong, 2019). The prevalence of DM is always increasing, globally over the last 10 years the population of patients with DM has a gap of close to 70 million. While it is predicted that in the next twenty years the population of DM patients will increase by more than 130 million people, which if averaged can exceed 6 million per year. In Indonesia, DM became fourth rank of the top five global prevalence, and have increased by 4 million people in the last 10 years (IDF, 2021 DM complications are acute and chronic, but the rate of macrovascular complications is higher than microvascular (Ekoru et al., 2019; Faselis et al., 2019; Viigimaa et al., 2019). This vascular disorder can lead to retinopathy, nephropathy, neuropathy, and peripheral artery disease which often ends in amputation of both major (3.6%) and minor (9.9%) (Faselis et al., 2019; Gazzaruso et al., 2021). Neuropathy and peripheral artery disease can cause foot ulcers that can complicate into infections.

Increased glucose levels in the blood, accompanied by a decrease in the supply of glucose into cells as raw material for metabolism. Such deficiency leads to insufficiency of energy produced by the body. In addition, damage to cells can also occur especially in the constituent cells of blood vessels (endothelial), both micro and macro blood vessels. Damage of

peripheral arteries can decrease blood flow to the leg area (Petrie et al., 2018). Over time, oxygenation in the area is disrupted, triggering tissue ischemia to cell death in the distal area (Mariadoss et al., 2022). Hyperglycemia conditions also trigger the use of sorbitol as a substitute for glucose which causes damage to nerve cells (Fakkal et al., 2020). Death of nerve cells due to lack of nutrients and oxygen causes the patient to be unaware of changes that occur in the leg area. The sensitivity of the feet to temperature changes and pain decreases so that the patient does not realize if there is a problem with the feet. The condition has an impact on unconscious wounds, infections, and often leads to amputation (Armstrong et al., 2017; Manickum et al., 2021).

Neuropathy and PAD in addition to complications can also be caused by other things related to self-care of DM patients. Some factors that are considered to have an impact on this are long suffering from DM, gender, age, and poor metabolic control, body mass index, hypertension, and smoking. This study will analyze the influence of each factor on the incidence of neuropathy and PAD in patients. Long suffering from DM is significantly a contributing factor to the incidence of neuropathy and PAD. Vascular and neurological disorders due to hyperglycemia will be aggravated in patients who have poor metabolic control. Based on previous research, DM patients begin with obesity so that this factor also affects the stability of blood glucose levels in patients. Hypertension and smoking can aggravate vascular disorders in people with DM. All of these factors increase the occurrence of neuropathy and PAD in DM patients (Alshammari et al., 2022; J. Liu et al., 2020).

DM patients can experience progressive nerve damage especially when the patient's blood glucose levels are unstable. These conditions can cause nerve function to be lost. High glucose in the blood indicates that glucose that enters to be metabolized by cells is reduced. The cause is lack of insulin as a mediator of glucose transport into cells and/or the occurrence of resistance to insulin. Nerve cells that experience this become deficient in nutrients and cause the metabolic process not to run properly. Sorbitol as a form of glucose will be formed due to metabolic stress to meet the needs of glucose in the nerves. However, sorbitol cannot be digested by nerve cells and consequently there is a buildup of sorbitol that disrupts nerve conduction (DeWit et al., 2017; Gautier et al., 1997; Harding & Kwong, 2019). Patients who have long had DM with unstable blood sugar will cause the disorder. In addition, neuropathy conditions can be preceded by hypoxia of nerve cells caused by vascular damage around neurons. This condition causes loss of myelin (demyelization) so that nerve conduction is disrupted (Feldman et al., 2019). Nerve damage can result in loss of pain sensation or other sensory damage (DeWit et al., 2017; Gautier et al., 1997; Harding & Kwong, 2019).

Neuropathy can be assessed by performing a Loss of Protection Sensation (LOPS) examination through a monofilament test and followed by neurological examination tests (pinprick, temperature difference, ankle reflex, and vibration with a 128Hz fork). The patient is declared to have a LOPS condition if the monofilament test results are obtained 2 areas are not felt and one of the neurological examination tests has a positive result (American diabetes association, 2023; Carmichael et al., 2021; Herman et al., 2012). This research aims to look at the factors that contribute to these two conditions

METHOD

Data collection of respondents begins by assessing the eligibility of respondents with predetermined inclusion criteria, namely DM patients aged >18 years, have never been amputated, and are willing to be respondents. The design used is a temporary sampling of factors related to neuropathy. Measuring respondent characteristic in the form of

questionnaires are given to obtain data on factors, while blood glucose measurements use glucometers, blood pressure is measured with an aneroid sphygmomanometer. Monofilament 10g is used to measure neuropathy with the limitation that if the patient does not feel 2 points from the entire examination, it is declared to have neuropathy (ADA, 2021b). While PAD is measured through examination of the dorsalis pedis artery, if it is not palpable, it will be declared at risk of PAD (ADA, 2021b). The condition of the feet is known through physical examination based on questionnaires from previous studies with good validity ($r > 0,361$) and reliability (cronbach's alpha 0,679) (Frisca, et al., 2019). This study had ethical clearance approval by UKMC DRPM (no. 39.02/II/B1-PN.10.01/8/23). Bivariate analysis using Kendall's-tau B used to see the relationship of factors to neuropathy and PAD. Ordinal regression tests are used to assess the contribution of each factor.

RESULTS

Respondents in the study were 40 DM patients according to inclusion criteria. All patients were given questionnaires, physical examinations, and diagnostics.

Table 1.
Respondent's Characteristics (n=40)

Factors		f	%	Factors		f	%
Age	Adult	8	20	Blood pressure	Pre-hypertension	1	35
	Older adult	2	60		Hypertension grade I	2	57.5
	Elderly	4	20		Hypertension grade II	3	7.5
Gender	Men	1	40	Blood glucose	Normal	1	25
	Women	6	60		High	3	75
Education	Elementary	2	70	Foot condition	Low risk ulcer	9	22.5
	High school	8	9		Moderate risk ulcer	1	27.5
	Higher education	3	3		High risk ulcer	2	50
Duration of illness	0-<5 years	1	35	Neuropathy	Not neuropathy	2	57.5
	5-<10 years	4	40		Neuropathy	3	42.5
	>10 years	1	25			7	
BMI	Normal	1	30	PAD	No PAD risk	4	100
	Overweight	2	57.		Has PAD risk	0	0
	Obesity	3	5				
		5	12.				

Univariate analysis shows that the majority of respondents were pre-elderly (24;60%), elementary education (28;70%), suffering from DM for 5-<10 years (16;40%), overweight (23;57.5%), high blood sugar (30;75%), female (24;60%), hypertension grade I (23;57.5%), foot conditions with high-risk ulcer (20, 50%), no neuropathy (23;57.5%), and all respondents were not at risk of PAD.

Table 2.
Bivariate analysis results of factors to neuropathy and PAD

Factors	Neuropathy		PAD		p-value*	
	No	Yes	Not risk	Has risk		
Age	Adult	6	2	8	0	0.295
	Older adult	13	11	24	0	
	Elderly	4	4	8	0	
Gender	Men	6	10	16	0	0.037
	Women	17	7	24	0	
Education	Elementary	16	12	28	0	0.932
	High school	6	3	9	0	
	Higher education	1	2	3	0	
Duration of illness	0-<5 years	5	9	14	0	0.05
	5-<10 years	11	5	16	0	
	>10 years	7	3	10	0	
BMI	Normal	6	6	12	0	0.916
	Overweight	15	8	23	0	
	Obesity	2	3	5	0	
Blood pressure	Pre-hypertension	8	6	14	0	0.569
	Hypertension grade I	12	11	23	0	
	Hypertension grade II	3	0	3	0	
Blood glucose	Normal	6	4	10	0	0.853
	High	17	13	30	0	
Foot condition	Low risk ulcer	7	2	9	0	0.003
	Moderate risk ulcer	9	2	11	0	
	High risk ulcer	7	13	20	0	

The incidence of neuropathy was greater in pre-elderly respondents (27.5%), have a primary education (30%), duration of illness 0-<5years (22.5%), overweight (20%), high blood sugar (42.5%), male (25%), hypertension grade I (22.5%), and high-risk foot conditions (42.5%). Based on these data, the significant correlation to neuropathy found are duration of illness (p= 0.05), gender (p= 0.038), and foot condition (p= 0.003).

Tabel 3.
Ordinal regression of factors to neuropathy

Factors	β	p-value	OR	Pseudo R ²
Constant	-0.216			0.277
Gender	-1.561	0.051	0.801	
Duration of illness	-0.529	0.277	0.562	
Foot condition	1.237	0.028	0.487	

The results of model fit test with the log likelihood method (p= 0.005) and goodness of fit (p= 0.259) shows that the regression model is good and can be used in interpreting further data. The regression model has a constant of 0.216 under the condition that all predictors are equal to zero (0). Gender has regression coefficient of -1,561 shows that neuropathy risk will increase significantly in male. Also, foot conditions with a regression coefficient of 1.237 shows that the higher risk of ulcers will rise the risk of neuropathy. Meanwhile, age and duration of illness does not have a significant effect. The determinant coefficient as pseudo R2-square value shows that gender, duration of illness, and foot conditions contributed 27.7% simultaneously to neuropathy. While the remaining 72.3% was influenced by other factors that were not correlated and not include in this study.

DISCUSSION

Obesity which shown by high level of BMI can increase damage of peripheral blood vessel. As a result lumen of blood vessel become narrow and change circulation to distal area

(Manickum et al., 2021; Rossboth et al., 2021). There is more neuropathy prevalence in DM patient with obesity (Callaghan, et.al, 2020). Meta-analysis research found that BMI and duration of diabetes significantly contribute to neuropathy (Fakkal et al., 2020). Analysis of factors contributing to neuropathy showed that BMI in the majority of respondents was in the overweight category. Being overweight is a factor in the occurrence of DM and also increases the occurrence of complications such as instability of blood glucose levels and also vascular complications (Alshammari et al.. 2022; Jalilian et al.. 2020; Viigimaa et al.. 2019; Ziauddeen et al.. 2018). Results of the main factors contributing to ulcer severity are high BMI, smoking, poor metabolic control, type of DM treatment and old age. This study also showed that the lower the metabolic control (blood glucose levels), the worse the incidence of ulcers in patients (Jalilian et al.. 2020).

Other studies say the age and duration of DM illness will be related to the patient's awareness of ulcers. A high level of alertness will also have a significant relationship with the level of understanding of patients and the ability to perform self-care (Fakkal et al., 2020; Ghobadi, et al, 2020). Checking the condition of the feet is one of the self-care behaviours that can be done independently by DM patients. Moreover, good foot care behaviour can effectively show better foot condition (Frisca. 2021). The incidence of neuropathy in patients was obtained at 42.5% which showed a fairly high number. Neuropathy conditions can reduce the patient's awareness of the incidence of injuries so that they do not treat early leg injuries (Harding & Kwong. 2019; X. Liu et al.. 2019). It is different from this study the incidence of neuropathy is more prevalent in men. The results of X.Liu's study (2019) showed that the incidence of peripheral neuropathy in women (29.49%) was higher than men (23.37%). Moreover. The incidence of neuropathy is also found more in urban than rural areas (2:1). Sex also significantly ($p = 0.21$) contributed to the degree of ulcer severity (Ghobadi et al.. 2020).

Another factor related to the incidence of neuropathy is poor metabolic control. The results showed that this factor did not have a significant relationship. Eventhough, poor metabolic control in other studies is a significant factor in neuropathy (Mariadoss et al.. 2022). High blood glucose contributes to causing nerve damage through the polyol pathway so that many nerve cells die, resulting in loss of protective sensation in patients (Harding & Kwong. 2019; Koerniawan & Frisca. 2023; Mariadoss et al.. 2022; Moattari et al.. 2012).

CONCLUSION

Factors that contribute to the significant incidence of neuropathy and PAD are foot condition and gender. Other factors still contribute but need to be explore studies related to each factor.

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