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Diabetic Peripheral Neuropathy in Adults with Type 2 Diabetes Mellitus

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ABSTRACT

Background: A complication of diabetes mellitus (DM) is diabetic peripheral neuropathy (DPN). Its causative factors include age, sex, duration of DM, body mass index (BMI), and a history of hypertension. **Purpose:** This study was aimed at identifying factors associated with DPN in adults with T2 DM. **Methods:** We employed a quantitative method with a cross-sectional approach and recruited 182 respondents through purposive sampling. We administered a diabetic neuropathy syndrome questionnaire and measured BMI and blood pressure. Data were analyzed univariately and bivariately using the chi-square test. **Results:** Of the 189 respondents, 139 (73.6%) were aged 45–59 years. The participants included 121 (67%) women and 8 (33%) men. Of all respondents, 108 (58.2%) had diabetes mellitus, 90 (49.4%) had an overweight BMI, 99 (51.6%) had a history of hypertension, and 139 (72.5%) had a history of DPN. The chi-square analysis showed a relationship between DPN and age ($p = 0.000$), duration of DM ($p = 0.001$), BMI ($p = 0.010$), and a history of hypertension ($p = 0.000$), but not with sex ($p = 0.688$). **Conclusion:** DPN can occur in patients with type 2 DM, and a high risk is associated with middle age, long duration of DM, overweight BMI, and a history of hypertension.

Keywords: Diabetes Mellitus; Hypertension; Diabetic Peripheral Neuropathy

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disease characterized by disturbances in glucose, fat, and protein metabolisms caused by insulin deficiency or resistance that cause hyperglycemia (Setiadi *et al.*, 2014). Type 2 DM (T2DM) is currently a global health threat (Perkeni, 2019). The International Diabetes Federation's data show a high prevalence of T2DM worldwide. In 2019, 463 million adults aged 20–79 years had DM, and this number is expected to reach 578 by 2030 (Atlas, 2019). The Basic Health Research data showed that the rate of T2DM occurrence in Indonesia at the age of 15 years in 2013 was 6.9%, which increased to 8.5% in 2018. With the highest prevalence of 1.7% in Aceh and the lowest in Papua at 0.8%, Jambi ranks fifth at 1.0% (Kemenkes, 2018).

Approximately 20%–40% of people with T2DM develop diabetic neuropathy (Perkeni, 2019). Diabetic peripheral neuropathy (DPN) is a long-term effect of microangiopathy-induced DM. Clinical manifestations of DPN include paresthesia, burning, numbness of the feet, decreased proprioceptive function, and decreased sensations of touch, pain, and temperature; thus, patients with neuropathy are at risk of injury and infection of the feet without being noticed (Smeltzer & Bare, 2013).

DPN is closely related to the age and duration of DM (Salawu *et al.*, 2018). Complications of DM arise when it is sustained for a long time. Prolonged poor glycemic control causes no enzymatic glycosylation reaction or Maillard reaction between protein and reactive carbonyl or dicarboxylic compounds. Degradation of protein glycosylation forms dicarboxylic and 3-deoxyglucosone, which in turn form advanced glycation end products, ultimately leading to DPN (Loughlin & Artlett, 2011). DPN causes symptoms of burning, numbness, prickling, and tingling.

Additionally, a history of hypertension is a risk factor for DPN, as explained by the vascular theory, neutropenic metabolism, immunology, and microvascular conditions that undergo hyalinization in the basal lamina of blood vessels, triggering thrombosis in intra-neural arterioles, reducing blood flow to nerves, and causing hypoxia and ischemia, resulting in peripheral neuropathy (Kowalak, Welsh, & Mayer, 2011).

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A previous study explored DPN in elderly individuals with an average age exceeding 70 years. However, only a few studies have examined adults aged 20 to 59 years. This study was aimed at determining the risk factors for DPN in adults with T2DM.

METHODOLOGY

Research Design

This study used a quantitative research method with a cross-sectional design to assess the risk factors for DPN by simultaneously collecting data on dependent and independent variables.

Setting and Samples

This study was carried out in Jambi City at the Puteri Ayu Health Center, which has the highest DM population in Jambi City (1,810 people). The sample comprised 182 respondents who underwent purposive sampling. The study was conducted from February to May, 2022. The inclusion criteria were as follows: age, 25–59 years; no history of diabetic ulcers; no trauma to the skin, such as burns; and no neurological disease or stroke.

Measurement and Data Collection

DPN was assessed using the Indonesian Version of the Diabetic Neuropathy Symptom Questionnaire (DNS-Ina) in 2016, which assesses sensory and motor clinical symptoms using a questionnaire that can be completed in a few minutes. The scoring system has a maximum score of four points, with one symptom receiving a score of 1. A score of 1 indicated diabetic neuropathy. The DNS-Ina assessment method observes symptoms of neuropathy caused by large fiber damage, such as numbness and shakiness when walking, and small fiber damage, such as pain, burning, throbbing pain, aches, and numbness. Testing of the DNS-Ina instrument was carried out by Mardastuti *et al.*, (2016) which showed a sensitivity of 80.0% and a specificity of 27.78%, and 82 participants tested positive (Mardastuti *et al.*, 2016). Asad *et al.*, (2010) conducted a neurological score reliability test to assess sensorimotor neuropathy in patients with T2DM to obtain a DNS score with a sensitivity of 64.41% and a specificity of 80.95% (Asad *et al.*, 2010). This study was conducted following ethical principles, including confidentiality, privacy, and self-determination. The respondents signed an informed consent form before commencement of the study.

Data were collected from February to May, 2022 for 182 respondent with T2DM. The body mass index (BMI) was calculated from the height and weight. The history of hypertension was determined based on the patient's medical record data, and blood pressure was measured using a digital sphygmomanometer.

Data Analysis

The respondents' characteristics were analyzed using descriptive statistics. The chi-square test was used to examine the data with a significance threshold of 5% (0.05) to determine the risk variables for DPN.

Ethical Consideration

The study protocol was approved by the Health Research Ethics Committee of the Jambi Ministry of Health Polytechnics on 31st January, 2022 with reference number L.B.02.06/2/0188/2022.

RESULTS

Table 1 shows the baseline characteristics of the 182 respondents. Table 2 shows the frequency distribution of the duration of DM, BMI, and history of hypertension and PDN. Table 3 shows factors associated with DPN.

Table 1: Characteristics of Respondents

Variable	n	%
Age		
25 -< 45 Years	43	26.4
45-59 Years	139	73.6
Sex		
Male	61	33
Female	121	67

Most of the respondents 139 [73.6%] were middle aged (45–59 years). Further, most (121 [67%]) respondents were women.

Table 2: Distribution by Duration of Diabetes Mellitus, Body Mass Index, and History of Hypertension and Peripheral Diabetic Neuropathy

Variable	n	%
Duration of DM		
Long	108	58.2
Short	74	41.8
BMI		
Underweight	8	2.2
Normal	84	48.4
Overweight	90	49.4
History of Hypertension		
No	83	48.4
Yes	99	51.6
Peripheral Neuropathy		
No	43	27.5
Yes	139	72.5

Of all respondents, 108 (58.2%) were old, 90 (49.4%) had an overweight BMI, 99 (51.6%) had a history of hypertension, and 139 (72.5%) had DPN.

Table 3: Factors Associated with Diabetic Peripheral Neuropathy

	Peripheral Neuropathy				Tot al	*p*
	Neuropathy		No neuropathy			
	n	%	N	%		
Age						
26-<45 years	17	39.5	26	60.5	43	0.000
45-59 years	122	87.8	17	12.2	139	
Sex						
Ma le	45	73.8	16	26.2	61	0.688
Fema le	94	77.7	27	22.3	121	
Duration of DM						
Short (<5 years)	92	85.2	16	14.8	108	0.001
Long (> 5 years)	47	63.5	18	36.5	74	
BMI						
Underw eight	8	100	0	0	8	0.010
Normal	56	66.7	28	33.3	84	
Over weight	75	83.3	15	16.7	90	
History of Hypertension						
Yes	93	83.9	6	6.1	99	0.000
No	46	55.4	37	44.6	83	

The bivariate statistical test revealed a significant relationship of DPN with age ($p = 0.000$), duration of DM ($p = 0.001$), BMI ($p = 0.010$), and history of hypertension ($p = 0.000$) in patients with DM, but not with sex ($p = 0.688$).

DISCUSSION

Age is a risk factor for DPN. In the present study, age was associated with DPN. The respondents' ages ranged from 45 to 59 years. Old age is associated with a higher risk of DPN, particularly in the elderly population. Age and DPN have a significant association (Hutapea *et al.*, 2016); (Mao *et al.*, 2019); (Pfannkuche *et al.*, 2020). Mao *et al*., showed that old age was independently associated with an increased DPN risk. Using other diagnostic criteria, age showed a nonlinear positive correlation with DPN Mao *et al.*, 2019; Popescu *et al.*, 2016. The occurrence of molecular aging or changes that occur due to aging are not fully understood. However, in general, with age, molecular and cellular damage accumulates, as in DPN, when damage to both large and tiny fibers may result from axonal damage.

We also found that sex is not associated with DPN. Consistent with studies by Abosrea, Elmasry & Oraby (2010) and Javed *et al.*, (2014), sex had no significant relationship with the occurrence of DPN (Abosrea, Elmasry & Oraby, 2010 ; Javed *et al.*, 2014). Few studies have examined the relationship between sex and the incidence of DPN. Lu *et al*., showed that women were more at risk of developing DPN compared to men ($p = 0.017$; Lu *et al.*, 2020). Additionally, the incidence of DPN is higher in women than in men (Pfannkuche *et al*., 2020).

The risk of DPN was significantly higher among respondents with DM who were older. The present study showed that respondents with DM for > 5 years had a higher risk than those diagnosed with DM ≤ 5 years, as well as a significant relationship between the duration of DM and DPN. A study showed that in patients with T2DM, the risk of developing NPD increased in those diagnosed 5–10 years before (Pfannkuche *et al.*, 2020; Jaiswal *et al.*, 2017). Consistent with Putri & Aghniya's study, a significant relationship was found between the duration of DM and the occurrence of DPN, with an average odds ratio of 0.25, implying that a longer duration of DM increases the risk of DPN by 25% (Putri & Waluyo, 2019; Aghniya, 2017). Similarly, several other studies have shown a significant relationship between the duration of DM and DPN (Liu *et al*., 2019; Khawaja *et al.*, 2018; Elmagboul, 2020).

According to the findings of this study, respondents with a BMI > 25 kg/m2 have a higher chance of developing DPN than those with a BMI ≤ 25 kg/m2, with a statistically significant association between BMI and DPN. Obesity is also associated with the risk of developing DPN. Respondents with a BMI > 30 kg/m2 were more at risk of developing DPN (Li *et al.*, 2015; Katz *et al.*, 2022). Similarly, Oh *et al.*, (2019) showed that central or abdominal obesity increases the risk of DPN. Obesity results in excessive fat storage. It forms a chemical compound in the form of triacylglycerol in adipose cells, which causes the production of fatty acids. Free fatty acids can circulate in the blood and cause oxidative stress, or lipotoxicity. Free fatty acids also contribute to hyperglycemia by decreasing glucose utilization in insulin-stimulated muscles. This prolonged duration accelerates the onset of complications (Setiadi *et al*., 2014).

Furthermore, a history of hypertension was associated with DPN in patients with DM ($p = 0.003$), with an average of 47 (51.6%) respondents having a history of hypertension. Similar to a study by Amour *et al.*, (2019) hypertension was a triggering factor for DPN in patients with DM, with an odds ratio of 4.3 (Amour *et al.*, 2019). Amour *et al.*, found that hypertension contributed to the incidence of DPN in patients with T2DM. A history of hypertension related to peripheral neuropathy is explained by microvascular conditions that cause hyalinization of the basal lamina of blood vessels, which triggers thrombosis in the intraneural arterioles and decreases blood flow to the nerves, resulting in hypoxia and ischemia of the nervous tissue, hypersensitization of peripheral neurons, and peripheral neuropathy (Zychowska *et al.*, 2013).

Implication and Limitations

This study has implications for nursing and health policy, where DM complications have a large impact on morbidity and mortality rates in patients with DM and on health financing owing to the length of hospitalization and long-term treatment. Complications of DM can be prevented by the seriousness of various parties in controlling the risk factors that accelerate the occurrence of complications by involving various multidisciplinary scientists and policymakers. Therefore, a special program should be created for controlling DM complications, including promotion,

education, and early detection of complications in patients with DM.

This study has limitations. PDN is only assessed based on the signs and symptoms experienced by the patient using a questionnaire. PDN could not be distinguished from other musculoskeletal conditions. In addition, we did not examine the glycemic history over a long period; therefore, a long duration of DM does not guarantee the occurrence of complications.

CONCLUSION

Patients with DM are at risk for several complications, including DPN. This risk increases in patients who are old, have an overweight BMI, or have a history of hypertension. Screening is necessary for the early detection of complications of DM, particularly DNP, based on risk factors.

Conflict of Interest

The authors have no conflict of interest to declare.

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