Correlation of nerve damage and peripheral neuropathy incidence using the MNSI and MDNS instrument approaches

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Abstract

The World Health Organization (WHO) reported that by 2030, diabetes mellitus would become the 7th leading cause of death. Diabetes mellitus is a chronic disease that causes various complications, one of which is peripheral neuropathy. Preventive efforts for peripheral neuropathy involve conducting detection examinations. The purpose of this study was to analyze nerve damage in peripheral neuropathy cases using the MNSI (Michigan Neuropathy Screening Instrument) and MDNS (Michigan Diabetic Neuropathy Score) instruments. The study employed a cross-sectional study approach with a sample of 50 people, using total sampling as the sampling technique. The independent variable in this study was nerve damage, and the dependent variable was peripheral neuropathy. Data collection in the study was carried out using the MNSI and MDNS instruments to link the dependent and independent variables. Hypothesis analysis in this study was conducted using the Spearman's rho correlation test. The study found that autonomic, sensory, and motor damage correlated with peripheral neuropathy, with a $p<0.05$. Examinations in the feet of diabetics were significantly related to the level of peripheral neuropathy. However, there was no evidence of a correlation between the characteristics of the respondents and the incidence of peripheral neuropathy. The results of the nerve damage examination demonstrated a correlation between different types of damage, and the MNSI and MDNS instruments proved effective in detecting peripheral neuropathy damage. Future research should focus on more in-depth studies to explore the correlation of nerve damage in patients with diabetes mellitus detected at a young age and consider other variables, such as HbA1c levels, as potential risk factors for peripheral neuropathy.

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Introduction

Chronic complications can occur in people with diabetes mellitus, and one of the causes is poor management of diabetes mellitus.[1] Individuals with diabetes mellitus may experience circulation problems and nerve innervation issues in their legs, putting them at risk of developing diabetic ulcers.[2] Neuropathy, a set of clinical symptoms that affect the nerves, is a major complication of diabetes mellitus, and the primary cause of neuropathy is usually damage to the peripheral and autonomic nerve parts.[3,4] Sensory neuropathy results in the loss of pain sensation, making the person unable to feel mild trauma to the foot. Even minor trauma can damage the skin's integrity. Autonomic neuropathy leads to dry and cracked skin due to the loss of sweat's moisturizing effect. Motor neuropathy causes an imbalance in leg muscle function, leading to biomechanical changes in the foot and resulting in deformity and uneven pressure distribution on the plantar aspect of the foot.[5] Indonesia, as one of the world's fifth most populous countries, also grapples with the issue of diabetes. According to the National Basic Health Survey in 2018, approximately 1.5% of Indonesians had diabetes, and one of the provinces with a prevalence rate exceeding the national average was East Java Province, where the prevalence reached 2%.[6] Peripheral neuropathy is often unrecognized because it typically asymptomatic nature, which can lead individuals with diabetes mellitus to face significant issues with their feet. However, when neuropathy does manifest symptoms like pain, tingling, and loss of sensation to temperature

changes, it can disrupt the quality of life for individuals with diabetes.[73,8] Reported worldwide, peripheral neuropathy is one of the most common complications in patients with diabetes mellitus, with an incidence ranging from 16% to 66%.[9] Individuals with type 2 diabetes mellitus experience a higher incidence of peripheral neuropathy compared to those with type 1 diabetes, with a rate of 6,100 cases per 100,000 people per year.[3,7] The results of research conducted in America and China found that as many as 6% to 51% of people with diabetes mellitus experienced peripheral neuropathy.[10] The incidence of peripheral neuropathy is also significant in Southeast Asian countries, including Malaysia (54.3%), the Philippines (58.0%), and Indonesia (58.0).[11] Questionnaires, namely the MNSI (Michigan Neuropathy Screening Instrument) and MDNS (Michigan Diabetic Neuropathy Score),[12,13] are used in addition to age. Other studies have also mentioned that the prevalence of peripheral neuropathy is related to other characteristics of the respondents, such as their education level, duration of suffering from diabetes mellitus, and gender.[14–16] The results of other studies have also identified changes in muscle strength and decreased muscle strength, particularly in men suffering from diabetes mellitus with peripheral neuropathy.[14,17] Therefore, the purpose of this study is to investigate the correlation between nerve damage and the incidence of peripheral neuropathy in patients with diabetes mellitus.

Recommendations for the prevention of peripheral neuropathy in patients with diabetes mellitus include the use of antiplatelet medication and routine foot care.[18] Currently, controlling blood sugar levels and adopting a healthy lifestyle are also crucial for preventing peripheral neuropathy.[19,20]According to a previous study conducted by Tintin *et al*., diabetic foot exercises can serve as an alternative approach to enhance sensory peripheral neuropathy.[21] Given that 50% of peripheral neuropathy cases are asymptomatic, conducting peripheral neuropathy examinations is essential. This emphasizes the need for healthcare practitioners to pay close attention to the symptoms of neuropathy in patients who have had diabetes mellitus for an extended period. This study offers a solution by using the MNSI (Michigan Neuropathy Screening Instrument) and MDNS (Michigan Diabetic Neuropathy Score) instruments to detect peripheral nerve damage. Diabetic individuals with specific characteristics have a higher potential for peripheral neuropathy damage.

Materials and Methods

The research design employed in this study is cross-sectional, which is a method used to assess the relationship between risk factors and their effects through one-time measurement observations.[22] The study involved a sample of 50 individuals with Type II Diabetes mellitus, and total sampling was used as the sampling technique. Data collection took place among respondents who routinely sought treatment and resided within the Anggana Samarinda Health Center's jurisdiction. The data collection period extended over one month, from March 1 to March 31, 2018. The collected data consisted of results from interviews and direct observations of the respondents.

In this study, the independent variable was nerve damage, while the dependent variable was peripheral neuropathy. The instruments used in this study were the MNSI and MDNS questionnaires. The MNSI serves as a clinical parameter for the early detection of neuropathy events, while the MDNS is used to assess the level of neuropathy. The peripheral neuropathy examination item from the MNSI involved a physical examination to check for the presence of dry (scaly), cracked, and calloused skin, as well as deformities.[23] Additional examination items were derived from the MDNS, including assessments of foot sensitivity, vibrational sensation, pain sensation, muscle strength, and reflex strength, which were consistent with the original examination item.[5] Tools used in this study included a 10 g monofilament, a 128 Hz tuning fork, a prick pin, and a reflex hammer. Based on the study's objectives, the examination results were categorized as follows: no neuropathy (score 0), mild neuropathy (scores 1-11), moderate neuropathy (scores 12-25), and severe neuropathy (scores 26-42).

Prior to commencing data collection, the researchers obtained ethics clearance from the Ethics Commission at Poltekkes Kemenkes Kalimantan Timur, which subsequently issued an ethics certificate with the number No.DP.04.03/7.1/07262/2018. The analysis in this study utilized univariate analysis to obtain an overview of the distribution and frequency of dependent and independent variables. Bivariate analysis employed the Spearman's rho correlation test.

Results

This section will present the research results that are relevant to the study's purpose, which is to analyze the correlation between respondent characteristics and nerve damage with the incidence of peripheral neuropathy using the MNSI and MDNS approaches. The study's findings will be presented in the form of both univariate and bivariate analyses, as follows:

Based on Table 1, it is evident that the average age of the respondents in this study was 52 years. Additionally, the average duration of suffering from diabetes mellitus was 5 years and 5 months, with the average blood sugar value among the respondents being 272.58 mg/dL. The table further reveals that 62% of the respondents are women, and a significant majority, approximately 82%, do not have a history of smoking. About 44% of the respon-

Table 1. Characteristics of respondents.

Variable	Value			
	Mean	Mode	Min	Max
Age	52.10	65	32	65
Long suffering from DM	5.5 years	-	2 months	20 years
Blood sugar	272.58	-	144	512
	n = 50		%	
Gender				
Man	19		38	
Woman	31		62	
Smoking status				
Already	9		82	
No	41		18	
Comorbidities				
Already	22		44	
No	28		56	
DFU history				
Already	8		16	
No	42		84	
Degree of peripheral neuropathy				
No neuropathy	5		10	
Mild neuropathy	35		70	
Moderate neuropathy	10		20	

dents had comorbidities, specifically hypertension, while 84% of them had no history of Diabetic Foot Ulcers (DFU). The results also indicate that 70% of the respondents experienced mild neuropathy.

Based on Table 2, the characteristics of peripheral neuropathy examination are evident, including assessments of autonomic, sensory, and motor damage in the right leg and left foot of diabetic respondents. Regarding the examination of autonomic damage in the right leg, 38% had single autonomic damage, while 14% had multiple autonomic damage. In the left leg, 40% of respondents had single damage, and 16% had multiple autonomic damage. In the second examination, which assessed sensory damage, it was found that 44% of respondents experienced decreased sensation in the left leg and 40% in the right foot. In the examination of motor damage, it was observed that 60% of respondents experienced a decrease in muscle strength in the right leg, and 64% experienced this decrease in the left leg.

Based on the results of statistical tests using the Spearman correlation analysis (Table 3), it is evident that there is no correlation between the characteristics of the respondents and peripheral neuropathy. The study's results indicate that the overall variable characteristics of the respondents have a p-value greater than 0.05.

The results of statistical tests using the Spearman correlation analysis reveal that the examination of autonomic, sensory, and motor nerves in the feet of diabetics is significantly associated with the level of peripheral neuropathy (Table 4). All relationships are in a positive direction, indicating that the higher the damage to autonomic, sensory, and motor nerves in diabetics, the greater the number of diabetics who experience peripheral neuropathy.

In Pearson's correlation analysis, it is revealed that the results of the sensory damage examination, specifically monofilament sensitivity, have a negative correlation with the examination of autonomic nerve damage ($p=0.016$; $r = -0.338$). The examination of sensory nerve damage using a pinprick shows a positive correlation with autonomic nerve damage ($p=0.007$; $r=0.376$) and a negative correlation with monofilament sensitivity damage ($p<0.001$; $r= -0.594$). Furthermore, it was observed that the examination of sensory nerve damage with a pinprick has a negative correlation with monofilament sensitivity ($p= 0.001$; $r= -0.457$) and a positive correlation with sensory nerve damage, assessed using garputala ($p<0.001$; $r=0.699$). Regarding the examination of motor nerve damage in leg muscles, a positive correlation was found with pinprick sensory nerve damage ($p=0.001$; $r=0.471$). In the reflex motor nerve examination, there was a positive correlation with pinprick sensory nerve damage ($p<0.000$; $r=0.555$) at a significance level of 0.01 (Table 5).

Discussion

The results of this study do not align with previous research indicating a correlation between age and the incidence of peripheral neuropathy.[24] In this study, mild peripheral neuropathy was observed in diabetics as young as 32 years old. These findings are consistent with retrospective research conducted in China, which reports a rapid increase in the prevalence of diabetes mellitus among young individuals (aged 18-40) due to changes in lifestyle and living standards. The study revealed that 9% of 655 newly diagnosed diabetic individuals within this age group suffered from one of the complications of diabetes mellitus, namely peripheral neuropathy.[25,26]

The relationship between age and neuropathy is closely associated with degeneration processes that can lead to damage to both large nerve cells and small nerve fibres. Neuropathy can occur as a result of blood vessel wall thickening, especially in the intima layer, causing vascular stiffness and reduced oxygen and nutrient flow. Prolonged exposure to such conditions can result in neuropathy.[27] Increasing age can lead to a decrease in cell function and a decline in overall bodily functions.. Diabetic neuropathy results from complex interactions between metabolic factors directly related to hyperglycemia and structural changes, including axonal degeneration and demyelination caused by microangiopathy. Both acute and chronic nerve damage can lead to anatomical and physiological alterations in peripheral nerves, affecting their structures, including myelin, axons, and supporting layers.[28] Beta cells in the pancreas can experience reduced function, potentially leading to hyperglycemia in people with diabetes, which can exacerbate the

Table 2. Characteristics of peripheral neuropathy examination.

Variable	Right foot		Left foot	
	N	%	N	%
Autonomic damage inspection				
Normal	24	48	22	44
Single autonomous damage	19	38	20	40
Multiple autonomous damage	7	14	8	16
Sensory damage inspection				
Normal	22	44	22	44
Decreased sensation	22	44	20	40
No sensation	6	12	8	16
Motor damage inspection				
Normal	20	40	18	36
Decreased muscle strength	30	60	32	64
No muscle strength	0	0	0	0

Table 3. Correlation analysis of respondent characteristics against peripheral neuropathy.

Variable	Diabetic peripheral neuropathy		
	p	R	Correlation direction
Age	0.059	0.269	+
Gender	0.296	0.151	+
Long suffering from DM	0.296	0.151	+
Smoking status	0.536	0.090	-
Blood sugar	0.211	0.180	+
Comorbidities	0.147	0.208	+
DFU history	0.120	0.223	+

Table 4. Correlation analysis of autonomic, sensory and motor impairment against peripheral neuropathy.

Variable.	Diabetic peripheral neuropathy		
	p	R	Correlation direction
Autonomic damage of the right leg	0.001	0.458	+
Autonomic damage of the left leg	0.002	0.426	+
Right leg sensory damage	0.001	0.667	+
Left leg sensory damage	0.001	0.569	+
Motor damage of the right leg	0.001	0.527	+
Motor impairment of the left leg	0.001	0.520	+

risk of peripheral neuropathy in elderly individuals with long-standing diabetes. Proper blood sugar control is crucial for diabetics as a preventive measure against peripheral neuropathy symptoms.[26,29] Additionally, a previous study has suggested a significant association between the Neutrophil–Lymphocyte Ratio (NLR) and arterial stiffness, with higher NLR counts corresponding to greater arterial stiffening.[30]

Another notable fact is that the signs and symptoms of peripheral neuropathy may decrease with age, along with an increased pain threshold in adulthood. Therefore, the severity of neuropathy may not always align with the symptoms experienced. As individuals age, complaints of neuropathy symptoms may diminish, but the severity of peripheral neuropathy can worsen.[31]

The occurrence of peripheral neuropathy is not influenced by gender. Therefore, this study aligns with previous research that has failed to establish a connection between gender and the incidence of peripheral neuropathy.[32] The fact in this study is that the incidence of peripheral neuropathy shows no difference based on gender, as it can occur in both men and women. While some theories suggest a higher incidence of diabetes in women, an interesting finding in this study is that the incidence of diabetes does not directly correlate with the incidence of neuropathy. When examining the results of this study, it becomes apparent that there are more female respondents than male respondents, which aligns with research indicating that women are at a six-fold higher risk of experiencing peripheral neuropathy compared to men.[31,32]

One of the causes of neuropathy is attributed to the hormone estrogen, with evidence suggesting that estrogen can disrupt iodine absorption in the intestines, consequently hindering the formation of nerve myelin.[33] Discrepancies in study outcomes can also stem from variations in the measuring instruments used.[34] Other research indicates that if diabetes mellitus onset occurs at a young age (18-40 years), the risk of mortality and complications is more common in men due to factors such as environmental influences, socioeconomic status, genetics, life pressures, and education level. Research results also mention that young women rarely suffer from diabetes, possibly due to their higher estrogen levels.[35,36]

Diabetes mellitus is also considered a risk factor in the incidence of peripheral neuropathy. However, this study contradicts previous research explaining that one of the causes of peripheral neuropathy is the duration of suffering from diabetes mellitus. In this study, it was observed that the duration of diabetes mellitus did not correlate with the incidence of peripheral neuropathy. The fact uncovered in this study is that mild peripheral neuropathy can occur in individuals with diabetes who have had the condition for a range of 3 to 18 years. However, some people with diabetes mellitus in this study did not experience peripheral neuropathy, even though they had been living with diabetes for 20 years. In theory, it is postulated that the longer an individual experiences hyperglycemia,[37] the more likely changes in nerve tissue occur due to the accumulation of sorbitol and increased activity in polyol pathways. Consequently, these changes can lead to alterations in nerve signal transduction, resulting in reduced sensitivity in the legs for people with diabetes.[38,39] In contrast, foot exercises significantly impacted the Ankle Brachial Pressure Index value and foot sensation in patients with diabetes mellitus.[40]

Another significant finding from prior studies suggests that patients with adult-onset diabetes mellitus, or those recently diagnosed with diabetes within one year, may already exhibit diabetes complications. This can occur due to delayed detection of diabetes. To avoid such delays in diagnosing diabetes, especially in young adults, the American Diabetes Association (ADA) guidelines for 2022 recommend diabetes screening starting at age 35.[26,35]

The smoking status in this study does not align with previous research, which suggests that actively smoking and having a history of smoking can increase the risk of microvascular and macrovascular complications.[41] The results of the current study indicate that smoking is not correlated with the incidence of peripheral neuropathy. In this study, it is observed that mild peripheral neuropathy events occur in diabetic patients who do not smoke (80%), and the same applies to diabetic patients who do not smoke and do not experience peripheral neuropathy (90%). Diabetics who do not smoke also account for those who do not experience peripheral neuropathy (98%). The difference between this study and previous research results is that out of the 50 respondents, only 9 had a smoking history.

In this study, it is found that current blood sugar values are not correlated with the incidence of peripheral neuropathy. This finding contrasts with previous research, which suggested that blood glucose levels correlated with the prevention of peripheral neuropathy.[42] The fact in this study is that mild peripheral neuropathy occurs in patients with diabetes mellitus with blood sugar values ranging from 144 to 512 mg/dL, peripheral neuropathy events occur in patients with diabetes mellitus with blood sugar values ranging from 214 to 472 mg/dL, and those who do not experience peripheral neuropathy have blood sugar values between 184 and 361 mg/dL. This study concludes that individuals with diabetes mellitus with unstable glucose levels do not necessarily suffer from peripheral neuropathy. This discrepancy may be due to researchers only measuring blood glucose without considering fluctuations in

Table 5. Correlation analysis on each examination variable.

	1	2	3	4	5	6	7	8	9	10
Blood sugar	1									
Long-suffering from DM	0.283*	1								
Age of respondents	-0.090	0.244	1							
Autonomic deterioration	0.070	0.180	0.243	1						
Sensory damage, monofilament sensitivity	-0.272	-0.323*	-0.334*	-0.338*	1					
Sensory damage, tuning fork	0.272	0.209	0.174	0.376**	-0.594**	1				
Sensory damage, pinprick	0.191	0.232	0.213	0.148	-0.457**	0.699**	1			
Motor deterioration, deformity	-0.083	0.074	0.308*	0.216	-0.253	0.171	0.070	1		
Motor impairment, leg muscle strength	0.105	0.216	0.112	0.206	-0.142	0.160	0.471**	-0.171	1	
Motor damage, reflexes	0.361*	0.310*	0.057	0.200	-0.487**	0.745**	0.555**	-0.037	0.218	1

* Correlation is significant at the 0.05 level (2-tailed); ** Correlation is significant at the 0.01 level (2-tailed).

blood sugar from the previous day. According to the results of a research survey, blood sugar fluctuations are strongly influenced by diet.[43] Additionally, this study did not examine whether respondents with diabetes mellitus received treatments for the prevention of peripheral neuropathy symptoms, such as folic acid and vitamin B12.[42]

Comorbidities were not correlated with the incidence of peripheral neuropathy in this study, contradicting previous research suggesting that comorbidities can influence the incidence of peripheral neuropathy.[42] The fact in this study is that peripheral neuropathy occurs in patients with diabetes mellitus, whether they have comorbidities or not. However, the study does not provide detailed information about the specific diseases that the patients may have. Previous research indicated that the most common comorbidities included gout and hypertension. Changes in smooth muscle cells, endothelial cells, blood vessel walls, and blood pressure can increase vascular risk in diabetics.[44] For patients with gout, it is known that high uric acid levels increase oxidation in the body and provoke inflammation. Elevated uric acid levels can stimulate the renin-angiotensin system, damage vascular endothelial cells, and increase proliferation in vascular smooth muscle.[45]

Patients with Type 2 diabetes may also experience foot ulceration as one of the major complications. The severity of these ulcers and the prevention of new wounds can be addressed through early detection interventions.[46] Diabetic Foot Ulcers (DFUs) are caused by prolonged instability in blood sugar levels, which affect the peripheral blood vessels and the nervous system.[47] The fact in this study is that the incidence of peripheral neuropathy occurs in patients with diabetes, whether or not they have a history of DFU. The results of this study align with research that suggests not all individuals with diabetes mellitus and DFU develop peripheral neuropathy. This discrepancy may arise from a delay in diagnosing peripheral neuropathy in DFU patients.[48] In this study, it was found that 84% of diabetics had not experienced DFU, emphasizing the need to expedite screening for peripheral neuropathy symptoms, as the study revealed that 50% of peripheral neuropathy sufferers did not exhibit symptoms.[7]

From the three assessments of neurological function for peripheral neuropathy, a correlation was observed between sensory, motor, and autonomic examinations and peripheral neuropathy. These findings are consistent with previous research indicating that peripheral neuropathy is often accompanied by sensory, motor, and autonomic damage.[49,50] Sensory nerve damage generally involves both small and large nerve fibers. Damage to small nerves affects a patient's ability to feel pain and temperature stimuli, while significant nerve damage may result in sensitivity or touch disorders.[32] Previous studies have shown that sensory and motor damage in patients with peripheral neuropathy can lead to reduced sensitivity, loss of ankle reflexes, joint mobility disorders, muscle weakness, and an increased risk of falling.[51–53]

The presence of tissue hypoperfusion, particularly in peripheral areas, can lead to increased oxidative stress, which may cause autonomic nerve damage. Patients with autonomic nerve damage may experience symptoms such as dry skin, cracked skin, and the development of calluses in their legs. These symptoms can occur due to oxidative stress, resulting in damage to endothelial tissue and increased blood flow in the arteries. The increased blood flow triggers sympathetic nerve activity, which can affect sweat gland production and lead to decreased sweating.[54] Sensory nerve damage involves small nerve fibers that are responsible for sensing pain and temperature sensations, while large fibers are used for perceiving vibrations and tactile sensations. Damage to these nerves interferes with sensitivity and touch perception.[55] Some research results suggest that motor nerve damage is not directly influenced by diabetes mellitus. However, respondents experiencing peripheral neuropathy may suffer from impaired balance and changes in plantar pressure. Other studies also indicate that individuals with diabetes mellitus may experience weakness in lower extremity muscles, particularly those with polyneuropathy.[56 57]

Peripheral neuropathy progresses slowly and can cause symptoms of sensory and autonomic damage, which are often followed by motor nerve damage. Most patients experience positive sensory symptoms, including exaggerated or spontaneous responses such as paresthesias and pain. These symptoms may manifest as numbness, tingling, imbalance, prickling, and a burning sensation. They tend to worsen, particularly at night. In general, these symptoms can range from mild to severe. Negative sensory symptoms, characterized by a decreased response to certain stimuli, indicate a loss of sensitivity in the affected segments. Severe neuropathic pain may also be present, in the form of hyperesthesia (an excessive response to tactile stimuli), hyperalgesia (an increased sensitivity to pain stimuli), hyperpathy (persistent pain), or even allodynia (pain sensations triggered by non-painful stimuli). These symptoms may progress to hypo/anesthetic sensitivity, resulting in reduced responsiveness to touch, vibration, and proprioception. Additionally, sensory impairment in large nerve fibres can lead to hypo or absence of deep reflexes, particularly in the Achilles reflex. In very severe cases, common reflexes may be entirely absent.[50,53]

Conclusions

The quicker the detection of peripheral neuropathy symptoms, the better the chances of preventing complications associated with it. Early detection of peripheral neuropathy can be achieved using the MNSI instrument, as it can identify damage in neurological nerves, typically encompassing autonomic, sensory, and motor nerves. The MDNS instrument is capable of assessing the extent of peripheral neuropathic damage. If a person with diabetes mellitus experiences nerve damage, it will lead to autonomic and motor damage, increasing the risk of peripheral neuropathy as the level of nerve damage rises.

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