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Neuropaty Detection In Diabetes Mellitus Patients

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A R T I C L E I N F O

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ABSTRACT

Diabetes mellitus (DM) is a metabolic disease that contains a collection of symptoms that arise in a person caused by an increase in blood glucose levels (hyperglycemia) due to a progressive decrease in insulin secretion, the prevalence of Diabetes Mellitus in the world continues to increase every year. Type 2 diabetes mellitus is a chronic disease that is increasing in the world and is the cause of various organ damage, one of which is diabetic peripheral neuropathy. Early detection of diabetic peripheral neuropathy and identification of risk factors can reduce the morbidity of diabetic peripheral neuropathy. Cases of diabetic neuropathy affect as many as 54% of patients with type 2 diabetes, the prevalence of neuropathy in patients with diabetes mellitus is approximately 30% in hospital patients and 20% in patients in the community. Complications of neuropathy can strike patients with diabetes mellitus at various ages. The longer a patient has diabetes, the risk of developing complications of Diabetes Mellitus will increase. The cause of this is due to degenerative factors, namely a decrease in body functions, especially the ability of pancreatic -cells to produce insulin and other organs of the body that also perform compensatory mechanisms during persistent hyperglycemia. The purpose of this study is to find a simple test that can be used by the public in detecting diabetes mellitus neuropathy, while the data collected by researchers from 2013 to 2018 used 3 databases (Pubmed, ScienceDirect, Google Scholar). So the results of this study explain that the Sudoscan method is a test that does not require special preparation and can be used by untrained people, of course, in detecting neuropathy in diabetes mellitus, while the neuropad method can be carried out by non-professional staff and takes 9 minutes to 13 minutes. minutes and is now easy to use. These methods are very effective, and do not require tools and can be used by the general public, so they can be used to detect neuropathy both in hospitals, health centers and in patients' private places.

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1. Introduction

Diabetes Mellitus (DM) is a chronic disease characterized by blood glucose (blood sugar) levels exceeding normal, i.e. blood sugar levels being equal to or more than 200 mg/dl, and fasting blood sugar levels being above or equal to 126 mg/dl. Diabetes Mellitus is known as the silent killer because the sufferer is often not aware of it while when it is known to have occurred at the level of complications, this disease can attack almost all systems of the human body, from the skin to the heart which eventually causes very crucial complications (Azaka et al., 2019).

Diabetes Mellitus (DM) is still one of the main health problems that we often encounter. The incidence rate has increased from time to time, even according to a survey by the International Diabetes Federation (IDF) which shows that the incidence of Diabetes Mellitus in the world for the last three consecutive years has always increased significantly, the details are as follows in 2013 (7.2%), 2014 (8.3%) and 2015 (8.8%).

As previously explained, Diabetes Mellitus is a metabolic disease caused by increased levels of glucose or blood sugar. Blood sugar is vital for human health because it is an important source of energy for cells and tissues. The disease is divided into several types, namely, type 1 diabetes, in which the body's immune system attacks and destroys the beta cells in the pancreas that produce insulin. Then Type 2 Diabetes, where the beta cells in the pancreas do not produce insulin in sufficient quantities, or the body's cells do not show a response to the insulin that is produced, there is also gestational diabetes, which is diabetes that occurs during pregnancy and other types of diabetes, which can cause diabetes. arising from hormonal, immunological, infectious, or other genetic disorders (Bagus et al., 2017).

If not managed properly, Diabetes Mellitus can cause various complications, such as coronary heart disease, stroke, obesity, and disorders of the eyes, kidneys, and nerves. In addition, Diabetes can also cause fluctuations in blood sugar levels in the body, this can lead to a sudden decrease (hypoglycemia) or increase in blood sugar levels (hyperglycemia), this disease can also cause chronic complications, both angiopathy and neuropathy. The method for managing neuropathy can be detected using a monofilament test, while angiopathy is detected through an ABI (Ankle Brachial Index) examination.

Enforcement of the diagnosis of Diabetes Mellitus is carried out by measuring blood sugar levels, the recommended blood sugar examination is enzymatically using venous blood plasma material. The criteria for the diagnosis of diabetes mellitus include four things, namely (1) fasting plasma glucose examination of approximately 200 mg/dl, fasting is a condition of no caloric intake for at least eight hours (2) plasma glucose examination of approximately 200 mg/dl 2 hours after oral glucose tolerance test (OGTT) with a glucose load of 75 grams (3) Examination of plasma glucose when approximately mg/dl with classic complaints (4) HbA1c examination of approximately 6.5% using the method standardized by the National Glychohaemoglobin Standardization Program (NGSP)) (Christia et al., 2015).

Examination results that do not meet the normal criteria or the criteria for diabetes mellitus are classified into the prediabetes group which consists of impaired glucose tolerance (TGT) and impaired fasting blood glucose (GDPT), this can occur when the results of the fasting plasma glucose examination are between 100-125 mg/dl and 2-hour plasma glucose OGTT examination < 140 mg/dl. The TGT is met if the results of the plasma glucose examination 2 hours after the OGTT are between 140-199 mg/dl and fasting plasma glucose <100 mg/dl. In addition, in someone who has been diagnosed with diabetes mellitus, HbA1c levels can be checked at least every three months if they have not reached their blood sugar target, and every 6 months for those with stable blood sugar levels.

Currently, there are many blood sugar measuring devices that are easy to use, the results obtained are generally reliable if the calibration of the equipment is carried out properly and the examination is carried out according to the recommended method, while the recommended time for self-monitoring of blood sugar is just before eating. , 2 hours after eating, at bedtime, or when experiencing certain symptoms. It is very important for someone to prevent diabetes mellitus early, especially if you have diabetes risk factors such as being overweight or have a family history of diabetes mellitus. For this reason, it is important to implement a healthy lifestyle and always consume healthy and balanced nutritious foods, as well as exercise regularly so that body weight is maintained (Desnita, 2018).

The most common complication of Diabetes Mellitus (DM) in the past few years is diabetic neuropathy, which is a painful symptom of nerve disorders that can cause numbness, this occurs because the axons and dendrites do not get enough nutrition, which causes the nerves to send impulses slowly. , plus the accumulation of sorbitol in the nervous tissue. Peripheral neuropathy is the most common form of diabetic neuropathy in people with diabetes mellitus, more than 40% of patients with type 2 diabetes mellitus have diabetic peripheral neuropathy. Diabetic neuropathy is a major cause of morbidity and mortality in patients with diabetes mellitus, and generates a large economic burden, besides diabetic neuropathy also predisposes to ulcers and gangrene of the feet that require proper treatment, diabetes mellitus patients who experience complications of peripheral neuropathy have a good quality of life. low due to signs and symptoms experienced such as neuropathic pain, mobility barriers, and balance disorders (Embuai, 2020).

Controlling blood glucose levels and early detection of neuropathy symptoms can prevent the occurrence of diabetic neuropathy in type 2 Diabetes Mellitus patients. Blood glucose control begins with non-pharmacologic therapy, namely lifestyle modification. . Therapy given to type 2

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Diabetes Mellitus patients is not only done for the short term, but with the aim of preventing and inhibiting the progression of microvascular and macrovascular complications that may arise so that patient compliance is needed in taking medication regularly so that blood glucose remains under control, detection of Neuropathy symptoms need to be done to prevent more severe complications. One of the simplest and easiest way to assess neuropathy symptoms is to use the Diabetic Neuropathy Symptom (DNS) questionnaire. So based on the background description above, researchers are interested in detecting and finding a simple test for detecting neuropathy in Type 2 Diabetes Mellitus patients that is easy and effective to use by the public.

2. Method

Researchers conducted a literature search relevant to the incidence of neuropathy and risk factors associated with complications of type 2 diabetes mellitus. The search was carried out through electronic databases such as (Pubmed, Science Direct and Google scholar). Then the literature is limited to full text articles, articles published between 2010 and 2018, and journal articles only. The results are successively found several literatures that are closest to the focus of the problem that the researcher is looking for. Then the literature that is most appropriate to the topic is selected regardless of the method or type of literature research, so that approximately 16 literatures are reviewed. all relevant articles were reviewed and analyzed (Halmar et al.,2019).

3. Results and Discussion

Sudoscan is a test that evaluates sweat gland function by measuring the ability of the sweat glands to release chloride ions in response to electrical stimulation on the palms of the hands and soles of the feet. Supported by research by Casellini et al., (2013) which states that Sudoscan is a significant and sensitive tool in detecting neuropathy (78% sensitivity and 92%). In addition, research by Calvet, Dupin, Winiecki, & Schwarz, (2012) This test was accepted by the subjects without complaint, safe and comfortable during the test with a required time of 2 minutes. The use of sudoscan was significant in detecting neuropathy in distal small fibers in diabetics less than and above 5 years of age (p= 0.0007 and p= 0.0058 respectively), very simple, requires no preparation and comfortable for the patient. The sudoscan method is one method of detecting neuropathy that is effective and easy to use in detecting neuropathy (Herlina et al., 2019).

The patch changes color from blue to pink when there is no disturbance, but remains blue or partially turns pink, if it is neuropathic. The adhesive pad contains the anhydrous blue salt of cobalt II chloride, which reacts and turns pink when exposed to water. In line with research (Ponirakis et al., 2014) Neuropads experience color changes at 10 minutes. The IpTT method is a simple test for detecting neuropathy. The IpTT touches the tips of the first, third and fifth toes using the examiner's finger for 1-2 seconds. The touch should be light and gentle. If the patient does not feel the touch 2 points, it is declared neuropathy (Hanifah, 2019).

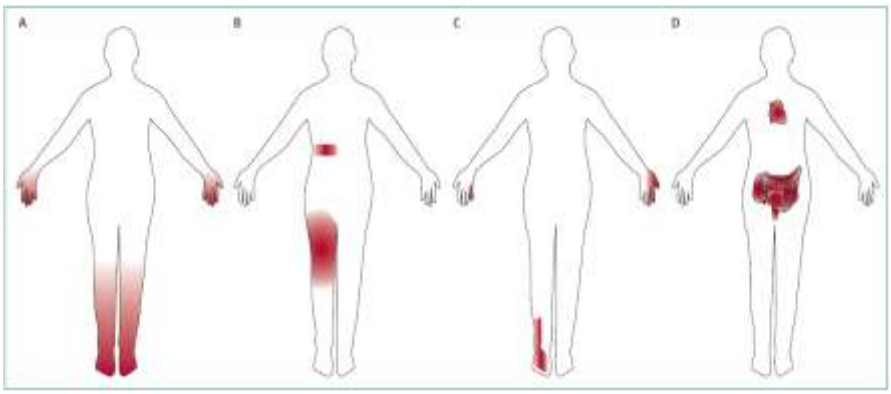

Figure 1. Classification of Diabetic Neuropathy

The most common form of generalized group neuropathy is distal symmetrical polyneuropathy as seen in the image above. Meanwhile, the focal and multifocal groups associated with diabetes mellitus can be broadly divided into recurrent, mild neuropathy, which is caused by mechanical trauma, compression, or entrapment and possibly associated with an inflammatory process with or without involvement of the ischemic process (LESTARI, 2014).

3.1 Pathophysiology

The pathogenesis of diabetic neuropathy is complex, and the mechanism of the disease is still not fully understood, and various hypotheses have been proposed. However, hyperglycemia or high blood glucose levels is believed to be the condition that is responsible for the changes that occur in the nervous tissue. There are two main mechanisms that are thought to have an important role in the occurrence of diabetic neuropathy, namely vascular disorders and metabolic disorders. Recently, a hypothesis has emerged which states that active neuroimmunity interactions contribute to the onset and onset of persistent pain in people with diabetes mellitus (Mulyaningsih & Handayani, 2021). In addition, the role of glial cells in the pathogenesis of diabetic neuropathy is also in further research. The pathogenesis of diabetic neuropathy usually progresses from metabolic changes, to ion current defects, and then the development of further structural and functional defects. Positive and negative clinical signs/symptoms will also develop in degree and severity as diabetic neuropathy worsens. Sensory sensitivity changes, reflecting sensory axon dysfunction, can be detected even in asymptomatic patients, as seen in the image below:

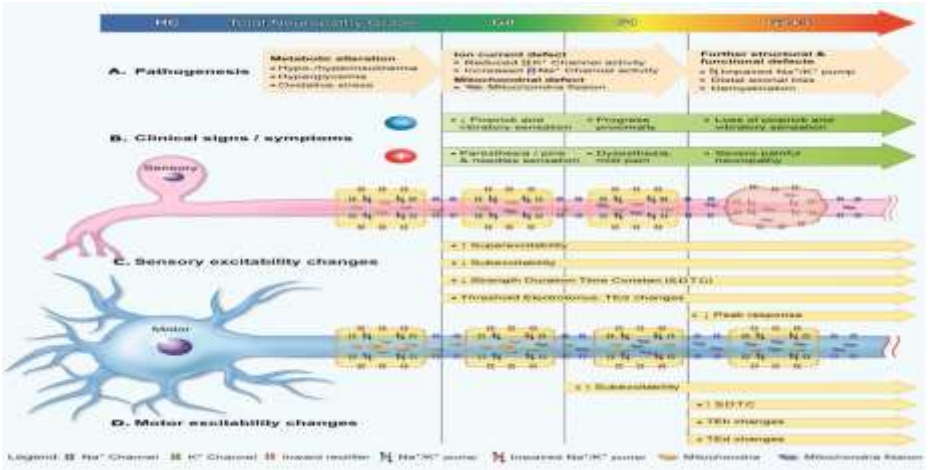

Figure 2. Stages of Nerve Damage in Diabetic Neuropathy

3.2 Diabetic neuropathy risk factors

There are several variables that influence neuropathy including age, gender, weight, height, body surface area, and body mass index. According to the research results in the article findings, there are various risk factors for diabetic neuropathy. As in a study in Romania found risk factors for age, duration of diabetes mellitus, HbA1c levels, hypertension, dyslipidemia, retinopathy, and nephropathy associated with the incidence of diabetic neuropathy in patients with type 2 diabetes mellitus. Furthermore, research in India found that the risk factors for diabetic neuropathy in patients with type 2 diabetes mellitus were age, microalbumin, duration of diabetes mellitus, and retinopathy. Glycemic control is the most important risk factor in the development of neuropathy, where an increase of 1% HbA1c increases 10-15% of neuropathy. Articles that discuss risk factors for peripheral neuropathy in type 2 diabetes mellitus find variations in risk factors. Research in India on patients with type 2 diabetes mellitus found that age and duration of diabetes mellitus were risk factors for diabetic neuropathy (Purwanti, 2013).

Symptoms of diabetic neuropathy vary widely. The most common symptom is tingling or numbness. These complaints usually begin to occur in the soles of the feet. Because the

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symptoms of this neuropathy appear very slowly, complaints of numbness sometimes go unnoticed by diabetics. Numbness or tingling should be suspected in people with diabetes who have sores on their feet but don't remember how these injuries occurred. In addition to a sense of loss of sensation, sometimes diabetic neuropathy actually gives symptoms of pain. The pain usually gets worse at night. Generally, sufferers describe the pain as cramping, burning, or like being slashed. Not infrequently, neuropathy also causes complaints of muscle weakness. People with diabetic neuropathy find it difficult to walk, and their muscles, especially in the calf area, appear to be shrinking.

If the neuropathy experienced is a type of autonomic neuropathy, complaints of dizziness, low blood pressure, difficulty defecating or diarrhea, and sexual dysfunction can also occur. The management of diabetic neuropathy requires the cooperation of neurologists and internal medicine specialists, especially endocrinologists. The presence of disturbances in sensation in the form of numbness or tingling often causes pain that is not realized how it occurs. Often these wounds are quite deep. It is necessary to take good care of the wound to prevent the wound from rotting and becoming gangrene. If there is erectile dysfunction due to neuropathy, sometimes the doctor will give the drug sildenafil or inject papaverine into the penis. To treat low blood pressure, patients are generally recommended to drink water and consume more salt (Putri & Waluyo, 2020).

Diabetic neuropathy can be prevented by (1) Controlling blood sugar. As much as possible try to keep HbA1C levels below 7%, fasting blood sugar levels less than 130 mg/dl, and blood sugar levels after eating below 180 mg/dl (2) Keeping blood pressure below 140/90 mmHg (3) Doing foot exercise for diabetics (3) Avoid exposure to cigarette smoke (4) Eat high-fiber and low-fat foods (5) Maintain ideal body weight (5) Check with the doctor at least once every three months. Complications of diabetes mellitus with neuropathy can be experienced by diabetics of various ages, someone who is more than 30 years old will experience physiological changes that can reduce a person's body functions. Diabetic neuropathy is often found after a person reaches the age of 50 years.

According to a Roman-Pintos review, age, gender, duration of diabetes mellitus, poor glycemic control, height, overweight, obesity, insulin therapy are risk factors for diabetic peripheral neuropathy in patients with type 2 diabetes mellitus. insulin and metformin, male gender and old age are risk factors for diabetic neuropathy, in addition, low socioeconomic and poor glycemic control can also be a risk for diabetic neuropathy. The length of time a person suffers from Diabetes Mellitus can exacerbate the risk of complications including neuropathy and diabetic ulcers. Long time suffering from Diabetes Mellitus has a close relationship with diabetic neuropathy (Yuliani et al., 2017).

Chronic hyperglycemia conditions cause decreased insulin secretion or decreased insulin sensitivity. Excess glucose will enter the Polyol pathway, so that glucose turns into sorbitol. Sorbitol formed will cause intracellular osmotic stress on nerve cells so that it can cause nerve cell damage. In reducing high intracellular glucose, the enzyme aldose reductase reduces the amount of glucose that enters the Polyol pathway, but this also causes a reduction in glutathione which then increases the production of Advanced Glycation End Products so that in the end it will still cause oxidative stress in nerve cells. The longer a person suffers from Diabetes Mellitus, this process will continue for longer and will continue to cause further damage to cells, especially nerves. The features of nerve cell dysfunction are segmental demyelination, damage to axons, and thickening of the basement membrane that surrounds the surface of Schwann cells. Over time, the nerve cell axons will disappear completely. In addition to morphological abnormalities, patients with Diabetes Mellitus will also find functional abnormalities of nerve cells in the form of impaired impulse conduction, both motor and sensory (Yulita et al., 2019).

In patients with diabetic neuropathy, there is a decrease in the rate of blood flow to the endoneurium caused by the presence of vascular resistance due to hyperglycemia.

From the results of the sural nerve biopsy of diabetic neuropathy patients, it was found that there was thickening of blood vessels, platelet aggregation, endothelial hyperplasia, and pseudo-blood vessels that contributed to the occurrence of ischemia. This ischemia causes disruption of axonal transport and Na+/K+ ATPase activity which in turn causes axonal degeneration and nerve dysfunction, this is also influenced by VEGF levels.

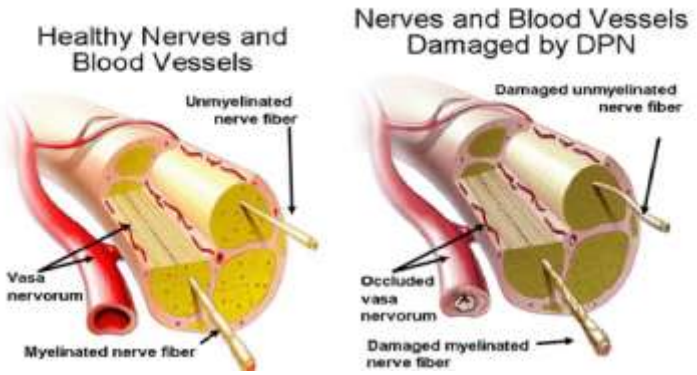

Figure 3. Differences between normal and ischemic nerve fibers

Measurement of HbA1c levels is one method used for monitoring glucose control in patients with DM. HbA1c assessment can assess the effectiveness of therapy by monitoring blood glucose regulation in the long term. The HbA1c value is a proportional plasma glucose concentration within 4 weeks to 3 months. Blood sugar control as assessed by HbA1c levels has been associated with the progression of DM complications, one of which is neuropathy. One of the scoring or scoring systems to diagnose diabetic neuropathy that has been validated and widely accepted is the Neuropathy Symptom Score (NSS). However, some of the criteria used in NSS are criteria that are rarely assessed, this is because the NSS is not made specifically for people with diabetic neuropathy. A large group of diabetics requires regular screening to diagnose diabetic neuropathy as early as possible so as to prevent the occurrence of diabetic ulcers. The consequence of this is the development and modification of several scoring systems that fully meet the methodological criteria for diagnostic tests (Yusuf et al., 2020).

The clinical manifestations of diabetic neuropathy are highly dependent on the type of nerve component involved, what part of the nerve is involved, and the underlying pathophysiological mechanism. Diabetic neuropathy can affect all the nerves in the patient's body and its manifestations can be in the form of positive symptoms and negative symptoms. Positive symptoms indicate an increase in the spontaneous activity of nerve fibers, for example the emergence of allodynia, paraesthesia, and hyperalgesia, while negative symptoms indicate a decrease in nerve fiber activity, for example the emergence of numbness and anesthesia Positive symptoms are closely related to the quality of life of diabetic neuropathy patients. because not infrequently these symptoms cause sleep disturbances and depression that occurs in 5-10% of patients. On the other hand, negative symptoms have a high level of morbidity and mortality because patients tend to ignore these symptoms so that they get treatment too late (Hanifah et al., 2021).

TABLE 1
CLINICAL MANIFESTATIONS OF DIABETIC NEUROPATHY

Types of Nerve Components	Clinical Manifestations	Examination Form
Sensory	Increased sensitivity to pain > Alodinia > Hiperestesia	Monofilamen 10 g
	Decreased sensitivity to pain > Hipoestesia > Parastesia > Anesthesia	*Pin Prick*
	Loss of perception	Garpu tala 128 Hz
Motorik	Atrofi kaki	PF muscle strength and physiological reflexes

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Otonom	Deformitas Impaired skin hydration Decreased skin turgor Atrophy of the skin and pads vasomotor network	Inspection: deformity Inspection: dry skin Inspection: cracked skin Inspeksi : *callus*

In terms of early detection of the incidence of diabetic neuropathy, there are several types of examinations that can be performed to diagnose a condition of peripheral nerve dysfunction/DPN. Screening for DPN is recommended to be carried out in every type 1 Diabetes Mellitus patient who has suffered for five years or more as well as in every type 2 Diabetes Mellitus patient. It is recommended that the examination be repeated every year. In the anamnesis, the patient's medical history that needs to be explored is a history of diseases associated with neuropathy, such as endocrine disorders (hyperthyroidism, hypothyroidism, etc.), renal insufficiency, liver dysfunction, HIV infection, vasculitis and malignancy. In addition, the patient's social history also needs to be explored, especially those related to work (possibility of exposure to toxic substances), living environment, lifestyle, alcohol consumption, and smoking. Medication history also needs to be asked about the types of drugs the patient has taken, duration of drug use, and history of drug allergies.

4. Conclusion

Examination to establish the diagnosis of diabetic neuropathy can be done by several methods such as sudoscan, neuropad and simple clinical neurological examination in stages every year, related to symptoms of sensory, motor, and autonomic sensitivity. Another cause that can occur in diabetic neuropathy patients is due to degenerative factors, namely a decrease in body function, especially the ability of the -cells of the pancreas to produce insulin and other body organs that also perform compensatory mechanisms during persistent hyperglycemia. Risk factors for diabetic peripheral neuropathy in diabetes mellitus Type 2 diabetes mellitus patients were age, gender, duration of diabetes mellitus, glycemic control (HbA1c and fasting plasma blood glucose levels and 2 hours postprandial), cardiovascular risk factors such as hypertension, dyslipidemia, overweight, obesity and microalbuminemia, the presence of other microvascular complications such as nephropathy and retinopathy. Education related to prevention of modifiable risk factors can be increased such as: weight loss, healthy lifestyle (healthy diet and physical activity), regular drug consumption, modification of specific risk factors related to cardiovascular risk factors.

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