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The Association between Waist Hip Ratio and Severity of Diabetic Peripheral Neuropaty in Diabetes Melitus Type 2 by Using Toronto Clinical Scoring System

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ABSTRACT

Introduction: Diabetic neuropathy is a common and progressive microvascular complication of diabetes, so early detection and prevention is very important. Other modifiable risk factors such as hypertension, dyslipidemia, or central obesity can be managed. Central obesity with insulin resistance is a key pathophysiological factor in the metabolic syndrome. Waist hip ratio (WHR) has been proposed as a tool for detecting central obesity. Toronto Clinical Scoring System (TCSS) is a diabetic neuropathy scoring system that has high sensitivity and specificity. The aim of this study was to determine the relationship between waist hip ratio and the severity of peripheral diabetic neuropathy in type 2 Diabetes Melitus (DM) according to the Toronto Clinical Scoring System (TCSS).

Method: This study used a cross-sectional design. Sampling was conducted at the Endocrinology Polyclinic and Neurology Polyclinic Hospital H. Adam Malik Medan. The research sample was taken as many as 45 subjects consecutively. TCSS examination is performed to diagnose and determine the severity of diabetic neuropathy Therefore, waist hip ratio was calculated to assess central obesity. Data analysis using Chi Square test.

Results: On the demographic characteristics of the research subjects were male, age range 51-60 years, high school education level, not working, history of DM 5-10 years. The mean value of WHR is 0.87±0.051. Median TCSS Score 10 (6-16). The majority of subjects had mild diabetic peripheral neuropathy. Patients with central obesity had a grading of neuropathy that was classified as severe as many as 13 people (56.5%), moderate as many as 7 people (30.4%), and mild as many as 3 people (13.0%). While patients who are not obese have a grading of neuropathy that is classified as severe as many as 1 person (4.5%), moderate as many as 5 people (22.7%), mild as many as 16 people (72.7%). Based on the Chi Square test, it was found that there was a significant association between the waist hip ratio and the severity of diabetic peripheral neuropathy in type 2 DM patients with $p<0.01$.

Conclusion: There is a statistically significant association between waist hip ratio and the severity of diabetic neuropathy in type 2 DM with $p < 0.01$.

Keywords

Waist hip ratio, Diabetic peripheral neuropathy, DM type 2, TCSS

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INTRODUCTION

Diabetes Mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia that occurs due to defects in insulin secretion, insulin action or both [1]. Diabetic neuropathy is a common and progressive microvascular complication of diabetes, so early detection and prevention is very important in reducing the

morbidity and mortality of diabetic neuropathy [2]. Therefore, risk factors for diabetic neuropathy must be identified. According to several previous epidemiological studies, age, duration of diabetes, smoking status, and components of the metabolic syndrome such as obesity are well-known risk factors for diabetic neuropathy [3,4].

Of all the complications of DM, neuropathy causes the greatest morbidity and reduces the patient's quality of life if not managed properly. Diabetic neuropathy can develop asymptomatically and undetected, can also show signs and symptoms that progress slowly and even serious complications occur [5]. Furthermore, diabetic neuropathy is associated with gait abnormalities and decreased balance which can therefore cause disability for the patient and reduce the patient's quality of life [6,7].

International Diabetes Federation (IDF) predicts an increase in the number of people with DM worldwide from 425 million in 2017 to 628 million in 2045 [8]. In Indonesia, the World Health Organization (WHO) predicts an increase in the number of people with DM from 8.4 million in 2000 to around 21.3 million in 2030. This report shows an increase in the number of people with DM by 2-3 times in 2035 [1]. Diabetic neuropathy is the most common complication in DM patients. DM sufferers have 11 times the risk of experiencing neuropathy compared to those who do not suffer. In the United States, 60-70% of DM patients are complicated by diabetic neuropathy. Meanwhile in Indonesia, 60% of diabetic neuropathy patients are found [1,8]. Diabetic neuropathy refers to a diverse collection of clinical disorders affecting the nervous system, with distinct anatomic features, clinical course, and phenotype [9].

There are five components of the metabolic syndrome: central obesity, high blood pressure, cholesterollow high-density lipoprotein (HDL), high triglycerides, and hyperglycemia. Patients with diabetes already have hyperglycemia, but other modifiable risk factors (modifiable) such as hypertension, dyslipidemia, or central obesity can be overcome. Central obesity with insulin resistance is a key pathophysiological factor of the metabolic syndrome [10].

Research by Oh et al. (2019) reported evidence showing that central obesity and insulin resistance play a role in the pathophysiology of diabetic neuropathy. Patients with diabetic neuropathy have higher insulin resistance and greater rates of obesity. Furthermore, physical examination in diabetic neuropathy patients has a significant relationship with HOMA-IR, body mass index (BMI), waist circumference, and visceral fat area. Central obesity, waist circumference, and visceral fat area were also found to be strongly associated with HOMA-IR. This suggests that insulin resistance acts as a key regulator between obesity and diabetic neuropathy [10].

Anthropometric measurements are generally used to assess disease risk factors because they are easy to monitor at the community level, and are used in epidemiological studies to predict the development of type 2 DM. BMI measurements are used to relate weight to height and are most often used to estimate the prevalence of obesity in a population. where BMI $\geqslant$25 kg/m2 is associated with increased morbidity of type 2 DM and BMI $\geqslant$30 kg/m2 is associated with an increased risk of morbidity and mortality due to diabetes and its complications. However, BMI only reflects total body fat and does not distinguish between different patterns of fat distribution. Waist size (waist circumference /WC) andwaist hip ratio (WHR) has been proposed as a tool to detect central obesity. Until now, the association between metabolic control and the development of microvascular complications (retinopathy, neuropathy and nephropathy) is a major concern of clinicians. The factors involved in the development of vascular complications in diabetes are long-standing diabetes, poor glycemic control, smoking, hypertension and dyslipidemia are well known, but there is still not much data showing the role of weight/body fat distribution. In this regard, research by Bulum et al. reported that WC and WHR can be used as a simple and non-invasive method to detect diabetic neuropathy in a population of type 2 DM with obesity [11].

The relationship between morphological changes and nerve function as determined by nerve conduction studies (NCS) has been shown previously for diabetic neuropathy and other polyneuropathies [12,13]. The gold standard for diagnosing diabetic small nerve fiber neuropathy is measurement of intraepidermal nerve

fiber density (IENFD) by skin punch biopsy. However, this invasive approach is rarely used in routine diagnosis and is mainly used for research purposes [14,15].

Recently, a different clinical scoring system was developed as a quantitative instrument to document the presence and severity of diabetic neuropathy. Toronto Clinical Scoring System (TCSS) is one of the scoring systems implemented as a simple screening method for diabetic neuropathy to classify patients into severity categories and has been reported to have a good relationship with NCS findings and complications in subjects withdistal sensory polineuropathy (DSP). Research by Supriyanta (2004) in Jakarta reported high sensitivity and specificity diagnostic values for the assessment of diabetic neuropathy [16]. Several other studies, such as research by Novriansyah et al. (2014), Purbasari et al. (2019), and Sinambela (2021), have also reported that TCSS can be used to assess Chemotherapy Induced Peripheral Neuropathy (NPTK) [17], neuropathy of Human Immunodeficiency Virus (HIV) patients [18], and leprosy neuropathy [19]. Therefore, TCSS can be considered as a simple method to evaluate the severity of diabetic neuropathy because of its high diagnostic value [13,20]. This study aims to determine the association between waist hip ratio and the severity of peripheral diabetic neuropathy in type 2 Diabetes Melitus (DM) according to the Toronto Clinical Scoring System (TCSS).

METHOD

This study was a descriptive analytic with cross-sectional data collection method without treatment on primary data sources obtained from all type 2 diabetes mellitus patients with diabetic neuropathy who are undergoing treatment at the Endocrine Polyclinic and Neurology Polyclinic at H. Adam Malik General Hospital Medan from April 2022 to November 2022. The number of samples required after calculation is 45 people. The determination of research subjects was carried out according to a consecutive non-random sampling method. Inclusion criteria in this study were all patients with type 2 diabetes mellitus with diabetic peripheral neuropathy who were on outpatient treatment at the Neurology and Endocrinology Polyclinic of RSUP. Haji Adam Malik Medan and willing to give consent to participate in this study, by signing an informed consent. Exclusion criteria in this study were patients with certain diseases (plexopathy, radiculopathy, autoimmune disorders /Guillain-Barre syndrome, brain lesions, aphasia, severe metabolic disorders and previous psychiatric disorders) and patients on certain medications (tuberculosis treatment, antiretrovirals, and chemotherapy / radiotherapy).

Determination of the severity of diabetic neuropathy was using the TCSS scoring system. Neuropathy examination using TCSS consists of a symptom score (presence or absence of symptoms of pain, numbness, tingling, weakness in the legs, feeling of imbalance), reflex scores (patella and achilles reflexes which are assessed as present, reduced or absent) and sensory examination scores (stab sensation, temperature, light touch, vibration and position). With measurement results: Score 0-5: no neuropathy; score 6-8: mild neuropathy; score 9-11: moderate neuropathy; score 12-19: severe neuropathy [13,17]. Waist Hip Ratio is the ratio of waist to hip circumference. This measurement is calculated as the waist measurement divided by the hip measurement. In this study WHR was measured using a measuring tape. According to WHO, WHR > 0.90 cm in male and > 0.85 cm in female indicates central obesity [21].

This research has been approved and passed the ethical review from the Health Research Ethics Committee of the Faculty of Medicine, University of North Sumatra with number 500 / KEPK / USU / 2022 which was issued on June 07, 2022 and from the Health Research Ethics Committee of Haji Adam Malik Hospital with number LB.02.02/XV.III.2.2.2/2133/2022 which was issued on June 23, 2022.

The research data were analyzed statistically with the help of the Windows SPSS computer program (Statistical Product and Science Service) versi 22.0, then displayed in tabular form. Univariate analysis in this study was conducted to analyze the demographic characteristics of subjects. Numerical variables are presented by displaying the mean, standard deviation, median, (minimum-maximum). Bivariate analysis in this study was conducted to analyze the association between the research variables, in this case to determine the

association between waist hip ratio and severity of diabetic peripheral neuropathy in diabetes melitus type 2 by using Toronto clinical scoring system. Data analysis using Chi Square test.

RESULT

Table 1 shows the average age group was 55.5 ± 10.13 divided into 31-40 years of age with 2 subjects (4.4%) with the youngest age 36 years, the age range of 41-50 years was 12 subjects (26.7%), the age range of 51-60 years was 17 subjects (37.8%), the age range 61-70 years was 11 subjects (24.4%), and the age range 71-80 years was 3 subjects (6.7%) with the oldest age of 77 years. There were 28 male subjects (62.2%) in the study and 17 female subjects (37.8%). The education level of the research subjects was divided into Elementary School (13.3%), Junior High (11.1%), High School (46.7%), Diploma (2.2%), Bachelor (24.4%), and Master (2.2%). Respondents' Job was divided into working, namely 18 subjects (40.0%) and not working as many as 27 subjects (60.0%). The most ethnic group is the Batak ethnic group with 20 subjects (44.5%). Long history of suffering from DM in all study subjects had a median value of 7 years with a range of 3-13 years divided into < 5 years for 13 subjects (28.9%), 5-10 years for 28 subjects (62.2%), and > 10 years as many as 4 subjects (8.9%).

Table 1 Distribution of Research Subject Demographic Characteristics

Demographics of stroke patients	Mean ± SD	n = 43 (%)
Gender		
• Male		28 (62.2)
• Female		17 (37.8)
Age Group	55.5±10.13	
• 31-40		2 (4.4)
• 41-50		12 (26.7)
• 51-60		17 (37.8)
• 61-70		11 (24.4)
• 71-80		3 (6,7)
Education		
• Elementary school		6 (13.3)
• Junior High		5 (11.1)
• Senior High School		21 (46.7)
• Diploma		1 (2.2)
• Bachelor		11 (24.4)
• Master		1 (2.2)
Occupation		
• Working		18 (40.0)
• Not Working		27 (60.0)
Ethnicity		
• Bataknese		20 (44.5)
• Melayu		6 (13.3)
• Karonese		11 (24.4)
• Javanese		8 (17.8)
Duration of DM	7 (3-13)	
• < 5 years		13 (28.9)
• 5 – 10 years		28 (62.2)
• > 10 years		4 (8.9)

The characteristics of the waist hip ratio in diabetic peripheral neuropathy patients with type 2 DM at Haji Adam Malik General Hospital are presented in table 2. Numerical data are not normally distributed, presented with median data (minimum value-maximum value). The median waist circumference of patients with diabetic peripheral neuropathy in type 2 DM at Haji Adam Malik General Hospital was 86 cm with the smallest waist circumference being 70 cm and the largest being 118 cm. The median hip circumference of patients with diabetic peripheral neuropathy in type 2 DM is 96 cm with the smallest hip circumference was

84 cm and the largest hip circumference was 128 cm. The mean waist hip ratio of diabetic neuropathy patients with type 2 DM is 0.87 ± 0.05. The total median score of the Toronto Clinical Scoring System (TCSS) for all diabetic neuropathy patients in type 2 DM is 10 with the smallest score of 6 and the largest score of 16, which are divided into 3 categories including: severe (31.1%), moderate (26.7%), and mild neuropathy (42.2%).

Table 2. Characteristics of WHR and TCSS Score in Diabetic Peripheral Neuropathy Patients with Type 2 DM at Haji Adam Malik General Hospital

Characteristics	Mean / Median	n = 45	%
Waist Circumference (cm)**	86 (70-118)		
Hip Circumference (cm)**	96 (84-128)		
WHR*	0,87± 0,05		
TCSS**	10 (6-16)		
Severe	12 (12-16)	14	31,1%
Moderate	10 (9-11)	12	26,7%
Mild	7 (6-8)	19	42,2%

* Data is normally distributed
** Data is not normally distributed

In table 3, it was found that patients with central obesity had a degree of neuropathy that was classified as severe in 13 people (56.5%), moderate in 7 people (30.4%), and a degree of neuropathy that was classified as mild in 3 people (13.0%). Meanwhile, patients who were not centrally obese had a degree of neuropathy that was classified as severe in 1 person (4.5%), moderate in 5 people (22.7%), and a degree of neuropathy that was classified as mild in 16 people (72.7%). Based on the Chi Square test, it was found that there was a significant association between waist hip ratio and the severity of diabetic peripheral neuropathy in type 2 DM patients with a p value <0.01.

Table 3. Association between WHR and the Severity of Diabetic Peripheral Neuropathy in Type 2 DM at Haji Adam Malik Central General Hospital

		TCSS			Total	P Value
		Severe	Moderate	Mild		
WHR	Obesity	13 (56,5)	7 (30,4)	3 (13,0)	23 (100)	<0,01
	Not Obesity	1 (4,5)	5 (22,7)	16 (72,7)	22 (100)	
	Total	14 (31,1)	12 (26,7)	19 (42,2)	45 (100)	

*Chi Square test, p <0.05 is significant

DISCUSSION

Based on this study, it was found that the average age of diabetic neuropathy patients was 55.5 ± 10.13 years, with the most age range being 51-60 years (37.8%). Characteristics of the average age of diabetic neuropathy patients is relevant to the study by Bansal et al. (2014), where it was reported that the mean age of subjects with diabetic neuropathy was 57.1 years [22]. Bulum et al. (2016) in Croatia reported that the median age of subjects with diabetic neuropathy was 58 years [11]. According to Iqbal et al (2018) stated that age is a risk factor that can also affect the development of diabetic neuropathy. Apart from age, there are several other factors that play a role in influencing the occurrence of diabetic neuropathy including prolonged diabetes, uncontrolled blood glucose levels, high LDL and triglyceride levels, hypertension, obesity and smoking. Age factor physiologically affects the occurrence of changes in the condition of blood vessels in connection with atherosclerosis [14].

In this study, it was found that the sex characteristics of diabetic peripheral neuropathy patients were mostly male (62.2%). The results of this study are relevant to research by Kiani et al. (2013) in Iran, who reported that the majority of diabetic neuropathy patients were male (51.5%) [24]. Almost the same results were also found in the study of Sina et al (2019) that the majority of diabetic neuropathy sufferers were more

prevalent in men (61.5%) than women (38.5%) [25]. Nonmodifiable risk factors for microvascular complications of diabetes include old age, genetics (polymorphism of the aldose reductase gene), increased duration of diabetes, and height. Tall diabetics are more prone to developing diabetic neuropathy because they have longer peripheral nerves. Because men are generally taller than women, more men have diabetic neuropathy than women [26].

In this study, it was found that the highest educational level of diabetic neuropathy patients was high school with 21 subjects (46.7%). These results are relevant to previous research conducted by Trisnawati (2014) which stated that the education level of most diabetic neuropathy patients in their study was high school, which was 34.9% [27]. According to Semana et al (2013) which states that the majority of diabetes mellitus sufferers are mostly high school graduates who are included in the low education category. People with diabetes mellitus who have low education tend not to have much knowledge about how to prevent and control a healthy daily lifestyle so that they do not develop type 2 diabetes mellitus and cause complications of diabetic neuropathy [28].

Characteristics of duration of suffering from type 2 DM in the subjects of this study obtained a median value of 7 years (3-13 years) with the longest range of history of suffering from DM, namely 5-10 years as many as 28 subjects (62.2%). Research by Bansal et al. (2014) reported that the average length of time subjects had type 2 DM was 10.8 years [22]. Meanwhile, Kiani et al. (2013) reported that type 2 DM patients with diabetic neuropathy had a longer duration of suffering from DM than patients without diabetic neuropathy [29]. Diabetic neuropathy is the most common complication experienced by patients with type 2 DM, the incidence increases according to the duration of DM, especially after suffering for 5 years. The length of time a DM is diagnosed is also associated with decreased function of pancreatic beta cells, causing complications that generally occur in patients with an illness of 5-10 years [30].

In this study, the median waist circumference of patients with diabetic peripheral neuropathy in type 2 DM at Haji Adam Malik General Hospital was 86 cm with the smallest waist circumference being 70 cm and the largest being 118 cm. The median hip circumference of patients with diabetic peripheral neuropathy in type 2 DM is 96 cm with the smallest hip circumference being 84 cm and the largest hip circumference being 128 cm. The mean waist hip ratio in diabetic neuropathy patients with type 2 DM is 0.87 ± 0.05. Almost the same results were found in the study of Akter et al (2020) where in that study the average WHR of diabetic peripheral neuropathy patients was 0.96 ± 0.05. 31 Although the exact pathophysiological pathway in which visceral adipose tissue plays a role in the development of microvascular complications has still not been clearly identified. Certainly, there are several hypotheses linking it to hypertension and dyslipidemia, which are confirmed to be one of the major risk factors causing vascular injury and several other homeostatic disturbances that may enhance the effect of both. Waist circumference and WHR have been proposed as tools for detecting central obesity. Until now, the relationship between metabolic control and the development of microvascular complications (retinopathy, neuropathy and nephropathy) is a major concern of clinicians. The factors involved in the development of vascular complications in diabetes, namely long duration of diabetes, poor glycemic control, smoking, hypertension and dyslipidemia are well known, but there is still not much data showing the role of weight/body fat distribution [11].

The median total TCSS score of all diabetic peripheral neuropathy patients with type 2 DM in this study was 10 with the smallest score of 6 and the largest score of 16. These results are relevant to Asir et al's (2020) study at the endocrine polyclinic and the internal medicine polyclinic at the National Central General Hospital Dr. Cipto Mangunkusumo, with a median TCSS value of 9.50 with a range (6 - 16) classified as moderate degree diabetic peripheral neuropathy [32]. In line with previous studies, the median total TCSS value of diabetic peripheral neuropathy patients in this study as a whole was 10 which was classified as moderate degree of neuropathy. This condition is caused by the more complex the damage experienced, the more severe the level of peripheral neuropathy. Based on the characteristics of the TCSS in this study, it was found that most subjects experienced mild degree of neuropathy (42.2%). These results are in line with a study conducted by Yuan et al (2012) in patients with diabetic peripheral neuropathy as measured by TCSS, it was found that the

majority of subjects had a relatively mild degree of neuropathy (47.12%) [33]. According to research conducted by Anggun (2020), the factors that influence the degree of severity of neuropathy in patients with diabetes mellitus are age, duration of diabetes, HbA1c, vitamin D deficiency, nutritional status (abdominal obesity), lipid levels, and the presence of plaque in the arteries. carotids [34]. In this study, factors that influence the severity of neuropathy based on the TCSS score include: patient characteristics such as age, duration of type 2 DM, and abdominal obesity.

In this study, it was found that patients with central obesity had a degree of neuropathy that was classified as severe in 13 people (56.5%), moderate in 7 people (30.4%), and mild in 3 people (13 .0%). Meanwhile, patients who were not obese had a degree of neuropathy that was classified as severe in 1 person (4.5%), moderate in 5 people (22.7%), mild in 16 people (72.7%). The results of this study also showed that there was a statistically significant association between the waist hip ratio and the severity of diabetic neuropathy in type 2 DM with a p value <0.01. The increasing severity of diabetic peripheral neuropathy associated with high WHR (central obesity) scores is related to the pathomechanism of the neuropathy. According to Oh et al. (2019) in Korea reported evidence showing that central obesity and insulin resistance play a role in the pathophysiology of diabetic peripheral neuropathy. Among the five components of the metabolic syndrome, central obesity is the most important risk factor for diabetic neuropathy in subjects with type 2 DM. In that study, the parameters of central obesity, waist circumference, and visceral fat area were highly correlated with HOMA-IR. Insulin resistance status exhibits low-grade inflammation, which predisposes to endothelial dysfunction and microvascular complications [10]. Another study by Look AHEAD Research Group (2017) in the United States shows that weight loss reduces the incidence of diabetic neuropathy [4]. Although secondary effects of increased hyperglycemia after weight loss cannot be ruled out, weight management is an important intervention strategy for diabetic neuropathy. Furthermore, a beneficial effect of bariatric/metabolic surgery on cardiac and sudomotor dysfunction has been found [10,35].

Research by Zhou et al (2021) in China demonstrated that obesity, especially central/abdominal obesity, is an important and independent risk factor for the development of diabetic neuropathy, indicating that central/abdominal obesity is an important component and that microangiopathy is a frequent sequel of the metabolic syndrome. may increase the risk of developing polyneuropathy in patients with diabetes. Because of the lack of protective blood-brain barrier, the peripheral nervous system (PNS) is susceptible to central obesity-driven dysfunction, including loss of peripheral sensory neurons and small intraepidermal nerve fibers, sensory polyneuropathy symptoms and signs that occur with stocking-gloves, and decreased motor and sensory nerve function. The potential underlying mechanism is that central obesity affects anabolic and catabolic processes by affecting the autonomic nervous system (ANS), which is a component of the peripheral nervous system (PNS). Moreover, central obesity is associated with an imbalance between the sympathetic and parasympathetic divisions of the ANS, resulting in sympathetic hyperactivation with sustained sympathetic outflow that decreases perfusion, so that ultimately, these physiological changes also promote further neurological dysfunction in the PNS [36].

A study by MONICA/KORA also reported that there was a relationship between the occurrence of diabetic peripheral neuropathy and waist circumference in the type 2 DM population. They also concluded that central obesity is an important component and macroangiopathy as a frequent sequel of the metabolic syndrome may increase the risk of developing polyneuropathy in diabetic subjects [37]. Limitation of this study was that this study only focused on scoring neuropathy with waist hip circumference, so that other factors that can affect the severity of diabetic neuropathy are not carried out further analysis.

CONCLUSION

There is a statistically significant association between the waist hip ratio and the severity of diabetic neuropathy in type 2 DM with a p value <0.01.

DECLARATIONS

Ethics approval and consent to participate. Permission for this study was obtained from the Ethics Committee of Universitas Sumatera Utara and H. Adam Malik General Hospital.

CONSENT FOR PUBLICATION

The Authors agree to publication in Journal of Society Medicine.

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COMPETING INTERESTS

None.

AUTHORS' CONTRIBUTIONS

All authors significantly contribute to the work reported, whether in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas. Contribute to drafting, revising, or critically reviewing the article. Approved the final version to be published, agreed on the journal to be submitted, and agreed to be accountable for all aspects of the work.

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