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Triglyceride-Glucose Index as a Predictor of Diabetic Foot Ulcer Severity in Type 2 Diabetes Mellitus: Cross-Sectional Study

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ABSTRACT

Introduction: Diabetic foot ulcers are a complication of type 2 diabetes mellitus that has a high global prevalence. Insulin resistance in type 2 DM patients tends to cause chronic wounds and can delay wound healing. TyG index is currently used as a surrogate biomarker to evaluate insulin resistance because it is easy to perform and low cost.

Methods: Analytic observational research with a cross-sectional approach at Diabetic Foot Poly Ulin Hospital Banjarmasin. The study sample was all patients diagnosed with type 2 DM and undergoing wound care at the Diabetic Foot Polyclinic of Ulin Hospital Banjarmasin starting in December 2024 who met the inclusion and exclusion criteria with a total of at least 74 people. Data analysis was performed with a simple binomial logistic regression test to estimate crude Prevalence Odds Ratio (POR) with 95% confidence intervals, and multiple binomial logistic regression tests were performed to estimate adjusted POR and 95%CIs.

Results: Compared with the lowest one-third TyG Index score, study subjects with the middle one-third TyG Index score were associated with a lower risk of severe diabetic foot ulcer incidence by 85.9% (Adj POR 0.141, 95% CI: 0.011-1.802). Subjects with the highest third TyG Index value were also associated with a lower risk of diabetic foot ulcer incidence of 87.1% (Adj POR 0.129, 95%CI: 0.008-1.959). The mean value of TyG Index+SD was 4.8872 + 0.4230 at severe foot ulcers.

Conclusion: TyG index is not a predictive factor for the severity of diabetic foot ulcers in type 2 DM patients at the Diabetic Foot Clinic of Ulin Hospital Banjarmasin ($p>0.05$).

Keywords: TyG index, type 2 DM, diabetic foot ulcers

INTRODUCTION

Diabetic foot ulcers are complications of type 2 diabetes mellitus (DM) that usually occur due to neuropathy and peripheral arterial disease with a high global prevalence. The occurrence of diabetic foot ulcers stems from the interaction between impaired tissue regeneration, vasculopathy, neuropathy, and inflammation caused by insulin resistance. Insulin resistance is a condition in which insulin exerts a lower biological effect than expected in both experimental and clinical settings.[1-4]

The global prevalence of diabetic foot ulcers is 6.3%. Nearly 15% of type 2 DM patients suffer from foot ulcers and the amputation rate of type 2 DM patients is 15 to 40 times higher than the general population. Diabetic foot ulcers are more common in men than women. Patients with diabetic foot ulcers have a lower body mass index, longer duration of diabetes, and more with a history of smoking than patients without diabetic foot ulcers. Previous studies have shown that insulin resistance is one of the important risk factors for cardiovascular diseases, such as hypertension, vascular stiffness, and is associated with the development of atherosclerosis.[1,3,5,6]

Individuals with insulin resistance tend to experience several metabolic abnormalities, such as hyperglycemia, dyslipidemia, and hypertension, all of which are strongly associated with cardiovascular disease. Currently, there is no specific method for accurate determination of insulin resistance. The gold standard euglycemic insulin clamp and intravenous glucose tolerance testing are invasive and expensive and, although used in academic studies, are not applied in clinical practice. Homeostasis model assessment insulin resistance (HOMA-IR) index is widely used today but has limited value in subjects receiving insulin treatment or those without functioning beta cells. To overcome these limitations, the TyG index was developed and shown to be superior to HOMA-IR in assessing insulin resistance in individuals with and without diabetes. According to previous studies, the TyG index is a simple, easy, and low-cost surrogate, does not require insulin quantification, and can be used in all subjects regardless of their insulin treatment status.[7]

Previous research on the relationship between TyG Index and the severity of diabetic foot ulcers was conducted by Zhang et al in 2023 at Wenzhou University Hospital China.[8] This study was conducted at Diabetic Foot Poli Ulin Hospital Banjarmasin with different population and demographics from previous studies. As far as the author's research is concerned, this research is the first research conducted at Ulin Hospital, Banjarmasin.

RESEARCH METHODS

Design

This research design is analytical observational research with a cross-sectional approach. This study was conducted at the Diabetic Foot Polyclinic of the Regional General Hospital Ulin Banjarmasin starting in December 2024 until the minimum sample size was met. Minimum sample at least 74 people. Inclusion Criteria: Patients diagnosed with type 2 DM with diabetic foot ulcers who seek treatment at the Diabetic Foot Clinic of Ulin Hospital Banjarmasin, Patients with age >18 years and Patients agree to participate in the study as evidenced by the signature on the informed consent sheet. Exclusion Criteria: Patients with type 1 DM or other types of DM with diabetic foot ulcers who seek treatment at the Diabetic Foot Clinic of Ulin Hospital Banjarmasin. This research has a Medical and Health Research Ethics Committee of FKIK ULM No.242 /KEPK- FKIK ULM/EC/ XII/2024, a certificate of ethical feasibility of research from RSUD Ulin Banjarmasin No.194/ XII-Reg Research/RSUDU/24, and a research permitNo.188/PPDS.IPD/Litbang/RSUDU/ XII/2024 dated December 28, 2024.

Table 1. The samples were classified according to wagner's criteria:[9]

Wagner's Classification	
Grade 0	The skin is intact but the bone abnormalities cause "risky feet."
Grade 1	Superficial ulcers
Grade 2	Deeper, with full thickness extension
Grade 3	Deep abscess formation or osteomyelitis
Grade 4	Partial gangrene of the forelegs
Grade 5	Extensive gangrene

The incidence of diabetic foot ulcers is categorized into 2 groups:[8]

1. Mild-Moderate: Wagner 0-2
2. Heavy (Severe): Wagner 3-5

The cutoff point for the TyG Index as a marker of insulin resistance is ≥ 4.5.[10]

Variable Identification

a. Independent variable: TyG index
b. Dependent variable: severity of diabetic foot ulcers
c. Confounding variables: age, gender, BMI, smoking habits, duration of suffering from DM, use of oral antihyperglycemic therapy and/or insulin, and antilipid therapy.

Data Analysis

All statistical analyses were performed using IBM SPSS version 27 statistical software. Data analysis was performed with a simple binomial logistic regression test to estimate crude Prevalence Odds Ratio (POR) with 95% confidence intervals, and multiple binomial logistic regression tests were performed to estimate adjusted POR and 95%CIs.

RESULT

Table 2. Baseline characteristics of study participants (n = 74)

Characteristics	Total n (%)
Age, mean (year, ± SD)	56.31 ± 9.12
Gender	
Male	32 (43.2)
Female	42 (56.8)
IMT	
Underweight	0 (0,0)
Normal	28 (37.8)
Overweight	18 (24.3)
Obesity	28 (37.8)
Smoker	
Yes	17 (23.0)
No	57 (77.0)
DM duration	
≤10 years	53 (71.6)
>10 years	21 (28.4)
Antihyperglycemic therapy	
Oral	18 (24.3)
Insulin	48 (64.9)
Combination	8 (10.8)
Antilipid	
Yes	41 (55.4)
No	33 (44.6)
Triglyceride	
Normal (<150 mg/dl)	52 (70.3)
Borderline (150-199 mg/dl)	11 (14.9)
High (>200 mg/dl)	11 (14.9)
Fast Blood Glucose	
Low (< 70 mg/dl)	4 (5.4)
Normal (70-125 mg/dl)	23 (31.1)
High (> 126 mg/dl)	47 (63.5)
HbA1C Level	
No data	32 (43.24)
HbA1C < 7,0	12 (16.22)
HbA1C ≥ 7,0	30 (40.54)

Table 2 shows that the average age of type 2 DM patients with diabetic foot ulcers involved in this study was 56.31 years (± 9.12). Female gender is more than male gender 42 people vs 32 people (56.8% vs 43.2%). Normal BMI and obesity (37.8%), overweight (24.3%) and none of the research subjects were underweight. Most of the study subjects did not smoke (77.0%) and had DM <10 years (71.6%). Most of the research subjects used antihyperglycemic therapy in the form of insulin (64.9%) and used antilipid therapy (55.40%). Most of the research subjects had normal triglyceride levels (70.3%). Most of the research subjects had high fasting glucose levels as 47 people (63.5%). Most of the research subjects had HbA1C levels > 7.0, as many as 32 people (40.54%).

Table 3 shows the bivariate analysis between the independent variables and other influencing variables with the dependent variable (severity of diabetic foot ulcers). For data with a numerical scale, namely age, a normality test was first performed using the Kolmogorov Smirnov statistical test p<0.05. This indicates that the data is normally distributed. Furthermore, an

Table 3. Association between TyG Index and diabetic foot ulcer severity

Characteristics	Classification of Diabetic Foot Ulcers (Wagner)		*p-value*
	Mild-Moderate (n =52)	Heavy (n= 6)	
Age, mean (year, ± SD)	**57,53 ± 9,11**	**51,88 ± 7,93**	**0,027[a]***
Gender			
Male	23 (71,9)	9 (28,1)	0,236[b]
Female	35 (83,3)	7 (16,7)	
BMT			
Underweight	0 (0,0)	0 (0,0)	<0,001[b]*
Normal	23 (82,1)	5 (17,9)	
Overweight	8 (44,4)	10 (55,6)	
Obesity	27 (96,4)	1 (3,6)	
Smoker			
Yes	12 (70,6)	5 (29,4)	0,502[c]
No	46 (80,7)	11 (19,3)	
DM duration			
≤10 years	39 (73,6)	14 (26,4)	0,132[c]
>10 years	19 (90,5)	2 (9,5)	
Antihyperglycemic therapy			
Oral	16 (88,9)	2 (11,1)	0,938[d]
Insulin	35 (72,9)	13 (27,1)	
Combination	7 (87,5)	1 (12,5)	
Antilipid			
Yes	33 (80,5)	8 (19,5)	0,632[b]
No	25 (75,8)	8 (24,2)	
Triglyceride			
Normal (<150 mg/dl)	39 (75,0)	13 (25,0)	0,966[d]
Borderline (150-199 mg/dl)	9 (81,8)	2 (18,2)	
High (>200 mg/dl)	10 (90,9)	1 (9,1)	
Fast Blood Glucose			
Low (< 70 mg/dl)	4 (100,0)	0 (0,0)	1,000[d]
Normal (70-125 mg/dl)	17 (73,9)	6 (26,1)	
High (> 126 mg/dl)	37 (78,7)	10 (21.3)	

Notes: *= statistically significant; a= unpaired t-test; b= Chi-square test; c= Fisher-exact test; d= Kolmogorov-Smirnov test; SD=...; BMI= Body Mass Index; DM= Diabetes Mellitus

Table 4. Association between TyG index and diabetic foot ulcer severity (logistic regression model)

TyG Index Category	Mild–Moderate DFU n (%)	Severe DFU n (%)	Adjusted POR (95% CI)	p-value
Lowest tertile (T1)	5 (71.4)	2 (28.6)	1.00 (Reference)	-
Middle tertile (T2)	39 (78.0)	11 (22.0)	0.141 (0.011–1.802)	0.132
Highest tertile (T3)	14 (82.4)	3 (17.6)	0.129 (0.008–1.959)	0.140

Adjusted for age, sex, BMI, smoking status, duration of diabetes, and medication use. DFU: diabetic foot ulcer; POR: prevalence odds ratio.

Table 5. Table of the relationship of tyg index values with the incidence of diabetic foot ulcers according to wagner

TyG Index	Classification of diabetic foot ulcers (Wagner)		Relationship between TyG index and diabetic foot ulcers			
	Mild-moderate (n=58)	Heavy (n=16)	Crude POR (95%CI)	p-value	Adj.* POR (95%CI)	p-value
TyG index, mean ± SD	4.8872 ± 0.4230	4.7881±0,3676	0.994 (0.980-1.008)	0.393	0.987 (0.969-1.004)	0.133

Adj. = Adjusted; CI = Confidence Interval; POR = Prevalence Odds Ratio; SD= Standard Deviation
*Adjusted for age, gender, BMI, smoking status, duration of DM, use of antihyperglycemic and antilipid medications.

unpaired t-test was conducted and the two- sided pvalue = 0.027 (<0.05). This indicates that the mean age of the study sample in mild moderate foot ulcers and severe foot ulcers is statistically significantly different.

Tables 3 and 4 show the results of bivariate and multivariate analyses of the association between TyG index and severity of diabetic foot ulcers using binomial logistic regression to estimate crude PORs and 95% CIs. A multiple binomial logistic regression test was then performed by incorporating confounding variables into the analysis, to adjust for conventional risk factors.

Table 3 shows the estimated Odds Ratio for the incidence of diabetic foot ulcer severity in patients with TyG Index one- third highest (T3) and one-third middle (T2), compared with one-third lowest (T1). Compared with the lowest one-third TyG index value, study subjects with the middle one-third TyG Index value were associated with a lower risk of severe diabetic foot ulcer incidence by 85.9% (Adjusted POR 0.141, 95% CI: 0.011-1.802). Study subjects with the highest one-third TyG Index score were also associated with a lower risk of diabetic foot ulcer incidence of 87.1% (Adjusted POR 0.129, 95%CI: 0.008-1.959). However, this association of severe diabetic foot ulcer incidence with both TyG Index values 2 and 3 was not statistically significant when compared to the association of severe diabetic foot ulcer incidence in patients with TyG Index value 1.

DISCUSSION

In this study, the average age of research subjects was 56.31 ± 9.12 years. In accordance with several previous studies such as that conducted by Hicks et al (2020), the incidence of diabetic foot ulcers mostly occurs at the age of 50 years and over (average 59.2 years). However, this is also related to the duration of DM, the cumulative effect of hyperglycemia, and the high prevalence of macro and microvascular complications in this age range.[11,12]

In this study, female gender was more than male gender, in line with the results of research conducted by Deltty A et al (2020), that women in physical activity tend to move less and use less glucose. Insulin resistance is exacerbated when activity is lacking, and glucose intake increases. This involves AMPK (AMP- activated protein kinase) which does not work properly which will cause women to tend to be at higher risk of developing type 2 DM compared to men. In the process of pregnancy there is also an increase in insulin resistance, so women tend to suffer more from type 2 DM than men. This is different from previous studies by Hicks et al (2020) and Roosboth et al (2020) where men experience more type 2 DM than women. Other risk factors such as blood sugar control status and other complications may also contribute to this difference.[12-15]

Several previous studies have shown that BMI is associated with abnormalities in the distribution of pressure on the surface of the soles of the feet both on the front, middle and rear feet. This mostly occurs in obesity with BMI <35. This study is in line with the results of research by Ananta et al (2023) which showed that most people with Type 2 DM have a normal BMI. This is because at the beginning of Type 2 DM, the patient's BMI will increase first, then because the muscles do not get enough glucose, the muscles cannot develop and convert glucose into energy. Fat and muscle eventually undergo lysis to meet energy needs. Insulin resistance is caused by an excess of fatty acids and proinflammatory cytokines, leading to impaired glucose transport and increased fat breakdown. Hyperinsulinemia results in vasculopathy, resulting in impaired circulation of medium and large blood vessels and limb ulcers or gangrene.[15-17]

The risk factor for smoking is also interrelated with other factors such as gender, duration of

diabetes, BMI, and duration of DM. Several previous studies have shown a link between smoking and the severity of diabetic foot ulcers in relation to peripheral neuropathy, vascular changes and wound healing. One of the mechanisms underlying these effects is oxidative stress. However, diabetic patients with foot ulcers will try to quit smoking to improve the prognosis of diabetic foot ulcers.[15,16]

For the duration of suffering from DM, most of the research subjects with DM duration < 10 years, namely 75.70%, research subjects with DM duration > 10 years, namely 24.30%. This is in accordance with several previous studies which show that diabetic foot ulcers begin to occur after patients suffer from diabetes for more than five years. Several other studies have shown that the longer diabetes, the greater the likelihood of ulcers. Previous research conducted by Safari et al (2023) showed that patients suffering from DM with recurrent diabetic foot ulcers suffered from DM for more than 10 years. Patients who suffer from DM disease for more than 10 years are risk factors that cause diabetic foot ulcers. DM patients who have suffered from DM for many years will experience vascular complications such as microangiopathy which will cause a decrease in blood circulation and then can develop as diabetic ulcers.[15,20,21]

Most of the study subjects used antihyperglycemic therapy in the form of insulin, 64.90%. Oral antihyperglycemic therapy was used in 24.30% of the study subjects, and a combination of oral antihyperglycemics and insulin was 10.80%. The use of antihyperglycemic drugs is related to the patient's blood sugar target that has not been achieved. Previous studies such as those conducted by Balakrishnan et al (2022) stated that the use of insulin in type 2 DM patients with diabetic foot ulcers showed better ulcer improvement than the use of oral antihyperglycemia.[22]

In this study, research subjects with high fasting glucose levels were 66.20%, normal fasting glucose levels were 28.40%, and low fasting glucose levels were 5.40%. Most of the research subjects still had high fasting glucose levels. This is in accordance with several previous studies, such as those conducted by Arismawati et al (2022). which shows the relationship between blood glucose levels and diabetic ulcers where high blood glucose levels can reduce blood vessel elasticity which will result in decreased distal limb tissue perfusion. High blood glucose levels are a fertile environment for the proliferation of anaerobic pathogens because blood plasma in uncontrolled DM patients has a high viscosity. [15]

Research subjects who had HbA1C levels >7.0 were 40.54%, greater than research subjects who had HbA1C levels < 7.0, namely 16.22%. This shows that most research subjects have uncontrolled blood sugar during the last three months. A total of 32 people (43.24%) of the research subjects did not have HbA1C data because the patients were anemic and there was a history of blood transfusion during treatment. Research subjects who used antilipid therapy (55.40%) were more than research subjects who did not use antilipid therapy (44.60%). Most of the research subjects had normal triglyceride levels of 66.20%, low triglyceride levels of 14.90%, and high triglyceride levels of 18.90%. Previous research by Nassaji et al (2017) showed the use of statins as a preventive for diabetic foot ulcers but based on research conducted by O'Dell et al (2024), the use of statins does not affect the healing rate of diabetic foot ulcers.[23,24]

TyG Index as a Predictive Factor of Diabetic Foot Ulcer Severity

Table 9.1 shows that research subjects with the middle third and highest third TyG Index values are associated with a lower risk of diabetic foot ulcer incidence compared to

research subjects with the lowest third TyG Index values, although it is not statistically significant. The results of this study differ from previous studies such as those conducted by Zhang et al (2023) which stated that an increase in TyG index was independently associated with the severity of diabetic foot ulcers. The subjects in this study have routinely undergone treatment and received antihyperglycemic and antilipid therapy which affects fasting blood glucose levels and triglyceride levels so that it can affect the results of this study.[8,10]

In this study, the subjects were type 2 DM patients with diabetic foot ulcers who came regularly to the diabetic foot clinic of Ulin Hospital Banjarmasin. Some underwent foot wound care twice a week and some once a week. During the treatment, changes occurred, namely the improvement of the degree of diabetic foot ulcers according to Wagner. The research subjects had also received routine therapy tailored to the patient's condition every month in the form of antihyperglycemic drugs both oral and insulin, antilipid drugs, antibiotics and other drugs according to other patient complaints such as high blood pressure drugs. This affects the results of the study, namely that some research subjects have fasting blood sugar and triglyceride levels under control, thus updating the results of the TyG index. In this study, the mean value of the TyG Index was 4.8872 (SD + 0.4230) in the classification of mild moderate leg ulcers and 4.7881 (SD + 0.3676) in the classification of severe leg ulcers, as shown in table 9.2. Based on research conducted by Salazar et al in 2017, the cutoff point for TyG Index as a marker of insulin resistance is ≥ 4.5. The results of this study show that both the classification of mild moderate leg ulcers and severe leg ulcers have an average TyG Index value ≥ 4.5 which indicates insulin resistance. Most of the research subjects had TyG Index above the cutoff value associated with the basic characteristics of this research data, namely most of the research subjects had uncontrolled fasting blood sugar levels. 63.5% of the study subjects had high fasting glucose levels. TyG Index is dynamic and may vary over time.[25]

The relationship between TyG Index and glycemic control can be explained through several mechanisms.[27] An increase in free fatty acids is caused by an increase in triglyceride levels which can have an impact on increasing the reflux of free fatty acids from adipose to non-adipose tissue thus affecting glycemic control. Several studies have reported that higher triglyceride levels in muscle and liver may affect glucose metabolism in each target organ. Insulin resistance plays an important role in the pathophysiology of type 2 diabetes; therefore, insulin resistance testing can be used as a marker of diabetes mellitus progression. In health services with limited laboratory facilities, the TyG index can be used as a substitute for predicting the development of diabetes.[26,27]

This study illustrates that by controlling fasting blood sugar levels including through the administration of oral antidiabetics, insulin, or a combination, it is possible to affect the results of the TyG index which will then reduce the risk of diabetic foot ulcers both mild moderate and severe degrees according to research by Balakrisnan et al (2023). Likewise, controlling triglyceride levels through the administration of antilipids is expected to improve the TyG index which is then expected to improve insulin resistance and reduce the risk of diabetic foot ulcers according to research.[21,24] This study has not involved other variables associated with the incidence of diabetic ulcers so that it can affect the results of research such as kidney function, albumin, physical activity of research subjects, diet and education. The subjects in this study have routinely undergone treatment and received antihyperglycemic and antilipid therapy which affects fasting blood glucose levels and

triglyceride levels so that it can affect the results of this study.[8,25]

CONCLUSION

The TyG index was not significantly associated with diabetic foot ulcer severity in Type 2 DM patients. Although it remains a practical indicator of insulin resistance, TyG alone may not predict ulcer severity in patients under comprehensive metabolic therapy. Further multicenter studies are recommended to validate these findings. It is necessary to conduct research by paying attention to other variables that have not been considered as confounding variables in this study.

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