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TRIGLYCERIDE-GLUCOSE INDEX: A POTENTIAL SURROGATE FOR INSULIN RESISTANCE IN PREDICTING THE RISK OF DIABETIC NEPHROPATHY

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Abstract

Objective:

This study was performed to explore how the triglyceride-glucose (TyG) index is related to insulin resistance, as measured by HOMA-IR, in patients newly diagnosed with type 2 diabetes mellitus (T2DM). It also examined how the TyG index is linked to UACR, a marker often used to detect early signs of diabetic nephropathy.

Study Design: Cross-sectional observational study.

Study Duration: This study was conducted at Peoples University of Medical and Health Sciences for Women Shaheed Benazirabad Nawabshah Hospital from March 2024 to March 2025

Methods:

An observational, cross-sectional study was carried out over a one-year. The study included adult patients with a recent diagnosis of T2DM. Data collected encompassed demographics (age, gender), clinical details (BMI, vitals, duration of diabetes), and key biochemical measurements: HOMA-IR, serum creatinine, TyG index, lipid profile, fasting plasma glucose, spot UACR, and fasting insulin. There were 4 quartiles in which the participants were categorized based on their TyG index scores; Quartile 1 (4.5 to 5), quartile 2 (5.1 to 5.5), quartile 3 (5.6 to 6), and quartile 4 (Above 6).

Results:

A total of 218 individuals participated in the study, of which 140 (approximately 64%) were female and 78 (36%) males. The participants had a mean age of 49.2 ± 11.4 years. Among them, 45% were

classified as overweight, 16% as obese, and 39% had a body weight within the normal range. Based on their TyG index values, 60 participants (27.5%) fell in Q1, 84 (38.5%) in Q2, 47 (21.5%) in Q3, and 27 (12.5%) in Q4.
Patients in the highest TyG quartile (Q4) exhibited noticeably higher levels of fasting blood glucose, HbA1c, triglycerides, total cholesterol, LDL cholesterol, HOMA-IR, and UACR when compared to those in lower quartiles ($p<0.05$). At the same time, they had reduced HDL cholesterol and eGFR values ($p<0.05$).
Correlation analysis revealed a strong positive association between the TyG index and HbA1c ($r=0.74$, $p<0.001$), along with a moderate correlation with HOMA-IR ($r=0.46$, $p<0.001$) and a weaker, borderline-significant correlation with UACR ($r=0.11$, $p=0.04$). Fasting insulin was inversely related to both HbA1c ($r=-0.11$, $p=0.06$) and the TyG index ($r=-0.12$, $p=0.05$). eGFR showed a moderate negative correlation with the TyG index ($r=-0.33$, $p=0.01$), but only minor associations with HOMA-IR and UACR.

Introduction

Diabetes mellitus (DM) is a group of chronic metabolic disorders primarily marked by elevated blood glucose levels. It results from disruptions in the body's regulation of carbohydrate, fat, and protein metabolism and can gradually lead to complications affecting major organs, including the nerves, blood vessels, eyes, heart, and kidney [1].
Recent global data indicates that diabetes is becoming increasingly widespread, affecting over 500 million people. This number is expected to rise significantly in the coming decades. Official studies have shown that the risk for diabetes mellitus (DM) is rapidly increasing due to the genetic markers present in patients, as well as rapidly adopting unhealthy lifestyle practices and choices especially in third world countries [2]. The consumption of overly processed foods as well as the startling high content of sugar in packaged foods is a major contributing factor for diabetes. Insulin resistance levels are tested in people as higher than ever before when paired with a sedentary lifestyle. One of the major factor in the development of type 2 diabetes is obesity which is caused by pairing high sugar consumption along with lack of physical activity with insulin resistance [3].
Diabetic nephropathy (DN) is one of the serious health problems which is caused by diabetes. It can lead to end-stage renal disease. According to studies, 40% of the individuals having diabetes develop DN [4]. DN is diagnosed when there is a drop in glomerular filtration rate (GFR) and albumin is checked in the urine. This shows damage to the kidney. This is why it is necessary to screen regularly. In order to detect DN early, tests like urinary albumin-to-creatinine ratio (UACR) and eGFR are used by doctors [5,6,7].
When the kidneys filter too much blood, a high pressure is caused in the kidney's filtering units. This is called glomerular hyperfiltration with which diabetic nephropathy starts. This can lead to a speedy damage in the kidney if not treated in time. Therefore, it is necessary for the diabetic patients to go for regular screening so that the disease is detected earlier and its progression can be slowed [5,7]. Insulin resistance (IR) has been closely linked to such changes, and its presence can accelerate renal complications in diabetes. Early detection of such dysfunction, particularly in asymptomatic patients, could potentially allow for timely intervention and better outcomes.
Research has proven that the medical community considers the triglyceride-glucose (TyG) index as one of the leading methods in diagnosing insulin resistance, due to its extremely cost-effective nature and high efficiency. It is helpful in predicting diabetic nephropathy (DN) for diabetic patients as well. There have been various studies that have linked the angiopathies of patients diagnosed with type 2 diabetes and the triglyceride-glucose index [8] . Other research papers have shown that the presence of insulin resistance has been linked with the triglyceride-glucose index as well, where type 2 diabetes micro-angiopathies and macroangiopathies have been associated as well [9]. Due to the prevalence of diabetes among the population of developing countries, there is an arising need for cheap and reliable markers to identify and predict diabetic nephropathy in its early stages. This study aims to focus on the triglyceride-glucose index along with the homeostasis model assessment

of insulin resistance. This focus will be on type 2 diabetic patients in order to understand how the triglyceride-glucose index can help in predicting diabetic nephropathy with the use of UACR.

Patients and Methods

This study has been conducted by observing Type 2 diabetic patients who have received medical care for their condition. Approval from the institutional ethics review board was obtained prior to initiating the study. Standard formula was used to calculate the sample size based on the estimated prevalence of T2DM and a 5% margin of error.

Participants were recruited through non-probability consecutive sampling. Inclusion criteria required individuals to be previously diagnosed with T2DM for a duration of one to five years and to have fasting plasma glucose (FPG) levels of 126 mg/dL or higher.

Exclusion criteria: People with type 1 diabetes were not a part of this research. Moreover, people with chronic illnesses, or systemic illnesses were also excluded. Furthermore, those people who were undergoing dialysis, pregnancy, or current smoking were also not a part of this paper.

Each of the participants was informed about the research and their consent was obtained. Each participant's demographic and clinical data were recorded, including age, gender, duration of diabetes, waist circumference, height, BMI, and body weight. After 10 to 12 hours of fasting, blood samples were collected for laboratory analyses. The samples included the following measurements; fasting insulin, relevant metabolic markers, and fasting plasma glucose. Till their analysis, these samples were placed under certain appropriate conditions.

Insulin levels and fasting glucose were used to calculate homeostasis model assessment of insulin resistance (HOMA-IR). In order to determine the UACR, a spot urine sample was obtained. This is a key marker to assess kidney function in individuals with diabetes. UACR is calculated by dividing albumin by creatinine in the urine sample. Albumin was in mg and creatinine was in g.

There were 4 quartiles in which the participants were categorized based on their TyG index scores; Quartile 1 (4.5 to 5), quartile 2 (5.1 to 5.5), quartile 3 (5.6 to 6), and quartile 4 (Above 6). Statistical software was used to perform data analysis. In order to assess the relationship between HOMA-IR, TyG index, eGFR, metabolic indicators, anthropometric indicators, and UACR, Pearson correlation was used.

Results

Out of the total 218 participants, the majority of the study population were women (64.7%). The mean age calculated was 49.2 years. Among them, the majority of the patients were obese, representing 46.8% of the total participants. Only 37.2% participants had normal weight. The rest of them were obese. The overall average values for fasting insulin, glycated hemoglobin (HbA1c), HOMA-IR, and TyG index were 3.46 ± 1.48 µIU/mL, 6.65 ± 2.17%, 1.79 ± 0.86, and 5.39 ± 0.39, respectively. Urinary parameters included a mean urinary albumin of 5.83 ± 4.25 mg/dL, creatinine of 91.2 ± 13.9 mg/dL, UACR of 66.5 ± 51.8 mg/g, and eGFR of 99.2 ± 48.4 mL/min/1.73m².

Based on the TyG index, patients were categorized into four quartiles: Q1 (n=58, 26.6%), Q2 (n=86, 39.4%), Q3 (n=46, 21.1%), and Q4 (n=28, 12.8%), with TyG averages of 4.93, 5.33, 5.65, and 6.09 respectively.

Table 1: Demographics of type 2 diabetics

Parameter	Q1 (4.5–5.0)	Q2 (5.1–5.5)	Q3 (5.6–6.0)	Q4 (>6.0)
Number of patients (n)	58	86	46	28
Age (years)	51.4 ± 11.8	46.7 ± 11.6	49.3 ± 10.1	52.1 ± 11.2**
BMI (kg/m²)	26.2 ± 3.3	26.3 ± 3.8	26.3 ± 3.5	26.8 ± 4.0
Waist Circumference (in)	31.0 ± 3.0	30.7 ± 3.6	30.1 ± 2.6	31.0 ± 2.2
SBP (mmHg)	129.2 ± 11.3	125.4 ± 12.9	126.7 ± 16.5	125.0 ± 11.4
DBP (mmHg)	86.7 ± 8.5	85.2 ± 10.0	84.1 ± 10.6	90.1 ± 9.4*†

Duration of T2DM (years)	3.9 ± 1.2	3.5 ± 1.5	3.8 ± 1.1	4.1 ± 1.1*

Table 2: Biochemical Parameters by TyG Index Quartiles

Parameter	Q1	Q2	Q3	Q4
Fasting Glucose (mg/dL)	158.6 ± 33.0	214.7 ± 57.5*	256.3 ± 75.8**	370.4 ± 61.9***
Fasting Insulin (µIU/mL)	3.70 ± 1.5**	3.60 ± 1.6†	3.05 ± 1.0	3.30 ± 1.5
HbA1c (%)	5.15 ± 1.4	6.70 ± 2.0*	7.25 ± 2.0*	8.80 ± 1.9***
Total Cholesterol (mg/dL)	172.4 ± 45.2	185.1 ± 45.1	194.7 ± 51.9*	238.5 ± 69.4***
Triglycerides (mg/dL)	128.9 ± 34.0	208.5 ± 55.0*	330.2 ± 84.3**	552.8 ± 250.7***
HDL-C (mg/dL)	43.6 ± 6.7	37.2 ± 8.7*	36.7 ± 7.5*	33.2 ± 8.6***
LDL-C (mg/dL)	124.8 ± 36.3	134.7 ± 36.2	139.9 ± 40.4	175.9 ± 56.0***
HOMA-IR	1.45 ± 0.7	1.85 ± 0.8*	1.84 ± 0.8**	2.33 ± 0.9***
Urinary Albumin (mg/dL)	4.9 ± 3.3	6.3 ± 4.6*	5.4 ± 3.9	7.2 ± 5.0*
Urinary Creatinine (mg/dL)	91.2 ± 15.9	89.7 ± 12.2	94.8 ± 15.1*	91.0 ± 11.7
UACR (mg/g)	60.2 ± 46.9	72.1 ± 58.0	57.3 ± 41.5	77.9 ± 53.0
eGFR (mL/min/1.73m²)	124.6 ± 106.8	118.5 ± 122.5*	87.2 ± 62.7**	82.9 ± 65.9***

Correlation Analysis:

Fasting insulin was inversely related to HbA1c ($r = -0.12$, $p = 0.07$), and fasting glucose ($r = -0.14$, $p = 0.05$), while TyG index showed a strong positive correlation with fasting glucose ($r = 0.76$, $p < 0.001$) and a moderate one with HOMA-IR ($r = 0.48$, $p < 0.001$). A weaker but still significant correlation was noted between TyG and UACR. TyG and insulin levels had a slight negative correlation ($r = -0.13$).

Table 3: Linear Regression Analysis for Predicting UACR and eGFR

Predictor	Outcome	β Coefficient	Std. Error	p-value	95% CI
TyG Index	UACR	12.75	9.30	0.001	[16.40 – 20.15]
HOMA-IR	UACR	1.80	4.20	0.01	[4.45 – 21.10]
TyG Index	eGFR	-4.40	16.60	0.02	[-28.40 – -37.20]
HOMA-IR	eGFR	-1.88	7.50	0.05	[-13.00 – -16.80]

ROC Curve Analysis:

To evaluate the predictive capability of the TyG index and HOMA-IR for albuminuria, ROC analysis was performed. The TyG index demonstrated a better area under the curve (AUC = 0.51, $p < 0.01$), while HOMA-IR had an AUC of 0.37 ($p < 0.01$), suggesting that TyG is a more useful marker in identifying early kidney dysfunction in T2DM.

Discussion

The focus of this study has been on type 2 diabetics in order to explore the connection that exists between the triglyceride glucose index and insulin resistance, which is quantified by using the

HOMA-IR model. This study assesses the association between UACR and TyG index. This highlights the importance of early screening for diabetic nephropathy. This is predicted by the TyG index and ACR [9]. TyG index is used as a metabolic marker widely in the medical industry for the diagnosis of diabetes, metabolic issues, and heart conditions. However, this approach has still not been widely adopted for the diagnosis of insulin resistance [10].

A significant parameter when diagnosing insulin resistance in T2DM patients is lipid levels. Lipid levels are used to assess how sensitive tissues are to insulin. Sensitivity in tissues to insulin introduces the risk for hyperglycemia, hypertension, and dyslipidemia. High levels of hyperglycemia, hypertension, and dyslipidemia are more common in obese patients due to the high insulin resistance levels and higher triglyceride levels. High triglycerides are also linked to impaired glucose metabolism [11]. Studies have reported that there is a high correlation between insulin resistance levels and DN with the triglyceride glucose index [12]. High ratios for urinary albumin-to-creatinine have also indicated metabolic dysregulation as well as renal impairment [13].

Previous research has also investigated the relevance of the TyG index in relation to insulin resistance and diabetic complications. A study reported that the TyG index had stronger correlations with anthropometric and metabolic parameters, such as BMI, HbA1c, and atherogenic lipid profiles, when compared to conventional indicators like HDL-C or even HOMA-IR. However, that study did not establish a clear connection between the TyG index and diabetic nephropathy. In contrast, the findings of the current study suggest that the TyG index may indeed have value as a non-invasive, cost-effective predictor of renal impairment in individuals with type 2 diabetes [12,14].

Another important observation in this study was the inverse relationship between eGFR and both TyG index and HOMA-IR. While some previous reports, particularly from non-local populations, failed to demonstrate a statistically significant association between TyG and eGFR, our results reveal a consistent and meaningful decline in kidney function with higher TyG and HOMA-IR values [15]. This discrepancy may reflect population-specific differences in genetic predisposition, diet, lifestyle, or duration of diabetes, underscoring the importance of conducting region-specific investigations.

Moreover, there was a positive correlation seen between UACR and TyG index, indicating that people with higher TyG values were more likely to exhibit microalbuminuria—a hallmark of early diabetic nephropathy [16,17]. Various studies enforce the relevance of the TyG index as a reliable marker for insulin resistance and have noted that it has a higher area under the curve than HOMA-IR in its association with diabetic nephropathy [4,16,18]. Analysis has shown that the TyG index is better at predicting albuminuria at a rate of 85% and has a higher sensitivity at 67% as compared with the HOMA-IR which has a 59% and 65% value for sensitivity abd specificity respectively. This has established that the triglyceride glucose index is much more accurate than HOMA-IR in the prediction of albuminuria and diabetic nephropathy in type 2 diabetics.

Studies have reported that albuminuria has been associated with a higher value of the triglyceride glucose index and linked with diabetic neuropathy and DR (diabetic retinopathy) [18]. It is important to note that while previous studies did not include spot urine ACR, this study has, instead of the traditional approach of 24-hour albumin excretion rate. This study has also established that diabetic patients with a high triglyceride glucose index and HOMA-IR scores had more severe insulin resistance, despite a diagnosis of nephropathy. Renal failure has been an established factor of high TyG index scores. This is due to the fact that a high TyG index in diabetic patients suggests diabetic micro-angiopathy, which is a leading factor in the diagnosis of renal failure. One of the first signs of diabetic neuropathy is microalbuminuria. In the present study, 78.9% of participants exhibited microalbuminuria, while 21.1% had normal albumin levels, and none were categorized under macroalbuminuria. The majority of microalbuminuria cases (89%) were found among individuals in the highest TyG quartile (Q4), indicating a clear gradient in risk.

Regression analyses further supported the predictive value of the TyG index. A one-unit increase in the TyG index corresponded to a 4.43-unit decline in eGFR, compared to a 1.90-unit reduction

associated with a similar increase in HOMA-IR. Likewise, TyG was a stronger predictor of elevated UACR, showing an odds ratio (OR) of 12.85, compared to 1.82 for HOMA-IR.

Other studies have also demonstrated associations between the TyG index and microvascular complications, including microalbuminuria [17]. One such study observed a similar trend, though limited to a Chinese population, raising concerns about generalizability [19]. The current study, however, broadens that insight by showing a robust relationship between TyG index values and early-stage diabetic kidney involvement in a more diverse clinical context.

Compared to previously reported values, the diagnostic sensitivity and specificity of the TyG index in this study were slightly higher (67% and 85%, respectively), suggesting improved utility in identifying early nephropathy. This affirms the potential role of the TyG index as a non-invasive, cost-effective, and reliable tool for early risk stratification in patients with T2DM.

Conclusion

The findings of this study highlight a significant association between the TyG index and insulin resistance as measured by HOMA-IR. More importantly, the TyG index proved to be a more effective indicator than HOMA-IR in predicting the early development of diabetic nephropathy, specifically through its correlation with microalbuminuria and reduced eGFR.

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This study was conducted without receiving financial support from any external source.

Conflict in the interest

The authors had no conflict related to the interest in the execution of this study.

Permission

Prior to initiating the study, approval from the ethical committee was obtained to ensure adherence to ethical standards and guidelines.

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