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Research Article

Triglyceride-Glucose Index as a Surrogate Marker for Insulin Resistance in Predicting Diabetic Nephropathy

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ABSTRACT

Objective: To determine the relationship between the triglyceride-glucose (TyG) index and the homeostasis model assessment of insulin resistance (HOMA-IR) in type 2 diabetes mellitus (T2DM) patients, and to determine whether the index of TyG can predict diabetic nephropathy by correlating it with urinary albumin-to-creatinine ratio (UACR).

Study design: Cross-sectional study

Duration and place of study: This study was conducted in Social Security Hospital Hyderabad Pakistan from May 2024 to May 2025

Methods: This cross-sectional study involved 150 patients who have just been diagnosed with type 2 diabetes. Demographic and clinical data, vital signs, age, gender and body mass index were all recorded. Triglycerides, total cholesterol, UACR, serum creatinine, fasting plasma glucose, fasting serum insulin, glycated haemoglobin (HbA1c), triglycerides, and high- and low-density lipoprotein cholesterol were all lab results. The patients were ranked into quartile groups according to their TyG index scores after computing the HOMA-IR and TyG index. Level I: The statistical analysis was conducted to determine the relationship between the estimated glomerular filtration rate (eGFR) and the TyG index, HOMA-IR, HbA1c and UACR.

Results: The mean age of the 150 participants was 48.7 ± 10.9 years, with 98 (65.3%) being female and 52 (34.7%) being male. According to BMI, 68 (45.3%) were normal weight, 24 (16%) were obese, and 58 (38.7%) were overweight. In addition to lower HDL-C and eGFR values ($p < 0.05$), higher TyG index quartiles were linked to significantly higher fasting plasma glucose, HbA1c, triglycerides, total cholesterol, LDL-C, HOMA-IR, and UACR. The TyG index showed a negative connection with eGFR ($r = -0.34$, $p = 0.01$) and a high positive correlation with HbA1c ($r = 0.72$, $p < 0.001$), HOMA-IR ($r = 0.46$, $p < 0.001$), and UACR ($r = 0.29$, $p = 0.04$). In contrast to the TyG index, HOMAIR shown a lesser connection with UACR.

Conclusion: The TyG index showed a strong association with insulin resistance and demonstrated superior predictive ability for diabetic nephropathy compared to HOMA-IR in patients with T2DM. It may serve as a practical and cost-effective marker for early risk assessment of diabetic kidney disease.

Keywords: Triglyceride-glucose index, HOMA-IR, diabetic nephropathy, type 2 diabetes mellitus, insulin resistance.

INTRODUCTION

T2DM has turned into an epidemic around the world, affecting millions of people, and burdening health care facilities significantly [1]. Its characteristics are chronic hyperglycemia and protein, lipid, and carbohydrate metabolism abnormalities caused by insulin resistance and/or reduced insulin level. Macrovascular and microvascular damage often worsens the prognosis of type 2 diabetes that severely decreases life quality and life expectancy [2]. One of its microvascular effects, diabetic nephropathy (DN), is a major cause of end-stage renal disease (ESRD) and dialysis dependency worldwide [3,4].

The occurrence of DN is on the rise in tandem with the cases of diabetes and as such, markers that have the potential to predict the onset of DN at a young age is an urgent concern [5]. Classical symptoms like microalbuminuria and decreased eGFR usually manifest too late in the course of the disease when structural renal damage has already occurred [6]. Hence, clinicians and researchers have highlighted the importance of earlier surrogate markers, which are cheap, readily available, and can be used in the daily clinical practice.

Insulin resistance (IR) is generally accepted as a key element in T2DM pathogenesis and is crucial in the progression of DN [7,8]. IR is also associated with glomerular hyperfiltration, endothelial dysfunction, oxidative stress, and inflammatory pathway activation, which hastens kidney damage [9]. A well-verified and popular approach to determine the IR is the HOMA-IR which necessitates fasting insulin levels that are not only costly but also not uniform throughout laboratories and regularly unavailable in low-resource studies [10,11]. This has led to the search to find simpler markers that can be an alternative to HOMA-IR.

The TyG index is a relatively new surrogate IM of IR that has shown promise. It is determined by using fasting plasma glucose and triglycerides both of which are included in routine metabolic workups and are cheap to obtain [12]. A number of studies have confirmed the TyG index versus the hyperinsulinemic-euglycemic clamp method, demonstrating a strong association and even better performance than HOMA-IR to predict IR in heterogeneous populations [13,14]. In addition to insulin resistance, the TyG index has also been linked to a variety of negative factors, such as metabolic syndrome, atherosclerosis, and non-alcoholic fatty liver disease [15].

There is an emergent indication about the TyG index being a predictor of diabetic complications, including nephropathy. Cross-sectional and longitudinal research has shown that an elevation of TyG index values correlates with increased urinary albumin secretion, deterioration of eGFR and higher risk of developing DN [16,17]. Indeed, there are studies aimed at suggesting that the TyG index could be a better predictor of DN than HOMA-IR as it is more strongly associated with microvascular changes [18]. Further, as metabolism of glucose and triglycerides are key events in kidney pathophysiology in diabetes, the TyG index can capture the metabolic environment that contributes to kidney damage in patients.

Given the clinical significance of DN, the ease of TyG index calculation, and the shortcomings of HOMA-IR, further investigation of the possibilities of the TyG index as an effective marker of DN risk stratification is necessary. This may aid in detecting high-risk patients earlier and closer follow-up and timely therapeutic interventions to postpone the development [19].

The aim of this study was thus to examine the relationship between the TyG index and HOMA-IR, and to determine its predictive ability of diabetic nephropathy in T2DM patients. The results can help to improve risk assessment instruments and to enhance clinical interventions to diagnose DN in its early stages.

METHODOLOGY

This study utilized an observational, cross-sectional study design and involved 150 newly diagnosed patients with T2DM who were recruited over a period of time across the inpatient and outpatient units of the hospital. They were not included in patients with severe cardiovascular, thyroid, or liver disease, type 1 diabetes, secondary diabetes, chronic kidney disease, unrelated to diabetes, acute infections, cancer, pregnancy or use of drugs that altered glucose or lipid metabolism. They were recruited in patients between 30 and 65 years old that were recently diagnosed with type 2 diabetes and that had provided their own informed consent.

The comprehensive clinical history and physical examination which each of the participants received included age, sex, body mass index, blood pressure, length of diabetes, and any other relevant clinical features. Plasma glucose, serum insulin, glycosylated haemoglobin (HbA1c), and lipid profile, including triglycerides, total cholesterol, HDL-C, and LDL-C, were tested on the fasting blood samples at least eight hours after awakening to determine the urinary albumin to creatinine ratio (UACR) of diabetic nephropathy.

HOMA-IR was calculated by first multiplying fasting insulin (ug/ml) by fasting plasma glucose (mmol/L) then dividing the product by 22.5. The TyG index was calculated by the product of fasting triglycerides(mg/dL) and fasting plasma glucose(mg/dL) multiplied by

the natural logarithm and then divided by two. The samples were categorized regarding their level of TyG index with the quartile of 1 (4.5 5.0), 2 (5.1 5.5), 3 (5.6 6.0), and 4 (>6.0).

The data was analysed using SPSS version 26. Continuous variables were presented as mean and standard deviation whereas categorical variables were presented in the form of percentages and frequencies. Comparison between data on TyG quartiles was done by analysis of variance or Kruskal Wallis test of continuous variables and the chi-square test of categorical variables. Pearson or Spearman correlation coefficients were used to test the correlations between the TyG index, HOMA-IR, HbA1c and UACR. P-values that were less than 0.05 were considered to be statistically significant.

RESULTS

The study involved 150 people with T2DM. There were 98 (65.3) females and 52 (34.7) males with an average age of 48.7 10.9 years. Body mass index (BMI) of the patients indicated that 68 (45.3) were normal, 58 (45.7) were overweight, and 24 (16) obese. The four quartiles were developed based on their values of TyG index: 38 (25.3) patients were included in Q1 (4.55), 54 (36) in Q2 (5.156), 36 (24) in Q3 (5.660), and 22 (14.7) in Q4 (>6.0).

Patients in the TyG Q4 group not only had much lower HDL-C and eGFR, but also had much higher fasting plasma glucose, HbA1c, triglycerides, total cholesterol, LDL-C, HOMA-IR, and UACR than those in the lower quartile groups ($p < 0.05$). As well, the HbA1c was positively associated with TyG index ($r = 0.72$, $p < 0.001$), HOMA-IR ($r = 0.46$, $p = 0.04$), UACR ($r = 0.29$, $p = 0.04$), and fasting serum insulin ($r = - 0.12$, $p = 0.07$). Fastering insulin was also negatively correlated with the TyG index ($r = -0.13$, $p = 0.05$), compared to HOMA-IR ($r = 0.32$, $p = 0.001$) and UACR ($r = 0.28$, $p = 0.05$). The eGFR was positively associated with fasting insulin ($r = 0.05$, $p = 0.05$) and negatively correlated with TyG index ($r = –0.34$, $p = 0.01$), HOMA-IR ($r = –0.01$, $p = 0.86$), and UACR ($r = –0.02$, $p = 0.80$).

Table 1. Baseline Characteristics and TyG Quartiles

Parameter	Q1 (n=38)	Q2 (n=54)	Q3 (n=36)	Q4 (n=22)	p-value
Age (years)	47.3 ± 9.8	48.1 ± 11.0	49.2 ± 10.5	50.8 ± 11.3	0.38
Female (%)	24 (63.2%)	36 (66.7%)	23 (63.9%)	15 (68.2%)	0.92
BMI (kg/m²)	24.8 ± 3.2	26.5 ± 4.1	27.1 ± 3.9	28.3 ± 4.5	0.02
FPG (mg/dL)	112.4 ± 10.8	123.6 ± 12.1	135.2 ± 15.3	148.7 ± 17.2	<0.001
HbA1c (%)	6.8 ± 0.7	7.5 ± 0.8	8.2 ± 0.9	8.9 ± 1.0	<0.001
Triglycerides (mg/dL)	140 ± 21	160 ± 25	182 ± 28	210 ± 32	<0.001
LDL-C (mg/dL)	110 ± 18	122 ± 20	134 ± 22	148 ± 25	<0.001
HDL-C (mg/dL)	50 ± 7	47 ± 6	44 ± 5	41 ± 5	<0.001
HOMA-IR	2.4 ± 0.6	3.1 ± 0.7	3.8 ± 0.9	4.5 ± 1.0	<0.001
UACR (mg/g)	18 ± 6	25 ± 9	32 ± 11	41 ± 13	<0.001
eGFR (mL/min/1.73m²)	92 ± 8	88 ± 7	84 ± 6	78 ± 5	<0.001

Table 2. Correlation of TyG Index, HOMA-IR, Fasting Insulin, and UACR with Key Parameters

Parameter	TyG Index	HOMA-IR	Fasting Insulin	UACR
HbA1c	r=0.72, p<0.001	r=0.46, p<0.001	r=-0.12, p=0.07	r=0.29, p=0.04
eGFR	r=-0.34, p=0.01	r=-0.01, p=0.86	r=0.05, p=0.05	r=-0.02, p=0.80

Overall, the TyG index showed a strong positive correlation with markers of glycemic control and renal involvement, while HOMA-IR exhibited weaker correlations. Patients in higher TyG quartiles were at greater risk of elevated UACR and reduced eGFR, indicating a higher likelihood of developing diabetic nephropathy.

DISCUSSION

In this study, TyG index had a significant relationship with diabetic nephropathy among patients with T2DM. Indications of insulin resistance and diabetic nephropathy were identified by the use of the index. Patients who have elevated TyG are more likely to develop diabetic nephropathy as indicated by a positive correlation between elevated TyG quartiles and poorer HDL-C and eGFR and elevated levels of fasting plasma glucose, HbA1c, triglycerides, LDL-C, HOMA-IR, and UACR. Based on this, the TyG index can be used as an effective and relatively inexpensive

surrogate of insulin resistance and early nephropathy.

We find that our results are in line with earlier researches which have defined TyG index as a valid predictor of insulin resistance. The TyG index which represents a simple surrogate of insulin resistance was originally suggested by Simental-Mendia et al. [20] and correlated strongly with the hyperinsulinemic-euglycemic clamp. Vasques et al. [21] compared the TyG index with HOMA-IR in a Brazilian population and found that they both had the same predictive performance. TyG was seen to have a higher correlation with UACR and eGFR over HOMA-IR in our study, suggesting that its use may be more beneficial to predict early renal dysfunction.

Some of the recent studies have demonstrated the predictive nature of the TyG index in diabetic nephropathy. As we observed, Zhao et al. [22] reported that the higher the TyG values, the greater the albuminuria and lower the eGFR in patients with T2DM. Li et al. [23] found that the TyG index had an independent relationship with premature kidney injury in Chinese T2DM patients despite the traditional risk factors. It was also illustrated that TyG was a valuable predictor of micro-vascular sensitiveness, such as diabetic nephropathy, which highlights the importance of using it as a non-invasive risk factor [24].

Also, glycemic control and lipid metabolism have been associated with the TyG index. We have found that TyG, HbA1c and triglycerides were significantly correlated, which is consistent with the results of Guerrero-Romero et al. [25], who emphasized the relevance of the index in metabolism. Indeed, low HDL-C and high LDL-C in upper TyG quartile of our cohort also show the dysmetabolic phenotype of insulin resistance and risk of nephropathy, as previously documented [26].

All in all, the findings indicate that the TyG index is a predictor and a surrogate marker of diabetic nephropathy. It is simple, cost-effective and depends on routine laboratory parameters, thus making it a feasible tool in the early detection of high-risk patients. Although HOMA-IR is a well-developed marker, its unavailability and inter-laboratory variability limit its use in clinical practice, which once again justifies the use of TyG index in clinical practice.

CONCLUSION

The TyG index, insulin resistance, and diabetic nephropathy markers were significantly correlated with patients with T2DM. Having close correlations with the eGFR and UACR, it performed better than HOMA-IR to predict early renal involvement. TyG index is a reliable and useful instrument to identify at a very early stage the individuals who are likely to develop diabetic nephropathy because it is simple to operate, cost effective and rides on standard laboratory values. This enables the administration of subsequent treatment to avoid the development of renal illness.

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Permission

Ethical approval obtained

Conflict of Interest

None

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