



## ASSOCIATIONS OF TYG INDEX WITH HOMA-IR AND UACR FOR PREDICTING DIABETIC NEPHROPATHY IN T2DM PATIENTS

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### ABSTRACT

**Background:** Diabetes mellitus (DM) damages blood vessels, kidneys, eyes, nerves, and the heart by increasing blood sugar levels and changing metabolism. A total of 10.5% of people worldwide suffered from diabetes in 2021; by 2030, that number is projected to increase to 643 million, and by 2045, it will reach 783 million. Pakistan has over 33 million people with a diabetes prevalence of 26.7%. Due to the slow course of type 2 diabetes mellitus (T2DM), patients should be screened for diabetic nephropathy (DN) at diagnosis and then once a year thereafter. Insulin-resistant kidneys exhibit hyper filtration, which is associated with the progression of diabetic nephropathy (DN) and severe illness. Microalbuminuria, which indicates endothelial dysfunction, can be treated early.

**Objective:** To determine the association of TyG index with HOMA-IR in T2DM patients, and to determine the association of TyG index with UACR for predicting DN.

**Study design:** A cross-sectional study

**Place and Duration:** This study was conducted in Sandeman Provincial Hospital Quetta from March 2023 to March 2024.

**Methodology:** The sample was acquired from Diabetic Clinic patients using a non-probability consecutive sampling technique. The study comprised T2DM patients with fasting plasma glucose (FPG) values of  $\geq 126$  mg/dl and a diagnosis of 1-5 years. Data was collected after patients provided informed consent and ensured their confidentiality. The demographic and clinical data gathered were gender, age, height, diabetes duration, blood pressure (BP), waist circumference (WC), weight, and body mass index (BMI).

**Results:** In all, 250 patients were included in this investigation. There were 88 (35.2%) male participants and 162 (64.8%) female participants, making up the majority of the participants. Overall 49.2 years of age was the average. Overall 3.46 was the mean fasting serum insulin. The mean HOMA-IR was 1.79. The mean glycated hemoglobin was 6.65. The mean TyG index levels were 5.39. 46% of the participants were overweight while 15% were obese and 39% were normal weighted. **Conclusion:** The TyG index showed a strong connection with HOMA-IR and was superior in predicting diabetic nephropathy (DN) in type 2 diabetes patients.

**Keywords:** diabetic nephropathy, type 2 diabetes, TyG index, HOMA-IR

## INTRODUCTION

Diabetes mellitus (DM) damages blood vessels, the kidneys, eyes, nerves, heart, and other organs by increasing blood sugar levels and changing metabolism [1]. A total of 10.5% of people worldwide suffered from diabetes in 2021; by 2030, that number is projected to increase to 643 million, and by 2045, it will reach 783 million [2]. Pakistan's diabetes prevalence is 26.7%, with around 33 million patients [3]. The World Health Organization reported 1.5 million diabetes-related fatalities in 2019, the majority of which occurred in low- and middle-income countries [4]. Genetics and an unhealthy lifestyle are major risk factors for obesity [5]. In Pakistan, 57.9% have generalized obesity, whereas 73.1% have central obesity [6]. Diabetic nephropathy (DN), which affects 40% of diabetics worldwide, is a major cause of end-stage renal failure [7]. In Pakistan, chronic renal impairment accounts for 31% of all DN cases [8].

Due to the slow course of type 2 diabetes mellitus (T2DM), patients should be screened for diabetic nephropathy (DN) at diagnosis and then once a year thereafter. Screening entails determining the estimated glomerular filtration rate (eGFR) and the spot urine albumin-to-creatinine ratio (UACR) from serum creatinine, urinary creatinine, and albumin in a spot urine sample [9]. ACRs between 30-300 mg/g indicate microalbuminuria, and ACRs greater than 300 mg/g suggest macro albuminuria [10]. ACR levels below 30 mg/g are considered normal. Albuminuria is a common sign of diabetic kidney disease, indicating kidney dysfunction.

Insulin-resistant kidneys exhibit hyper filtration, which is associated with the progression of diabetic nephropathy (DN) and severe illness [11]. Microalbuminuria, which indicates endothelial dysfunction, can be treated early. The triglyceride-glucose (TyG) index, a low-cost test of insulin resistance, predicts DN and could replace HOMA-IR. Studies in Taiwan, China, India, and Pakistan have linked the TyG index to type 2 diabetes mellitus (T2DM), angiopathies, and metabolic syndrome (MS) [12].

Relevant data has remained scarce in Pakistan. There is a need for a new, accessible, affordable and reliable marker to predict early-stage DN in the Pakistani population. The current study was planned to determine the association of TyG index with HOMA-IR in T2DM patients, and to determine the association of TyG index with UACR for predicting DN.

## METHODOLOGY

This research was approved by the Ethical Review Committee. The sample was acquired from Diabetic Clinic patients using a non-probability consecutive sampling technique. The study comprised T2DM patients with fasting plasma glucose (FPG) values of  $\geq 126$  mg/dl and a diagnosis of 1-5 years.

**Exclusion criteria:** Those patients who had systemic or chronic illnesses, pregnancy, type 1 diabetic mellitus were not a part of this research. Moreover, those people who smoked or were on dialysis were also removed from this study.

Data was collected after patients provided informed consent and ensured their confidentiality. The demographic and clinical data gathered were gender, age, height, diabetes duration, blood pressure (BP), waist circumference (WC), weight, and body mass index (BMI). After fasting for 10-12 hours,

5 ml of venous blood was drawn, stored in specific tubes for various assays, and kept at -20°C. The fasting plasma glucose (FPG) and insulin concentrations were examined to determine HOMA-IR. A spot urine sample was taken to calculate the albumin-to-creatinine ratio (ACR). The urinary ACR is computed by dividing the albumin content (mg) by the creatinine concentration (mg) in a spot urine specimen.

Participants were divided into four groups based on TyG index scores. SPSS version 26 was used for data analysis, and Pearson correlation was used to investigate connections between the TyG index, UACR, anthropometric measures, eGFR, HOMA-IR, and biochemical variables. Linear regression evaluated HOMA-IR and TyG index as predictors of UACR and eGFR, with significance set at  $p < 0.05$ .

## RESULTS

In all, 250 patients were included in this investigation. There were 88 (35.2%) male participants and 162 (64.8%) female participants, making up the majority of the participants. Overall 49.2 years of age was the average and 3.46 was the mean fasting serum insulin level. Overall 1.79 was the mean HOMA-IR. Glycated hemoglobin was 6.65 on average. The mean TyG index levels were 5.39. 46% of the participants were overweight while 15% were obese and 39% were normal weighted. Table number 1 shows the demographics of the participants according to TyG index quartiles.

**Table No. 1: demographics of the participants according to TyG index quartiles.**

Demographics	Q1 (n=68)	Q2 (n=100)	Q3 (n=52)	Q4 (n=30)
	(4.5-5)	(5.1-5.5)	(5.6-6)	(>6)
Age (years)	51.5	46.7	49.6	51.7
Waist circumference (inches)	30.8	30.6	30.1	30.9
BMI	26.3	26.2	26.3	26.7
Duration of T2DM (years)	3.9	3.5	3.8	4.1
Diastolic Blood Pressure (mmHg)	86.7	85.3	84.1	90.1
Systolic Blood Pressure (mmHg)	129.1	125.3	126.7	125.1

Table number 2 shows correlation of biochemical parameters with HOMA-IR, TyG index, and UACR.

**Table No. 2: correlation of biochemical parameters with HOMA-IR, TyG index, and UACR.**

Parameters	TyG Index	Fasting serum insulin	UACR	HOMA-IR
	r-value	r-value	r-value	r-value
LDL-C	0.55	-0.01	0.16	0.34
HDL-C	-0.35	0.13	0.11	-0.22
eGFR	-0.35	0.05	-0.02	-0.01
Fasting plasma glucose	0.76	-0.14	0.10	0.48
TyG Index	1	-0.13	0.28	0.32

<b>Total Cholesterol</b>	0.39	-0.01	0.08	0.11
<b>Glycated Haemoglobin</b>	0.35	-0.12	0.15	0.05

Table number 3 shows the relationship of TyG index quartiles with albuminuria.

**Table No. 3: relationship of TyG index quartiles with albuminuria.**

Albuminuria Categories	Q1 (n=68)	Q2 (n=100)	Q3 (n=52)	Q4 (n=30)
	(4.5-5)	(5.1-5.5)	(5.6-6)	(>6)
<b>Normal (&lt;30 mg/g)</b>	22 (32.4%)	20 (20%)	9 (17.3%)	3 (10%)
<b>Microalbuminuria (30–300 mg/g)</b>	46 (67.6%)	80 (80%)	43 (82.7)	27 (90%)

## DISCUSSION

The study looked at how the TyG index connects to HOMA-IR in T2DM patients and how it works with UACR to predict diabetic nephropathy (DN). While the TyG index has been extensively studied for its link to diabetes, metabolic problems, and heart disease, it has not gotten the same level of scrutiny as other measures for detecting insulin resistance [13, 14].

Lipid levels are critical in determining insulin action, which refers to decreased tissue sensitivity to insulin, raising the risk of hyperglycemia, hypertension, and dyslipidemia [15]. People who are overweight or obese frequently have increased insulin resistance (IR) and lipoprotein metabolism abnormalities, such as elevated levels of triglyceride-rich lipoprotein remnants, remnant-like particle cholesterol, and Apo lipoprotein B. Low insulin sensitivity is associated with greater triglyceride levels, and vice versa. Research indicates that muscles with high triglyceride levels have poor glucose metabolism [16]. The current study demonstrated that fasting plasma glucose (FPG) and triglycerides have separate correlations with diabetic nephropathy (DN).

In 2018, a study in Pakistan looked at how the TyG index interacted with insulin resistance (IR) and diabetic nephropathy (DN) [17]. The TyG index had a greater linear connection with BMI, atherogenic dyslipidemia, HbA1c, and IR than other indicators such as fasting triglycerides, HOMA-IR, and HDL-C. The study revealed that the TyG index was a more reliable predictor of metabolic syndrome (MS), but there was no evidence associating it to DN. The current investigation found a significant inverse relationship between eGFR and the TyG index, HOMA-IR, and UACR. In contrast, a study conducted on a Chinese population found no significant association between the TyG index and eGFR [18]. However, similar to our findings, it discovered a strong link between a higher TyG index and type 2 diabetic nephropathy (DN), as well as a favorable relationship between the TyG index and 24-hour albumin excretion rate.

A 2020 study in India, similar to the current one, looked into the relationship between the TyG index and diabetic nephropathy (DN), neuropathy, and retinopathy [19]. It discovered that fasting plasma glucose (FPG) and triglycerides were independently correlated with DN, but albuminuria was associated with higher TyG index levels. However, unlike the current investigation, it excluded eGFR and used 24-hour albumin excretion rate rather than spot urine ACR.

Patients with type 2 diabetes, whether with or without nephropathy, exhibit more severe insulin resistance (IR), as indicated by a higher TyG index and HOMA-IR scores. This study discovered a strong relationship between an elevated TyG index and microalbuminuria, which indicates early diabetic nephropathy (DN). IR causes increased glomerular pressure and vascular permeability, which leads to glomerular hyper filtration. Dyslipidemia contributes significantly to renal impairment in T2DM. Previous research has also linked IR to an increased risk of progressive DN [20].

The current study has limitations. For starters, as an observational cross-sectional study, it has intrinsic design limits. Prospective studies are required to investigate the relationship of TyG index

scores with the start and progression of diabetic nephropathy (DN) in type 2 diabetic individuals. Second, the study was conducted at a single location, emphasizing the need of multicenter epidemiological studies.

## CONCLUSION

The TyG index showed a strong connection with HOMA-IR and was superior in predicting diabetic nephropathy (DN) in type 2 diabetes patients.

## Funding source

None

## Conflict in the interest

None

## Permission

It was taken from the review committee

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