Section: General Medicine

Original Research Article

UTILITY OF TRIGLYCERIDE-GLUCOSE INDEX AS A MARKER OF DIABETIC RETINOPATHY AND NEPHROPATHY IN TYPE 2 DIABETES MELLITUS: A CROSS-SECTIONAL STUDY

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Received *: 15/05/2026*
Received in revised form *: 25/06/2026*
Accepted *: 07/07/2026*

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DOI: 10.70034/ijmedph.2026.3.150

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2026; 16 (3); 926-932

ABSTRACT

Background: The triglyceride-glucose (TyG) index is a simple, low-cost surrogate marker of insulin resistance proposed as a predictor of diabetic microvascular complications, but its association with diabetic retinopathy and nephropathy remains incompletely defined in Indian populations. **Objective:** To evaluate the utility of the TyG index as a marker of diabetic retinopathy and nephropathy, and to correlate it with these complications in type 2 diabetes mellitus (T2DM).

Materials and Methods: This hospital-based cross-sectional study enrolled 90 adults with T2DM. Fasting triglycerides and glucose were used to calculate the TyG index, and participants were categorized into tertiles. Retinopathy was graded by ETDRS classification and nephropathy assessed by urinary albumin excretion and eGFR. Chi-square test, independent t-test, ANOVA, and Pearson correlation were used, with $p<0.05$ considered significant.

Results: Retinopathy was present in 31 (34.44%) and nephropathy in 61 (67.78%) of 90 participants; 28 (31.11%) had both. Retinopathy and nephropathy prevalence rose across TyG tertiles, from 38.71% and 64.52% in the lowest tertile to 56.67% and 73.33% in the highest. Mean TyG index was numerically higher with retinopathy (5.29 vs 5.19) and nephropathy (5.27 vs 5.16), though not statistically significant ($p=0.247$, $p=0.212$). Fasting and post-prandial glucose were significantly higher with retinopathy ($p=0.028$, $p=0.024$), while HbA1c was significantly associated with nephropathy ($p=0.009$). TyG index correlated significantly with fasting glucose ($r=0.622$), post-prandial glucose ($r=0.570$), triglycerides ($r=0.755$), and HbA1c ($r=0.538$), all $p<0.001$.

Conclusion: The TyG index shows a graded association with diabetic retinopathy and nephropathy across tertiles and correlates strongly with glycemic and lipid parameters, supporting its potential as an inexpensive adjunct for risk stratification, although larger studies are needed to establish significant thresholds for individual complications.

Keywords: Triglyceride-glucose index; diabetic retinopathy; diabetic nephropathy; type 2 diabetes mellitus; insulin resistance.

INTRODUCTION

Diabetes mellitus is one of the most prevalent chronic metabolic disorders worldwide, characterized by persistent hyperglycemia resulting from defects in insulin secretion, insulin action, or both; the World Health Organization estimated approximately 422 million people were living with diabetes in 2014, a figure projected to rise steadily.1 Type 2 diabetes mellitus (T2DM) constitutes nearly 90% of all cases and is closely linked to lifestyle-related risk factors such as obesity, sedentary behaviour, and poor dietary habits.[2] India carries a disproportionate share of this burden, with the International Diabetes Federation estimating approximately 74 million adults living with diabetes in 2021, projected to exceed 124 million by 2045.[3]

Beyond its metabolic derangements, T2DM is associated with a wide spectrum of chronic complications that substantially increase morbidity and mortality. Diabetic retinopathy is the most common microvascular complication and remains the leading cause of preventable blindness among working-age adults worldwide, resulting from chronic hyperglycemia-induced retinal microvascular damage.[4] Diabetic nephropathy is a major cause of chronic kidney disease and end-stage renal failure in diabetic individuals, characterized by persistent albuminuria and progressive decline in glomerular filtration rate, affecting nearly 20-40% of patients with diabetes.[5]

The development and progression of these microvascular complications are influenced not only by glycemic control but also by underlying insulin resistance, dyslipidemia, and hypertension, which contribute to endothelial dysfunction, oxidative stress, and inflammatory pathways. Identifying reliable, accessible surrogate markers of insulin resistance may therefore aid early detection and risk stratification. The triglyceride-glucose (TyG) index, derived from fasting triglyceride and fasting plasma glucose values, has been proposed as a practical alternative to more complex and invasive techniques such as the hyperinsulinemic-euglycemic clamp.[6,7]

Guerrero-Romero et al. demonstrated that the TyG index strongly correlates with insulin sensitivity measured by the gold-standard clamp technique,[8] and subsequent work has linked elevated TyG index values with increased arterial stiffness, progression of diabetic nephropathy, and greater severity of diabetic retinopathy.[9,10] Despite this growing evidence, data evaluating the TyG index's association with diabetic retinopathy and nephropathy remain limited, particularly in Indian populations, where simple and cost-effective markers may offer substantial clinical utility in resource-limited settings.

This study was therefore designed to evaluate the association of the TyG index with diabetic retinopathy and nephropathy among patients with type 2 diabetes mellitus, with the aim of enhancing early detection strategies and contributing to the growing literature on the applicability of the TyG index as a surrogate marker of microvascular risk in diverse populations.

Aims and Objectives

1. To evaluate the utility of the triglyceride-glucose index as a marker of diabetic retinopathy and nephropathy in patients with type 2 diabetes mellitus.
2. To correlate the triglyceride-glucose index with diabetic retinopathy and nephropathy in type 2 diabetes mellitus.

MATERIALS AND METHODS

Study design and setting: This was a hospital-based cross-sectional observational study conducted at PES Medical College Hospital, Kuppam, Andhra Pradesh, over 18 months (April 2024 to September 2025).

Study population and eligibility: Patients aged more than 18 years diagnosed with type 2 diabetes mellitus as per American Diabetes Association (ADA) guidelines, attending the medical outpatient department or admitted to the medical wards, were eligible. Patients with end-stage renal disease (eGFR <15 mL/min/1.73m²), active urinary tract infection, malignancy, pregnancy, statin therapy, or type 1 diabetes mellitus were excluded.

Sample size and sampling: The minimum sample size was calculated using the standard formula for estimating a single proportion at 95% confidence, based on a previously reported diabetic retinopathy prevalence of 34.6% (Z=1.96, p=0.346, d=0.10), yielding a minimum of 87 participants; the final sample size, accounting for feasibility and attrition, was 90. A purposive sampling technique was used, with eligible patients consecutively enrolled after informed consent until the target was reached.

Study procedure: After institutional ethics committee approval, each participant underwent structured clinical assessment including diabetes history, blood pressure, anthropometry, and fasting blood samples for glucose, lipid profile, and HbA1c, together with renal function tests and urine protein-creatinine ratio. The TyG index was calculated as ln[fasting triglycerides (mg/dL) x fasting plasma glucose (mg/dL)/2], and participants were categorized into tertiles (T1 low, T2 mid, T3 high) based on the 33rd and 66th percentile values of the cohort distribution.[11] Diabetic retinopathy was assessed by dilated fundus examination performed by an ophthalmologist and graded using the Early Treatment Diabetic Retinopathy Study (ETDRS) classification (no retinopathy, mild/moderate/severe non-proliferative, or proliferative diabetic retinopathy). Diabetic nephropathy was assessed using urinary albumin excretion (microalbuminuria/macroalbuminuria) and estimated glomerular filtration rate.

Variables: Independent variables included TyG index, age, gender, duration of diabetes, BMI, blood pressure, and HbA1c. Outcome variables were presence and severity of diabetic retinopathy, eGFR, and presence of nephropathy based on protein-creatinine ratio.

Statistical Analysis: Data were entered in Microsoft Excel and analysed using SPSS version 23. Categorical variables were expressed as frequencies and percentages and compared using the chi-square test; continuous variables were expressed as mean ± standard deviation and compared using the independent-samples t-test between two groups or one-way ANOVA across more than two groups. Pearson correlation was used to assess the relationship between the TyG index and continuous biochemical parameters. A two-sided p value <0.05 was considered statistically significant.

RESULTS

A total of 90 patients with type 2 diabetes mellitus were enrolled. The baseline demographic profile of the cohort is summarized in Table 1. The majority of participants were aged 60-69 years (31.11%), followed by 41-49 years (25.56%); males predominated markedly (88.89%). Just under a third of participants were current smokers (31.11%) and 44.44% reported alcohol use.

Table 1: Baseline demographic profile (N=90)

Parameter	Frequency (n)	Percentage (%)
Age group (years)		
18–30	1	1.11
30–39	10	11.11
41–49	23	25.56
51–59	15	16.67
60–69	28	31.11
≥70	13	14.44
Sex		
Female	10	11.11
Male	80	88.89
Smoking		
No	62	68.89
Yes	28	31.11
Alcohol use		
No	50	55.56
Yes	40	44.44

Baseline clinical, biochemical, and urine parameters are summarized in Table 2. The cohort showed poor glycemic control (mean HbA1c 10.44 ± 2.89%; fasting glucose 194.46 ± 79.26 mg/dL), dyslipidemia with elevated triglycerides (239.09 ± 185.95 mg/dL) and low HDL (34.67 ± 13.26 mg/dL), and a mean TyG index of 5.23 ± 0.39. Dipstick proteinuria (1+ to 3+) was present in 38.89% of participants, and 3+ glycosuria was the most common urine sugar finding (47.78%).

Table 2: Baseline clinical, biochemical and urine parameters (N=90)

Parameter	Mean	SD
Clinical and biochemical parameters (Mean ± SD)		
Systolic BP (mmHg)	127.07	18.15
Diastolic BP (mmHg)	89.98	97.56
Fasting blood sugar (mg/dL)	194.46	79.26
Post-prandial blood sugar (mg/dL)	284.48	78.26
HbA1c (%)	10.44	2.89
Triglycerides (mg/dL)	239.09	185.95
Total cholesterol (mg/dL)	165.46	44.74
HDL (mg/dL)	34.67	13.26
LDL (mg/dL)	82.07	38.95
VLDL (mg/dL)	35.91	18.88
Serum urea (mg/dL)	35.63	19.53
Serum creatinine (mg/dL)	1.11	0.83
eGFR (mL/min/1.73m²)	90.12	37.37
Urine protein–creatinine ratio	0.94	1.93
TyG index	5.23	0.39
Urine protein (dipstick), n (%)		
Nil	46	51.11
Trace	9	10.00
1+	16	17.78
2+	11	12.22
3+	8	8.89
Urine sugar (dipstick), n (%)		
Nil	28	31.11
1+	4	4.44
2+	15	16.67
3+	43	47.78

The distribution of diabetic retinopathy, nephropathy, and TyG tertiles is presented in Table 3. On fundus examination, 61.11% of participants had no diabetic retinopathy, while mild, moderate, and severe non-proliferative changes were seen in 6.67%, 24.44%, and 2.22% respectively. Overall, diabetic retinopathy was present in 34.44% and nephropathy in 67.78% of participants, with 31.11% having both complications, 36.67% nephropathy alone, 7.78% retinopathy alone, and 24.44% neither.

When cross-tabulated against TyG tertile, the proportion of participants with retinopathy present rose from 38.71% in the lowest (T1) tertile to 56.67% in the highest (T3) tertile, and nephropathy present rose from 64.52% to 73.33% across the same tertiles, with combined complications rising from 32.26% to 43.33%, indicating a graded increase in microvascular complication burden with increasing TyG index category.

Table 3: Distribution of diabetic retinopathy, nephropathy and TyG tertiles (N=90)

Parameter	Frequency (n)	Percentage (%)
Fundus findings (ETDRS stage)		
No diabetic retinopathy	55	61.11
Stage 1 – Mild NPDR	6	6.67
Stage 2 – Moderate NPDR	22	24.44
Stage 3 – Severe NPDR	2	2.22
TyG tertile		
T1 (Low, TyG ≤5.00)	31	34.44
T2 (Mid, TyG 5.01–5.54)	29	32.22
T3 (High, TyG >5.45)	30	33.33
Diabetic retinopathy status		
Present	31	34.44
Absent	59	65.56
Diabetic nephropathy status		
Present	61	67.78
Absent	29	32.22
Combined retinopathy / nephropathy status		
Both present	28	31.11
Nephropathy only	33	36.67
Retinopathy only	7	7.78
Neither	22	24.44

TyG tertile distribution of the combined retinopathy/nephropathy phenotype (raw counts, % of total N=90):

TyG tertile	Both present n (%)	Nephropathy only n (%)	Retinopathy only n (%)	Neither n (%)
T1 (Low, n=31)	10 (11.11)	10 (11.11)	2 (2.22)	9 (10.00)
T2 (Mid, n=29)	5 (5.56)	14 (15.56)	1 (1.11)	9 (10.00)
T3 (High, n=30)	13 (14.44)	9 (10.00)	4 (4.44)	4 (4.44)

TyG tertile distribution expressed as percentage within each tertile:

TyG tertile	Retinopathy present n (% within tertile)	Nephropathy present n (% within tertile)	Both present n (% within tertile)
T1 (Low, n=31)	12 (38.71)	20 (64.52)	10 (32.26)
T2 (Mid, n=29)	6 (20.69)	19 (65.52)	5 (17.24)
T3 (High, n=30)	17 (56.67)	22 (73.33)	13 (43.33)

The association of TyG index and other biochemical parameters with retinopathy, nephropathy, and combined complication status, together with correlation analyses, is detailed in Table 4. Mean TyG index was numerically higher among participants with diabetic retinopathy (5.29 vs 5.19, p=0.247), diabetic nephropathy (5.27 vs 5.16, p=0.212), and combined complications (5.29 vs 5.20, p=0.371), though none of these differences reached statistical significance. In contrast, fasting blood sugar and post-prandial blood sugar were both significantly higher among patients with retinopathy (178.24 vs 219.94 mg/dL, p=0.028; 268.09 vs 310.23 mg/dL, p=0.024 respectively), while HbA1c was significantly associated with nephropathy status (11.58% in those without nephropathy vs 9.91% in those with nephropathy, p=0.009), but not with retinopathy or combined complication status. TyG index did not differ significantly across proteinuria grades (p=0.932) or across the four combined DR/DN categories (p=0.421). TyG index showed a strong, statistically significant positive correlation with triglycerides (r=0.755), fasting blood sugar (r=0.622), post-prandial blood sugar (r=0.570), and HbA1c (r=0.538), all p<0.001, confirming its close metabolic relationship with the glycemic and lipid parameters from which it is derived.

Table 4: Association of TyG index and biochemical parameters with diabetic retinopathy, nephropathy and combined status, and correlation with TyG index

Parameter	No DR vs DR present	No DN vs DN present	Not both vs Both DR&DN
TyG index	5.19 vs 5.29 p=0.247	5.16 vs 5.27 p=0.212	5.20 vs 5.29 p=0.371
FBS (mg/dL)	178.24 vs 219.94 p=0.028	194.83 vs 194.28 p=0.975	183.71 vs 218.25 p=0.097
PPBS (mg/dL)	268.09 vs 310.23 p=0.024	295.62 vs 279.18 p=0.368	275.85 vs 303.57 p=0.173
HbA1c (%)	10.59 vs 10.44 p=0.522	11.58 vs 9.91 p=0.009	10.64 vs 9.90 p=0.287
Triglycerides (mg/dL)	248.75 vs 223.91 p=0.492	205.45 vs 255.08 p=0.197	244.87 vs 226.29 p=0.612

Values shown as No/Absent group mean vs Yes/Present group mean, with p value from independent t-test.

Category	TyG index Mean (SD)	p value
TyG index by proteinuria grade — one-way ANOVA		
Nil	5.22 (0.36)	
Trace	5.16 (0.33)	
1+	5.25 (0.46)	
2+	5.25 (0.44)	
3+	5.32 (0.50)	0.932
TyG index by combined DR/DN status — one-way ANOVA		
Neither	5.11 (0.37)	
Nephropathy only	5.24 (0.39)	
Retinopathy only	5.30 (0.28)	
Both present	5.29 (0.43)	0.421

Variables (vs TyG index)	Pearson r	p value	N
Fasting blood sugar	0.622	<0.001	90
Post-prandial blood sugar	0.570	<0.001	90
HbA1c	0.538	<0.001	90
Triglycerides	0.755	<0.001	90

DISCUSSION

This cross-sectional study of 90 patients with type 2 diabetes mellitus evaluated the association of the TyG index with diabetic retinopathy and nephropathy, and demonstrates a graded, though not always statistically significant, relationship between metabolic dysregulation and microvascular complication burden.

Diabetic retinopathy was observed in over a third of our cohort, with severity ranging from mild non-proliferative changes to more advanced forms, consistent with global epidemiological data identifying retinopathy as one of the most common microvascular complications of type 2 diabetes.[1] The International Diabetes Federation has highlighted the growing prevalence of diabetes and its complications, particularly in low- and middle-income countries,[12] and our prevalence rates are broadly comparable to hospital-based studies in other Asian populations, where moderate non-proliferative retinopathy tends to predominate.

Fasting and post-prandial blood sugar levels were significantly higher among patients with retinopathy in our analysis, consistent with Zhang et al.'s validation of the relationship between plasma glucose levels and retinopathy, which emphasized chronic hyperglycemia as a major determinant of retinal microvascular damage.[13] Higher TyG values, reflecting combined hyperglycemia and hypertriglyceridemia, were also more frequently observed in patients with retinopathy, and the moderate-to-strong positive correlations between glucose parameters and TyG index further reinforce this metabolic interdependence.

With regard to diabetic nephropathy, our study demonstrated a substantial proportion of patients with isolated nephropathy as well as combined retinopathy and nephropathy, suggesting widespread microvascular injury. Deckert et al. proposed that albuminuria reflects generalized vascular damage rather than isolated renal pathology,[14] while Nakagawa et al. described endothelial dysfunction as a central mechanism in diabetic nephropathy.[15] The numerically higher mean TyG index among patients with nephropathy in our cohort is consistent with these pathophysiological models, suggesting that insulin resistance may contribute to renal microvascular damage even where statistical significance was not reached.

Stratification into TyG tertiles revealed a progressive gradient of microvascular complications, with the highest tertile showing a greater frequency of both retinopathy and nephropathy compared to the lowest tertile. This gradient is consistent with Simental-Mendía et al.'s work establishing the TyG index as a surrogate of insulin resistance closely related to metabolic abnormalities,[16] and mirrors Tiongco et al.'s meta-analysis among Asian populations demonstrating that elevated TyG index was significantly associated with increased likelihood of nephropathy development.[17] Ran et al. similarly reported correlations between TyG index and microvascular complications in early-onset type 2 diabetes, noting that younger patients with higher TyG values were more likely to develop retinopathy and nephropathy;18 although our cohort was not limited to early-onset cases, the observed gradient across tertiles suggests TyG may have predictive relevance irrespective of disease onset timing.

Srinivasan et al. explored the relationship between TyG index, retinopathy, and nephropathy specifically in Indian patients and demonstrated a positive association between higher TyG and microvascular damage,[19] a finding our results parallel, particularly in the increased frequency of combined complications among individuals with higher metabolic indices-a similarity that may reflect shared genetic, dietary, and lifestyle patterns within the Indian population.

The strong positive correlation between triglycerides and TyG index observed here is expected given the index's derivation formula; Budoff highlighted the role of triglyceride-rich lipoproteins in vascular injury and inflammation,[20] and elevated triglycerides may accelerate endothelial dysfunction, contributing to both retinal and renal damage. With respect to glycemic control, HbA1c did not differ significantly between patients with and without retinopathy, but did differ significantly by nephropathy status, suggesting that chronic glycemic exposure may have a more direct association with renal microvascular involvement than with retinal changes in this cohort, potentially reflecting the differential impact of sustained hyperglycemia on glomerular basement membrane thickening and mesangial expansion relative to retinal vasculature.

The absence of statistically significant differences in mean TyG index across retinopathy, nephropathy, and combined complication categories in ANOVA analysis may reflect limited statistical power in this comparatively modest sample; Kassab et al. reported significant associations between TyG and microvascular complications in a larger cohort, which may explain the discrepancy.[21] The coexistence of retinopathy and nephropathy in a considerable proportion of participants underscores the systemic nature of diabetic microangiopathy, consistent with Klein et al.'s observation that microalbuminuria often coexists with retinopathy as parallel vascular injury,[22] and the pathophysiological role of inflammation described by Vinik et al. in diabetic vascular complications.[23]

Non-linear relationships have also been proposed: Zhou et al. reported a U-shaped relationship between TyG index and retinopathy risk, suggesting both very low and very high values may carry risk,[24] while Low et al. demonstrated that the TyG index prospectively predicted chronic kidney disease progression in type 2 diabetes.[25] Although our cross-sectional design cannot establish causality, the tertile-based gradient observed here is compatible with these findings and supports the hypothesis that elevated TyG may identify patients at risk for microvascular deterioration, warranting longitudinal follow-up. Jabeen et al. and Pan et al. have similarly reported associations between the TyG index and both microvascular and macrovascular complications of diabetes, reinforcing its broader role as a marker of vascular vulnerability.[26,27]

From a clinical perspective, identification of high-TyG-tertile patients may facilitate earlier ophthalmologic and nephrologic evaluation; Chamroonkiadtikun et al. demonstrated the TyG index's predictive capacity for incident type 2 diabetes itself,[28] and Raman et al. emphasized the substantial burden of metabolic syndrome on microvascular complications specifically in Indian populations,[29] supporting integration of metabolic risk assessment with routine complication screening. Prospective studies similar to those described by Neelam et al. in a Singaporean population could further clarify the temporal relationship between TyG index and incident retinopathy.[30]

Strengths and Limitations

- The cross-sectional design limits the ability to establish temporal or causal relationships between the TyG index and diabetic retinopathy or nephropathy.
- The sample size, while adequate for the primary analysis, was relatively modest and may have limited statistical power to detect smaller associations between TyG index and individual complications.
- Being a single-centre, hospital-based study, the findings may not be fully generalizable to the broader diabetic population.
- No universally accepted cut-off values exist for the TyG index, and the tertile boundaries used here were derived from the study cohort's own distribution rather than externally validated thresholds.

CONCLUSION

This cross-sectional study demonstrates that individuals with type 2 diabetes mellitus commonly exhibit suboptimal glycemic control, dyslipidemia, and a substantial burden of microvascular complications, particularly diabetic nephropathy and retinopathy. Retinopathy was significantly associated with higher fasting and post-prandial glucose levels, while nephropathy showed a stronger association with HbA1c, indicating differential relationships between glycemic parameters and specific complications. The TyG index, a surrogate marker of insulin resistance, showed a progressive increase in microvascular complication burden across tertiles and a strong, statistically significant positive correlation with glucose and triglyceride parameters, supporting its potential role as an inexpensive, readily available tool for early risk stratification in type 2 diabetes, even though its association with individual complications did not reach statistical significance in this cohort. Larger, prospective, multicentric studies are warranted to validate the TyG index's predictive utility for diabetic retinopathy and nephropathy.

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