Section: Diabetes

Original Research Article

BEYOND HBA1C: TYG INDEX AND TG/HDL RATIO AS WINDOWS INTO GLYCEMIC BURDEN IN TYPE 2 DIABETES MELLITUS — A CROSS-SECTIONAL STUDY

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ABSTRACT

Background: The triglyceride–glucose (TyG) index and the triglyceride/HDL-cholesterol (TG/HDL) ratio are inexpensive surrogate markers of insulin resistance that have been proposed as predictors of glycemic status and diabetic microvascular complications. Data from South Asian outpatient populations remain limited.

Materials and Methods: In this cross-sectional study, 116 adults with type 2 diabetes mellitus (T2DM) attending a diabetes outpatient clinic were classified as having good (HbA1c <7%, n=39) or poor (HbA1c ≥7%, n=77) glycemic control. Anthropometric, biochemical, fundoscopic and urine albumin data were recorded. TyG index and TG/HDL ratio were compared between groups and correlated with glycemic and vascular outcomes; discriminative ability was assessed with receiver operating characteristic (ROC) curves and associations with diabetic retinopathy (DR) and nephropathy (albuminuria) were examined using multivariable logistic regression.

Results: Both TyG index (9.58±0.38 vs 9.04±0.41, p<0.001) and TG/HDL ratio (5.51±1.82 vs 3.71±1.24, p<0.001) were significantly higher in the poor-control group, as were diabetes duration, systolic/diastolic blood pressure, fasting glucose and triglycerides. TyG index correlated strongly with fasting glucose (r=0.71, p<0.001) and moderately with HbA1c (r=0.41, p<0.001); TG/HDL ratio showed weaker correlations (r=0.28–0.29). TyG index and TG/HDL ratio discriminated poor glycemic control with AUCs of 0.85 and 0.80, respectively. Neither marker differed significantly by presence of DR (TyG: p=0.63; TG/HDL: p=0.32) or nephropathy (TyG: p=0.31; TG/HDL: p=0.68), and neither showed useful discrimination for these complications (AUC 0.51–0.55). On multivariable logistic regression, TyG index was not independently associated with DR or nephropathy after adjustment for age, sex, BMI, diabetes duration, systolic blood pressure and HbA1c.

Conclusion: In this cohort, TyG index and TG/HDL ratio tracked closely with glycemic control status but were not independently associated with diabetic retinopathy or nephropathy. These indices may be useful adjunct markers of metabolic/glycemic burden in T2DM, but larger, adequately powered studies are needed before they can be recommended as screening tools for microvascular complications.

Keywords: triglyceride-glucose index; TG/HDL ratio; insulin resistance; type 2 diabetes mellitus; diabetic retinopathy; diabetic nephropathy; glycemic control.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder whose microvascular complications — retinopathy, nephropathy and neuropathy — remain leading causes of blindness, end-stage renal disease and disability worldwide. Chronic hyperglycemia is the principal driver of

microvascular injury, but insulin resistance and atherogenic dyslipidemia are increasingly recognized as parallel contributors to vascular damage in T2DM. Direct measurement of insulin resistance by the hyperinsulinemic-euglycemic clamp or homeostasis model assessment (HOMA-IR) requires a fasting insulin assay that is costly and not widely available in routine practice. The triglyceride-glucose (TyG) index — calculated as Ln[fasting triglycerides (mg/dL) × fasting plasma glucose (mg/dL)/2] — was proposed by Simental-Mendía et al. as an inexpensive surrogate for insulin resistance derived from two routinely measured analytes, and has since been validated against the clamp technique by Guerrero-Romero et al. Similarly, the triglyceride/HDL-cholesterol (TG/HDL) ratio, first popularized by McLaughlin et al., is a simple lipid-based marker that correlates with insulin resistance and atherogenic small dense LDL particles.

Both indices have been linked to cardiometabolic risk, incident type 2 diabetes and, in several recent Asian cohorts, to diabetic retinopathy; a 2023 meta-analysis of ten observational studies (13,716 patients) reported that a higher TyG index was associated with increased odds of retinopathy (pooled OR 2.34, 95% CI 1.31–4.19). However, evidence linking these markers to microvascular complications in South Asian, hospital-based outpatient populations is still limited, and findings across studies have not been uniformly consistent. This study examines the relationship of the TyG index and TG/HDL ratio with glycemic control status and with the presence of diabetic retinopathy and nephropathy in a cohort of T2DM patients attending a diabetes outpatient clinic.

Objectives:

(1) To compare the TyG index and TG/HDL ratio between patients with good (HbA1c <7%) and poor (HbA1c ≥7%) glycemic control. (2) To evaluate the correlation of these indices with glycemic parameters (fasting plasma glucose, HbA1c) and diabetes duration. (3) To assess the association of TyG index and TG/HDL ratio with diabetic retinopathy (by fundoscopy) and nephropathy (by urine albumin category), including their discriminative performance (ROC-AUC) and independent association on multivariable analysis.

MATERIALS AND METHODS

Study design and setting: This was a cross-sectional, observational study conducted among adults with type 2 diabetes mellitus attending a diabetes outpatient clinic. Data were compiled into a de-identified master chart comprising demographic, anthropometric, clinical, biochemical, and complication-screening variables for 116 patients.

Participants: Adult patients with a confirmed diagnosis of T2DM were consecutively enrolled. Variables recorded included age, sex, education level, socioeconomic status (modified scale), body mass index (BMI), duration of diabetes, smoking and alcohol use, seated systolic and diastolic blood pressure (SBP/DBP), fasting plasma glucose, glycated hemoglobin (HbA1c), fasting lipid profile (triglycerides, HDL-cholesterol, total cholesterol, LDL-cholesterol), dilated fundus examination findings, and semi-quantitative urine albumin status.

Definitions and derived variables: Glycemic control was dichotomized as good (HbA1c <7%) or poor (HbA1c ≥7%), consistent with commonly applied clinical targets. The TyG index was calculated as Ln[fasting triglycerides (mg/dL) × fasting plasma glucose (mg/dL)/2]. The TG/HDL ratio was calculated as fasting triglycerides (mg/dL) divided by HDL-cholesterol (mg/dL). Diabetic retinopathy was categorized by dilated fundoscopy as normal, non-proliferative diabetic retinopathy (NPDR), or proliferative diabetic retinopathy (PDR); for binary analyses, any NPDR/PDR was classified as 'retinopathy present'. Diabetic nephropathy was assessed by urine albumin category (nil, microalbuminuria, macroalbuminuria); for binary analyses, any microalbuminuria/macroalbuminuria was classified as 'albuminuria present'.

Statistical analysis: Continuous variables are presented as mean ± standard deviation and were compared between groups using the independent-samples t-test, with the Mann–Whitney U test as a non-parametric check; one-way ANOVA was used for comparisons across ordinal complication stages (Normal/NPDR/PDR;
Nil/Micro/Macroalbuminuria). Categorical variables are presented as counts and percentages and compared using the chi-square test. Pearson correlation coefficients were calculated between TyG index/TG-HDL ratio and glycemic and clinical parameters. Discriminative ability of TyG index and TG/HDL ratio for poor glycemic control, retinopathy, and nephropathy was assessed using receiver operating characteristic (ROC) curves and the area under the curve (AUC). Multivariable logistic regression (standardized predictors) was used to assess the independent association of TyG index with retinopathy and nephropathy after adjustment for age, sex, BMI, diabetes duration, systolic blood pressure, and HbA1c. A two-tailed p-value <0.05 was considered statistically significant. Analyses were performed in Python (pandas, SciPy, scikit-learn).

RESULTS

Baseline characteristics: Of 116 patients with T2DM, 39 (33.6%) had good glycemic control (HbA1c <7%) and 77 (66.4%) had poor glycemic control (HbA1c ≥7%). Mean age was 60.7±8.7 years and 56.0% were female. Compared with the good-control group, the poor-control group had significantly longer diabetes duration, higher systolic and diastolic blood pressure, higher fasting glucose, higher triglycerides, higher TG/HDL ratio and higher TyG index (Table 1). Total cholesterol, LDL-cholesterol, HDL-cholesterol, age, and BMI did not

differ significantly between groups. Education level and urine albumin category differed significantly across groups ($\chi 2$ p=0.023 and p=0.003, respectively), with more macroalbuminuria in the poor-control group; gender, socioeconomic status, smoking, alcohol use, and fundoscopy category did not differ significantly.

Table 1: Baseline characteristics by glycemic control group (n=116)

Variable	Good control (HbA1c<7%) n=39	Poor control (HbA1c≥7%) n=77	p-value*
Age (years)	62.2 ± 7.7	59.9 ± 9.1	0.170
BMI (kg/m²)	29.4 ± 3.3	30.6 ± 4.1	0.111
Diabetes duration (years)	4.0 ± 2.1	5.8 ± 2.3	<0.001
SBP (mmHg)	131.0 ± 11.6	139.0 ± 11.9	0.001
DBP (mmHg)	79.8 ± 5.3	90.6 ± 7.3	<0.001
Fasting glucose (mg/dl)	118.7 ± 18.2	146.8 ± 26.8	<0.001
HbA1c (%)	6.4 ± 0.3	9.1 ± 0.8	<0.001
Triglycerides (mg/dl)	151.1 ± 45.7	209.1 ± 55.6	<0.001
HDL-C (mg/dl)	42.0 ± 8.6	39.3 ± 6.9	0.065
TG/HDL ratio	3.71 ± 1.24	5.51 ± 1.82	<0.001
TyG index	9.04 ± 0.41	9.58 ± 0.38	<0.001
Total cholesterol (mg/dl)	199.4 ± 29.8	199.3 ± 32.9	0.986
LDL-C (mg/dl)	112.0 ± 24.7	113.3 ± 28.1	0.805

*Independent-samples t-test. Values are mean ± SD. SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

TyG index and TG/HDL ratio across glycemic control groups: [Figure 1] illustrates the distribution of TyG index and TG/HDL ratio by glycemic control group. Both markers were significantly higher in patients with poor glycemic control (p<0.001 for both), consistent with the expected relationship between hyperglycemia, hypertriglyceridemia and these composite indices.

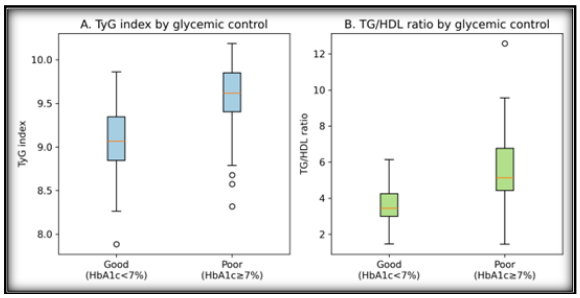

Figure 1: TyG index (A) and TG/HDL ratio (B) by glycemic control group. Boxes show median and interquartile range; whiskers show range.

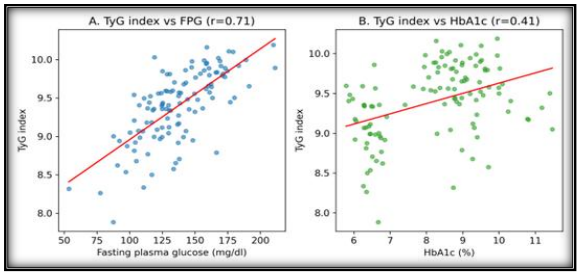

Figure 2: Scatter plots of TyG index against fasting plasma glucose (A, r=0.71) and HbA1c (B, r=0.41), with linear fit.

Correlation with glycemic parameters: TyG index correlated strongly with fasting plasma glucose (r=0.706, p<0.001) and moderately with HbA1c (r=0.405, p<0.001) and systolic blood pressure (r=0.278, p=0.003); correlation with BMI and diabetes duration was weak and non-significant. TG/HDL ratio showed weaker correlations with HbA1c (r=0.289, p=0.002), fasting glucose (r=0.282, p=0.002) and SBP (r=0.199, p=0.032). These correlations are illustrated in [Figure 2].

Discriminative ability for glycemic control status: On ROC analysis, both markers discriminated poor glycemic control reasonably well: TyG index AUC=0.849 and TG/HDL ratio AUC=0.797 [Figure 3]; HbA1c AUC=1.000 by definition, shown for reference only since it was the classifying variable).

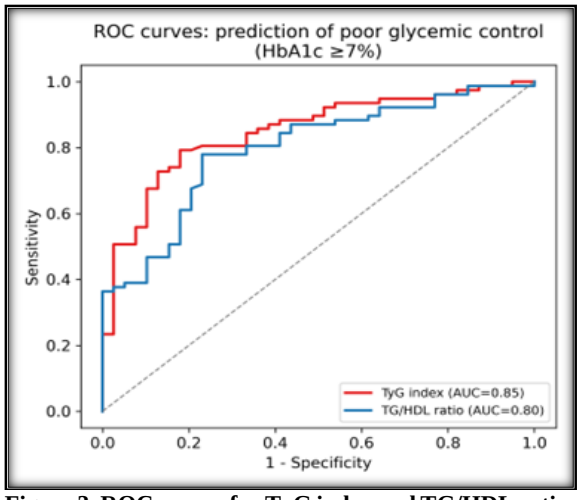

Figure 3. ROC curves for TyG index and TG/HDL ratio in identifying poor glycemic control (HbA1c ≥7%).

Association with diabetic retinopathy and nephropathy: Fundoscopy was normal in 84 patients (72.4%), showed NPDR in 27 (23.3%) and PDR in 5 (4.3%). Urine albumin was nil in 84 (72.4%), microalbuminuria in 25 (21.6%) and macroalbuminuria in 7 (6.0%). Neither TyG index nor TG/HDL ratio differed significantly between patients with and without retinopathy, or with and without albuminuria, whether analyzed as a binary presence/absence comparison or across ordinal disease stages [Table 2].

Table 2: TyG index and TG/HDL ratio by presence of diabetic retinopathy and nephropathy

Comparison	TyG index (mean±SD)	p-value	TG/HDL ratio (mean±SD)	p-value
No retinopathy (n=84)	9.39 ± 0.45	0.625	4.79 ± 1.62	0.317
Retinopathy present (n=32)	9.43 ± 0.49		5.18 ± 2.38	
No albuminuria (n=84)	9.37 ± 0.49	0.310	4.86 ± 1.84	0.678
Albuminuria present (n=32)	9.47 ± 0.37		5.02 ± 1.91	

p-values from independent-samples t-test.

Consistent with the absence of a mean difference, ROC analysis showed poor discrimination of TyG index and TG/HDL ratio for both complications: AUC for retinopathy was 0.538 (TyG) and 0.533 (TG/HDL); AUC for nephropathy was 0.551 (TyG) and 0.506 (TG/HDL) — all close to the 0.5 line of no discrimination. On multivariable logistic regression adjusting for age, sex, BMI, diabetes duration, systolic blood pressure and HbA1c, TyG index was not independently associated with retinopathy (standardized OR 1.30, per 1-SD increase) or nephropathy (standardized OR 0.91). For nephropathy, HbA1c retained the strongest independent association among the variables modeled (standardized OR 2.86), while no single variable reached conventional significance for retinopathy in this modestly sized sample.

DISCUSSION

In this cross-sectional cohort of 116 patients with T2DM, both the TyG index and the TG/HDL ratio were significantly higher among patients with poor glycemic control and correlated meaningfully with fasting glucose and HbA1c — an expected finding given that fasting glucose and triglycerides are direct components of the TyG formula, and that hyperglycemia commonly co-occurs with atherogenic dyslipidemia in poorly controlled T2DM. Both markers also showed good discriminative ability (AUC 0.80–0.85) for identifying poor glycemic control status, supporting their potential utility as simple, low-cost adjunct indicators of overall metabolic burden in outpatient diabetes care.[1-3]

However, contrary to several recently published Asian cohort studies — including a 2023 meta-analysis reporting an approximately two-fold higher odds of retinopathy with elevated TyG index, and hospital-based studies from China and Nepal reporting similar associations — neither the TyG index nor the TG/HDL ratio was significantly associated with diabetic retinopathy or nephropathy in this cohort, either on univariate comparison or multivariable-adjusted analysis, and both indices showed essentially no discriminative value (AUC ≈0.5–0.55) for these outcomes. Several explanations should be considered. First, the sample size (116 patients, with only 32 retinopathy cases and 32 albuminuria cases) provided limited statistical power to detect modest effect sizes of the kind reported in larger cohorts. Second, this was a single time-point, cross-sectional assessment; TyG index and TG/HDL ratio are dynamic markers that may better reflect cumulative or longitudinal insulin resistance exposure than complications that develop over years, so single measurements may under-capture the biologically relevant exposure window. Third, diabetes duration — a well-established determinant of microvascular complications — showed only a weak, non-significant correlation with TyG index in this cohort (r=0.03), suggesting that in this population, duration and metabolic-index pathways to complications may be at least partly independent, diluting any composite association. Finally, differences in population characteristics, complication ascertainment methods, and covariate adjustment across studies may all contribute to inconsistent findings across the literature.[4-6]

These findings should be interpreted as hypothesis-generating rather than as evidence against a biological relationship between insulin resistance markers and diabetic microvascular disease. The pathophysiological rationale for such a relationship — insulin resistance promoting endothelial dysfunction, low-grade inflammation, and dyslipidemia-driven microvascular injury — remains well supported in the broader literature. What this study adds is a cautionary, real-world data point from a South Asian outpatient setting: that a significant association between TyG index/TG-HDL ratio and glycemic control does not automatically translate into a significant association with retinopathy or nephropathy in every population, and that such associations should not be assumed without local validation.[7-9]

Strengths: Strengths of this study include a well-characterized cohort with complete biochemical, fundoscopic and urine albumin data (no missing values), calculation of both TyG index and TG/HDL ratio using standard validated formulae, and the use of both simple bivariate comparisons and multivariable-adjusted, ROC-based analyses to characterize the relationships comprehensively.

Limitations: This study has several limitations. The cross-sectional, single-center design precludes causal inference and is subject to selection bias inherent to an outpatient clinic sample. The relatively modest sample size, and particularly the small number of PDR (n=5) and macroalbuminuria (n=7) cases, limited power to detect associations with advanced-stage complications and precluded stable stage-specific multivariable modeling. HOMA-IR or direct insulin measurements were not available for comparison with the TyG index. Retinopathy was staged by fundoscopy rather than fundus photography/OCT, and nephropathy was assessed by semi-quantitative urine albumin category rather than

the quantitative albumin-to-creatinine ratio; both may have introduced some outcome misclassification. Finally, single fasting measurements of glucose and lipids do not capture within-patient variability over time.

CONCLUSION

In this cohort of Indian patients with type 2 diabetes, the TyG index and TG/HDL ratio were strongly and consistently associated with glycemic control status, supporting their value as simple, inexpensive markers of overall glycemic-metabolic burden. However, neither marker showed a significant or clinically useful association with diabetic retinopathy or nephropathy in this sample. These indices should not, on the basis of these data, be assumed to serve as stand-alone screening tools for microvascular complications; larger, adequately powered, and preferably longitudinal studies are warranted to clarify their role in predicting diabetic retinopathy and nephropathy in South Asian populations.

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