Section: General Medicine

Original Research Article

TRIGLYCERIDE GLUCOSE INDEX AS A PREDICTOR OF CARDIAC AUTONOMIC NEUROPATHY AMONG PATIENTS WITH TYPE 2 DIABETES MELLITUS: A CROSS-SECTIONAL STUDY IN A TERTIARY CARE HOSPITAL IN TAMIL NADU

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ABSTRACT

Background: Cardiac autonomic neuropathy (CAN) is a serious complication of type 2 diabetes mellitus (T2DM). It affects the nerves that control the heart and is associated with increased illness and death. The triglyceride-glucose (TyG) index is an easy, marker of insulin resistance that can be calculated quickly and may help in early identification of metabolic risk. **Objectives:** To measure TyG index levels in patients with T2DM and to assess how well it can predict the presence of CAN.

Materials and Methods: This cross-sectional study included 63 patients with T2DM aged 18–60 years at MAPIMS, Tamil Nadu, from April to September 2024. We recorded clinical details, body measurements, and laboratory parameters, and performed Ewing's cardiovascular autonomic function tests. Based on test results, patients grouped as CAN or non-CAN. Groups were compared using independent t-tests, with $p<0.05$ considered significant.

Results: CAN was present in 41.3% of patients. Compared to those without CAN, patients with CAN had higher fasting blood glucose (242.22±29.92 vs 166.26±10.92 mg/dL), triglycerides (246.31±9.41 vs 153.08±4.37 mg/dL), HbA1c (9.14±1.27 vs 7.12±0.99%), and TyG index (10.30±0.12 vs 9.45±0.07), and all these differences were highly significant ($p<0.001$). Autonomic function test results were significantly worse in the CAN group. Among body measurements, only waist circumference was significantly linked with CAN ($p=0.014$).

Conclusion: The TyG index clearly separated T2DM patients with CAN from those without CAN. Since it is simple, inexpensive, and easy to calculate, it can be used as a screening tool to identify high-risk patients early, especially in settings with limited resources.

Keywords: Triglyceride-glucose index, Cardiac autonomic neuropathy, Type 2 diabetes mellitus, Ewing tests, Insulin resistance.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is increasing rapidly worldwide. Around 537 million adults were affected in 2021, and this number is expected to rise to 783 million by 2045.[1] Long-term high blood sugar and related metabolic problems can cause small blood vessel complications such as eye disease, kidney disease, and nerve damage, and can also increase the risk of major heart and blood vessel disease.[2] One important complication is cardiac autonomic neuropathy (CAN), which occurs when diabetes damages the nerves that control the heart. CAN is often missed in routine practice, but it is linked to abnormal heart rhythms, silent heart attacks, and sudden cardiac death.[3,4,5]

Studies show that the prevalence of CAN varies widely, from 20% to 80%. This difference is mainly due to variation in patient populations, diagnostic methods, and duration of diabetes.[6] Detecting CAN early is important because it can develop before obvious symptoms appear, and early detection allows timely intervention. However, standard testing using Ewing's battery, though considered the gold standard, needs special equipment, trained staff, and time. This makes it difficult to use widely in everyday clinical settings.[7]

The Triglyceride-Glucose (TyG) index is calculated from fasting triglyceride and fasting glucose values using a logarithmic formula, and it is a simple marker of insulin resistance.[8,9] Many studies have shown that a higher TyG index is associated with metabolic syndrome, higher risk of cardiovascular events, and diabetic complications including neuropathy.[10,11,12] Insulin resistance, high blood sugar, and abnormal lipids can together damage nerves and disturb autonomic function through mechanisms such as oxidative stress, endothelial dysfunction, and inflammation.[5,13,14]

In India, diabetes has become a major public health problem, affecting more than 77 million people and creating a large economic burden.[15] Even so, only limited studies have specifically explored the link between TyG index and CAN, although several regional studies report a high prevalence of CAN in patients with T2DM.[16,17,18] Because the TyG index is easy to calculate, low-cost, and based on routine blood tests, it may be useful for early identification of autonomic dysfunction in clinical practice. Therefore, this study aimed to compare TyG index levels in T2DM patients with and without CAN and to assess how well the TyG index can predict autonomic impairment.

The Objective of this study is, to determine the Triglyceride Glucose Index among individuals diagnosed with T2DM and to assess the predictive capability of the TyG index for detecting CAN.

MATERIALS AND METHODS

Study Design and Setting

This prospective cross-sectional observational study was carried out in the Department of General Medicine at MAPIMS, Tamil Nadu, for six months from April to September 2024.

Study Population

Adults aged 18–60 years with confirmed type 2 diabetes mellitus (19) who gave written informed consent were included. Those who did not consent and those outside the age range were excluded.

Sample Size

Using prevalence data from similar studies (16), the sample size was calculated as 63 using the formula $4pq/d^2$ with suitable values chosen for confidence level and precision.

Data Collection

Detailed clinical history was taken for each participant. Body measurements included body mass index (BMI) calculated using Quetelet's formula (20), waist circumference, hip circumference, waist–hip ratio, and blood pressure. Electrocardiography was done for all participants.

Biochemical Assessment

Fasting blood samples were tested for glucose, triglycerides, total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and glycated hemoglobin (HbA1c). The TyG index was calculated using: TyG = ln [(fasting triglycerides × fasting glucose) / 2] (8).

Autonomic Function Testing

Heart-related autonomic function was assessed using Ewing's battery of tests (7). These included heart rate variation with deep breathing, heart rate response to standing (30:15 ratio), Valsalva ratio, fall in blood pressure on standing, and blood pressure response to sustained handgrip. Based on the number and type of abnormal test results, patients were classified as CAN or non-CAN using standard diagnostic criteria.

Statistical Analysis

Data were analyzed using SPSS version 20. Continuous variables were presented as mean ± standard deviation. Differences between CAN and non-CAN groups were compared using independent t-tests. A p value <0.05 was considered statistically significant.

Ethical Considerations

Ethical approval was obtained from the Institutional Ethics Committee, MAPIMS. Written informed consent was taken from all participants before enrolment and all ethical standards were followed in line with Helsinki Declaration.

RESULTS

Demographic and Clinical Characteristics

The study included 63 patients, and most were men (60.3%, n=38). The average age was 48.78±7.66 years, with a median age of 49 years (IQR: 42–55 years). On average, participants had diabetes for 6.15±1.89 years. The mean BMI was 28.35±4.42 kg/m², showing that most participants were overweight. The average waist–hip ratio was 1.04±0.09, indicating central (abdominal) obesity. The mean TyG index was 9.80±0.43, suggesting a higher risk of insulin resistance. [Table 1]

Table 1: Baseline Clinical and Metabolic Characteristics (N=63)

Characteristic	Mean ± SD	Median (IQR)
Age (years)	48.78 ± 7.66	49.00 (42.00, 55.00)
Duration of DM (years)	6.15 ± 1.89	5.90 (4.90, 7.00)
BMI (kg/m²)	28.35 ± 4.42	27.90 (25.10, 30.20)
Waist-Hip Ratio	1.04 ± 0.09	1.04 (0.98, 1.09)
TyG Index	9.80 ± 0.43	9.51 (9.44, 10.29)

Abbreviations: DM, diabetes mellitus; BMI, body mass index; TyG, triglyceride-glucose; IQR, interquartile range

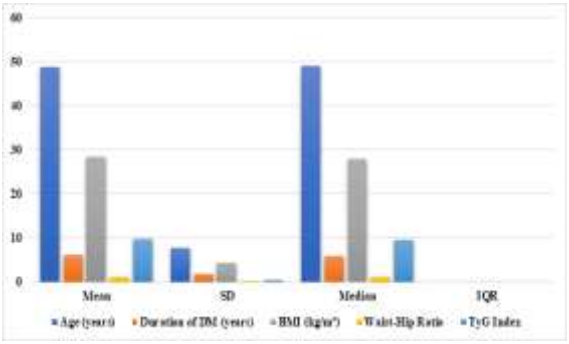

Figure 1: Baseline Clinical and Metabolic Characteristics

Interpretation

The mean age was approximately 49 years, indicating a middle-aged group. The average duration of diabetes was just over 6 years. The mean BMI was 28.35 kg/m², showing that most participants were overweight. The mean waist-hip ratio (1.04) and TyG index (9.80) suggest a high prevalence of central obesity and insulin resistance in this cohort. These baseline values provide context for understanding the metabolic risk profile of the study group.

Prevalence and Severity of CAN

CAN was found in 26 participants (41.3%). The remaining 37 participants (58.7%) did not have CAN. Among the 26 patients with CAN, most were diagnosed at an advanced stage: 16 (61.5%) had severe CAN, 9 (34.6%) had definite CAN, and only 1 (3.8%) had early CAN. This shows that CAN was mainly detected in later stages in this study.

Lifestyle Factors

CAN was present in 40% of smokers and was similar among non-smokers; this difference was not statistically significant (p=0.929). Among people who consumed alcohol, 58.8% had CAN compared to non-consumers, but this difference was also not statistically significant (p=0.085).

Comparison of Autonomic and Metabolic Parameters

Table 2 compares patients with CAN and those without CAN. All autonomic test results were worse in the CAN group. The deep breathing difference was much lower in CAN patients (11.01±3.49 vs 20.18±3.07, p<0.001). Similarly, the 30:15 ratio (1.03±0.07 vs 1.19±0.07, p<0.001) and the Valsalva ratio (1.22±0.21 vs 1.52±0.06, p<0.001) were also lower in the CAN group. Both parasympathetic and sympathetic abnormality scores were significantly higher in CAN patients (p<0.001 for both), showing greater autonomic dysfunction.

Table 2: Comparison of Parameters Between CAN and Non-CAN Groups

Variables	CAN Status	Mean ± SD	t value	p value
Deep Breathing Difference	No	20.18 ± 3.07	11.040	<0.001*
	Yes	11.01 ± 3.49		
HR 30:15 Ratio	No	1.19 ± 0.07	8.788	<0.001*
	Yes	1.03 ± 0.07		
Valsalva Ratio	No	1.52 ± 0.06	8.156	<0.001*
	Yes	1.22 ± 0.21		
Fasting Blood Glucose (mg/dL)	No	166.26 ± 10.92	-14.19	<0.001*
	Yes	242.22 ± 29.92		
Fasting Triglycerides (mg/dL)	No	153.08 ± 4.37	-52.83	<0.001*
	Yes	246.31 ± 9.41		
HbA1c (%)	No	7.12 ± 0.99	-7.097	<0.001*
	Yes	9.14 ± 1.27		
TyG Index	No	9.45 ± 0.07	-34.95	<0.001*
	Yes	10.30 ± 0.12		

Abbreviations: CAN, cardiac autonomic neuropathy; HR, heart rate; HbA1c, glycated hemoglobin; TyG, triglyceride-glucose
**Note: Statistically significant at p<0.05*

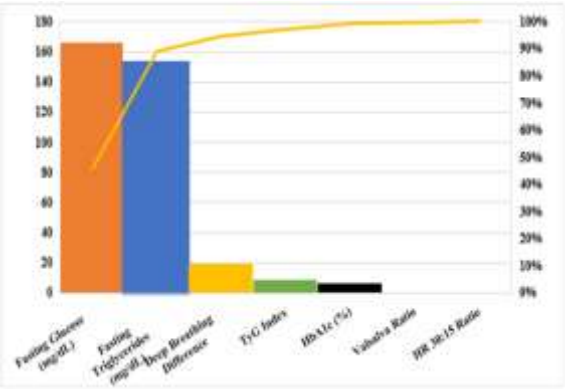

Figure 2: Comparison of Clinical Parameters Between CAN and Non-CAN Groups

Interpretation

- Autonomic Function Tests: Deep breathing difference, HR 30:15 ratio, and Valsalva ratio were all significantly lower in the CAN group, indicating greater autonomic dysfunction.
- Metabolic Parameters: The CAN group had much higher mean fasting blood glucose (242.22 vs 166.26 mg/dL), fasting triglycerides (246.31 vs 153.08 mg/dL), HbA1c (9.14% vs 7.12%), and TyG index (10.30 vs 9.45) compared to the non-CAN group.
- Pattern: The chart highlights that patients with CAN consistently have worse metabolic control and autonomic function, supporting the association between poor glycemic/lipid control, higher TyG index, and the presence of CAN.

DISCUSSION

This study showed that 41.3% of patients with T2DM had CAN. This is similar to other Indian studies, where CAN prevalence has been reported between 34% and 80% in comparable groups.[16,17,18] The wide difference in prevalence across studies is likely due to variations in patient characteristics, duration of diabetes, diagnostic methods, and healthcare setting. Our result lies in the middle of this range, suggesting it reflects a typical tertiary care diabetic population.

CAN is an important problem because it is linked to higher risk of death, poor exercise capacity, and more chances of arrhythmias and silent myocardial infarction.[3,4,5] Pop-Busui reported that CAN can independently predict cardiovascular death in diabetes, with about a 3.5 times higher relative risk compared to patients without CAN.[21] In our study, patients with CAN had much higher fasting glucose, triglycerides, HbA1c, and TyG index, supporting the idea that poor metabolic control is strongly related to autonomic nerve damage.

The link between insulin resistance and CAN occurs through various mechanisms. Insulin resistance may cause endothelial dysfunction by reducing nitric oxide availability, which leads to poor blood supply to nerves vasa nervorum.[13] Long-term high blood sugar also activates pathways such as the polyol and hexosamine pathways thus forming advanced glycation end products and increasing oxidative stress and inflammation.[14] These changes damage autonomic nerve fibers. Usually, parasympathetic damage occurs first and sympathetic damage follows later, which matches our findings where heart rate variability tests were abnormal in CAN patients. Findings from our study are consistent with Akbar et al., who showed that TyG index is significantly associated with CAN in Type 2 DM.[22] They suggested a TyG cut-off of 9.5 to predict CAN, with 78% sensitivity and 72% specificity. In our study, the mean TyG index in CAN patients (10.30±0.12) was clearly above this value, indicating high insulin resistance. Jeyaseeli et al. also reported that patients with abnormal Ewing's tests had higher TyG index values, and the mean difference between groups was around 0.8 units, which is close to our observed difference of 0.85 units.[16] Other studies have also shown that TyG index is linked with several diabetic complications, supporting its role as a useful insulin resistance marker. Liu et al. reported that higher TyG index was associated with worsening diabetic nephropathy.[10] Wei-Yu et al. found that TyG index predicted cardiovascular events better than fasting glucose or HbA1c alone in diabetic patients.[11] Vijan's review also highlighted the usefulness of simple metabolic markers in routine diabetes care.[12] Together, these findings suggest TyG index can help identify diabetic patients at higher risk for multiple complications.

All Ewing test results were clearly worse in CAN patients in our study. This supports the understanding that hyperglycemia, oxidative stress, and microvascular damage can affect both parasympathetic and sympathetic systems.[5,13,14] Typically, parasympathetic dysfunction appears first, shown by reduced heart rate changes with deep breathing and Valsalva, and later sympathetic dysfunction is seen as postural blood pressure changes. Our results followed this pattern, and parasympathetic abnormality scores were consistently higher in CAN patients. Waist circumference was significantly associated with CAN in our study. This supports findings from the ADDITION-Denmark study, which reported central obesity as an independent risk factor for CAN.[6] Visceral fat increases inflammation through disturbed adipokines, and higher inflammatory mediators like tumor necrosis factor-alpha and interleukin-6 can contribute to nerve inflammation and autonomic dysfunction.[22] This may explain why waist circumference showed a stronger relationship with CAN than BMI alone. The importance of body size measures in health risk assessment has long been recognized since Quetelet's work.[20]

In our study, smoking and alcohol use were not significantly linked with CAN. This differs from some other reports. A likely reason is that the number of smokers and alcohol users in our sample may have been small, reducing the ability to detect a statistical association. Another possibility is that strong metabolic factors such as hyperglycemia,

dyslipidemia, and insulin resistance had a larger impact and may have masked any smaller lifestyle effects.

A key finding was that most CAN cases were severe (61.5%), showing that many patients were detected late. CAN often remains silent until advanced stages, when treatment options are less effective. This highlights the need for earlier screening. In this context, a simple marker like the TyG index could help identify high-risk patients earlier, before severe autonomic damage occurs.

In many Indian healthcare settings, the burden of diabetes is high and resources are limited.[15] Ewing's autonomic testing can be costly and not easily available everywhere. The TyG index is simple, low-cost, and needs only fasting glucose and triglycerides, which are routinely tested in diabetes care. In our study, TyG index clearly differed between CAN and non-CAN groups, supporting its potential use as a screening marker in routine practice.

A practical approach could be a stepwise screening method. TyG index could be calculated during routine follow-up, and patients with higher values (TyG >9.5) could then be referred for detailed autonomic testing for confirmation. This would help use resources efficiently and improve early detection, potentially reducing complications related to undiagnosed CAN.

Strengths and Limitations

This was the first study from Tamil Nadu to evaluate the link between the TyG index and cardiac autonomic neuropathy (CAN). Using the full Ewing's test battery,[7] with standardized methods improved the accuracy and reliability of CAN diagnosis, and diabetes classification followed standard guidelines.[19]

Key limitations were the cross-sectional design (association only, not cause), single-center setting with a small sample (n=63), and a mainly middle-aged group, which may reduce generalizability. There was no long-term follow-up to track CAN progression or confirm whether TyG predicts future CAN, and potential confounders such as medications, comorbidities, and diet were not assessed.

Future multicenter, larger, and long-term studies are needed, and ROC analysis can help decide the best TyG cut-off values for Indian populations to improve screening accuracy.

CONCLUSION

The TyG index was much higher in diabetic patients who had CAN and clearly helped to differentiate them from those without CAN. Since it can be easily calculated using routine fasting glucose and triglyceride tests and is inexpensive, it can be used as a simple screening tool in daily clinical practice. Using the TyG index for early screening may help identify high-risk patients sooner, allowing earlier treatment and better outcomes, especially in resource-limited settings. Adding it to routine diabetes follow-up could improve CAN detection and support earlier interventions.

Clinical Implications

During routine follow-up visits, patients with type 2 diabetes can use the TyG index as a fast-screening tool. It can assist in the early detection of people with increased metabolic risk because it is simple to compute from fasting glucose and triglyceride testing. To prevent missing CAN, doctors should think about conducting thorough autonomic function tests if the TyG score is high (>9.5). This method may promote early detection and intervention before autonomic nerve damage becomes irreparable, and it is particularly helpful in rural and resource-constrained situations where Ewing's tests may not be easily accessible.

Future Directions

Future research should include larger multicenter studies in India to decide the best TyG cut-off value for predicting CAN, using ROC curve analysis to balance sensitivity and specificity. Long-term follow-up studies are also needed to confirm whether TyG can predict future CAN and to track disease progression. Studies should examine whether TyG levels change with treatment and whether improving insulin resistance can delay or prevent CAN. Adding the TyG index into digital diabetes risk calculators and clinical decision-support tools may help clinicians detect high-risk patients earlier. Finally, cost-effectiveness studies comparing TyG-based screening with standard testing methods will help decide the best approach for resource-limited healthcare settings.

Declarations

Ethical Approval: Approved by Institutional Ethics Committee, MAPIMS

Informed Consent: Obtained from all participants

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Conflict of interest: This work does not present any conflicts of interest.

Data Availability: Upon reasonable request, data is available from the respective author.

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