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Profiling triglyceride-glucose index in Filipinos with type 2 diabetes mellitus: a single-center study

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Abstract

Background In this study, we evaluated the utility of the TyG index among Filipino patients with type 2 diabetes mellitus (T2DM) and explored its association with various laboratory markers.

Methods An analytical cross-sectional study was conducted by retrospectively obtaining data from the medical records of 109 Filipino T2DM patients from a tertiary level teaching hospital. Data obtained were then statistically analyzed.

Results Results revealed an overall TyG index of 9.15 ± 0.71 among the participants. A significant dose-response relationship was observed between the TyG index and HbA1c. The AUC result has an acceptable discriminating ability among patients with varying glycemic control. The optimal cut-off value of >8.4 has a sensitivity of 92.5% and a specificity of 47.1% in identifying patients with poor glycemic control.

Conclusion Overall, our findings show the potential of TyG index in glycemic control assessment among Filipinos with T2DM. However, further analysis must be performed to verify its clinical utility and applicability in different populations.

Keywords Triglyceride-glucose index, Type 2 diabetes mellitus, Filipino, Glycemic control, HbA1c, AUC

Introduction

Among the leading causes of mortality worldwide is diabetes mellitus (DM), a metabolic disease characterized by hyperglycemia due to defects in the secretion or action of insulin [25, 42]. The incidence of this metabolic disease continues to rise, affecting around 463 million individuals globally as of 2019. This represents approximately 9.3% of the global adult population aged 20 to 79 [19]. In the Philippines, over 3.7 million individuals were diagnosed with DM, according to the Philippine Center for Diabetes Education Foundation in 2016. This is expected to have increased in the following years [11]. Most DM cases are classified as type 2 DM, accounting for about 90% of diabetes cases worldwide [19, 40].

Early detection and continuous monitoring are needed to correctly manage T2DM and prevent the development of DM-related conditions. Currently, the markers used for its diagnosis and monitoring are the following: (1) random plasma glucose; (2) fasting plasma glucose, which requires 8 to 10 h of fasting before sample collection; (3) 2-h plasma glucose, which is measured during the oral glucose tolerance test; and the (4) hemoglobin A1c which

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reflects long-term glycemic control [1, 20]. Despite their current significance in disease diagnosis, they are still subjected to certain limitations. For instance, hemoglobin A1c levels may change due to glycemia and erythrocyte turnover rates, making it unreliable for patients with erythrocyte disorders. It is also more costly and may not be as widely available in primary healthcare settings as routine tests [15]. On the other hand, the other glucose parameters may be invasive and time-consuming [12]. Due to the disadvantages of currently available methods, alternative or supplemental markers such as the triglyceride-glucose index (TyG index) are being examined.

The TyG index is a noninsulin-based marker that is simple and inexpensive. It requires tests for triglyceride and fasting glucose levels, which are widely available and routinely performed in clinical laboratories. Previous studies have noted its correlation with insulin resistance (IR) as measured by conventional methods, including the hyperinsulinemic-euglycemic clamp (HIEC) and the homeostatic model assessment of insulin resistance (HOMA-IR). These supported its utility as a reliable and reproducible alternative tool for identifying IR [13, 35, 41]. It has also been associated with different conditions, including metabolic syndrome, T2DM, chronic kidney disease, non-alcoholic fatty liver disease, and cardiovascular risk among certain populations [3, 6, 9, 44]. However, data regarding the TyG index of Filipino T2DM patients has not been sufficiently explored. Its association with routine liver function, renal function, and coagulation markers such as the ALT, eGFR, platelet count, prothrombin time (PT), and activated partial thromboplastin time (APTT), particularly in these populations, are still limited as well. To contribute to the gap on this topic, this study will focus on profiling the TyG index of Filipinos with T2DM and determining the index's association with selected laboratory markers. Establishing the mean level of the index in this population and identifying possible associations with other routine markers may be a preliminary step in determining its potential role as an alternative, supplemental, or additional biomarker for predictive, diagnostic, or prognostic purposes.

Methods

Study design and sampling

This study employed an analytical cross-sectional research design. This study design allowed the determination of possible associations among variables that were measured and assessed simultaneously. The study retrospectively obtained data from T2DM patients admitted from January to December 2021 at a level III training and teaching hospital in Central Luzon, Philippines. Random sampling was employed in selecting the 109 T2DM patients. A sample size of 100 is needed to estimate the mean TyG index with a 95% confidence interval, assuming a mean index value of 9.1 and a standard deviation of 0.6 based on the study of Unger et al. This was used as a basis for this study, which utilized an actual sample size of 109.

Included in the study are data from patients who met the following criteria:

- With complete demographic data on age and sex
- With type 2 diabetes mellitus as the working diagnosis
- With laboratory findings on triglyceride and fasting glucose levels
- With laboratory findings on one or more of the following tests: HbA1c, ALT, creatinine, platelet count, PT, and/or APTT

Collection and screening of data from medical records

Data from medical records were collected and compiled using an electronic spreadsheet, which served as the data abstraction form. The following data were obtained from the medical records of T2DM patients who were included in the study: age, sex, working diagnosis, and their laboratory findings on selected tests upon admission, including fasting glucose, triglyceride, HbA1c, ALT, serum creatinine, platelet count, PT, and APTT. The collection and screening of data were done through a three-step process. The first step involved identifying patients with complete demographic data and T2DM as their working diagnosis. Any patients with incomplete entries were not included in the second step. The next step involved checking if the patients had triglyceride and fasting glucose results to be used to compute the TyG index. Those who had both results were included in the third step, where it was determined if they had results on at least one of these tests: HbA1c, ALT, creatinine, platelet count, PT, and APTT.

Computation of derived data

The TyG index and eGFR were derived from the obtained laboratory findings per patient. The fasting glucose and triglyceride results were used in computing the TyG index using this formula: *Ln [triglyceride (mg/dL)*×*fasting glucose (mg/dL)/2]* [21]. On the other hand, the patient's age, sex, and serum creatinine results were used to compute the eGFR using the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) formula: $GFR = 175 \times \text{standardized } S_{cr}^{-1.154} \times age^{-0.203} \times 1.212$ (if black) × 0.742 (if female), where GFR is expressed as mL/min/1.73 m^2 of body surface area [41] and S_{cr} is expressed in mg/dL. According to previous studies, this formula

provides better estimation among those with normal and decreased kidney function and is considered the most accurate among the three available eGFR formulas [5].

Ethical considerations

The study was approved by the Research Ethics Committee of the Jose B. Lingad Memorial General Hospital (JBLMGH-REC 2021–81). Data collection and processing were done in compliance with the Philippine Data Privacy Act of 2012. All data were treated with utmost confidentiality and were only accessible to the researcher, research assistant, and those who evaluated the study. Patients were anonymized throughout the study.

Data analysis

STATA was used to run various statistical tests to address the study's objective. In all the tests, a *p*-value below 0.05 was considered significant. Descriptive statistics were used to present the overall summary of the data. The comparison of the mean TyG index among the subgroups on patient demographics was performed using the independent samples *t*-test (if there are two groups) or the one-way analysis of variance or ANOVA (if there are ≥ 3 groups). The comparison of the mean TyG index obtained in this study with the indices from different populations was tested using the two-sample *t*-test. This was performed under the assumptions of equal and unequal variances since the homogeneity of variance cannot be determined. The dose–response relationship between the TyG index and the various laboratory parameters was determined through linear regression. This tool helped quantify the estimated changes in the other laboratory markers in response to the changes in the TyG index while controlling for age and sex. The logarithm base 10 (Log10) of the results was obtained before performing the regression analysis as performed by Yu et al. [45]. The ability of the index to predict poor glycemic control (HbA1c ≤ 7%) among T2DM patients was assessed using the receiver operating characteristic (ROC) curve analysis.

Results

Demographic and clinical characteristics of the participants

The baseline characteristics of the participants are shown in Table 1. A total of 109 patients were included in this study, most female and middle-aged adults with a mean age of 56.21. Regarding the laboratory findings, most participants had elevated fasting blood sugar and hemoglobin A1c upon admission, with a median value of 142.16 mg/dL and 9.1%, respectively. These findings are consistent with their T2DM diagnosis. The median values of the other findings were within the reference range, indicating that most patients had normal ALT levels, platelet count, PT, and APTT. The overall eGFR (70.50 mL/min/1.73 m^2) is also within normal limits. Still, it is close to the cut-off value of 60 mL/min/1.73 m^2 since 46 participants had reduced filtration rates, attributable to their secondary renal conditions. Lastly, the TyG index of the Filipino T2DM patients included in the study ranged from 9.02 to 9.28.

Table 1 Demographic and clinical characteristics of the participants

Demographics	Total (*n* = 109)
Age (years)	56.21 ± 11.75
Sex	
Female *n* (%)	56 (51.38%)
Male *n* (%)	53 (48.62%)
Biochemical parameters	
Fasting blood sugar (mg/dL) *n* = 109	142.16 (110.45)
Triglyceride (mg/dL) *n* = 109	133.63 (83.19)
Hemoglobin A1c (%) *n* = 70	9.1 (4.7)
Alanine aminotransferase (IU/L) *n* = 36	33 (37)
Estimated GFR (mL/min/1.73 m^2) *n* = 108	70.50 (52.86)
Platelet count (10^9/L) *n* = 109	279 (141)
Prothrombin time (s) *n* = 47	12.3 (1.8)
Activated partial thromboplastin time (sds) *n* = 47	27.5 (5.4)
Triglyceride-glucose index	9.15 ± 0.71

Continuous variables were presented as mean ± SD or median (interquartile range). Categorical variables were presented as *n* (%)

Table 2 Comparison of the mean TyG index per demographic subgroups

	No. of patients per subgroup N (%)	TyG index (mean + SD)	*p*-value
Age (*n* = 109)			0.02*
25–44	17 (15.60%)	9.09 ± 0.69	
45–64	68 (62.39%)	9.28 ± 0.68	
> 6 5	24 (22.02%)	8.81 ± 0.69	
Sex (*n* = 109)			0.41
Females	56 (51.38%)	9.20 ± 0.71	
Males	53 (48.62%)	9.09 ± 0.70	

* *p*-value below 0.05 is considered significant

TyG index according to subgroups on patient demographics

The TyG index of each age group was also determined (Table 2). The highest computed index of 9.28 ± 0.68 belonged to patients aged 45 to 64, while the lowest

index of 8.81 ± 0.69 belonged to elderly patients aged 65 and above. A significant difference in the TyG indices of patients from different age groups was observed, as reflected by the *p*-value of 0.02. Regarding sex, a higher mean index (9.20 ± 0.71) was obtained from females, but this did not significantly differ from the mean index of male patients (9.09 ± 0.70).

TyG index of different populations

Table 3 compares the overall TyG index of the participants (9.15 ± 0.71) with those obtained by other studies in different populations. This analysis aims to determine whether TyG levels obtained in our population differ from other ethnic groups. All studies included adult patients with T2DM, similar to this research. Based on the obtained *p*-value of < 0.001, the mean TyG index from this study was found to be significantly lower than the mean index obtained from Iraqi (9.46 ± 0.68) and Nepalese (9.40 + 0.66) T2DM patients who were included in the study of Hameed and Timalsina et al. [15, 39]. In contrast to this, it did not differ from the indices obtained by Chamroonkiadtikun et al. (9.02 ± 0.42) and Pan et al. (9.20 ± 0.78) among Thai and Chinese DM patients, respectively [6, 32].

Dose–response relationship between TyG index and other laboratory parameters

Linear regression analysis revealed a significant association between the TyG index and hemoglobin A1c ($p < 0.001$) after adjusting for age and sex, indicating a linear dose–response relationship between the two parameters. The regression coefficient shows that for every one-unit increase in the TyG index, there is a 1.290% increase in the HbA1c. This is further supported by a higher mean TyG index among patients with elevated HbA1c (TyG index = 9.29 ± 0.62) compared to those with normal results (TyG index = 8.39 ± 0.71). However, this significant dose–response relationship was not observed between the index and the other laboratory parameters, as reflected by their *p*-values in Table 4.

Table 4 Dose–response relationship between TyG index and other laboratory parameters adjusted for age and sex

Laboratory parameter	*p*-value	10^ regression coefficient
Hemoglobin A1c	< 0.001*	1.290
ALT	0.19	1.304
eGFR	0.51	1.095
Platelet count	0.81	0.984
Prothrombin time	0.45	0.977
APTT	0.11	0.954

Abbreviations: *ALT* alanine aminotransferase, *eGFR* estimated glomerular filtration rate, *APTT* activated partial thromboplastin time

* *p*-value of < 0.05 is statistically significant

TyG index as a potential predictor of glycemic control

Further analysis was done since a significant association was observed between the TyG index and HbA1c, a marker of glycemic control. Figure 1 illustrates the ROC curve of the TyG index in predicting glycemic control as reflected by HbA1c results. Based on the AUC result of 0.757 (95% *CI* = 0.640 to 0.852), the TyG index has an acceptable discriminating ability [27], particularly when distinguishing patients with good glycemic control (HbA1c < 7.0%) from those with poor control (HbA1c ≥ 7.0%). The optimal cut-off value of > 8.4 has a sensitivity of 92.5% (95% *CI* = 81.8 to 97.9%) and a specificity of 47.1% (95% *CI* = 23.0 to 72.2%) in identifying patients with poor glycemic control. The cut-off point has a positive predictive value (PPV) of 84.5% and a negative predictive value (NPV) of 66.7%.

Discussion

Based on the findings of this study, the TyG index of T2DM patients from different age groups differed significantly, with the highest index obtained from middle-aged patients (45 to 64 years old) and the lowest from elderly patients aged 65 years and above. Similar findings were obtained in the study of Pan et al., which observed a negative correlation between the TyG index and age, and Lv et al., which found that younger participants tend to have higher indices [26, 32]. Other studies also noted

Table 3 Comparison of the study's mean TyG index with the indices of other populations

TyG index of current study	Author and publication year	Country	TyG index Mean ± SD	*p*-value[a]	*p*-value[b]
9.15 ± 0.71	Chamroonkiadtikun et al. [6]	Thailand	9.02 ± 0.42	0.06	0.09
	Hameed [15]	Iraq	9.46 ± 0.68	< 0.001*	< 0.001*
	Pan et al. [32]	China	9:20 ± 0:78	0.51	0.47
	Timalsina [39]	Nepal	9.40 + 0.66	0.003*	0.004*

a assuming equal variances, *b* assuming unequal variances

* *p*-value below 0.05 is considered significant

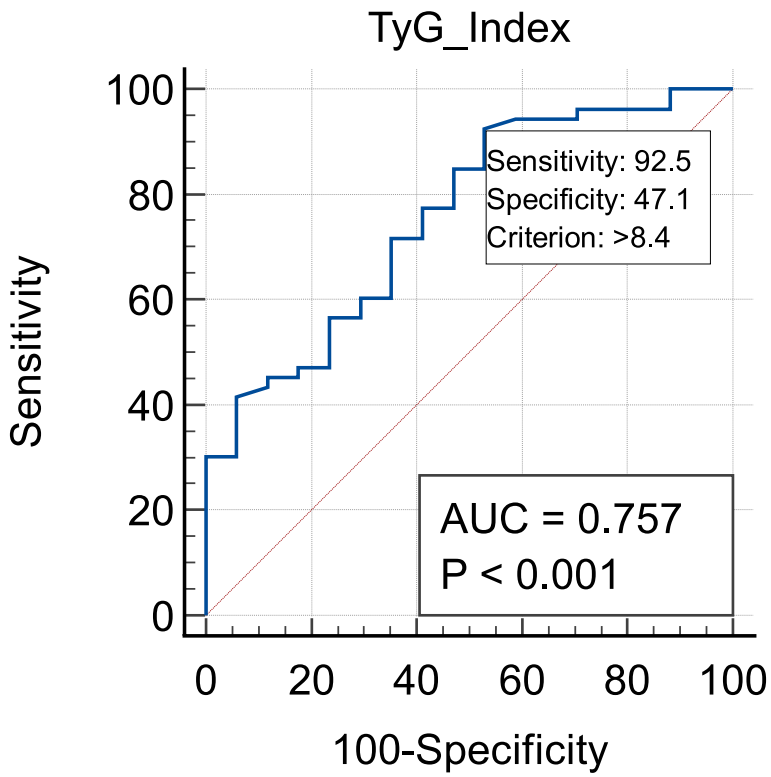

Fig. 1 ROC curve analysis of the TyG index in predicting poor glycemic control

significantly different TyG indices among patients of varying ages, but some obtained contrasting results regarding the trend across age groups. These studies divided the participants into four groups based on TyG quartiles, with quartile 4 having the highest mean index. They observed that age was likely to increase across quartiles of the TyG index, with older patients usually belonging to groups with higher indices [29, 46]. These results may be explained by age-related changes in glucose metabolism and a progressive decline in glucose tolerance as people age [7, 38]. However, lifestyle-related risk factors are now commonly observed among young and middle-aged adults. Prediabetes and obesity are becoming increasingly prevalent in these age groups [2, 37]. Moreover, one study found that older patients may have better glucose and lipid management than middle-aged ones due to better diet, medication adherence, and healthier lifestyle choices [8]. These may explain the findings in this research wherein lower indices were observed among elderly patients.

Regarding sex, female patients in this study had a slightly higher mean TyG index, but this did not significantly differ from males. This is similar to the study of Pan et al., which also did not observe any significant correlation between the index and sex [32]. However, Zhang et al. found that those in higher TyG quartiles were frequently women, while other studies noted more male patients [23, 24, 46]. These may be due to abdominal fat distribution, hepatocellular lipids, muscle mass, and glucose uptake, which may differ among men and women. Aside from these, insulin sensitivity and hormonal responses may, at times, be varied as well [28, 46]. However, this study did not observe significant differences in the laboratory parameters of male and female patients, including their TyG indices.

The overall TyG index obtained from Filipino T2DM participants included in this study was 9.15 ± 0.71, which differed significantly from the overall index obtained in the study of Hameed in Iraq and Timalsina et al. in Nepal [15, 39]. These may signify differences based on ethnicity since certain findings may not universally apply to other populations from different races or ethnic groups [6, 49]. These may be due to variations brought about by socioeconomic, cultural, and heritable factors [17, 18]. Genome studies have also identified genes that may contribute to variations in glucose homeostasis, and the frequency of these genes may differ among ethnic groups [30]. Lastly, analytical variations in the assays used for testing may also account for the differences in certain parameters, including the TyG index [16, 43].

Despite the differences in the mean TyG index of different populations, as indicated previously, the study of

Da Silva et al. stated that a value of at least 8.31, in general, is associated with T2DM risk as observed in previous studies on the topic [10]. Another study stated that a cut-off value between 8.7 and 8.9 had a 54% sensitivity and 71% specificity in predicting T2DM [33]. Moreover, a one-unit increase in the index may increase the risk of developing DM by 2.26-fold after adjusting for age and sex [23]. In studies with TyG quartiles, DM risk progressively increased across quartiles, with those in the fourth quartile having up to 3.4 times higher risk than those in the first one [6, 22, 24]. These findings support the association of the index with T2DM, which may be explained by metabolic mechanisms. Both glucose and triglyceride levels are metabolic components related to insulin resistance, which may precede the development of T2DM [10, 46]. Thus, monitoring these laboratory parameters and prompt interventions may mitigate the risk. Additionally, the measurement of the TyG index is being explored as a possible supplemental or alternative screening marker to promote early DM prevention.

Regarding the laboratory findings, no significant association was obtained between the TyG index and ALT. However, a different finding was obtained in the study of Yu et al., which noted a significant linear dose–response relationship between these parameters. They found that ALT levels increased by 1.222, and the odds ratio of having impaired liver function, as reflected by an abnormal ALT result, increased by 2.0444 per 1 unit increase in the TyG index. This may be explained by the presence of insulin resistance and impaired metabolic status among these patients, both of which may be associated with the progression of abnormal liver function and may result in higher TyG indices. The researchers concluded that the index might be used as a screening marker for adults at risk for IR-related impairment in liver function [43].

The two lab parameters utilized in the index are crucial metabolic variables that may affect IR and liver diseases. These may account for the relationship between impaired liver function and the TyG index [45, 47]. In this study, the index was slightly higher among those with elevated ALT, but the aforementioned findings from other studies regarding the dose–response relationship were not obtained. This may be due to normal ALT levels in most participants, indicating that their liver function had not been compromised during testing.

The eGFR also did not have a significant association with the TyG index. However, conflicting results were obtained in other studies. Zheng et al. observed an inverse trend where the eGFR decreased as TyG increased [48]. Similarly, Okamura et al. observed significantly higher indices among participants with mildly decreased eGFR [31]. The findings of other studies also stated that the TyG index correlated linearly with the risk of reduced eGFR, indicating that the risk elevates proportionally with the increase in the index [26, 36]. These findings may also be explained by insulin resistance in renal diseases, with dyslipidemia and hyperglycemia playing critical roles in IR development. Together with hyperinsulinemia, these findings may contribute to the progression of renal abnormalities, which may influence the glomerular filtration rate.

Moreover, these may also result in corresponding changes in the TyG index since IR-induced changes in glucose and lipid homeostasis may occur during disease development. However, contradicting results are currently obtained among different renal function markers and TyG since some studies noted that the blood urea nitrogen and serum creatinine were not significantly associated with the index. Still, other studies found that the risk for reduced eGFR and microalbuminuria were correlated with this novel marker [26, 36, 48]. A contradicting finding between the index and reduced eGFR was also obtained in this study since no association was observed between these two variables. Thus, the findings necessitate further analysis of renal markers and TyG to establish their association.

This study also revealed that T2DM patients with elevated HbA1c had higher TyG indices than those with normal HbA1c levels. In addition, linear regression analysis showed a significant dose–response association between the TyG index and HbA1c after controlling for age and sex. These are supported by Hameed and Timalsina et al., which found that the index was significantly higher in diabetics with poor glycemic control (9.69 ± 0.61; 9.73 ± 0.58) than in those with good control (9.19 ± 0.67; 9.07 ± 0.56). Together with the one conducted by Babic et al., these studies also stated that the index correlated significantly, independently, and positively with this glycemic marker after controlling for confounding variables. However, the latter study further stratified patients based on their BMI and found that the association only remained among overweight and obese patients [4, 15, 39]. Regarding the index's ability to identify patients with poor glycemic control, this study obtained an AUC of 0.757, indicating that the marker has an acceptable discriminating capacity, again in line with other studies that obtained AUC values of 0.839 and 0.803. An optimal cut-off value of ≥ 9.12 with a sensitivity of 86.1% and specificity of 61.5% for predicting glycemic control was also specified in one of these studies, which was slightly different from the cut-off point identified in this study (> 8.4), but this may be explained by the ethnic

differences of the participants and by the analytical variations in the methods used for testing [15, 39].

These findings show that the TyG index is a potential alternative marker for glycemic control. This may be advantageous in the clinical setting since HbA1c is relatively expensive and not routinely available in certain healthcare facilities. The presence of erythrocyte disorders and other factors that influence erythrocyte survival and age may also influence HbA1c levels, unlike fasting glucose and triglyceride levels [15, 16]. Furthermore, the TyG index may be computed from cost-effective laboratory parameters that are readily available and routinely tested [14, 34]. These make the index more accessible, particularly in screening individuals at risk for DM or in monitoring patients already diagnosed. Previous studies have explored these clinical uses, which found that the TyG index may help identify individuals who are normoglycemic but still have an early risk of developing DM [6, 29]. Individuals whose glucose parameters are either within normal limits or borderline are not traditionally considered a high-risk group, thus may not be given prompt action for disease prevention. This may be detrimental since studies have found that these patients may still be susceptible to DM development. However, some researchers have discovered that the TyG index may be increased to a certain point among these individuals. Therefore, this index may serve as a simple screening tool for risk assessment even among this population, which is beneficial since lifestyle modification may be immediately advised and practiced [6, 24].

This study presented preliminary findings on the TyG index of Filipinos with T2DM. However, certain limitations were encountered in this research. As an analytical cross-sectional study, determining the correlation of variables is possible, but establishing causation among them cannot be performed. As a retrospective study, other data on patient demographics, medical history, or risk factors were not considered. Further analysis through a population-based study using a cross-sectional, case–control, or longitudinal research design may be performed to further examine the association among the variables, verify the index's reliability as a marker of glycemic control, and adjust for other possible confounding variables.

Conclusion

This is the first study published on the TyG index among Filipinos with T2DM in the locale. Given the limitations of the study's retrospective nature, the analysis is limited only to the association of TyG with diabetes-related parameters available in medical records. Based on the study's findings, the participants' mean TyG index varies across different age groups, with elderly patients having the lowest computed mean index. This difference may necessitate the establishment of separate reference ranges or cut-off points for individuals of varying ages. Regarding the overall result among the participants, the mean TyG index is 9.15 + 0.71, which is similar to other Asian populations. When considered collectively, the findings of these studies indicate a TyG result of at least 8.4 among T2DM patients. Lastly, the linear dose relationship of the TyG index with HbA1c and its discriminating capacity among T2DM patients with varying glycemic control specify its potential role as a marker of glycemic control. Thus, the index may serve as a potential alternative for HbA1c in low-resource settings, due to its availability and cost-efficiency.

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None.

Authors' contributions
CCF and RET conceptualized the study. All authors participated in the data collection, data analysis, and writing of the manuscript. All authors agree to the present version of the manuscript.

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Availability of data and materials
Data associated with this study is available upon request.

Declarations

Ethical approval and consent to participate
The study was approved for conduct by the Research Ethics Committee of the Jose B. Lingad Memorial General Hospital (*JBLMGH-REC 2021–81*).

Consent for publication
All authors agree to have the manuscript and its associated results published.

Competing interests
The authors declare that they have no competing interests.

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