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Original Research Article

Diagnostic accuracy of the triglyceride-glucose index for gestational diabetes screening: evidence from an Indian cohort

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ABSTRACT

Background: Gestational diabetes mellitus (GDM) is associated with significant maternal and fetal complications, yet current screening methods such as the oral glucose tolerance test (OGTT) remain cumbersome, costly and inconvenient. The triglyceride-glucose (TyG) Index is an emerging surrogate marker of insulin resistance and may offer a simpler alternative for GDM screening. To evaluate the diagnostic accuracy of the TyG Index for screening GDM at 24–28 weeks of gestation in an Indian population.

Methods: This cross-sectional study included 270 pregnant women (19–40 years) attending antenatal care at Lady Hardinge Medical College, New Delhi (January 2021–August 2022). Women with pre-existing diabetes, hypertension, liver disease or medications affecting glucose or triglycerides were excluded. All participants underwent fasting OGTT using IADPSG criteria and simultaneous fasting triglyceride measurement. The TyG Index was calculated as: TyG=Ln (fasting triglycerides (mg/dl) ×fasting plasma glucose (mg/dl))/2. ROC analysis was conducted to determine the optimal cut off and diagnostic performance metrics were computed.

Results: The TyG Index demonstrated a strong discriminative ability with an AUC of 0.874 (95% CI: 0.829–0.912). A cut off value of 4.9 yielded a sensitivity of 82.72%, specificity of 78.31%, PPV of 62.04%, NPV of 91.36% and overall accuracy of 79.63%. Using this threshold, GDM prevalence was overestimated (40%) compared to OGTT-based prevalence (30%). Women with TyG>4.9 had significantly higher Fasting, 1-hour and 2-hour glucose levels ($p<0.001$) and higher systolic blood pressure ($p<0.05$).

Conclusions: The TyG Index demonstrates good diagnostic accuracy and high sensitivity for detecting GDM, suggesting its potential as a simple, single-step screening tool that may reduce the need for OGTTs. However, it overestimates GDM prevalence and larger multicentric studies are required before widespread implementation in India.

Keywords: Gestational diabetes mellitus, Insulin resistance, OGTT, Pregnancy, Screening, TyG index

INTRODUCTION

Gestational diabetes mellitus is defined as "any degree of glucose intolerance with onset or first recognition during pregnancy". It affects 7% of all pregnancies worldwide and in India, it ranges from 6 to 9% in rural and 12 to 21% in urban area.[1-3] It has been associated with a myriad of complications for both the mother and baby, therefore, it needs to be appropriately screened for and treated.[4] GDM is a topic of considerable controversy when it comes to its screening and diagnosis. Despite almost 50 years of research, there is still no agreement regarding optimal gestational diabetes screening.

The IADPSG (International Association of the Diabetes and Pregnancy Study Group) recommends the most widely accepted fasting OGTT-based guidelines for the diagnosis of GDM while the Ministry of Health and Family Welfare of India recommends its own DIPSI criteria due to the latter's non-fasting nature.[5,6] On the other hand, the ACOG

still advocates for the 2 step screening method and follows the Carpenter and Couston criteria for diagnosis.[7] Thus, these OGTT-based tests can be confusing, inconvenient, cumbersome and costly.

The pathogenesis of GDM revolves around the decrease in insulin sensitivity towards the second half of pregnancy. Also, the decrease in activity of hepatic lipase leads to an increase in triglyceride (TG) levels in pregnancy and this resulting hypertriglyceridemia further contributes to insulin dysfunction.[8] Several studies have found that hypertriglyceridemia, even in early pregnancy, is associated with insulin resistance as well as GDM.[9,10] Enquobahrie et al found that each 20 mg/dl increase in TG concentration leads to a 10% rise in the risk of GDM and TG levels more than 137 mg/dl were 3.5 times more likely to develop GDM.[11] As our understanding of these intricate mechanisms continues to grow, there is also a need for updating our screening methods in order to provide better care to our patients.

The TyG has been shown in recent studies as a reliable and simple surrogate index for insulin resistance as it correlates well with the HOMA-IR index.[12,13] It is a single-step test that is defined as the log product of an individual's serum levels of fasting TG and fasting plasma glucose (FPG). It is calculated as.[12,14]

TyG= Ln (TG×FPG)/ 2

Where Ln= log (e)

TG= fasting triglyceride value (mg/dl); FPG= fasting plasma glucose (mg/dl)

Various diseases such as type 2 diabetes mellitus, coronary artery disease and Non-alcoholic fatty liver disease have all found to positively and significantly correlate disease severity with a rising TyG Index.[13,15-17] The PURE (Prospective Urban Rural Epidemiology) study was a prospective cohort study published in the Lancet which studied 141243 individuals aged 35–70 years across 5 continents and used the TyG Index as a surrogate marker for insulin resistance.[13]

They concluded that the TyG Index was a predictor of incidence of diabetes, cardiovascular events and related mortality in low and middle income countries (cardiovascular mortality (LICs: 1·44; 1·15-1·80; $p_{interaction}$=0·01), myocardial infarction (LICs: 1·29; 1·06-1·56; MICs: 1·26; 1·10-1·45; $p_{interaction}$=0·08), stroke (LICs: 1·35; 1·02-1·78; MICs: 1·17; 1·05-1·30; $p_{interaction}$=0·19) and incident diabetes (LICs: 1·64; 1·38-1·94; MICs: 2·68; 2·40-2·99; $p_{interaction}$ <0·0001).Thus, this index has been shown as a useful marker in its ability to triage patients who were at a higher risk of developing metabolic diseases. Sanchez et al first determined the diagnostic accuracy of TyG index as a screening test for gestational diabetes mellitus.[18] The IADPSG criteria was used as the gold standard and the diagnostic performance of TyG Index was calculated. A high sensitivity of 89% and a negative predictive value of 93% were obtained of the TyG Index as a marker for detection of GDM.

Although they did not find any differences among the fetomaternal outcomes, they concluded that the TyG index might be a useful screening test to reduce the need for OGTTs by about 37% and improve maternal antenatal care, especially in low-income regions. Hence, we conducted this study in India to study its utility in our setups and population.

METHODS

Pregnant women between the age of 19-40 years attending the ANC OPD of Lady Hardinge Medical College, New Delhi at 24-28 weeks period of gestation carrying a singleton live fetus were recruited in this study from January 2021 to August 2022 after taking ethical clearance from Institutional Ethical Committee, LHMC, New Delhi. Women who were already diabetic, hypertensive, had liver disease or were taking any drugs that could influence the plasma glucose or serum triglyceride value were excluded.

Patients who met the inclusion criteria were called the following morning in a fasting state of 10-12 hours wherein OGTT was performed and GDM was diagnosed if one or more venous blood glucose values exceeded the following thresholds: fasting ≥92 mg/dl, one-hour ≥180 mg/dl or two-hour ≥153 mg/dl in accordance with the IADPSG criteria.

Simultaneously, fasting triglyceride values were also measured. The GODPOD (Glucose Oxidase-Peroxidase) method was used for blood glucose estimation and GPOPAP (Glycerol Phosphate Oxidase Peroxidase) method was used for serum triglyceride estimation. Subsequently, the TyG index was calculated in all women at the same time using a scientific calculator. The formula used was, TyG= Ln [fasting triglycerides (mg/dl) × fasting glucose (mg/dl)]/2.

Statistical analysis

Data was entered in MS Excel and analysis was done using SPSS software version 21.0. Unpaired T test was used to compare two group means and Chi-square test was done to compare two categorical variables. A p-value of less than 0.05 was considered as significant. ROC analysis along with Youden index calculation was done to establish a cut-off value of the TyG index for maximum accuracy in screening for GDM above which the patients were diagnosed with GDM.

To express the validity of the TyG index, a 2×2 table was constructed (Table 1) between cases detected by TyG index and cases diagnosed by OGTT by which sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio were calculated.

RESULTS

A total of 270 women were recruited in our study. The mean age of our cases was 25.7±4.5 years (Table 2) and 58 women (21.5%) had a first degree relative with a history of diabetes mellitus (Table 3). The mean systolic blood pressure of our cases was 116.1±16mm Hg and the mean diastolic blood pressure of our cases was 71.6±11.6mm Hg. OGTT was performed as the routine screening test in all the patients recruited. Fasting blood sugar was found to be in the range of 63-144 mg/dl with a mean of 86.2±11.8 mg/dl.

One-hour post OGTT blood sugar ranged between 71-253 mg/dl with a mean of 149.8±29.3 mg/dl and Two-hour post OGTT blood sugar ranged between 69-215 mg/dl with a mean of 119.1±28.5 mg/dl (Table 4). Fasting triglyceride values were estimated in all the women to calculate the TyG Index. The range of fasting triglyceride lied between 90-477 mg/dl and the mean triglyceride value was 209.6±73.6 mg/dl. The triglyceride-glucose index of the cases ranged between 4.4 to 5.5 with a mean of 4.9± 0.2 (Table 4). ROC curve was constructed between sensitivity and 100-specificity (Figure 1).

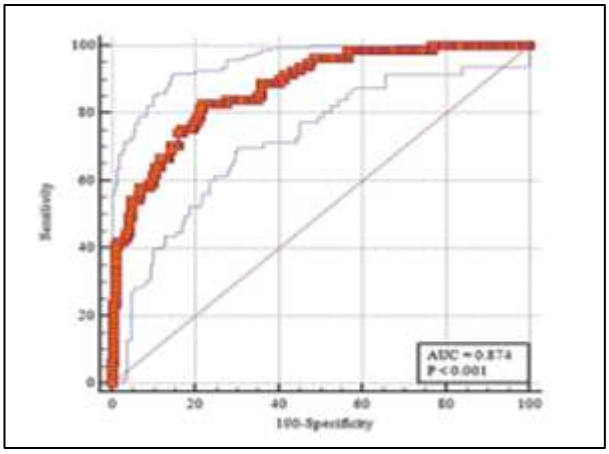

Figure 1: ROC analysis curve between sensitivity vs 1-specificity.

Table 1: Diagnostic performance of TyG index.

	GDM+	GDM-
GDM+	True positive	False positive
GDM-	False negative	True negative

Table 2: Age distribution of recruited cases.

Parameter	Mean	SD	Minimum	Maximum
Age (in years)	25.7	4.5	18	39

Table 3: Presence of family history of diabetes mellitus in the cases.

Family h/o DM	Frequency	GDM by OGTT	Chi square Test P value
Yes	58	34	<0.001

Table 4: Biochemical values in our recruited cases.

Parameters	Mean	SD	Minimum	Maximum
FBS (mg/dl)	86.2	11.8	63.0	144.0
BS after 1 hr of OGTT (mg/dl)	149.8	29.3	71.0	253.0
BS after 2 hr of OGTT (mg/dl)	119.1	28.5	69.0	215.0
Fasting triglyceride values (mg/dl)	209.6	73.6	90.0	477.0
Triglyceride glucose index	4.9	0.2	4.4	5.5

Table 5: Difference between various clinical and biochemical parameters among the cases who were diagnosed with GDM v/s those who were not diagnosed with GDM using the TyG index.

Parameters	TYG index				Unpaired t test P value
	>4.9		≤4.9		
	Mean	SD	Mean	SD	
Age (in years)	26.2	4.8	25.3	4.3	0.106
Systolic blood pressure (SBP) (mmHg)	118.5	16.7	114.4	15.2	0.037
Diastolic blood pressure (DBP) (mmHg)	72.3	12.7	70.8	10.8	0.273
Fasting blood sugar (mg/dl)	93.8	13.4	81.2	6.9	<0.001
1 hour post OGTT blood sugar (mg/dl)	168.1	28.5	137.6	22.8	<0.001
2 hour post OGTT blood sugar (mg/dl)	136.0	31.9	107.9	19.1	<0.001

Table 6: ROC analysis.

Area under the ROC curve (AUC)	0.874
Standard error	0.0223
95% confidence interval	0.829 to 0.912
Z statistic	16.776
Significance level P (Area=0.5)	<0.001
Youden index J	0.6102
Associated criterion (CUT OFF)	>4.9

Table 7: Number of cases who had triglyceride glucose index above the cutoff v/s who were diagnosed with GDM by OGTT (2 x 2 table).

Triglyceride glucose ratio	GDM BY OGTT				Total	Chi square test P value
	Yes		No			
	N	%	N	%		
>4.9	67	62.0	41	38.0%	108	<0.001
≤4.9	14	8.6	148	91.4%	162	

Table 8: Diagnostic performance of the TYG index.

Statistic	Value	95% CI
Sensitivity	82.72%	72.70 to 90.22
Specificity	78.31%	71.74 to 83.96
Positive likelihood ratio	3.81	2.86 to 5.09
Negative likelihood ratio	0.22	0.14 to 0.36
Disease prevalence by OGTT (81/270)	30.00%	
Disease prevalence by TyG index (108/270)	40.00%	
Positive predictive value	62.04%	55.05 to 68.56
Negative predictive value	91.36%	86.71 to 94.48
Accuracy	79.63%	74.33 to 84.27

The point of maximum sensitivity was chosen and Youden's Index was applied. A cut-off of 4.9 was obtained for TyG index above which patients were diagnosed with GDM in our study (Table 6). The disease prevalence was estimated at 30% when OGTT was used but increased to 40% when the cut-off of TyG index ≥4.9 was taken. Sensitivity of TyG Index in its ability to screen for GDM at 24-28 weeks of POG was 82.72%, Specificity was 78.31%, PPV was 62.04% and the NPV was 91.36%. The positive likelihood ratio was 3.81 and the negative likelihood ratio was 0.22. The overall accuracy of this test was 79.63%. (Table 7 and 8).

DISCUSSION

The TyG index showed a high sensitivity of 82.72% and negative predictive value (NPV) of 91.36% for diagnosis of GDM and in consequence, may be used as a screening strategy that would reduce the need for many OGTTs. To our knowledge, this is the first study to explore the use of the TyG index for GDM screening at 24-28 weeks POG in an Indian setup. The study conducted by Sanchez-Garcia estimated a cut-off of 4.69 whereas our study found a cut-off of 4.9 (Table 6).[18] This could be due to the higher mean fasting triglyceride value found in our population, which has led to the higher cut-off.[19] Indians have higher TG values and lower HDL-c values and therefore different cut-off points for the TyG index may need to be calculated for different populations.[19] Various studies have demonstrated that TyG index calculated in first trimester or even pre-pregnancy is a good predictor of LGA and GDM where mothers with a higher TyG index were significantly more likely to develop GDM and deliver LGA babies.[20-22] Another study showed that the TyG Index correlated with HOMA-IR during the first and second trimester of pregnancy ($p<0.05$) and the value also correlated with the blood pressure among these women where the value of TyG Index among pre-eclamptic pregnant was significantly higher than in normotensive women.[23] In our study also, SBP was significantly higher ($p<0.05$) in women with a TyG Index cutoff higher than our calculated of ≥4.9 (Table 5). There have been conflicting results to determine the accuracy of the TyG index in the first trimester.[20,21,24,25] The study conducted by Pazhohan et al revealed that TyG index is a predictor of giving birth to LGA babies and developing GDM than other measurements such as TG/HDL-c ratio.[20] Mothers in the top tertile of the TyG index in the first trimester of pregnancy were 4.9 and 5.3 times more likely to develop GDM and deliver LGA infant than their bottom tertiles

respectively. Another study conducted by Liu et al found a high risk of development of GDM in women with top tertile of TyG Index value (OR TyG=3.535 (95% CI 1.483–8.426)).[21] The risk for LGA infant delivery in women of the top tertile was also significantly higher than in women with the lowest tertile (OR TyG=3.011, (95% CI 1.012–8.962)). Though first-trimester detection of insulin resistance may be useful in predicting GDM, it may subsequently add to the high costs of healthcare and may even unnecessarily add to the apprehension of the pregnant lady who may not ultimately be diagnosed with GDM at 24-28 weeks. Further cost-benefit studies are required to estimate the utility of the TyG index in first trimester. The measurement of TyG at 24-28 weeks is at the crucial time when the insulin resistance sets in and it requires blood sampling only once instead of the OGTT, which requires samples to be drawn thrice. Performing OGTT adds to the burden of healthcare and becomes cumbersome as patients frequently vomit and sometimes even go back without completing the full test. Though many types of biomarkers such as such as adiponectin, sex hormone-binding globulin and C-reactive protein have been tested for their ability in predicting GDM, these markers are expensive and are not available in most settings.[26-28] Therefore, these markers at present cannot be recommended as routine screening tools for GDM.

The fasting plasma glucose, as well as fasting triglyceride, can be both estimated from one sitting of blood sampling and don't require patients to wait to undergo repeated sampling. The gold-standard method of measuring insulin resistance is the Hyperinsulinemic-Euglycemic clamp test, compared to which TyG index is easy, inexpensive, fast and can be conveniently obtained.[29] Since, the comparative studies were mainly from Mexico and Asian countries, the generalizability of these findings could be limited. Large, randomized controlled trials across different regions will be needed to internationally standardize the cut-off of TyG index for detection of GDM.

Limitations

Although this study provides promising results, there are limitations, which warrant future research. A major limitation of this study is the small number of existing research, which may introduce small sample bias and restrict some of the analyses such as meta-regression to control for confounders among studies. Secondly, authors compared the TyG index with the OGTT using the IADPSG criteria. Both of these tests require the patient to be called a second time in the fasting state which in Indian settings may be unfeasible for the patients because of various social, economic and geographical constraints. This is precisely the reason why the Government of India has endorsed the DIPSI test, which can be performed in the non-fasting state in the same antenatal visit.[6] Though fasting blood values better predict insulin resistance, which is the underlying pathology of GDM, we still need to perform more wide-scale studies in various places to determine the feasibility of this test in India before it can be adopted.

CONCLUSION

The overall diagnostic accuracy of the TyG index in its ability to detect GDM is 79.63%. A cut off of TyG index at 4.9 puts its sensitivity in detecting GDM at 82.72%, which shows that TyG index can effectively detect the cases of GDM in the population. This one-step test can bring down the complexities of performing repeated blood samples, which the OGTT requires. However, it overestimates the prevalence of GDM (40% v/s 30% by OGTT).

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