Section: Obstetrics and Gynecology

Original Research Article

CORRELATION OF TRIGLYCERIDE GLUCOSE INDEX AND SERUM URIC ACID LEVELS IN EARLY PREGNANCY (<20 WEEK PERIOD OF GESTATION) WITH THE DEVELOPMENT OF GESTATIONAL DIABETES MELLITUS

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ABSTRACT

Background: GDM is a growing public health concern in lieu of its higher prevalence and ever- increasing burden on health care. Elevated serum uric acid is a feature of hyperinsulinemia and insulin resistance. Triglyceride glucose (TyG) index, is also a valuable surrogate marker of insulin resistance. This study was intended to explore the utility of these parameters and asses if the same can be used for early detection of GDM. The objective is to explore the relationship between the TyG index and serum uric acid levels in early pregnancy and their potential association with the development of GDM.

Materials and Methods: Hospital based prospective Cohort study was conducted among 270 Antenatal mothers enrolled during June 2023 to December 2024, in their early pregnancy i.e. at <20 weeks gestational age. Data regarding the age, parity, history of GDM, history of DM in family, history of macrosomia in previous pregnancy, weight and height were collected and serum uric acid, fasting plasma triglyceride and fasting plasma glucose values were estimated. GDM was diagnosed using DIPSI criteria.

Results: About 34(12.6%) women developed GDM. A significant association between elevated TyG index and serum uric acid levels in early gestation with the development of GDM was found. The TyG index, predicts GDM with an AUC of 0.715 (95% CI: 0.617–0.814). The serum uric acid, predicted GDM with an AUC of 0.928 (95% CI: 0.863–0.994).

Conclusion: Both the Triglyceride-Glucose (TyG) index and serum uric acid levels, when measured before 20 weeks of gestation, are significantly associated with the subsequent development of Gestational Diabetes Mellitus (GDM). These findings suggest that early metabolic alterations, reflected by these markers, may precede the clinical manifestation of GDM and serve as useful predictors.

Keywords: Gestational Diabetes Mellitus (GDM), Triglyceride-Glucose (TyG) Index, Serum Uric Acid

INTRODUCTION

Gestational Diabetes Mellitus is a form of hyperglycaemia that develops or is first recognized during pregnancy and poses risks to both mother and foetus.[1] It is one of the commonest complications of pregnancy, with a prevalence of about 11.7% South East Asian Countries.[2,3] Women with gestational diabetes are at an increased risk of complications during pregnancy and at delivery. GDM also raises the long-term risk of type 2 diabetes mellitus and cardiovascular disease in mothers and metabolic disorders in offspring

Recent studies have suggested that certain biomarkers may provide valuable insights into the early prediction of GDM. Among these, the

Triglyceride Glucose (TyG) index has gained attention as a potential indicator of insulin resistance, which is a key pathophysiological factor in the development of GDM. The TyG index is a simple and cost-effective marker calculated from fasting triglyceride and glucose levels and has been associated with the development of metabolic disorders, including diabetes.

The TyG index, calculated using fasting triglyceride and fasting glucose levels, has emerged as a reliable marker for insulin resistance. TyG index is obtained as a product of fasting Triglycerides (TG) and plasma glucose levels, which serves as arithmetical expression of Insulin Resistance.

Triglyceride glucose (TyG) index, has been proposed as a very valuable surrogate marker of insulin resistance.[4] TyG index is useful in the risk stratification of metabolic syndrome, non-alcoholic fatty liver disease, type 2 diabetes mellitus, atherosclerosis and cardiovascular disease (CVD).[5] Due to its excellent relevance in predicting insulin resistance, it can be used to identify women who are prone to GDM. Several studies have been done in the recent years which have established positive correlation between higher values of TyG index and incidence of GDM.[6,7] However, extensive research of the online database showed no evidence from the Indian subcontinent.

Serum uric acid is a routine biochemical marker that can be measured inexpensively, making it an attractive candidate for early GDM risk assessment.

Serum uric acid levels have been found to be elevated in conditions associated with insulin resistance, such as obesity and metabolic syndrome. Uric acid is thought to contribute to endothelial dysfunction and inflammation, both of which are involved in the pathogenesis of GDM. It has been suggested that hyperuricemia in early pregnancy may be a predictor of GDM development.

This study aims to explore the relationship between the TyG index and serum uric acid levels in early pregnancy and their potential association with the development of GDM. These markers are cost-effective and routinely measurable, making them feasible in resource-limited settings. Monitoring these indices may provide valuable insights into identifying high-risk women early in their pregnancies, allowing for proactive management strategies to improve maternal and fetal health outcomes.

MATERIALS AND METHODS

This hospital based prospective Cohort study was conducted among Pregnant women coming for routine antenatal care to Outpatient Department of Obstetrics and Gynecology at S. Nijalingappa Medical College, Bagalkot. Duration of Study was from June 2023 to December 2024

Inclusion Criteria

- Antenatal mothers enrolled in early pregnancy i.e. at <20 weeks period of gestation and are available for follow up.

Exclusion Criteria

- Known pregestational diabetes mellitus
- Receiving steroids in any form
- Known cases of Gout and hyperuricemia
- Mothers with known renal disease
- Severe anemia (Hb < 7g%)
- Known haemoglobinopathies.

Sample Size Estimation

According to the study conducted by Sánchez-García A et al,[6] the prevalence of GDM was found to be 10-14.3%=10

The Relative risk for GDM with Triglycerides index levels in first trimester was found to be 1.03.

α (two-tailed) =0.050 and at 95% confidence level. β =0.200 and 80% of power of the study.

The standard normal deviate for $\alpha = Z\alpha = 1.960$ The standard normal deviate for $\beta = Z\beta = 0.842$ Sample size estimated is 262-270 pregnant women.

Sampling method: Purposive sampling method.

Method of collection of data:

A detailed history and complete clinical examination of patients was done to rule out the exclusion criteria. The aim and objectives of the intended study was properly explained to the subjects and informed consent was taken on the proforma sheet. The preliminary data regarding the age, parity, history of GDM, history of DM in family, history of macrosomia in previous pregnancy, weight and height were collected.

Blood sample collected for routine antenatal check-up during the first antenatal visit was utilized for measuring the serum uric acid, fasting plasma triglyceride and fasting plasma glucose values.

S.uric acid levels was measured by enzymatic uricase method, fasting plasma glucose was measured using the glucose oxidase assay and fasting triglycerides was analyzed by the glycerol phosphate oxidase method in the laboratory of S. Nijalingappa medical college.

Diagnosis of GDM: All Antenatal mothers during their follow up visit between 24-28 week period of gestation were subjected to glucose challenge with 75grams of glucose irrespective of the fasting state as is routinely done in our OPD. GDM was diagnosed using DIPSI criteria8 i.e., plasma glucose >/= 140mg/dl after 2h of glucose challenge is diagnostic.

Timing of the tests: After a fasting period of 12 hours; serum uric acid, fasting plasma triglyceride and fasting plasma glucose values are measured in early pregnancy i.e. at <20weeks period of gestation. During follow up, Glucose challenge with 75gram glucose is given at 24 to 28 weeks of gestation to diagnose GDM.

Based on S. uric acid levels, the patients were divided into two groups i.e. between the levels of <4.2mg/dl and >4.2 mg/dl. Calculated triglyceride glucose indices were divided into quartiles. These groups were then analysed for the risk of development of

GDM and their role as screening tests. The relation of S. uric acid levels and triglyceride glucose index in early pregnancy (<20weeks) with the development of GDM will be studied as the primary outcome. Their role as early predictors of GDM will be studied as secondary outcome.

Statistical analysis: Data analysis was done using IBM SPSS version 24.0 Statistical analysis was done using SPSS software 24.0. Data obtained were tabulated in the Excel sheet and analysed. Quantitative data were expressed as mean±standard deviation and nonparametric data were expressed as median and min-max values. Percentages were used for representing qualitativedata. Relative risk, Absolute risk and Attributable risk were calculated. Chi-square test for proportions in Qualitative data and Student's unpaired t – test for Quantitative data. Women were categorized by tertiles of the triglyceride glucose index to compare GDM case distribution and the risk of developing GDM, using the lowest tertile as reference.

RESULTS

The mean age of the study participants was 25.91 ± 4.57 years. Participants belonged to age group 18-36 years Mean BMI of the study participants was 25.78 ± 3.68. Majority of the study participants were in the Obese category (48.9%). The mean Fasting Blood Sugar values was 80.61 ± 12.08mg/dL

The mean uric acid level 3.23±1.22 mg/dL The table 6 compares two groups based on their uric acid levels: Uric acid ≤4.2 mg/dL (229 participants) and Uric acid >4.2 mg/dL (41 participants).

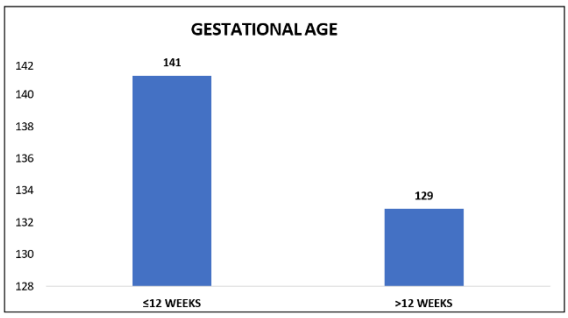

Figure 1: Gestational age of study subjects

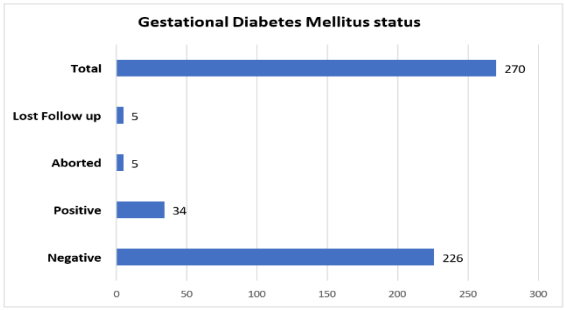

Figure 2: Gestational Diabetes Mellitus status of study subjects

Table 1: Assessment of study subject characteristics based on uric acid levels

	Uric acid ≤4.2 (229/270)	Uric acid >4.2 (41/270)
Mean Age	25.57±4.69	27.80±3.34
BMI	25.29±3.02	28.49±5.49
Fasting Blood Sugar	80.28±11.54	82.41±14.80
Triglyceride	106.32±48.08	114.77±54.73
Family history of DM	78 (34.1%)	16 (39.0%)
History of Macrosomia	3(1.3%)	1(2.4%)
GDM Diagnosis	5(2.2%)	29(70.7%)
Abortion	4(1.7%)	1(2.4%)

The mean triglyceride level was 107.6 ± 49.13. Triglyceride glucose index: The mean triglyceride glucose index was 8.258 ± 0.543. The prevalence of GDM among the study participants was found to be 12.6%. Association of various parameters with GDM was evaluated by excluding lost follow up and abortions. The total sample size was assessed to be 260.

Table 2: Association of triglyceride index with Gestational Diabetes Mellitus among the study subjects

Triglyceride Index	GDM negative	GDM positive	P value
First quartile	64(98.5%)	1(1.5%)	0.000*
Second quartile	56(86.2%)	9(13.8%)	
Third quartile	61(93.8%)	4(6.2%)	
Fourth quartile	45(69.2%)	20(30.8%)	
Total	226(86.9%)	34(13.1%)	

On assessment of association [Table], it was found that in the Lower TGI (First Quartile) almost (98.5%) are GDM-negative, with only 1.5% GDM-positive. In the higher TGI (Fourth Quartile) the percentage of GDM-negative cases (69.2%) and percentage of GDM-positive cases (30.8%). A statistically significant association was found between Triglyceride Index and GDM status.

Table 3: Risk Estimate between gestational Diabetes mellitus and TyG Index

Risk Estimate			
	Value	95% Confidence Interval	
		Lower	Upper
Odds Ratio for TyG 2 quartile (1st quartile / higher TyG index)	13.037	1.746	97.336
For cohort GDM DIAGNOSIS BY DIPSI = negative	1.185	1.105	1.271
For cohort GDM DIAGNOSIS BY DIPSI = positive	.091	.013	.652

N of Valid Cases	260		

On assessment of risk ratio, it was found that individuals in the 1st quartile of TGI have significantly higher odds of the outcome (GDM Negative) compared to those with higher TGI. GDM-negative individuals have slightly increased odds of the outcome, but the association is weak. All confidence intervals indicate statistical significance.

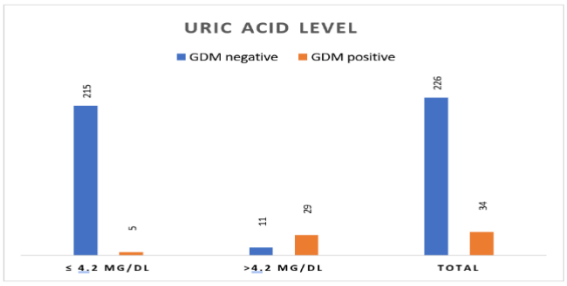

Figure 3: Association of Serum Uric Acid with Gestational Diabetes Mellitus among the study subjects

A significant association ($p < 0.05$) was found between uric acid level diagnosis of Gestational Diabetes Mellitus.

On assessment of risk ratio, it was found that A very high odds ratio (113.364) for the recoded variable suggests a strong association. GDM-negative individuals have higher odds compared to the reference group, while GDM-positive individuals have significantly lower odds for having uric acid level >4.2mg/dl. Confidence intervals indicate statistical significance.

Regression analysis shows that the odds of developing Gestational Diabetes mellitus in cases with uric acid > 4.2mg/dl is 128.992 times compared to ≤ 4.2mg/dl category. Regression analysis of TyG index after dividing into quartiles it was found that the odds of developing GDM in the elevated TyG index category was 18.6 times compared to first quartile.

Triglyceride glucose index and serum uric acid as early predictors of gestational diabetes mellitus

To explore the predictive ability of serum UA and TGI in < 20 weeks gestation for the prediction of GDM, ROC curve analysis was performed.

Comparison of Predictivity of Uric acid and TGI

On assessment it was found that serum uric acid is a better predictor compared to TGI (greater area under the curve).

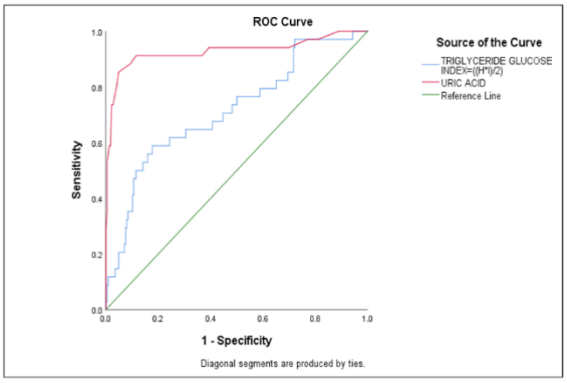

Table 4: Area Under the Curve

Test Result Variable(s)	Area	Std. Errora	Asymptotic Sig.b	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
Triglyceride Glucose Index=((H*I)/2)	.715	.050	.000	.617	.814
URIC ACID	.928	.033	.000	.863	.994

Receiver Operator curve (ROC) to assess the predictivity of uric acid for Gestational Diabetes mellitus showed an area under the curve of 0.902, Sensitivity 85.3% and Specificity 95.1% and was found to be statistically significant ($p< 0.05$). Receiver Operator curve (ROC) to assess the predictivity of Triglyceride Glucose Index (TyG index) for Gestational Diabetes mellitus showed an area under the curve of 0.715, Sensitivity 58,8% and Specificity 82.4% and was found to be statistically significant ($p< 0.05$).

Table 5: Area Under the Curve for combined probability of TyG and S. Uric acid

Test Result Variable(s): Predicted probability				
Area	Std. Errora	Asymptotic Sig.b	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.955	.017	.000	.922	.988

Upon assessment of combined probabilities of prediction using Tyg and Serum Uric Acid levels for prediction of GDM it was found to have a statistically significant ($p<0.001$) higher area under the ROC curve (AUC=0.955).

Combined Predictivity of Triglyceride Glucose Index and Serum Uric Acid in Diagnosis of Gestational Diabetes Mellitus

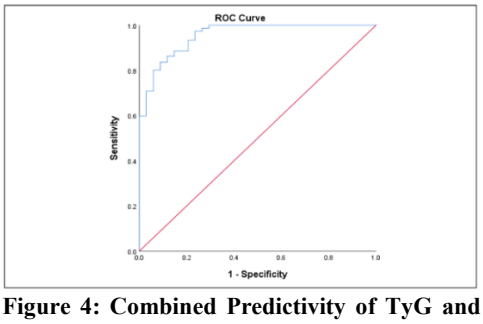

Figure 4: Combined Predictivity of TyG and SUA in Diagnosis of GDM

DISCUSSION

Gestational diabetes mellitus (GDM) is a growing global health concern, with implications for both maternal and foetal outcomes. Identifying reliable early predictors is essential to initiate timely interventions. In this study, we explored the relationship between two potential biomarkers—Triglyceride-glucose (TyG) index and serum uric acid levels, measured in early pregnancy (<20 weeks)—with the subsequent development of GDM. The findings of the current study can provide potential insights on the role of TGI and Serum Uric Acid as early predictors of GDM.

Our findings suggest a significant positive correlation between elevated TyG index and serum uric acid levels in early gestation with the development of GDM.

TyG index and GDM

Multiple studies have assessed the correlation between early pregnancy TyG index and subsequent development of GDM. Previous study by Wang et al. found that an elevated TyG index in the first trimester was significantly associated with a higher risk of developing GDM. They proposed a specific cut-off value for risk stratification, demonstrating a sensitivity of 74% and specificity of 69% for GDM prediction.9 Zhang et al. reported similar findings in a Chinese cohort, highlighting that the TyG index was not only a strong predictor of GDM but also outperformed traditional risk factors such as BMI and maternal age when used in early pregnancy.[10]

The current study showed a significant higher odd of developing GDM among cases with elevated Triglyceride Glucose Index. The results of a retrospective cohort study by Zhang J et al involving 631 singleton pregnant women indicated that an elevated TyG index in early pregnancy was independently associated with an increased risk of GDM.[10] Specifically, each 1-unit increase in the TyG index corresponded to 3.11-fold higher odds of developing GDM. The study also noted that higher TyG index levels were associated with increased incidences of premature birth and hypertensive disorders during pregnancy. In a prospective cohort study by Guo Y et al, it was found that each 1-unit increase in the TyG index resulted in a 2.10-fold increase in GDM risk. Women in the highest quintile of the TyG index had 3.25 times higher odds of developing GDM compared to those in the lowest quintile. The study concluded that the TyG index in early pregnancy is a valuable predictor of GDM risk.[11]

Diagnostic and Predictive Utility of TyG index

The present study indicates that the TyG index, predicts GDM with an AUC of 0.715 (95% CI: 0.617–0.814). In a study by Mo Z et al Involving 589 pregnant women, it was found that the TyG index had a higher predictive value for GDM compared to other factors like triglycerides (TG), fasting plasma glucose (FPG), and insulin. The optimal TyG index cutoff was 8.632, yielding a sensitivity of 72.2% and specificity of 78.7%.[12] In a study by Sánchez-García A et al, TyG index as a screening tool for GDM at 24–28 weeks of pregnancy was evaluated. The TyG index demonstrated a sensitivity of 89% and specificity of 50%, with a high negative predictive value of 93%, suggesting its potential utility in GDM screening.[6]

These studies underscore the potential of the TyG index as a predictive marker for GDM, with AUC values ranging from 0.715 to 0.807, indicating moderate to strong predictive capabilities. Variations in AUC values may be attributed to differences in study populations, timing of assessments, and methodological approaches.

Combined Predictive Value

Both the markers are found to be independently associated with GDM, and when combined, they may improve sensitivity and specificity, allow earlier intervention, serve as a non-invasive, accessible screening method before OGTT An important contribution of this study is the evaluation of both markers in combination. The TyG index and serum uric acid levels together showed better predictive capacity for GDM than either marker alone, as reflected in improved AUC (area under curve) values in ROC analysis.

Studies have shown that combining SUA and TyG index provides better predictive performance (higher AUC values in ROC curves) compared to either marker alone. This suggests a potential synergistic role in early screening strategies. Future large- scale, longitudinal studies are needed to validate optimal cut-off points and integrate these markers into routine prenatal care.

CONCLUSION

This study demonstrates that both the Triglyceride-Glucose (TyG) index and serum uric acid levels, when measured before 20 weeks of gestation, are significantly associated with the subsequent development of Gestational Diabetes Mellitus (GDM). These findings suggest that early metabolic alterations, reflected by these markers, may precede the clinical manifestation of GDM and serve as useful predictors The TyG index showed a strong association with GDM, reinforcing its value as a practical, low-cost screening tool in early pregnancy. Importantly, the combined assessment of both markers enhanced predictive performance, supporting a multi-marker approach to early risk stratification. Given that both indicators are derived from routine biochemical tests, their incorporation into early antenatal screening protocols could enable timely interventions aimed at preventing GDM and its associated complications.

Further prospective, large-scale studies are warranted to validate these findings, explore underlying mechanisms, and establish clinically applicable cut-off values. This may contribute to the development of

accessible and cost-effective strategies for the early identification and management of GDM, particularly in resource-constrained settings. Their integration into screening protocols could enable earlier interventions, improving maternal and fetal outcomes.

Elevated serum uric acid and TyG index in early pregnancy are promising, cost- effective biomarkers for GDM prediction. Their integration into screening protocols could enable earlier interventions, improving maternal and fetal outcomes. Further research should clarify combined thresholds and mechanistic pathways.

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