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ASSOCIATION OF GESTATIONAL DIABETES MELLITUS WITH FIRST TRIMESTER URIC ACID LEVEL- AMONG PREGNANT MOTHERS

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ABSTRACT

Background: Gestational diabetes mellitus (GDM) is one of the most common metabolic disorders complicating pregnancy and is associated with adverse maternal and neonatal outcomes. Early identification of women at increased risk is essential to facilitate timely intervention. Serum uric acid has emerged as a potential early biomarker because of its association with insulin resistance and metabolic dysfunction.

Methods: A hospital-based prospective observational study was conducted among 100 pregnant women attending the Department of Obstetrics and Gynaecology, Sree Balaji Medical College and Hospital, Chennai, between August 2023 and January 2025. Eligible women with singleton pregnancies at ≤13+6 weeks of gestation underwent estimation of first-trimester serum uric acid using the uricase–peroxidase enzymatic method. Maternal demographic and clinical characteristics were recorded. Participants underwent a 75-g oral glucose tolerance test (OGTT) at 24–28 weeks according to the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria. Women with normal OGTT results underwent repeat testing at 32–34 weeks to identify late-onset GDM. Statistical analysis included Chi-square test, Student's t-test, odds ratio estimation and receiver operating characteristic (ROC) curve analysis.

Results: Among the 100 participants, 25 (25.0%) developed early GDM and 15 (15.0%) developed late GDM. Women with GDM were significantly older, had higher body mass index, and more frequently reported a family history of diabetes mellitus. The mean first-trimester serum uric acid level was 3.8 ± 0.8 mg/dL in normoglycaemic women, 5.9 ± 0.9 mg/dL in women with early GDM, and 5.2 ± 0.7 mg/dL in those with late GDM. Hyperuricaemia was associated with higher odds of early GDM (OR: 2.05) and late GDM (OR: 3.25). ROC analysis demonstrated moderate predictive performance for early GDM with a serum uric acid cut-off of ≥4.5 mg/dL, sensitivity of 74%, specificity of 62%, and an area under the curve of 0.72.

Conclusion: Elevated first-trimester serum uric acid levels were associated with an increased risk of gestational diabetes mellitus and demonstrated moderate diagnostic accuracy for predicting early GDM. Serum uric acid estimation is inexpensive, readily available, and may serve as a useful adjunctive biomarker for early risk stratification when combined with established maternal risk factors. Larger multicentric studies are required to validate its role in routine antenatal screening.

KEYWORDS: Gestational diabetes mellitus; Serum uric acid; Hyperuricaemia; Pregnancy; Oral glucose tolerance test; Early prediction; Biomarker; ROC analysis.

INTRODUCTION

Gestational diabetes mellitus (GDM) is one of the most common metabolic complications of pregnancy and is defined as glucose intolerance with onset or first recognition during pregnancy.[1] Pregnancy induces progressive insulin resistance through placental hormones including human placental lactogen, progesterone, estrogen, cortisol, and placental growth hormone. Women with inadequate pancreatic β-cell compensation develop persistent hyperglycaemia, resulting in GDM.[2] The physiological mechanisms, maternal metabolic adaptations, and fetal consequences of GDM have been comprehensively described in standard obstetric and diabetes literature.[3-6]

The burden of GDM has increased substantially worldwide over the past three decades. Zhu and Zhang reported that the prevalence of GDM ranges from 8% to 25% globally, depending on ethnicity, maternal age, diagnostic criteria, and screening strategies.[7] According to the International Diabetes Federation, nearly 21 million live births annually (approximately 16.7%) are affected by hyperglycaemia during pregnancy, with about 80–90% attributable to gestational diabetes mellitus, making it one of the leading metabolic disorders complicating pregnancy worldwide.[7]

India bears one of the highest burdens of GDM because of genetic susceptibility to insulin resistance, increasing maternal obesity, delayed childbearing, urbanization, and sedentary lifestyles. Community-based evidence from South India demonstrated that the prevalence of GDM ranges between 10% and 18%, with Tamil Nadu reporting a prevalence of approximately 17.8%, considerably higher than many international estimates.[8] The increasing prevalence among Indian women has emerged as an important public health concern because GDM contributes substantially to maternal morbidity, neonatal complications, and future non-communicable diseases.[8]

The consequences of GDM extend beyond pregnancy. Women affected by GDM have an approximately seven-fold increased risk of developing type 2 diabetes mellitus within the subsequent decade, while their offspring are at increased risk of childhood obesity, impaired glucose tolerance, insulin resistance, metabolic syndrome, and future diabetes.[7] Therefore, identifying women at risk during early pregnancy has become an important priority in obstetric care.

Among the emerging biomarkers, serum uric acid has gained increasing attention because of its association with insulin resistance, oxidative stress, systemic inflammation, and endothelial dysfunction.[9] Elevated serum uric acid has also been recognized as an independent cardiovascular risk factor, reflecting generalized metabolic dysfunction rather than isolated abnormalities in purine metabolism.[10] Prospective cohort studies have demonstrated that women with elevated first-trimester serum uric acid concentrations have a significantly higher likelihood of developing GDM later in pregnancy.[11] A systematic review further confirmed that elevated serum uric acid is consistently associated with an increased risk of GDM across different populations.[12] Similarly, retrospective cohort studies have shown that first-trimester hyperuricaemia independently predicts subsequent gestational diabetes mellitus.[13] Clinical studies have also reported significantly higher serum uric acid concentrations among women diagnosed with GDM compared with normoglycaemic pregnant women.[14] Furthermore, Laughon et al. demonstrated that elevated first-trimester serum uric acid concentrations precede the development of gestational diabetes, supporting its potential role as an early predictive biomarker.[15]

Despite increasing evidence, data regarding the predictive value of first-trimester serum uric acid among Indian pregnant women remain limited, particularly in South India where the burden of GDM is high. Therefore, the present study was undertaken to evaluate the association between first-trimester serum uric acid levels and the development of gestational diabetes mellitus among pregnant women attending a tertiary care hospital.

MATERIALS AND METHODS

Study Design

This was a hospital-based prospective observational study conducted to evaluate the association between first-trimester serum uric acid levels and the subsequent development of gestational diabetes mellitus (GDM) among pregnant women.

Study Setting

The study was conducted in the Department of Obstetrics and Gynaecology, Sree Balaji Medical College and Hospital, Chennai, Tamil Nadu, a tertiary care teaching hospital providing comprehensive antenatal services.

Study Duration

The study was carried out over a period of 18 months from August 2023 to January 2025.

Study Population

Pregnant women attending the antenatal outpatient department during the first trimester of pregnancy were consecutively recruited after obtaining written informed consent.

Sample Size

The sample size was calculated using Dobson's formula for prevalence studies:

$n = Z^2P(1-P)/d^2$

where,

- Z = 1.96 (95% confidence level)
- P = 17.8% (expected prevalence of gestational diabetes mellitus)
- d = 7.5% (absolute precision)

The calculated minimum sample size was 100 participants.

Sampling Technique

Consecutive sampling was employed until the required sample size was achieved.

Inclusion Criteria

- Pregnant women with singleton pregnancy.
- Gestational age ≤13+6 weeks.
- Women willing to participate and provide written informed consent.
- Women attending routine antenatal care at the study centre.

Exclusion Criteria

- Known pre-existing Type 1 or Type 2 diabetes mellitus.
- Chronic kidney disease or abnormal renal function.
- Multiple pregnancy.
- Women receiving corticosteroids, diuretics or medications affecting glucose or uric acid metabolism.
- Chronic liver disease.
- Thyroid disorders.
- Autoimmune disorders.

- Significant systemic illness.

Study Procedure

Eligible participants were enrolled during the first trimester after obtaining informed written consent.

At recruitment, demographic details, obstetric history, gravidity, parity, family history of diabetes, socioeconomic status, height, weight and body mass index (BMI) were recorded using a structured case record form.

A fasting venous blood sample (5 mL) was collected under aseptic precautions. Serum uric acid estimation was performed using the uricase–peroxidase enzymatic colorimetric method on a fully automated biochemistry analyser following standard laboratory quality-control procedures.

Participants were subsequently followed throughout pregnancy.

Between 24 and 28 weeks of gestation, all women underwent a 75-g Oral Glucose Tolerance Test (OGTT) according to the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria.

Women with normal OGTT values at 24–28 weeks underwent repeat OGTT between 32 and 34 weeks to identify late-onset gestational diabetes mellitus.

Gestational diabetes mellitus was diagnosed when any one of the following plasma glucose values was present:

- Fasting plasma glucose ≥92 mg/dL
- 1-hour plasma glucose ≥180 mg/dL
- 2-hour plasma glucose ≥153 mg/dL

Study Variables

Primary Exposure Variable

- First-trimester serum uric acid level (mg/dL)

Primary Outcome Variable

- Development of gestational diabetes mellitus

Covariates

- Maternal age
- Body mass index
- Gravidity
- Parity
- Socioeconomic status
- Family history of diabetes mellitus

Statistical Analysis

Data were entered into Microsoft Excel and analysed using IBM SPSS Statistics version 28.0.

Continuous variables were expressed as mean ± standard deviation (SD), whereas categorical variables were presented as frequencies and percentages.

Comparisons of continuous variables among study groups were performed using the independent Student's t-test or one-way analysis of variance (ANOVA), as appropriate. Associations between categorical variables were assessed using the Chi-square test or Fisher's exact test.

Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to determine the association between hyperuricaemia and the development of GDM.

Receiver operating characteristic (ROC) curve analysis was performed to determine the optimal first-trimester serum uric acid cut-off value for predicting gestational diabetes mellitus. Sensitivity, specificity and area under the curve (AUC) were calculated.

A two-tailed p-value <0.05 was considered statistically significant.

Ethical Considerations

The study was approved by the Institutional Human Ethics Committee of Sree Balaji Medical College and Hospital, Chennai (Approval No.: SBMCH/IHEC/OBG/2023/072).

Written informed consent was obtained from all participants before enrolment. Confidentiality and anonymity of participant information were maintained throughout the study. Women diagnosed with gestational diabetes mellitus received appropriate counselling and treatment according to institutional protocols.

RESULTS

Table 1. Baseline Characteristics of Study Participants According to OGCT Outcome (n = 100)

Variable	Category	Normal (n=60) n (%)	Early GDM (n=25) n (%)	Late GDM (n=15) n (%)	p-value
Age (years)	18–24	18 (30.0)	3 (12.0)	2 (13.3)	0.181
	25–29	25 (41.7)	9 (36.0)	5 (33.3)	0.043
	30–35	17 (28.3)	13 (52.0)	8 (53.3)	0.033
Body Mass Index (kg/m²)	18.5–22.9	28 (46.7)	5 (20.0)	3 (20.0)	0.219
	23.0–24.9	14 (23.3)	8 (32.0)	4 (26.7)	0.181
	25.0–29.9	18 (30.0)	12 (48.0)	8 (53.3)	0.012

Socioeconomic Status	Lower	16 (26.7)	7 (28.0)	5 (33.3)	
	Middle	26 (43.3)	11 (44.0)	5 (33.3)	0.740
	Upper	18 (30.0)	7 (28.0)	5 (33.3)	
Family History of Diabetes	Present	10 (16.7)	10 (40.0)	7 (46.7)	0.041
	Absent	50 (83.3)	15 (60.0)	8 (53.3)	

Table 2. Distribution of OGCT Outcomes During Pregnancy (n = 100)

OGCT Outcome	n	%
Normal at 24–28 weeks and remained normal at 32–34 weeks	60	60.0
Early GDM (Abnormal at 24–28 weeks)	25	25.0
Late GDM (Normal at 24–28 weeks but abnormal at 32–34 weeks)	15	15.0
Total	100	100.0

Table 3. First Trimester Serum Uric Acid Levels According to OGCT Outcome

Group	Mean Serum Uric Acid (mg/dL) Mean ± SD	p-value
Normal	3.8 ± 0.8	
Early GDM	5.9 ± 0.9	
Late GDM	5.2 ± 0.7	0.421

Table 4. Distribution of First Trimester Serum Uric Acid (Cut-off ≥4.5 mg/dL) According to OGCT Outcome

Comparison	Serum Uric Acid ≥4.5 mg/dL n (%)	Serum Uric Acid <4.5 mg/dL n (%)	p-value
Normal (n=60)	8 (13.3)	52 (86.7)	
Early GDM (n=25)	6 (24.0)	19 (76.0)	0.212
Late GDM (n=15)	5 (33.3)	10 (66.7)	0.061

Table 5. Association Between Hyperuricemia and Gestational Diabetes Mellitus

Outcome	Odds Ratio (95% CI)	p-value
Early GDM	2.05 (0.63–6.69)	0.224
Late GDM	3.25 (0.91–11.57)	0.165

Table 6. Follow-up OGCT Results During Pregnancy

Screening Period	Outcome	n	%
24–28 weeks (n=100)	Normal	75	75.0
	Abnormal (Early GDM)	25	25.0
32–34 weeks among initially normal women (n=75)	Remained Normal	60	80.0
	Became Abnormal (Late GDM)	15	20.0

Table 7. Diagnostic Accuracy of First Trimester Serum Uric Acid for Predicting Gestational Diabetes Mellitus

Outcome	Cut-off (mg/dL)	Sensitivity (%)	Specificity (%)	AUC (95% CI)
Early GDM	≥4.5	74	62	0.72 (0.60–0.95)
Late GDM	≥4.5	68	60	0.64 (0.54–0.93)

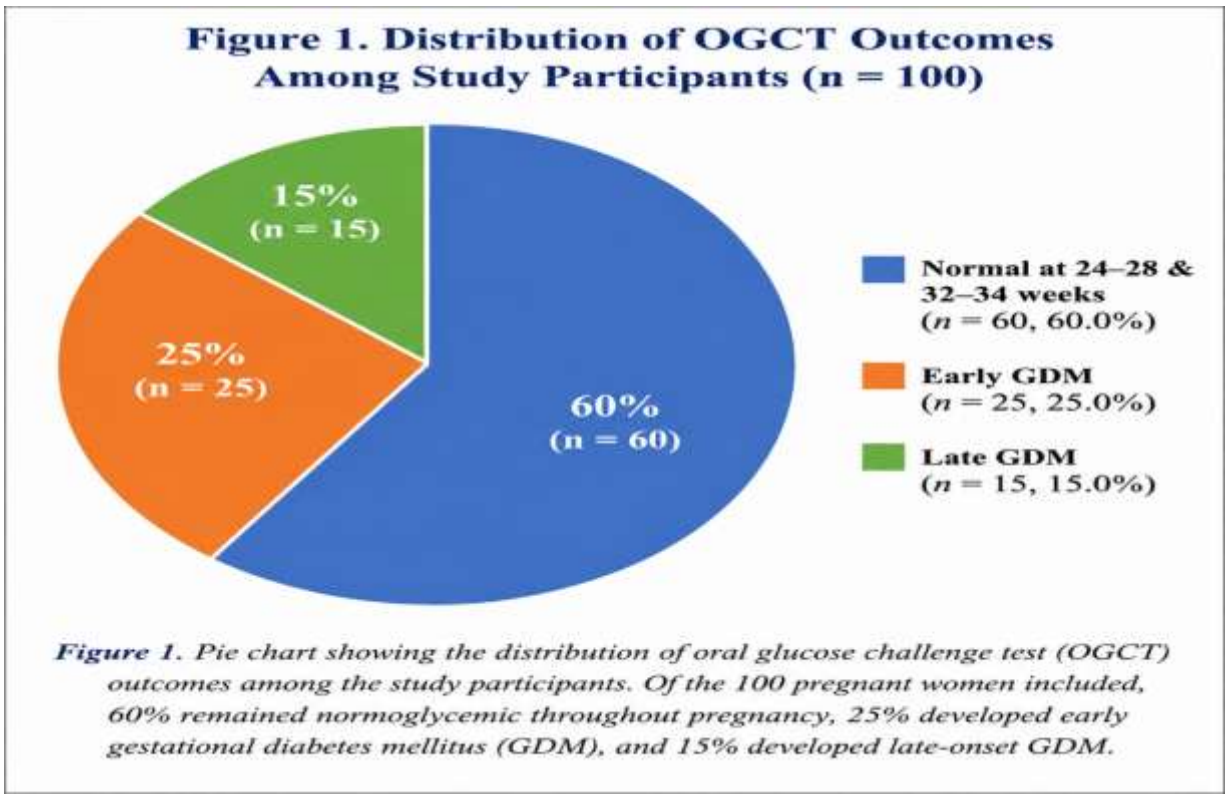


Figure 1. *Pie chart showing the distribution of oral glucose challenge test (OGCT) outcomes among the study participants. Of the 100 pregnant women included, 60% remained normoglycemic throughout pregnancy, 25% developed early gestational diabetes mellitus (GDM), and 15% developed late-onset GDM.*

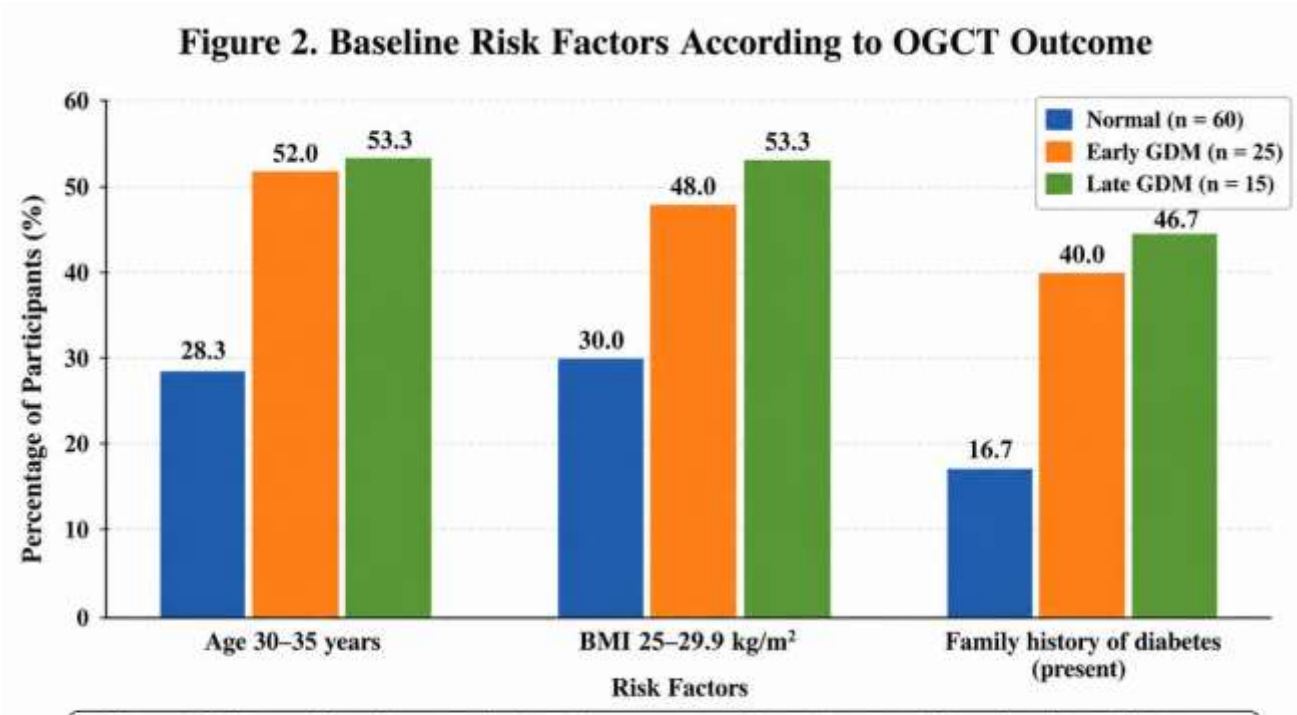


Figure 2. *Clustered bar diagram showing the percentage of participants with key baseline risk factors across OGCT outcome groups. A higher proportion of women in the Early and Late GDM groups had advanced maternal age (30–35 years), higher BMI (25–29.9 kg/m²), and a family history of diabetes compared to the Normal group.*

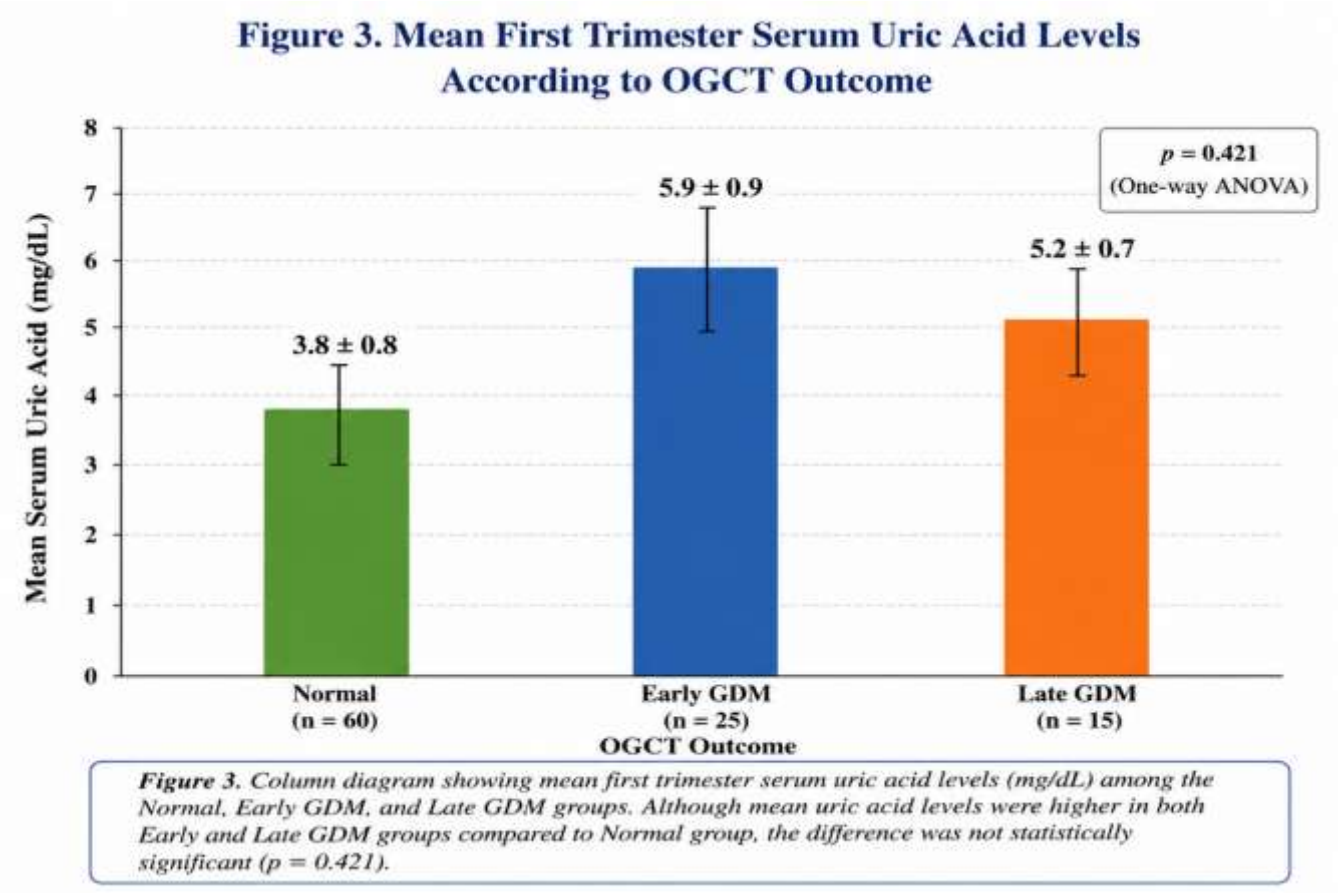
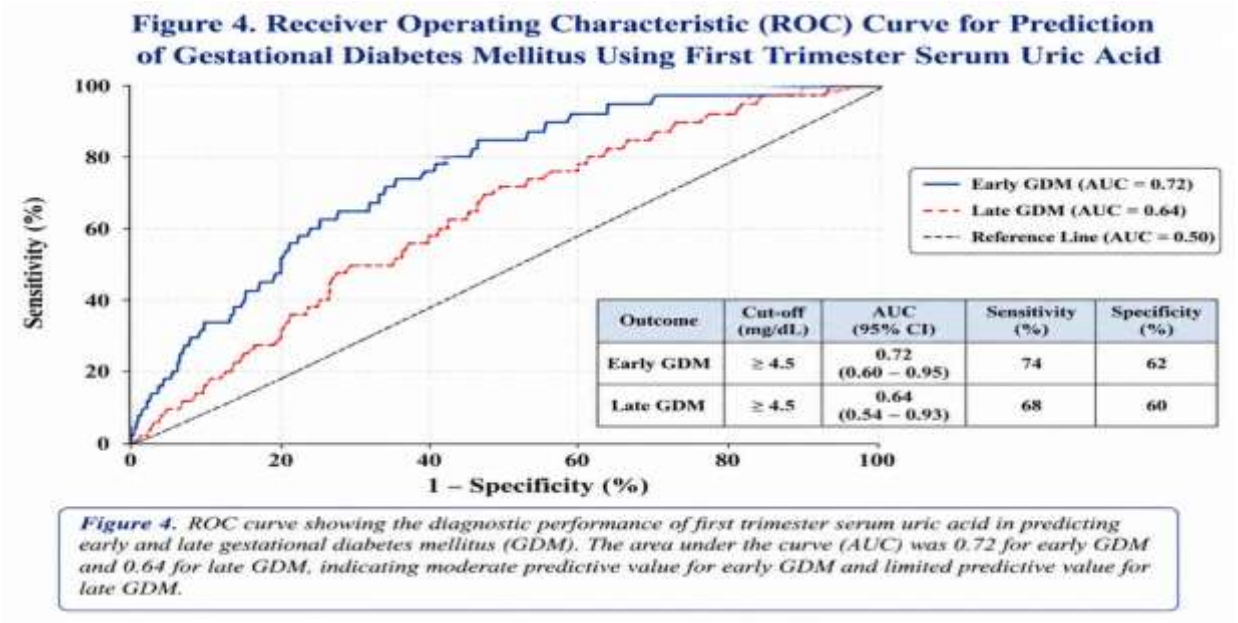


Figure 3. Column diagram showing mean first trimester serum uric acid levels (mg/dL) among the Normal, Early GDM, and Late GDM groups. Although mean uric acid levels were higher in both Early and Late GDM groups compared to Normal group, the difference was not statistically significant (p = 0.421).



Outcome	Cut-off (mg/dL)	AUC (95% CI)	Sensitivity (%)	Specificity (%)
Early GDM	≥ 4.5	0.72 (0.60 – 0.95)	74	62
Late GDM	≥ 4.5	0.64 (0.54 – 0.93)	68	60

Figure 4. ROC curve showing the diagnostic performance of first trimester serum uric acid in predicting early and late gestational diabetes mellitus (GDM). The area under the curve (AUC) was 0.72 for early GDM and 0.64 for late GDM, indicating moderate predictive value for early GDM and limited predictive value for late GDM.

DISCUSSION

The present prospective observational study evaluated the role of first-trimester serum uric acid in predicting gestational diabetes mellitus among 100 pregnant women attending a tertiary care hospital. Of the total participants, 25% developed early gestational diabetes mellitus and 15% developed late-onset gestational diabetes mellitus during follow-up, resulting in an overall incidence of 40%. Women who subsequently developed gestational diabetes mellitus were more likely to be older, overweight, and have a positive family history of diabetes mellitus. In addition, first-trimester serum uric acid levels were higher among women who developed gestational diabetes mellitus, and receiver operating characteristic analysis demonstrated moderate predictive ability for early gestational diabetes mellitus (AUC = 0.72).

In the present study, 25.0% of women developed early GDM and 15.0% developed late GDM, resulting in an overall GDM incidence of 40.0%. Yuan et al. reported that elevated maternal serum uric acid was significantly associated with

an increased risk of gestational diabetes mellitus in their systematic review and meta-analysis.[16] The findings of the present study are consistent with those of Yuan et al., supporting the role of elevated serum uric acid as an early predictor of GDM.

In the present study, the mean first-trimester serum uric acid level was 3.8 ± 0.8 mg/dL among normoglycaemic women, 5.9 ± 0.9 mg/dL among women with early GDM, and 5.2 ± 0.7 mg/dL among women with late GDM, indicating higher serum uric acid concentrations among women who subsequently developed GDM. Li et al. demonstrated a dose-dependent increase in GDM risk with rising maternal serum uric acid levels.[17] The present findings closely agree with those of Li et al., confirming that higher first-trimester serum uric acid is associated with an increased risk of gestational diabetes mellitus.

In the present study, women with GDM had higher serum uric acid concentrations than normoglycaemic women (5.9 ± 0.9 vs. 3.8 ± 0.8 mg/dL). Wolak et al. also observed significantly higher first-trimester serum uric acid levels among women who subsequently developed GDM.[18] This finding is similar to the present study and supports hyperuricaemia as an early marker of impaired glucose metabolism.

In the present study, elevated serum uric acid was associated with increased odds of gestational diabetes, with an odds ratio of 2.05 for early GDM and 3.25 for late GDM. Liu et al., in a cohort of 85,609 pregnant women, also reported that elevated early-pregnancy serum uric acid independently increased the risk of GDM.[19] The findings are comparable, indicating that elevated serum uric acid is an independent predictor of gestational diabetes mellitus.

In the present study, higher first-trimester serum uric acid levels preceded the diagnosis of gestational diabetes during follow-up. Amnioti et al. similarly demonstrated that elevated serum uric acid before pregnancy significantly predicted subsequent GDM.[20] The present findings support their conclusion that serum uric acid can be used for early identification of women at increased risk of gestational diabetes mellitus.

In the present study, 25.0% of women developed early gestational diabetes mellitus during OGTT at 24–28 weeks, while an additional 15.0% developed late-onset GDM during repeat screening, resulting in an overall GDM incidence of 40.0%. Sahin Aker et al. reported that women with elevated first-trimester serum uric acid had a significantly higher incidence of gestational diabetes during pregnancy.[21] The findings of the present study are comparable with those of Sahin Aker et al., indicating that elevated serum uric acid is associated with an increased risk of subsequent GDM.

In the present study, women with serum uric acid ≥4.5 mg/dL were more frequently observed among the early GDM (24.0%) and late GDM (33.3%) groups than among normoglycaemic women (13.3%), suggesting an increasing trend of hyperuricaemia among women who developed GDM. Amalraj et al. similarly demonstrated that hyperuricaemia during early pregnancy significantly increased the risk of gestational diabetes mellitus and hypertensive disorders of pregnancy.[22] The findings of the present study are in agreement with those of Amalraj et al., supporting serum uric acid as an early metabolic marker of GDM.

In the present study, the mean first-trimester serum uric acid level was 5.9 ± 0.9 mg/dL among women with early GDM compared with 3.8 ± 0.8 mg/dL among normoglycaemic women, indicating higher serum uric acid concentrations in women who subsequently developed GDM. Liang et al. reported that elevated first-trimester serum uric acid independently predicted gestational diabetes mellitus even after adjustment for maternal risk factors.[23] The present findings are similar to those of Liang et al., confirming that higher first-trimester serum uric acid levels are associated with subsequent development of GDM.

In the present study, women with elevated serum uric acid had increased odds of developing gestational diabetes, with an odds ratio of 2.05 for early GDM and 3.25 for late GDM. Jiang et al. demonstrated that elevated early-pregnancy serum uric acid significantly increased the risk of gestational diabetes and adverse pregnancy outcomes.[24] The present findings are comparable with those of Jiang et al., indicating that hyperuricaemia is associated with an increased likelihood of GDM.

In the present study, higher first-trimester serum uric acid levels were observed among women who subsequently developed both early and late gestational diabetes compared with women who remained normoglycaemic. Huang et al. reported that elevated serum uric acid during early pregnancy was significantly associated with subsequent gestational diabetes in a prospective cohort study.[25] The findings of the present study are consistent with those of Huang et al., further supporting the usefulness of serum uric acid as an early predictor of gestational diabetes mellitus.

In the present study, women with elevated first-trimester serum uric acid had increased odds of developing gestational diabetes mellitus, with an odds ratio of 2.05 for early GDM and 3.25 for late GDM. Liu et al. conducted a systematic review and meta-analysis and concluded that elevated maternal serum uric acid was consistently associated with a significantly increased risk of gestational diabetes across different populations.[26] The findings of the present study are in agreement with those of Liu et al., confirming that elevated serum uric acid is associated with an increased likelihood of GDM.

In the present study, the mean first-trimester serum uric acid level was higher among women who developed early GDM (5.9 ± 0.9 mg/dL) and late GDM (5.2 ± 0.7 mg/dL) than among normoglycaemic women (3.8 ± 0.8 mg/dL). Gungor et al. similarly reported significantly higher serum uric acid concentrations in women with gestational diabetes compared with healthy pregnant women.[27] The present findings are comparable with those of Gungor et al., supporting the association between hyperuricaemia and abnormal glucose metabolism during pregnancy.

In the present study, women with serum uric acid concentrations ≥4.5 mg/dL were more frequently observed among the GDM groups than the normoglycaemic group, indicating a positive association between hyperuricaemia and gestational diabetes. Zhao et al. reported that elevated maternal serum uric acid significantly increased the risk of gestational diabetes

mellitus and adverse pregnancy outcomes in a large retrospective cohort study.[28] The findings of the present study are similar to those of Zhao et al., demonstrating that elevated serum uric acid is associated with increased susceptibility to GDM.

Although the present study primarily evaluated gestational diabetes mellitus, elevated serum uric acid levels were observed during the first trimester before the onset of clinical disease, suggesting that hyperuricaemia reflects early metabolic dysfunction during pregnancy. Rasika et al. demonstrated that serum uric acid is an early biochemical marker of placental dysfunction and adverse pregnancy outcomes, particularly pre-eclampsia.[29] Although their study focused on hypertensive disorders rather than GDM, both studies indicate that elevated serum uric acid serves as an early marker of pregnancy-related metabolic abnormalities.

In the present study, receiver operating characteristic analysis demonstrated that first-trimester serum uric acid predicted early gestational diabetes with a cut-off value of ≥4.5 mg/dL, a sensitivity of 74%, specificity of 62%, and an area under the curve of 0.72. For late GDM, the corresponding sensitivity, specificity and AUC were 68%, 60% and 0.64, respectively, indicating moderate diagnostic performance. Ozturk et al. also demonstrated that elevated first-trimester serum uric acid was significantly associated with subsequent development of gestational diabetes mellitus and concluded that serum uric acid could serve as an early screening biomarker.[30] The findings of the present study are consistent with those of Ozturk et al., supporting the clinical utility of first-trimester serum uric acid as a simple, inexpensive and readily available adjunctive marker for identifying pregnant women at increased risk of gestational diabetes mellitus.

CONCLUSION

The present prospective observational study demonstrated that elevated first-trimester serum uric acid levels were associated with an increased risk of subsequent gestational diabetes mellitus. Women who developed gestational diabetes had higher mean serum uric acid levels than those who remained normoglycaemic and were more likely to be older, overweight, and have a positive family history of diabetes. These findings highlight the contribution of established maternal risk factors in addition to biochemical markers in the development of gestational diabetes.

Although the association between hyperuricaemia and gestational diabetes did not reach statistical significance in all analyses, elevated serum uric acid showed moderate diagnostic performance in predicting early gestational diabetes, with a cut-off value of ≥4.5 mg/dL, sensitivity of 74%, specificity of 62%, and an area under the ROC curve of 0.72. These results suggest that first-trimester serum uric acid may serve as a useful adjunctive biomarker for identifying women at increased risk of gestational diabetes during early pregnancy.

Serum uric acid estimation is inexpensive, widely available, minimally invasive, and can be incorporated into routine antenatal investigations. When interpreted alongside maternal age, body mass index, and family history of diabetes, it may facilitate early risk stratification and closer antenatal surveillance. Larger multicentric prospective studies are warranted to validate optimal cut-off values and establish its role in routine screening protocols. Overall, first-trimester serum uric acid shows promise as an adjunctive early screening marker for gestational diabetes mellitus, particularly in resource-limited healthcare settings.

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