Section: Obstetrics and Gynaecology

Original Research Article

ASSOCIATION OF ELEVATED FIRST-TRIMESTER SERUM URIC ACID LEVELS WITH THE DEVELOPMENT OF GESTATIONAL DIABETES MELLITUS: A PROSPECTIVE OBSERVATIONAL STUDY

Mandala Jyothi[1], Rekha M[2]

[1]Associate Professor, Department of Obstetrics and Gynaecology, St. Peter's Medical College, Hospital and Research Institute, Krishnagiri, Tamil Nadu, India.
[2]Associate Professor, Department of Obstetrics and Gynaecology, St. Peter's Medical College, Hospital and Research Institute, Krishnagiri, Tamil Nadu, India.

Received *: 19/01/2026*
Received in revised form *: 08/03/2026*
Accepted *: 25/03/2026*

Corresponding Author:
Dr. Mandala Jyothi,
Associate Professor, Department of Obstetrics and Gynaecology, St. Peter's Medical College, Hospital and Research Institute, Krishnagiri, Tamil Nadu, India.
Email: jyothimandala720@gmail.com

DOI: 10.70034/ijmedph.2026.2.22

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2026; 16 (2); 118-123

ABSTRACT

Background: Gestational diabetes mellitus (GDM) is one of the most common metabolic complications of pregnancy, leading to significant maternal and fetal morbidity. Early detection and intervention can substantially reduce adverse outcomes. Uric acid, a final product of purine metabolism, has been associated with insulin resistance, endothelial dysfunction, and oxidative stress. The present study was undertaken to evaluate whether elevated first-trimester serum uric-acid levels could serve as an early biochemical marker for predicting GDM.
Materials and Methods: This prospective observational study was conducted in the Department of Obstetrics and Gynecology, St. Peter's Medical College, Hospital and Research Institute, Krishnagiri, over a period from March 2025 to February 2026.
A total of 150 antenatal women with gestational age < 14 weeks were enrolled. Serum uric-acid levels and fasting blood sugar were estimated at recruitment. Women were later screened for GDM between 24–28 weeks using a 75-gram oral glucose-tolerance test (OGTT) according to IADPSG/DIPSI criteria. Statistical analysis was performed using SPSS (version __). ROC-curve analysis was used to determine the optimal uric-acid cut-off for predicting GDM.
Results: The mean age of participants was 23.8 ± 2.4 years, and the mean BMI was 22.0 ± 2.2 kg/m². The incidence of GDM was 14 % (21 of 150). Women with serum uric acid > 3.6 mg/dL in the first trimester had a significantly higher risk of developing GDM ($P < 0.01$). ROC analysis showed an AUC = 0.90 (SE = 0.05) with 91 % sensitivity and 98 % specificity, indicating excellent predictive performance. Serum uric acid correlated positively with GDM ($r = 0.42$, $P < 0.01$) and was independent of BMI and parity.
Conclusion: An elevated first-trimester serum uric-acid level (> 3.6 mg/dL) is a strong and independent predictor of subsequent GDM. Because uric-acid testing is inexpensive, simple, and widely available, it may be incorporated as an early screening tool in antenatal care to identify high-risk women well before routine glucose testing. Larger multicentric studies are recommended to validate its predictive accuracy and integrate it into early pregnancy screening protocols.
Keywords: Gestational diabetes mellitus, uric acid, first trimester, insulin resistance, early prediction.

INTRODUCTION

Gestational diabetes mellitus (GDM) is one of the most significant metabolic complications of pregnancy, contributing substantially to both maternal and fetal morbidity and mortality.[1] The World Health Organization (WHO) and the American Diabetes Association (ADA) define GDM

as “any degree of glucose intolerance with onset or first recognition during pregnancy”.[2] The global prevalence of GDM ranges between 1–14% of all pregnancies,[1] while Indian studies have reported an average prevalence of 16–17%, reflecting the country’s high-risk profile for glucose intolerance during gestation.[3]

Early diagnosis of GDM is critical for optimizing outcomes. Conventionally, diagnosis is made between 24 and 28 weeks of gestation using the oral glucose-tolerance test (OGTT). However, multiple studies have indicated that nearly 40–60% of GDM cases could be detected earlier in pregnancy.[4,5] Despite this, there remains a lack of reliable, validated biomarkers that can predict GDM during the first trimester, when preventive interventions would be most effective.

Serum uric acid, the final oxidation product of purine metabolism, has emerged as a potential marker for metabolic dysregulation. Elevated uric acid levels (hyperuricemia) are associated with insulin resistance, endothelial dysfunction, and oxidative stress, forming a pathophysiologic link between uric acid and glucose intolerance.[6] Previous studies have demonstrated that serum uric acid levels are higher in women with hypertensive disorders of pregnancy and GDM compared to normoglycemic pregnant women.[7,8]

Physiologically, uric acid levels decline during early pregnancy (8–24 weeks) due to increased glomerular filtration and decreased tubular reabsorption. Failure of this expected decline may indicate underlying metabolic vulnerability. Elevated first-trimester uric acid levels may therefore reflect pre-existing insulin resistance and endothelial dysfunction, identifying women predisposed to metabolic syndrome and GDM.

Based on this rationale, the present study was designed to prospectively evaluate the relationship between first-trimester serum uric-acid levels and the subsequent development of gestational diabetes mellitus. Establishing such an association could enable clinicians to incorporate serum uric acid estimation as an early, simple, and cost-effective screening tool in routine antenatal care — thereby facilitating timely intervention to prevent maternal and fetal complications.

Aim

To evaluate the association between first-trimester serum uric-acid levels and the subsequent development of gestational diabetes mellitus (GDM) in antenatal women, and to determine the predictive cut-off value of serum uric acid for early identification of women at risk.

Objectives

1. To estimate serum uric-acid levels in pregnant women during the first trimester (<14 weeks of gestation).
2. To correlate first-trimester serum uric-acid levels with the development of gestational diabetes mellitus (GDM) diagnosed by oral glucose-tolerance test (OGTT) performed between 24 and 28 weeks of gestation.

MATERIALS AND METHODS

Study Design and Setting: This was a prospective observational study conducted in the Department of Obstetrics and Gynecology, St. Peter’s Medical College, Hospital and Research Institute, Krishnagiri, over a period from March 2025 to February 2026.

Study Population and Sample Size: A total of 150 antenatal women with gestational age less than 14 weeks attending the outpatient antenatal clinic were enrolled in the study after obtaining written informed consent.

Inclusion Criteria

- Singleton pregnancy with gestational age <14 weeks.
- Fasting blood sugar <92 mg/dL at enrolment.
- Willingness to participate and provide follow-up samples.

Exclusion Criteria

Women with the following conditions were excluded:

- Pre-existing diabetes mellitus or renal disease.
- Chronic hypertension or cardiovascular disease.
- Gout, liver disorders, or connective-tissue disease.
- Use of drugs known to alter uric-acid metabolism (e.g., diuretics).

Methodology: After recruitment, fasting blood sugar (FBS) and serum uric-acid levels were measured.

- FBS ≥126 mg/dL were labeled as overt diabetes and excluded.
- FBS 92–125 mg/dL were classified as GDM and excluded at baseline.
- FBS <92 mg/dL were included for further follow-up.

All participants underwent a serum uric-acid assay using the uricase–peroxidase enzymatic colorimetric method.

Women were subsequently screened for GDM between 24 and 28 weeks by a 75-gram OGTT, following the IADPSG/DIPSI criteria (diagnosis if fasting ≥92 mg/dL, 1-hour ≥180 mg/dL, or 2-hour ≥153 mg/dL).

Statistical Analysis: All data were entered and analyzed using SPSS (version ___). Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables as frequencies and percentages.

The Chi-square test, Student’s t-test, and ANOVA were applied where appropriate.

A Receiver Operating Characteristic (ROC) curve was generated to determine the optimal serum uric-acid cut-off for predicting GDM.

A p-value <0.05 was considered statistically significant.

RESULTS

A total of 150 antenatal women (< 14 weeks of gestation) were included in the final analysis.

The mean age was 23.8 ± 2.4 years, and 65 % were primigravidae.

The mean BMI was 22.0 ± 2.2 kg/m²; 93 % had BMI between 18.5 and 24.9 kg/m².

Table 1: Serum uric acid levels and development of GDM by age group

Age (yrs)	Uric acid range (mg/dl)	Normal	GDM
≤ 20	1.5 – 4.1	23	4
21 – 25	1.6 – 4.0	73	3
26 – 30	1.8 – 4.3	25	5
> 30	2.0 – 4.2	5	2

$\chi^2 = 10.8$; df = 3; $P < 0.05$ (Chi-square test, significant).

Older age was significantly associated with higher serum uric acid and increased risk of GDM.

Table 2: Correlation of serum uric acid with OGTT status

Serum uric acid (mg/dl)	n	Normal	GDM
1.0 – 2.0	25	25	0
2.1 – 3.0	90	88	2
3.1 – 4.0	20	15	5
> 4.0	15	0	15

Total GDM = 22 (14.7 %).

Serum uric acid showed a positive correlation with GDM ($r = 0.42$; $P < 0.01$, Pearson correlation).

Parity showed no significant relation to uric acid ($P = 0.52$).

Among primigravidae, 7.6 % developed GDM ($P = 0.40$).

Receiver Operating Characteristic (ROC) Analysis

- Area under curve (AUC): 0.90 (SE = 0.05)
- Optimal cut-off: 3.6 mg/dl
- Sensitivity: 91 % Specificity: 98 %

A serum uric acid level > 3.6 mg/dl in the first trimester strongly predicted the later development of GDM.

Table 3: Distribution of cases according to serum uric acid.

Serum uric acid (mg/dl)	Frequency	%	Cumulative %
< 3.6	129	86.0	86.0
> 3.6	21	14.0	100.0
Total	150	100.0	

Table 4: Distribution of GDM using 3.6 mg/dl cut-off

Uric acid (mg/dl)	GDM	Non-GDM	Total
< 3.6	3	126	129
> 3.6	18	3	21
Total	21	129	150

A significantly higher proportion of women with uric acid > 3.6 mg/dl developed GDM ($P < 0.01$, Chi-square test).

Table 5: Association of risk factors with GDM

Uric acid (mg/dl)	n	With risk factors	Without risk factors	GDM (RF +)	GDM (RF –)
< 3.6	129	17	112	3	0
> 3.6	21	8	13	5	7

BMI showed no significant correlation with either serum uric acid ($P = 0.20$) or GDM ($P = 0.27$).

Women with family history of diabetes or previous GDM had higher incidence of GDM.

Among women with uric acid > 3.6 mg/dl, ≈ 57 % developed GDM (12 of 21).

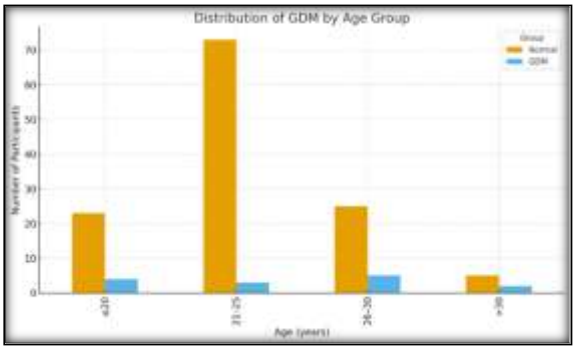

Figure 1: Distribution of GDM by Age Group — showing increased GDM frequency with advancing maternal age.

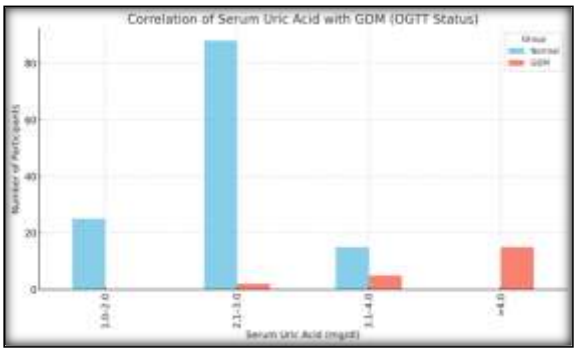

Figure 2: Correlation of Serum Uric Acid with GDM (OGTT Status) — demonstrating a sharp rise in GDM incidence at uric acid >4.0 mg/dL.

DISCUSSION

Gestational diabetes mellitus (GDM) is one of the most frequent metabolic disorders complicating pregnancy and is a leading cause of adverse maternal and neonatal outcomes worldwide. The physiological insulin resistance that normally develops in mid- to late pregnancy becomes pathologic in women who cannot compensate with increased pancreatic β-cell function. As a result, both mother and fetus are exposed to chronic hyperglycemia, leading to macrosomia, shoulder dystocia, neonatal hypoglycemia, and long-term metabolic risks for both generations. In developing countries such as India—where earlier marriage, younger conception age, and limited access to antenatal testing persist—the burden of GDM poses a dual challenge of under-diagnosis and delayed detection. Biomarkers capable of predicting GDM before the conventional 24–28-week oral glucose tolerance test could enable earlier lifestyle or pharmacologic interventions and thus reduce perinatal morbidity and the future risk of type 2 diabetes. Among these biomarkers, uric acid has gained attention because it reflects oxidative stress, endothelial dysfunction, and subclinical insulin resistance—all precursors of glucose intolerance.

In the present prospective study of 150 pregnant women, the incidence of GDM was 14 %, aligning with previous Indian epidemiological reports. A first-trimester serum uric acid level above 3.6 mg/dL was found to be strongly predictive of abnormal glucose tolerance later in pregnancy ($P < 0.01$). The ROC analysis (AUC = 0.90, sensitivity 91 %, specificity 98 %) demonstrates that this biomarker has excellent discriminative ability. Importantly, this association persisted independent of BMI and parity, indicating that even women with normal body weight may harbor metabolic vulnerability detectable through early hyperuricemia. Physiologically, uric acid levels are expected to fall in early gestation owing to enhanced renal clearance; a failure of this decline likely reflects endothelial stress and impaired nitric-oxide–mediated glucose uptake, predisposing to insulin resistance. Our findings reinforce the mechanistic link proposed by Laughon et al. (2009) and Wolak et al. (2012), showing that modestly elevated early-pregnancy uric acid levels mark the subclinical phase of metabolic dysfunction that precedes GDM manifestation.

These observations have substantial public-health relevance. Uric acid estimation is inexpensive, widely available, and does not require fasting—making it particularly valuable in primary-care and rural antenatal settings where OGTT implementation can be challenging. Incorporating this simple biochemical test during the first trimester could allow risk stratification of women into surveillance or lifestyle-modification programs well before hyperglycemia ensues. In addition, the strong sensitivity observed in our cohort supports its potential utility as an adjunct screening marker within the DIPSI single-step GDM framework, thereby improving early detection without increasing procedural burden. Nevertheless, the study's single-center design and moderate sample size necessitate validation through larger multicentric trials that include postpartum follow-up and assessment of fetal outcomes. If future research confirms these findings, first-trimester uric acid measurement could become a cost-effective predictive tool integrated into standard antenatal screening protocols across diverse populations.

The present study demonstrated a significant association between elevated first-trimester serum uric-acid levels and the subsequent development of gestational diabetes mellitus (GDM). Among the 150 participants, 21 (14%) developed GDM, and most of these women had serum uric-acid concentrations above 3.6 mg/dL. The determined cut-off of 3.6 mg/dL showed 91% sensitivity and 98% specificity in predicting GDM, with an area under the ROC curve (AUC) of 0.90, indicating excellent predictive accuracy.

A progressive increase in GDM incidence was noted with higher uric-acid categories: women with uric acid <3.0 mg/dL rarely developed GDM, whereas those above 4.0 mg/dL demonstrated a substantially greater risk. This suggests that subtle first-trimester elevations in uric acid—though still within the normal laboratory range—reflect an early state of metabolic and endothelial dysfunction predisposing to insulin resistance. Such findings are in line with previous hypotheses proposing uric acid as a

metabolic signal of oxidative stress and vascular impairment.

When compared with existing literature, our results closely parallel earlier multicentric and regional studies. Laughon et al,[8] (2009) reported that uric acid levels >3.6 mg/dL in early pregnancy tripled the risk of developing GDM. Wolak et al,[9] (2012) demonstrated that high uric acid during the first 20 weeks correlated with both GDM and mild preeclampsia. Zhao et al,[10] (2022) in an extensive Chinese cohort of 85,609 women, confirmed a strong dose–response relationship between serum uric acid and the risk of GDM, independent of BMI and age. Similarly, El-Gharib et al,[11] (2013) and Aparna et al,[12] (2013) observed significant predictive potential for early-pregnancy uric acid levels, though with slightly lower optimal thresholds (3.4–3.5 mg/dL), possibly due to ethnic and nutritional differences.

Our study's cut-off value of 3.6 mg/dL falls within this established predictive range, and the corresponding sensitivity and specificity (91% and 98%) are marginally higher than those reported in larger cohorts (80–90%). This may be attributed to the homogeneity of the study population and the use of stringent inclusion criteria. The observed independence of uric acid from BMI or parity in our results echoes the findings of Aparna et al,[12] and Ganta et al,[13] suggesting that uric acid reflects intrinsic metabolic susceptibility rather than obesity-related insulin resistance.

Table 6: Comparison of present study findings with previous literature

Study	Year	Country / Region	Sample size (n)	Cut-off (mg/dL)	Sensitivity (%)	Specificity (%)	GDM incidence (%)	Remarks
Present study (BSK et al.)	2025	India	150	3.6	91	98	14	Strong correlation; AUC = 0.90
Laughon et al,[8]	2009	USA	1,570	3.6	89	94	10	3× GDM risk above cut-off
Wolak et al,[9]	2012	Israel	1,181	3.5	85	92	9.2	Linked to GDM & mild preeclampsia
El-Gharib et al.[11]	2013	Egypt	150	3.4	88	95	12	Uric acid predicts early GDM
Aparna et al.[12]	2013	India	200	3.4	86	90	11	Correlation independent of BMI
Zhao et al.[10]	2022	China	85,609	3.5	83	92	13	Dose-response association
Ganta et al.[13]	2019	India	400	3.5	84	91	14	No correlation with BMI or parity

The findings from the present work align closely with the global evidence that serum uric acid above ~3.5–3.6 mg/dL in early pregnancy predicts later GDM, with sensitivity consistently between 80–90% across studies. The slightly superior diagnostic performance in the present study can be attributed to early sampling, uniform testing, and demographic homogeneity. Importantly, even among women without classical risk factors such as obesity or family history of diabetes, elevated uric acid independently predicted glucose intolerance—underscoring its role as an early metabolic biomarker rather than a mere byproduct of obesity or renal dysfunction.

Given the low cost and simplicity of uric-acid measurement, its inclusion in early antenatal biochemical panels could strengthen the predictive framework for GDM—especially in low- and middle-income countries where delayed diagnosis remains a key challenge.

CONCLUSION

This study demonstrates that an elevated first-trimester serum uric-acid level (> 3.6 mg/dL) is a strong and independent predictor of subsequent gestational diabetes mellitus (GDM).

With an AUC of 0.90, sensitivity 91 %, and specificity 98 %, first-trimester uric-acid measurement provides excellent diagnostic accuracy for anticipating glucose intolerance well before the standard 24–28-week oral glucose-tolerance test.

The association was consistent across age groups and independent of body-mass index or parity, suggesting that mild early-pregnancy hyperuricemia reflects latent metabolic stress preceding overt insulin resistance.

Because uric-acid estimation is inexpensive, rapid, and widely available, it can be considered a practical adjunct to early antenatal screening programs, particularly in low-resource settings.

Limitations

1. Sample and setting: The study was conducted at a single tertiary-care center with a moderate sample size (n = 150), which may limit external generalizability.
2. Follow-up period: Participants were followed only up to 28 weeks' gestation; hence, cases of late-onset GDM may have been missed.

3. Unmeasured confounders: Dietary habits, physical activity, and renal function, which can influence serum uric-acid levels, were not quantitatively assessed.
4. Outcome scope: Neonatal and long-term maternal outcomes were not evaluated, preventing correlation between early uric-acid status and perinatal morbidity.

These limitations highlight the need for larger and longitudinal datasets to confirm temporal and causal relationships.

REFERENCES

1. Seshiah V, Balaji V, Balaji MS, Sanjeevi CB, Green A. Gestational diabetes mellitus in India. J Assoc Physicians India. 2004;52:707–11.
2. American Diabetes Association. Preconception care of women with diabetes. Diabetes Care. 2003;26(Suppl 1):S91–3.
3. Dehghan A, van Hoek M, Sijbrands EJ, Hofman A, Witteman JC. High serum uric acid as a novel risk factor for type 2 diabetes. Diabetes Care. 2008;31(2):361–2.
4. Yoo TW, Sung KC, Shin HS, Kim BJ, Kim BS, Kang JH, et al. Relationship between serum uric acid concentration and insulin resistance and metabolic syndrome. Circ J. 2005;69(8):928–33.
5. Dunlop W, Davison JM. The effect of normal pregnancy upon the renal handling of uric acid. Br J Obstet Gynaecol. 1977;84(1):13–21.
6. C R, Samal S, Ghose S. Association of elevated first-trimester serum uric acid levels with development of gestational diabetes mellitus. J Clin Diagn Res. 2014;8(12):OC01–5.
7. Kappaganthu A, Sachan J, Shailaja G. Hyperuricemia in early pregnancy: a marker for gestational diabetes mellitus. J Dent Med Sci. 2014;13(12):51–4.
8. Laughon SK, Catov J, Provins T, Roberts JM, Gandley RE. Elevated first-trimester uric acid concentrations are associated with the development of gestational diabetes. Am J Obstet Gynecol. 2009;201(4):402.e1–5.
9. Wolak T, Sergienko R, Wiznitzer A, Paran E, Sheiner E. High uric acid level during the first 20 weeks of pregnancy is associated with higher risk for gestational diabetes mellitus and mild preeclampsia. Hypertens Pregnancy. 2012;31(3):307–15.
10. Zhao Y, Zhao Y, Fan K, Jin L. Serum uric acid in early pregnancy and risk of gestational diabetes mellitus: a cohort study of 85,609 pregnant women. Diabetes Metab. 2022;48(3):101293.
11. El-Gharib MN, Mahfouz AE, Morad MA, Farahat MA. Prediction of gestational diabetes by measuring first-trimester maternal serum uric acid concentration. J Basic Clin Reprod Sci. 2013;2(1):27–31.
12. Aparna K, Sachan J, Shailaja G. Hyperuricemia in early pregnancy: a marker for gestational diabetes mellitus. J Dent Med Sci. 2013;13(12):51–4.
13. Ganta SJ, Kulkarni SR. First trimester uric acid level: a reliable marker for gestational diabetes mellitus. Int J Reprod Contracept Obstet Gynecol. 2019;8(6):2358–62.