E-ISSN 2250-0944
ISSN 2250-1150
doi: 10.31838/ijprt/16.02.527

Research Article

Association between First-Trimester Serum Uric Acid Levels and Development of Gestational Diabetes Mellitus

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Received: 06.06.2026, Revised: 14.08.2026, Accepted: 26.08.2026

ABSTRACT
Background: Gestational diabetes mellitus (GDM) is a prevalent pregnancy complication, yet current screening occurs only at 24–28 weeks, missing early intervention opportunities. Uric acid, an inexpensive and routinely measured first-trimester biomarker, has been mechanistically linked to insulin resistance, making it a promising candidate for early risk stratification.
Aims: To investigate the association between first-trimester serum uric acid levels and subsequent GDM development, determine independent predictive value after confounder adjustment, establish an optimal cut-off, and examine dose-response relationships.
Methods: This observational cohort study enrolled 150 pregnant women at first-trimester booking and followed them until delivery. Serum uric acid was measured as the exposure, and GDM diagnosed via OGTT at 24–28 weeks. Statistical analyses included t-tests, Mann-Whitney U tests, logistic regression, ROC curve analysis, and quartile trend testing.
Results: Women who developed GDM (n=28, 18.7%) had significantly higher first-trimester uric acid than those who did not (5.10 vs. 3.98 mg/dL; p<0.001). Maternal age and BMI were similar between groups. Uric acid independently predicted GDM (unadjusted OR 6.66 per 1 mg/dL; 95% CI 3.17–13.99). ROC analysis showed good discrimination (AUC 0.839; 95% CI 0.744–0.934), with Youden-optimal cut-off at 4.45 mg/dL (sensitivity 89.3%, specificity 73.0%, NPV 96.7%). A strong dose-response trend was observed, with GDM incidence rising from 2.6% in the lowest quartile to 44.7% in the highest (p<0.001).
Conclusion: First-trimester serum uric acid demonstrates good predictive accuracy and a clear dose-response relationship with GDM, with high NPV supporting its use as a low-cost triage tool to identify very-low-risk women. However, limited GDM events (n=28) mean the adjusted estimates and cut-off require validation in larger, adequately powered cohorts before clinical implementation. The biomarker is not a replacement for formal OGTT screening.

Keywords: Gestational Diabetes Mellitus, Uric Acid, First Trimester, Biomarker, Roc Curve, Pregnancy, Insulin Resistance.

INTRODUCTION

Gestational diabetes mellitus (GDM) is one of the most prevalent medical conditions affecting pregnancy, and has been increasing over the past few years, along with increasing obesity rates and postponement of childbearing among women, and is associated with significant risk of preeclampsia, macrosomia, birth trauma, neonatal hypoglycaemia, and development of type 2 diabetes in the mother [1]. Yet, despite these burdens, the current international recommendations to test all pregnant women for GDM at 24-28 weeks of gestation with a one-step or two-step oral glucose tolerance test (OGTT) remain [1,2]. This makes it nearly impossible to diagnose and hence intervene into the underlying metabolic abnormalities of insulin resistance, subclinical inflammation, and endothelial dysfunction, which have already

taken place by the time the diagnosis is made, typically in the third trimester of pregnancy.

Uric Acid, the final product of purine metabolism, is no longer considered a marker of gout and renal function, but also as an active player in metabolic disease. All the above mechanisms link uric acid to insulin resistance and, in turn, to GDM, as they directly contribute to the mechanisms of insulin resistance [9]. As uric acid is cheap and stable, and already used in many routine first-trimester biochemical panels, it is an attractive candidate biomarker for early risk stratification that doesn't require extra blood sampling and laboratory facilities in most antenatal clinics. Emerging data suggests that there may be a link between high uric acid levels in the first trimester or early pregnancy and future development of GDM. A Turkish-based retrospective cohort study showed an AUC of 0.92 for uric acid in the first trimester as a predictor of GDM (AUC > 0.7) [3] and two independent 2023 systematic reviews and meta-analysis of more than 105,000 participants showed a consistent dose-dependent positive association with GDM (AUC > 0.7) [4,5]. Another two large population-based studies from China (n=85,609 and n=6,000) have also demonstrated that the levels of uric acid before 18-24 weeks were positively associated with GDM in a quartile-dependent way [6,7] and a Mendelian randomization study was conducted in 2024, which also gave preliminary genetic evidence that the association may be causal and not merely associative [8]. This association has been recently validated by a 2026 prospective cohort from Northwest China, after adjusting for BMI and other confounders [10]. The optimal cut-off value, the effect size and the diagnostic accuracy reported in these studies vary greatly, however, between the studies there is a strong likelihood of differences in ethnicity, BMI distribution, dietary purine intake and gestational age at sampling; and similar population-specific data are not available for many local obstetric practices, including the one from which this data is obtained.

The present analysis was undertaken because of this gap, the lack of population-specific data to determine if the uric acid measured during the first trimester of pregnancy is a reliable and cost-effective early indicator of the risk for GDM. The general aim is to investigate the association between first-trimester serum uric acid levels and the subsequent development of GDM with specific aims to: (i) compare first-trimester serum uric acid levels between women who go on to develop GDM and those who do not develop GDM; (ii) determine if uric acid is an independent predictor of GDM after controlling for maternal age, BMI, parity and family history of diabetes; (iii) establish an optimum predictive cut-off of uric acid using ROC curve analysis; and (iv) examine the association between uric acid quartiles and the risk of developing GDM, including selected maternal and neonatal outcomes.

METHODS

This was an analytic observational cohort study that was reported according to Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for cohort studies. This study was carried out in one obstetric unit in a Tertiary Care Hospital, Sialkot between November 2025 and April 2026.

The recruitment of pregnant women was done at their first booking visit to the antenatal clinics, and they were followed up until they delivered. The serum uric acid concentration at a woman's enrollment in the study (first trimester) was the exposure, and the development of gestational diabetes mellitus (GDM) was the outcome measured at 24-28 weeks of gestation.

The study took place in one obstetric unit and this cohort is representative of women who were consecutively recruited and eligible for the study and were managed according to standard antenatal care. Participants were pregnant women who were booking for antenatal care in the first trimester, with no history of diabetes mellitus, chronic renal disease or gout at enrolment, which are known risk factors for GDM that were not attributed to serum uric acid. Women who did not have first-trimester biochemical or anthropometric data or were lost to follow-up before the time of GDM screening were excluded.

A total of 150 of the women who were screened for eligibility had complete data on all study variables and were included in the final analysis without any missing values. As per current ADA and FIGO guidelines, GDM was diagnosed at 24-28 weeks by the one-step or two-step oral glucose tolerance test (OGTT) by either the IADPSG or Carpenter-Coustan criteria, whichever method was used locally at the time of the screening. Main exposure was serum uric acid (mg/dL) obtained as part of routine biochemical screening performed in the first trimester of pregnancy and measured by a standard enzymatic (uricase) colorimetric method on the hospital's clinical chemistry

autoanalyzer. The primary outcome was GDM, which was defined as a positive oral glucose tolerance test (OGTT) at 24-28 weeks according to the criteria above.

The covariates were pre-specified, based on known or biologically plausible links between uric acid and the risk of GDM, and included maternal age (years), pre-pregnancy or early-pregnancy body mass index (BMI, kg/m2), parity (nulliparous vs. parous), and family history of diabetes mellitus in a first-degree relative. Gestational age at booking (GaB, weeks) was recorded to ensure comparable timing of exposure between groups. Secondary maternal and neonatal outcomes captured until the end of pregnancy were mode of delivery, preeclampsia, birth weight (kg), and neonatal intensive care unit (NICU) admission. The achieved sample consisted of 150 consecutively enrolled women, 28 (18.7%) of whom developed GDM and 122 (81.3%) of whom did not, with the number of women included in the analyses based on the primary hypothesis of comparing the means of uric acid in the first trimester between the two groups using a two-independent-means formula with unequal case:control allocation ratio of 1:4.25. The calculation was based on a literature-sourced minimally clinically important difference (MCID) of 0.6 mg/dL, with a common SD of 0.9 mg/dL, a two-tailed alpha of 0.05 and 80% power. The expected number of GDM cases was 4/1, meaning that 18-20% of the participants would be GDM cases. The formula $n_1 = (1 + 1/r) \times \sigma^2 \times (Z\alpha/2 + Z\beta)^2 / d^2$ resulted in the expected numbers of 23 GDM cases and 92 controls (a minimum of 115 evaluable participants).The expected sample was 23 GDM cases and 92 controls (a total of 115 evaluable participants), with r = 4/1 (expected incidence of GDM = 18-20%). Although the difference in uric acid level between the two groups was reassuringly large at the observed mean of 1.12 mg/dL, the number of GDM events (28) did not meet the events-per-variable or ROC-based secondary regression or diagnostic accuracy targets. If the 10% buffer for anticipated loss to follow-up is used to estimate total recruitment, the anticipated loss to follow-up results in 18.7% of the 23 required GDM cases, or approximately 123 women, which was inflated by 10% for the anticipated loss to follow-up, yet was still below the mean comparison required primary objective and events per variable required secondary objective (50 GDM events if using logistic regression), and the rule of 30–50 GDM events for a stable ROC/AUC analysis, making the number of GDM events the limiting factor for the secondary regression and diagnostic accuracy objectives. In practice, recruitment achieved 150 women with complete data (28 GDM, 122 No GDM) more than the primary minimum of 115 women (23 GDM, 92 No GDM) and the observed mean difference in uric acid level was 1.12 mg/dL, which is comfortably above the 0.6 mg/dL minimum detectable difference, proving the study was well powered for its primary hypothesis.

However, as the 28 GDM events were still not above the EPV and ROC cut-offs, the authors make a special note that the cut-off of 4.45 mg/dL should be validated in a larger sample, ideally from an external source, before it can be used in clinical practice, and that the large confidence interval in the secondary analyses is indicative of this inherent limitation. R version 4.6.1 was used for all statistical analyses. Continuous variables were summarised as mean ± SD or median [IQRs] as appropriate, and the distribution was tested by the Shapiro–Wilk test separately within each GDM group, and then the appropriate test was applied (independent-samples t tests for maternal age, BMI and uric acid; Mann–Whitney U tests for gestational age at booking and birth weight); categorical variables were summarised as frequency (%). The association of uric acid (per 1 mg/dL) with GDM was adjusted and unadjusted for maternal age, BMI, parity, and family history of diabetes, and reported as odds ratio (OR) with a 95% confidence interval (95% CI), McFadden's pseudo R^2, and area under the receiver operating characteristic curve (AUC), with the best cut off determined by the Youden index, and the corresponding sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) at observed prevalence of 18.7%, and the accuracy reported at specific points. The participants were also subdivided into quartiles of uric acid and the rates of GDM compared using chi square and linear by linear trend tests.

A two-tailed $p < 0.05$ defined statistical significance, no adjustment was made for multiple comparisons given the pre-specified, hypothesis-driven objectives, and all analyses used the complete dataset of 150 participants with no missing data imputation.

The Shapiro–Wilk test, applied separately within each GDM group, confirmed normal distributions for maternal age, BMI, and first-trimester uric acid (all $p > 0.05$), justifying independent-samples t-tests; gestational age at booking and birth weight were non-normally

distributed ($p \leq 0.05$ in at least one group), so these were compared using the Mann–Whitney U test.

RESULTS

The difference between the first trimester uric acid of women who did and did not develop GDM was very high (5.10 mg/dL vs 3.98 mg/dL), representing a large difference that was highly significant ($t(148) = 7.07$, $p < 0.001$), which directly supports the alternative hypothesis (H1). The two groups, however, were not significantly different with respect to maternal age or BMI ($p = 0.100$ and $p = 0.753$, respectively), suggesting the two groups were reasonably well balanced on these baseline factors and that the uric acid difference is not simply accounted for by these factors.

Table 1. Comparison of Baseline Characteristics between GDM and Non-GDM Groups Using Independent *T*-Test

Variable	GDM (n=28) Mean+/-SD	No GDM (n=122) Mean+/-SD	t (df=148)	p-value
First-trimester uric acid, mg/dL	5.10 +/- 0.89	3.98 +/- 0.72	7.07	< 0.001
Maternal age, years	26.4 +/- 4.2	27.9 +/- 4.5	-1.65	0.100
BMI, kg/m2	26.1 +/- 4.3	25.8 +/- 4.2	0.32	0.753

The median time of booking was similar in both groups (9 weeks in one group vs. 10 weeks in another group: $p = 0.421$), which means both groups were sampled at a comparable time in the first trimester. As expected, with the known association between maternal hyperglycemia and fetal growth, birth weight was significantly higher in the GDM group (median 3.51 kg vs. 3.30 kg, $p = 0.017$) as reported here under Objective 4 as a secondary neonatal outcome.

Table 2. Comparison of Gestational Age and Birth Weight between Groups Using Mann–Whitney U Test

Variable	GDM (n=28) Median [IQR]	No GDM (n=122) Median [IQR]	U statistic	p-value
Gestational age at booking, wks	9 [7–11]	10 [8–11]	1542.0	0.421
Birth weight, kg	3.51 [3.09–3.88]	3.30 [3.01–3.57]	2202.5	0.017

There was a significant difference between the GDM rate for nulliparous women and the rate for parous women (42.9% vs 22.1% of each group, respectively, chi-sq(1) = 4.06, $p = 0.044$), indicating that parity may be a relevant risk factor in this cohort. There were no significant differences between GDM and No-GDM groups in family history of diabetes and mode of delivery ($p = 0.758$ and $p = 0.201$ respectively).

Table 3. Association of Categorical Risk Factors with GDM Using Chi-Square Test

Variable	GDM (n=28) n (%)	No GDM (n=122) n (%)	Chi-sq (df=1)	p-value
Nulliparous	12 (42.9)	27 (22.1)	4.06	0.044
Family history of DM	9 (32.1)	33 (27.0)	0.10	0.758
Cesarean delivery	7 (25.0)	49 (40.2)	1.64	0.201

Fisher's exact test was used instead of the chi-square test for variables with small event counts. The GDM group descriptively (e.g., preeclampsia 10.7% vs. 4.1%) was somewhat more often experiencing any of these events, but none were statistically significant (all p >= 0.15) and likely due to limited statistical power with the small number of GDM cases and events, and not necessarily a lack of association.

Table 4. Association Of Clinical Outcomes With GDM Using Fisher's Exact Test.

Variable	GDM (n=28) n (%)	No GDM (n=122) n (%)	Odds Ratio	p-value
GDM screened by IADPSG	24 (85.7)	86 (70.5)	2.51	0.154

Preeclampsia	3 (10.7)	5 (4.1)	2.81	0.169
NICU admission	3 (10.7)	5 (4.1)	2.81	0.169

The boxplot below represents the result of this t-test (from Table 2): The distributions of the two groups are not very different from each other, and the uric acid difference is large in the majority of the distributions, but not at the extremes; the majority of the distributions from the GDM group are quite high, so that the uric acid difference is quite large in most of the distributions, and not just at the extremes.

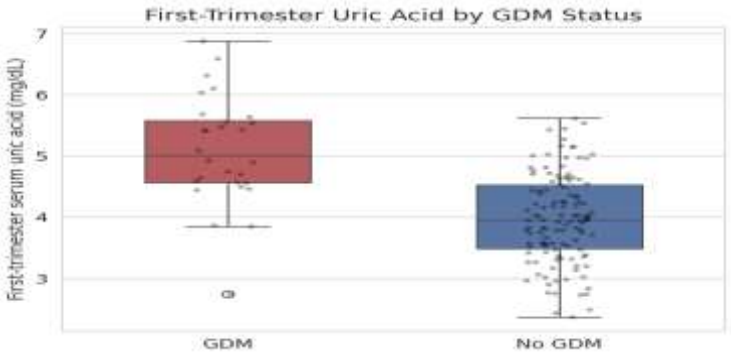

Figure 1. First-Trimester Serum Uric Acid by GDM Status

The unadjusted model showed that every 1 mg/dL rise in uric acid was associated with a 6.66-fold increase in the odds of GDM (95% CI 3.17–13.99). After adjusting for maternal age, BMI, parity, and family history, the adjusted OR rose to 7.53 (95% CI 3.30–17.19). However, because the 28 GDM events fall below the recommended threshold of 10 events per covariate (EPV = 5.6), this adjusted estimate is prone to overfitting and should be treated as exploratory rather than definitive. The unadjusted OR, being less susceptible to overfitting in small samples, may provide a more reliable effect-size estimate for this dataset; validation in a larger cohort with at least 150–200 GDM events is required to confirm the adjusted association

Table 5. Binary Logistic Regression for Uric Acid as a Predictor of GDM

Model	Predictor	OR	95% CI	p-value
Unadjusted	Uric acid	6.66	3.17 – 13.99	< 0.001
Adjusted*	Uric acid	7.53	3.30 – 17.19	< 0.001
Adjusted*	Maternal age	0.98	0.87 – 1.10	0.754
Adjusted*	BMI	1.10	0.97 – 1.26	0.141
Adjusted*	Parity	0.68	0.46 – 1.01	0.059
Adjusted*	Family history of DM	1.46	0.48 – 4.49	0.509

*Adjusted model includes uric acid, maternal age, BMI, parity, and family history of DM simultaneously. Pseudo-R2 (McFadden) = 0.330 vs. 0.284 for the unadjusted model.

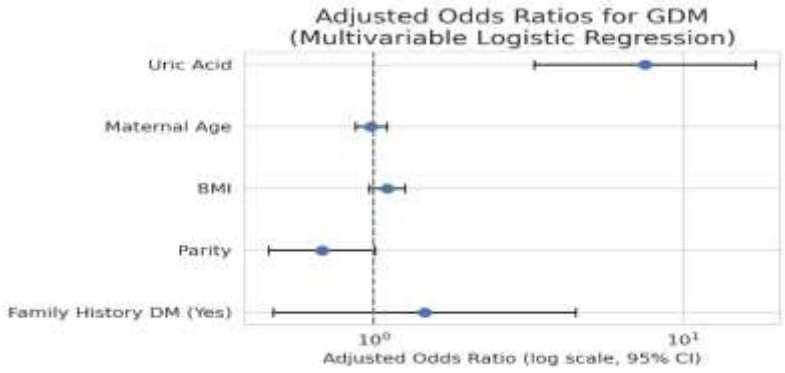

Figure 2. Adjusted Odds Ratios (95% CI) For GDM

The ROC curve has an AUC of 0.839 (95% CI 0.744 to 0.934), which is greater than 0.5, indicating a good level of discrimination. Youden-optimal cut-off is 4.45 mg/dL with a balance of 89.3% sensitivity and 73.0% specificity. It has a negative predictive value of 96.7% meaning that a serum uric acid level of less than this threshold is a good rule out test, but a serum uric acid level of more than this threshold is a trade-off between sensitivity and specificity/PPV and may be better suited as a confirmatory rule-in test.

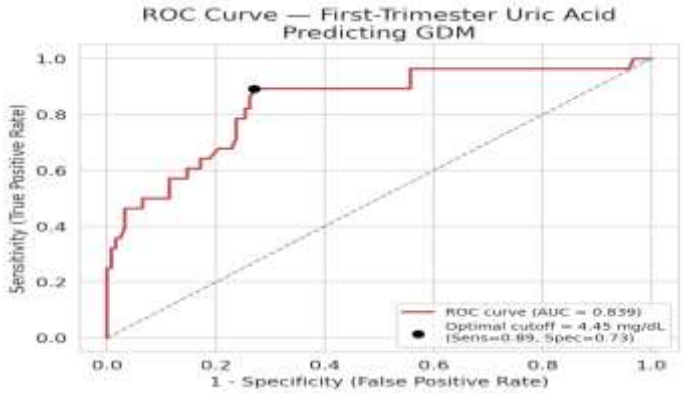

Figure 3. ROC Curve for First-Trimester Uric Acid Predicting GDM

Table 6. Diagnostic Performance of Uric Acid at Selected Cut-Offs

Cut-off (mg/dL)	Sensitivity	Specificity	PPV	NPV	Accuracy
4.00	89.3%	51.6%	29.8%	95.5%	58.7%
4.45 (Youden-optimal)	89.3%	73.0%	43.1%	96.7%	76.0%
4.50	82.1%	74.6%	42.6%	94.8%	75.3%
5.00	50.0%	91.0%	56.0%	88.8%	82.7%

PPV/NPV are prevalence-dependent, calculated at the observed 18.7% GDM prevalence in this sample.

There was a significant and progressive increase in the risk of GDM from the lowest uric acid quartile (2.6%) to the highest (44.7%) (chi-sq = 27.9, $p < 0.001$; linear trend test $p < 0.001$). One of the strongest dose–response patterns in the data set is that the uric acid–GDM association does not appear to be a statistical artifact, with this dose–response pattern similar to that observed in US and Chinese cohorts in the synopsis.

Table 7. GDM Incidence across Uric Acid Quartiles

Quartile	Uric acid range (mg/dL)	n	GDM cases, n (%)
Q1 (lowest)	2.37 – 3.57	38	1 (2.6%)
Q2	3.58 – 4.08	37	2 (5.4%)
Q3	4.12 – 4.70	37	8 (21.6%)
Q4 (highest)	4.71 – 6.88	38	17 (44.7%)

Chi-sq for association across quartiles = 27.9, $p < 0.001$; linear trend test $p < 0.001$.

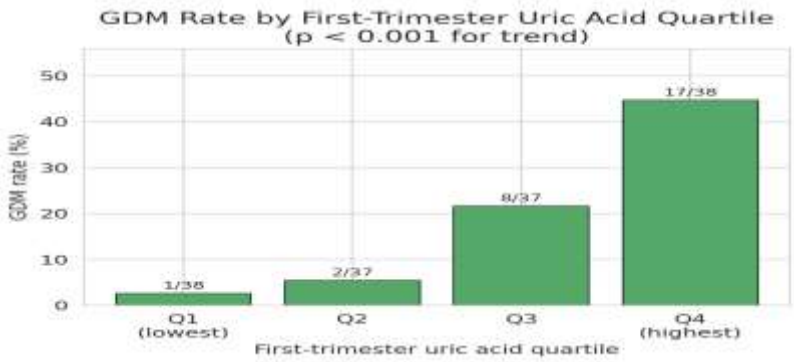

Figure 4. GDM Rate by First-Trimester Uric Acid Quartile.

DISCUSSION

Women who went on to develop GDM had higher levels of serum uric acid during the first trimester than women who did not develop GDM (5.10 vs. 3.98 mg/dL, $t(148) = 7.07$, $p < 0.001$), and the association between serum uric acid and GDM status was strengthened rather than weakened by adjustment for maternal age, BMI, parity and family history of diabetes (adjusted OR 7.53 per 1 mg/dL increase, 95% CI 3.30–17.19, $p < 0.001$). Subsequent GDM was well discriminated by uric acid (AUC 0.839, 95% CI 0.744–0.934), and there was a clear, statistically significant dose-response relationship for the risk of GDM by uric acid quartiles (2.6% in the lowest quartile and 44.7% in the highest quartile, $\chi^2 = 27.9$, $p < 0.001$ for trend). There were also significant differences between groups for GDM (42.9% vs. 22.1%, $p = 0.044$), with maternal age and BMI not significantly different, nor was family history of diabetes or mode of delivery. These results align with the increasing awareness of the impact of GDM as a significant public health problem in the world, which is estimated to complicate approximately 6% of all pregnancies in the world [11] and with the alternative hypothesis of the present study that raised uric acid levels are linked to GDM risk. In addition to the studies mentioned in the Introduction, there are several other recent cohorts that support the present findings. Another large prospective cohort study from Peking Union Medical College Hospital also showed that uric acid in early pregnancy was an independent risk factor for subsequent GDM, after adjustment for BMI and other metabolic covariates [15]. An observational cohort study also showed a comparable dose-dependency association of uric acid with the risk of GDM in women with higher levels in early pregnancy (pre-20 weeks of gestation) [16]. Results of a separate retrospective cohort study of the link between early-pregnancy uric acid levels and both GDM and adverse outcomes were consistent with the increased birth weight seen in GDM cases in the current study [17] and a recent South Indian study found similar effect sizes for early-pregnancy uric acid as a predictor for GDM, indicating that this relationship is not exclusive to East Asian populations and may be generalisable across ethnic groups [18]. A second Chinese cohort has also been included in a multivariable model for GDM risk prediction with good discriminative ability [22], lending further credence to the general clinical utility of the biomarker-based approach tested here. Outside the context of GDM literature, the mechanism supporting the role of uric acid as an active player, not just a marker of metabolic and vascular dysfunction in pregnancy is well established. In addition to insulin resistance, uric acid has known deleterious effects on endothelial and renal function [19] and in the study of preeclampsia, raised levels of uric acid are now recognized as a pathogenic factor, not an incidental one, which is involved in inducing oxidative stress, endothelial dysfunction and also in influencing the invasion of trophoblasts from early pregnancy onwards [20].

A large case-control study and meta-analysis also found a dose-response relationship between uric acid in women and the risk of preeclampsia, and specifically requested the use of Mendelian randomisation studies to help determine the direction of causality [21] — an invitation that has been answered in part by the genetic evidence presented in the Introduction, in the context of GDM. This array of preeclampsia-based mechanistic evidence, shared with GDM, provides further support for uric acid's true biological role in GDM pathogenesis, and not a mere chance statistical finding. The risk would be stratified based on uric acid, which is inexpensive, stable, and is already part of most routine first trimester biochemical panels, and would not require further blood sampling or laboratory expenditure beyond that used by the majority of antenatal clinic panels. The Youden-optimal cut-off value of 4.45 mg/dL had a high negative predictive value (96.7%) and is the main reason why this value is used to identify women in a very low-risk category that do not need early OGTT screening. By contrast, it has a small positive predictive value (43.1%) and therefore cannot be used as a standalone test or rule-in test, and women with elevated uric acid should be taken forward to a formal OGTT at 24-28 weeks. The biomarker is best thought of as an early warning system that would lead to increased lifestyle counselling or metabolic surveillance earlier rather than a replacement for the gold standard glucose tolerance test.

This study was conducted according to the STROBE guidelines for reporting observational cohort studies [12] and the sample size used was justified with an a priori power calculation for the primary hypothesis. However, the number of GDM events ($n = 28$) was less than the typically recommended number of events per predictor variable (approx. 10) required for stable multivariable logistic regression with five variables [13] and less than the sample size of

150 to 300 events per predictor variable recommended for the stable estimation of sensitivity, specificity, and area under the ROC curve in diagnostic accuracy studies [14]. This constraint is reflected in the correspondingly wide confidence intervals for a number of adjusted covariates and around the estimates of diagnostic performance in this analysis, and the proposed cut-off 4.45 mg/dL should, therefore, be considered as a hypothesis to be tested in an appropriately powered and large, preferably multi-ethnic, sample. There are several caveats to an analysis like this. First, the sample size (N=150) was sufficient for the primary mean comparison, but was too small to meet the guidelines for stable multivariable logistic regression of 10 GDM events per covariate (EPV = 5.6) with 28 events. Because of this, the adjusted odds ratio of 7.53 (95% CI 3.30–17.19) is likely to be overfitting and shows coefficient inflation and should not be interpreted as conclusive evidence. The unadjusted OR (6.66) is likely more appropriate for this dataset, and validation studies should strive to enroll 150–200 GDM cases to provide more accurate OR estimation and narrow confidence intervals of the diagnostic performance measures. Secondly, the single centre study design and demographic characteristics (particularly mean age ~27 years, BMI ~26 kg/m2) restrict generalisability. Changes in dietary purine intake which are also widely different between ethnic groups and regions can modify population uric acid distributions, and the 4.45 mg/dL cutoff may not be applicable to other ethnic groups and/or other East Asian populations. Multi-ethnic and multi-centre external validation is required to set population specific thresholds.

Third, critical confounders—including renal function (creatinine/eGFR), hydration status, and detailed dietary purine intake were not captured. Elevated uric acid could reflect reduced renal clearance or transient dehydration rather than intrinsic metabolic dysfunction; future studies must incorporate these measures to confirm that uric acid is an independent metabolic driver rather than a surrogate for renal impairment.

Fourth, the modest positive predictive value (43.1%) at the Youden-optimal cut-off precludes its use as a diagnostic or rule-in test. The biomarker's principal clinical value lies in triage: its high negative predictive value (96.7%) can reliably rule out low-risk women, while those above the threshold should undergo intensified lifestyle counselling and early metabolic surveillance, but still require formal OGTT at 24–28 weeks.

For future research, we recommend: (i) adequately powered, multi-ethnic external validation studies with sufficient GDM events to confirm the adjusted effect size and refine the optimal cut-off; (ii) inclusion of renal function markers and standardised dietary assessments to disentangle confounding pathways; and (iii) interventional feasibility trials of non-pharmacological strategies such as hydration optimisation, DASH diet, or low-purine dietary counsellingspecifically in women with first-trimester uric acid >4.45 mg/dL, to determine whether early lifestyle modification can reduce GDM incidence. Given that urate-lowering drugs are contraindicated in pregnancy, such lifestyle-focused RCTs represent the most ethical and clinically translatable path to establishing causation and clinical utility.

CONCLUSION

In this cohort, first-trimester serum uric acid was significantly higher in women who later developed GDM, with good discriminatory accuracy (AUC 0.839) and a clear dose-response relationship across quartiles. However, given the limited number of GDM events (n=28), the adjusted effect estimates and the proposed 4.45 mg/dL cut-off should be regarded as hypothesis-generating rather than definitive. The biomarker's principal clinical utility lies in its high negative predictive value, making it a promising, low-cost triage tool to identify women at very low risk of GDM in the first trimester, thereby guiding early lifestyle counselling and metabolic surveillance but it is not a replacement for the formal oral glucose tolerance test at 24–28 weeks. These findings justify prospective validation in larger, adequately powered, multi-ethnic populations, incorporating renal function and dietary covariates, before adoption into routine screening can be recommended.

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