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Original Research Article

Association of maternal serum uric acid levels with gestational diabetes mellitus: a hospital-based case-control study

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ABSTRACT

Background: Gestational diabetes mellitus is a common metabolic complication of pregnancy. Serum uric acid has been investigated as an inexpensive biomarker linked to insulin resistance and metabolic dysfunction. This study examined the relationship between maternal serum uric acid and its association with glycaemic control.

Methods: This case-control study enrolled 120 pregnant women between 24 and 40 weeks of gestation- 60 with GDM and 60 normoglycaemic controls. Demographic and clinical data were recorded, and serum uric acid was measured using an enzymatic uricase-peroxidase method. We assessed its association with GDM, random blood sugar (RBS), glycated hemoglobin (HbA1c) and treatment modality were evaluated and receiver operating characteristic (ROC) analysis were performed.

Results: Women with GDM were older and more often overweight or obese than controls. Serum uric acid was significantly higher in the GDM group: 50.0% of cases had levels above 5.7 mg/dl, compared with 18.33% of controls ($p < 0.003$). Uric acid correlated with RBS ($r = 0.29$, $p = 0.02$) and, more strongly, with HbA1c (Spearman $\rho = 0.690$, $p < 0.001$). Women who required insulin had higher mean uric acid than those managed on medication alone (6.70 ± 0.86 versus 5.35 ± 1.18 mg/dl; $p < 0.001$). ROC analysis gave an area under the curve of 0.7325, with an optimal cut-off of ≥ 5.1 mg/dl (sensitivity 71.67%, specificity 66.67%).

Conclusions: Maternal serum uric acid was associated with GDM and with markers of poorer glycemic control and greater treatment intensity. It may be a useful adjunctive biomarker, but its moderate discriminatory power means it cannot stand alone as a diagnostic test.

Keywords: Gestational diabetes mellitus, HbA1c, Serum uric acid

INTRODUCTION

Gestational diabetes mellitus (GDM)- carbohydrate intolerance of varying severity first recognized during pregnancy- carries significant maternal and perinatal consequences.^{1,2} It is linked to hypertensive disorders, operative delivery, fetal overgrowth, and neonatal metabolic complications, and it raises long-term cardiometabolic risk for both mother and child.³⁻⁵

Pregnancy is characterized by progressive insulin resistance, particularly from the second trimester onward.

GDM develops when pancreatic β -cell compensation is insufficient to maintain normoglycemia.³⁻⁵ This metabolic backdrop has prompted interest in biomarkers that might flag women at higher risk or track disease severity. Uric acid, the end product of purine metabolism, has traditionally been treated mainly as a marker of renal function. Increasing evidence implicates it to oxidative stress, inflammation, endothelial dysfunction, and impaired insulin signaling.⁶⁻⁹

Experimental and epidemiological data suggest that higher uric acid concentrations track with insulin resistance,

giving a plausible biological basis for a link with GDM.⁷⁻¹⁰ Serum uric acid follows a characteristic pattern across normal pregnancy: it decreases during early and mid-pregnancy, as renal clearance and plasma volume increase, then rises again in late pregnancy.¹¹ Several studies have linked elevated first-trimester uric acid to subsequent GDM, and more recent analyses have reinforced the association between higher uric acid and GDM, though heterogeneity across studies remains substantial.¹³⁻¹⁶

The evidence is not entirely consistent, though. Güngör et al found higher uric acid levels in women with GDM, but the difference did not reach statistical significance—suggesting that gestational age at sampling, renal function, BMI, and other metabolic factors may modify the relationship.¹⁷ Mendelian randomization studies, moreover, have not established causality, raising the possibility that uric acid reflects metabolic dysfunction rather than driving it.¹⁵ Against this backdrop, we set out to compare serum uric acid levels between pregnant women with GDM and normoglycemic controls between 24 and 40 weeks of gestation, and to examine how uric acid relates to glycemic indices and treatment requirement.

METHODS

Study design and setting

This case-control study was conducted in the department of obstetrics and gynecology, Sardar Patel Medical College and Associated Group of Hospitals, Bikaner, Rajasthan, India, between June 2025 and May 2026. Participants were recruited from the outpatient, inpatient, and antenatal clinics.

Participants

We enrolled 120 pregnant women between 24 and 40 weeks of gestation by convenience sampling—60 with a diagnosis of GDM [cases were women previously diagnosed GDM based on oral glucose tolerance test (OGTT) and other standard diagnostic criteria] and 60 healthy pregnant women free of GDM or other medical complications (controls). Eligible women were aged 18–40 years, carrying a singleton live pregnancy, and willing to take part. Women were excluded if they declined consent, or had pre-existing diabetes mellitus, cardiovascular disease, an endocrine disorder, essential hypertension, metabolic syndrome, pre-existing liver disease, acute or chronic kidney disease, gouty arthritis, a multifetal pregnancy, or a known fetal abnormality.

Clinical and biochemical assessment

A structured proforma was used to record maternal age, residence, booking status, obstetric history, gestational

age, BMI, hemoglobin, blood pressure, random blood sugar, and HbA1c. Approximately 3–5 ml of venous blood was drawn aseptically from the antecubital vein, allowed to clot, and centrifuged for 10 minutes to obtain serum. Serum uric acid was measured by the uricase-peroxidase enzymatic colorimetric method on an AU680 fully automated analyser. The reference ranges used were 2.4–4.9 mg/dl for the second trimester and 3.1–6.0 mg/dl for the third trimester.

Assessment of GDM severity

Among women with GDM, disease severity was explored through RBS, HbA1c, and treatment modality, classifying participants by whether they required insulin or were managed on medication (metformin/glyburide/combination). Treatment intensity was treated as a marker of treatment requirement rather than as a direct biological measure of disease severity.

Statistical analysis

Data were entered into a predesigned proforma and analysed using IBM SPSS Statistics version 22.0. Categorical variables are reported as frequencies and percentages, and continuous variables as mean±standard deviation or median with interquartile range, as appropriate. Pearson correlation was used to assess the relationship between serum uric acid and RBS, and Spearman correlation for uric acid and HbA1c. Differences in uric acid by treatment modality were tested with an independent-samples t-test, and ROC analysis was used to assess how well uric acid discriminated GDM. A two sided p value below 0.05 was considered statistically significant.

RESULTS

The study included 120 pregnant women, 60 in each group, with one serum sample contributed per participant. Baseline and biochemical findings are summarized below.

The age distribution differed significantly between the two groups ($p<0.001$). Most women with GDM were aged 30–35 years (55.0%), whereas most women in the non-GDM group were aged 25–29 years (61.67%).

The distribution of gestational age was comparable between the groups, with no statistically significant difference ($p=0.24$).

Place of residence and gravidity showed no statistically significant result with p values 0.72 and 0.58 respectively. Overweight or obesity was reported in 13.33% of women with GDM compared with none of the controls. The difference was statistically significant ($p=0.039$).

Table 1: Selected baseline characteristics of the study population.

Age (in years)	GDM (n=60) (%)	Non-GDM (n=60) (%)	P value
<20	0 (0.00)	2 (3.33)	<0.001
20-24	5 (8.33)	16 (26.67)	
25-29	17 (28.34)	37 (61.67)	
30-35	33 (55.00)	5 (8.33)	
36-40	5 (8.33)	0 (0.00)	
Gestational age (in weeks)			
≤30	14 (23.33)	7 (11.67)	0.24
31-32	6 (10.00)	2 (3.33)	
33-34	6 (10.00)	8 (13.33)	
35-36	16 (26.67)	25 (41.67)	
37-38	14 (23.33)	13 (21.67)	
39-40	4 (6.67)	5 (8.33)	
Other variables			
Rural residence	36 (60.0)	38 (63.3)	0.72
Urban residence	24 (40.0)	22 (36.7)	
Primigravida	29 (48.3)	26 (43.3)	0.58
Multigravida	31 (51.7)	34 (56.7)	
Overweight/obese	8 (13.33)	0 (0)	0.039

Table 2: Hemoglobin and blood pressure.

Parameters	GDM (n=60), mean±SD	Non-GDM (n=60), mean±SD	P value
Haemoglobin (gm/dl)	11.03±1.18	10.39±1.55	0.013
Systolic BP (mmHg)	124.7±7.42	123.2±6.95	0.255
Diastolic BP (mmHg)	80.0±6.45	79.97±4.68	0.976

Table 3: Distribution according to serum uric acid.

Serum uric acid (mg/dl)	GDM (n=60) (%)	Non-GDM (n=60) (%)	P value
<2.4	0 (0)	5 (8.33)	<0.003
2.4-5.7	30 (50.0)	44 (73.34)	
>5.7	30 (50.0)	11 (18.33)	

Table 4: Association of serum uric acid with glycemic indices and treatment requirement in GDM.

Analysis	Result	P value
Serum uric acid versus RBS	Pearson $r=+0.29$ (weak positive)	0.02
Serum uric acid versus HbA1c	Spearman $\rho=0.690$ (strong positive)	<0.001
Insulin therapy (n=18)	6.70±0.86 mg/dl	<0.001
Medication (n=42)	5.35±1.18 mg/dl	

The mean hemoglobin level was significantly higher in the GDM group than in the non-GDM group (11.03±1.18 versus 10.39±1.55 gm/dl; $p=0.013$).

The mean SBP was 124.7±7.42 mm Hg in the GDM group and 123.2±6.95 mmHg in the non-GDM group. The difference was not statistically significant ($p=0.255$).

The mean DBP was comparable between the GDM and non-GDM groups (80.0±6.45 versus 79.97±4.68 mmHg; $p=0.976$).

Serum uric acid distribution differed significantly between the groups. Half of the women with GDM had serum uric acid concentrations above 5.7 mg/dl, compared with 18.33% of controls. Conversely, most controls (73.34%) fell within the 2.4-5.7 mg/dl range, compared with 50.0% of women with GDM.

Serum uric acid showed a weak positive correlation with RBS ($r=0.29$), which was statistically significant ($p=0.02$).

A strong positive correlation was observed between serum uric acid and HbA1c (Spearman's $\rho=0.690$; $p<0.001$).

Participants requiring insulin therapy had significantly higher mean serum uric acid concentration than women managed with medication (6.70 ± 0.86 versus 5.35 ± 1.18 mg/dl; $t=4.95$, $p<0.001$)- an absolute difference of 1.35 mg/dl.

Table 5: ROC performance of serum uric acid for discrimination of GDM.

Measure	Value
Area under ROC curve	0.7325
Optimal cut-off	≥ 5.1 mg/dl
Sensitivity	71.67%
Specificity	66.67%
Positive predictive value	68.25%
Negative predictive value	70.18%
P value	<0.001

The AUC was 0.7325, indicating moderate discriminatory performance of serum uric acid for distinguishing women with GDM from controls.

A cut-off of ≥ 5.1 mg/dl yielded a sensitivity of 71.67%, indicating that 71.67% of women with GDM were correctly identified as positive at this cut-off.

The specificity was 66.67%, indicating that 66.67% of women without GDM were correctly identified as negative.

The reported PPV was 68.25%, NPV was 70.18% and p value was below 0.001.

Overall finding

Serum uric acid demonstrated moderate discriminatory ability for GDM at a cut- off of ≥ 5.1 mg/dl. However, its sensitivity and specificity do not support its use as a standalone diagnostic test.

DISCUSSION

This study identified a significant association between maternal serum uric acid and GDM among women assessed between 24 and 40 weeks of gestation. Higher uric acid also tracked with higher HbA1c, higher RBS, and a greater likelihood of needing insulin. Together, these findings support serum uric acid as a plausible adjunctive marker of metabolic risk in pregnancy, though the ROC results make clear it cannot substitute for standard diagnostic testing.

Maternal age differed markedly between groups: 55% of women with GDM were 30-35 years old, versus 8.33% of controls. Advancing maternal age is a well-established GDM risk factor, likely reflecting cumulative insulin resistance and declining β -cell reserve, and similar age associations have turned up in other cohort studies of uric acid and GDM.^{12,13}

BMI also differed significantly between the groups. Most participants in both groups had a normal BMI, but overweight or obesity appeared only among women with GDM in our data. Because adiposity drives insulin resistance and can independently influence uric acid metabolism, BMI remains an important potential confounder when interpreting the uric acid–GDM relationship.

The central finding here is the higher prevalence of elevated uric acid among women with GDM: half had levels above 5.7 mg/dl, compared with 18.33% of controls. This lines up with other observational work linking higher uric acid to GDM. Laughon et al reported a 3.25-fold increase in GDM risk among women in the highest first-trimester uric acid quartile, independent of age and BMI.¹² Sahin Aker et al likewise found higher first-trimester uric acid in women who went on to develop GDM, and a 2023 systematic review and dose-response meta-analysis spanning more than 105,000 participants reported a pooled odds ratio of 2.58 for the association between elevated maternal uric acid and GDM.^{14,16}

There is a plausible biological story behind this: uric acid appears to promote oxidative stress, endothelial dysfunction, inflammation, and impaired insulin signaling.^{7,18-20} It has also been linked to type 2 diabetes in population studies, reinforcing its ties to metabolic dysfunction more broadly.^{9,21}

Serum uric acid was positively correlated with glycemic indices. The correlation with RBS was weak ($r=0.29$) but statistically significant, while the correlation with HbA1c was considerably stronger ($p=0.690$)- suggesting that higher uric acid may track with poorer glycemic control once GDM is established. Nevertheless, the observational design precludes causal interpretation.

A notable secondary finding was the higher uric acid concentration among women who needed insulin- 6.70 mg/dl versus 5.35 mg/dl in those on medication alone. Since insulin requirement often signals greater difficulty achieving glycemic control, this points to a possible link between uric acid and treatment intensity, echoing recent work examining uric acid alongside GDM severity and pregnancy outcomes.^{22,23}

ROC analysis produced an AUC of 0.7325, and a cut-off of ≥ 5.1 mg/dl yielded 71.67% sensitivity and 66.67% specificity- moderate discriminatory performance. That is clinically relevant given how inexpensive and widely available uric acid testing is, but the sensitivity and specificity fall short of what is needed for it to stand alone as a diagnostic test. It is better viewed as a complement to conventional risk assessment.

Evidence remains heterogeneous. Güngör et al found higher uric acid in women with GDM, but the difference was not statistically significant, particularly at 24-28 weeks.¹⁷ More recent Mendelian randomization work also failed to establish a causal link between genetically

predicted uric acid and GDM, suggesting uric acid may be a marker of metabolic risk rather than a direct driver.¹⁵ Differences in gestational age at sampling, BMI, renal function, ethnicity, study design, and diagnostic criteria likely explain much of this heterogeneity.

Indian data point in the same direction, with reports of elevated uric acid preceding GDM and a substantial burden of GDM across Indian populations more broadly.^{24,25}

Retained, followed by more formally structured limitations. It was conducted at a single centre with a relatively small, convenience-sampled cohort, which may limit generalizability and introduce selection bias. Its case-control design cannot establish temporality or causality. Because uric acid was measured only after 24 weeks of gestation, our findings cannot establish its value as an early-pregnancy predictor of GDM. We did not adjust for BMI and other metabolic confounders through multivariable regression in the thesis analysis. And treatment requirement, while a pragmatic marker of severity, is also shaped by clinical practice patterns and not purely by biochemical severity.

Even with these limitations, the study adds data from a tertiary-care population in Rajasthan and supports further prospective investigation of uric acid- particularly when measured earlier in pregnancy and combined with established clinical and biochemical risk factors.

CONCLUSION

In this hospital-based case-control study, maternal serum uric acid was significantly higher among women with GDM than among normoglycemic pregnant women, and higher levels were linked to higher RBS and HbA1c and a greater likelihood of needing insulin. ROC analysis showed fair discrimination, with an optimal cut-off of ≥ 5.1 mg/dl. Serum uric acid may therefore be considered a potential adjunctive marker for metabolic risk stratification in GDM, though it should not be used as a standalone diagnostic test. Larger, prospective, multicentre studies are needed to establish gestation-specific thresholds and to determine whether early-pregnancy uric acid adds predictive value beyond established risk factors.

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