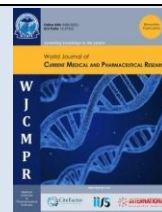




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UNVEILING SERUM URIC ACID AS AN EARLY BIOMARKER FOR GESTATIONAL DIABETES RISK: A PROSPECTIVE OBSERVATIONAL VALIDATION

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ARTICLE HISTORY	ABSTRACT
Received on: 03-07-2026 Revised on: 16-08-2026 Accepted on: 30-09-2026	Background: Serum uric acid, a marker linked to oxidative stress, endothelial dysfunction and insulin resistance, has been proposed as an inexpensive early biomarker of gestational diabetes mellitus (GDM), but the evidence remains heterogeneous.
Keywords: Uric acid; Diabetes; Gestational; Biomarkers; ROC Curve; Pregnancy Outcome; Prospective Studies.	Objective: To examine the association between serum uric acid measured at 0–18 weeks of gestation and the subsequent development of GDM, and to describe maternal and neonatal outcomes according to GDM status.
Corresponding Author Jaffar Ahmad Bhat Postgraduate Scholar, Department of Obstetrics and Gynaecology, Sher-i- Kashmir Institute of Medical Sciences (SKIMS), Soura, Srinagar, Jammu and Kashmir, India (190011).	Methods: This prospective observational study was conducted over 18 months in the Department of Obstetrics and Gynaecology, SKIMS, Srinagar. Women with singleton pregnancies registered early for antenatal care and without pre-existing chronic disease were enrolled (N = 225). Serum uric acid was measured at the first antenatal visit. GDM was diagnosed at 24–28 weeks by a 75 g oral glucose tolerance test using the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria. Groups were compared using the chi-square test and the unpaired t test, and the discriminative ability of uric acid was assessed by receiver operating characteristic (ROC) analysis.
	Results: GDM developed in 56 women (24.9%). Mean serum uric acid was 5.54 ± 2.23 mg/dL in women who developed GDM and 3.60 ± 1.28 mg/dL in those who did not ($p < 0.01$). At a cut-off of 4.95 mg/dL, the reported sensitivity was 70.6% and specificity 83% (area under the curve 0.770; $p < 0.001$). Family history of diabetes (23.2% vs 1.2%) and of gestational hypertension (46.4% vs 10.1%) was more frequent in the GDM group (both $p < 0.001$). Women with GDM more often delivered by lower segment caesarean section (58.9% vs 16.0%; $p < 0.001$), had infants weighing more than 4 kg (30.4% vs 0%; $p < 0.001$) and had neonates admitted to intensive care (28.6% vs 5.9%; $p = 0.002$). No maternal or neonatal deaths occurred.
	Conclusions: Higher serum uric acid at booking was associated with later GDM, with moderate reported discrimination. These unadjusted findings from a single centre support further evaluation of uric acid as a low-cost adjunct for early risk stratification, but do not justify its use as a stand-alone screening test.

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INTRODUCTION

Pregnancy is accompanied by substantial metabolic adaptation that supports fetal growth while preserving maternal homeostasis [1]. Early gestation is characterised by enhanced insulin sensitivity and maternal energy storage, whereas insulin resistance progresses through the second

and third trimesters [2]. This shift is driven largely by placental hormones, including human placental lactogen, progesterone, oestrogen, cortisol and placental growth hormone, which antagonise insulin action at the periphery [3]. When insulin resistance is exaggerated, or pancreatic β -cell compensation is inadequate, maternal glucose

homeostasis is disrupted [4,5], and gestational diabetes mellitus (GDM) may result.

GDM is defined as glucose intolerance first recognised during pregnancy, irrespective of its persistence after delivery [6]. Its prevalence has risen with advancing maternal age, obesity and changing lifestyles, and the burden is particularly high in many low- and middle-income countries [7]. GDM is associated with pre-eclampsia, polyhydramnios, operative delivery, fetal macrosomia, neonatal hypoglycaemia and a long-term risk of type 2 diabetes in both mother and child; differences in diagnostic criteria complicate comparisons of prevalence, but early identification and effective management remain central [8]. The underlying pathophysiology is an imbalance between rising insulin resistance and inadequate β -cell compensation, amplified by inflammation, oxidative stress and adipokine dysregulation [9–11]. Because GDM is frequently asymptomatic, systematic screening is required [10]. Screening is conventionally undertaken at 24–28 weeks of gestation, when insulin resistance peaks, with earlier testing recommended for women with risk features such as obesity, previous GDM or a strong family history of diabetes [12]. Both one-step and two-step strategies are in use [13,14], and diagnostic thresholds differ between organisations [15]. The IADPSG criteria, derived from the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study [16,17], recommend a one-step 75 g oral glucose tolerance test (OGTT), with GDM diagnosed if any one of the following is met or exceeded: fasting plasma glucose 92 mg/dL (5.1 mmol/L), 1-hour value 180 mg/dL (10.0 mmol/L) or 2-hour value 153 mg/dL (8.5 mmol/L) [18]. These outcome-based criteria increase the number of women identified, and their adoption has been accompanied by higher reported prevalence [19,20].

Predicting GDM before it becomes clinically apparent could allow earlier intervention. Candidate markers reflecting inflammation, oxidative stress, endothelial function, adipocyte activity and metabolic homeostasis, together with placental proteins, microRNAs and metabolites, have been investigated [21,22]. However, variability between populations, inconsistent assay methods and limited predictive accuracy have hindered clinical adoption [23]. A simple, inexpensive and widely available marker would be particularly valuable in resource-limited settings.

Uric acid, the end product of purine metabolism, has been linked to insulin resistance, oxidative stress and endothelial dysfunction, and elevated concentrations early in pregnancy may reflect metabolic stress or altered renal handling that precedes glucose intolerance [24]. Hyperuricaemia has been associated with reduced nitric oxide availability, a greater oxidative burden and pro-inflammatory signalling, and several studies report higher first-trimester uric acid concentrations in women who later develop GDM [25]. Published studies nevertheless differ in the gestational age at sampling, in the thresholds proposed (roughly 3.5 to 4 mg/dL) [26–30], in the diagnostic criteria applied, and in their conclusions, with some reporting no significant difference between women with and without GDM [31,32]. We therefore measured serum uric acid at the first antenatal visit (0–18 weeks) in women attending a tertiary referral hospital in Kashmir and screened them for GDM at 24–28 weeks using the IADPSG criteria. Our objectives were to compare early-pregnancy uric acid between women who did and did not develop GDM, to assess the

discriminative ability of a uric acid threshold of 4.95 mg/dL, and to describe maternal and neonatal outcomes according to GDM status. We hypothesised that women who subsequently develop GDM have higher uric acid concentrations early in pregnancy.

MATERIALS AND METHODS

Study design and setting

This prospective observational study was conducted in the Department of Obstetrics and Gynaecology, Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Srinagar, over a period of 18 months. The study is reported in accordance with the STROBE recommendations [33].

Participants

Pregnant women attending and registered at the antenatal outpatient department were assessed for eligibility. Women were eligible if they registered early for antenatal care, were compliant with follow-up, had a singleton pregnancy and were between 0 and 18 weeks of gestation at their first visit. Women were excluded if they had a multiple pregnancy, registered late, or were non-compliant with antenatal care; had a history of chronic disease or comorbidity before pregnancy, including abnormal liver or kidney function tests, chronic hypertension, overt diabetes or diabetes in pregnancy, and thyroid disorders; or had a recent acute infection.

Measurement of serum uric acid

Women were examined clinically and investigated according to institutional protocol. At the first antenatal visit, a venous blood sample was collected under aseptic conditions for estimation of serum uric acid (mg/dL). On the basis of this measurement, participants were categorised as having elevated (>4.95 mg/dL) or normal serum uric acid, and were followed throughout pregnancy.

Diagnosis of gestational diabetes mellitus

Screening for GDM was performed between 24 and 28 weeks of gestation using the IADPSG one-step OGTT. Participants fasted overnight and a fasting venous sample was obtained; 75 g of glucose was then given orally and venous samples were collected at 1 and 2 hours for plasma glucose. GDM was diagnosed if any one of the following was met: fasting plasma glucose ≥ 5.1 mmol/L (92 mg/dL), 1-hour glucose ≥ 10.0 mmol/L (180 mg/dL) or 2-hour glucose ≥ 8.5 mmol/L (153 mg/dL) [18].

Other variables and outcomes

Recorded variables were age (<20 , 20–24, 25–29 and ≥ 30 years), residence (rural or urban), socioeconomic status (classes I–IV), gravidity, family history of diabetes mellitus and of gestational hypertension, previous GDM, polycystic ovarian disease (PCOD), bad obstetric history and previous macrosomia. Glycaemic values were also recorded using the Diabetes in Pregnancy Study Group of India (DIPSI) test in the first trimester and at 24–28 weeks. Maternal and neonatal outcomes were mode of delivery (lower segment caesarean section [LSCS] or normal vaginal delivery [NVD]), neonatal birth weight (<2.5 , 2.5–4 and >4 kg), admission to the neonatal intensive care unit (NICU), and maternal and neonatal death.

Sample size

All eligible women attending the antenatal outpatient department during the study period were included.

Ethical considerations

All investigations formed part of routine antenatal care. Serum uric acid estimation at the first antenatal visit and

the OGTT at 24–28 weeks were performed free of cost at the SKIMS laboratory under the Janani Shishu Suraksha Karyakram (JSSK) scheme. Participants gave informed consent, and confidentiality of patient data was maintained. Ethical clearance was obtained from Ethics Committee SKIMS.

Statistical analysis

Continuous variables are presented as mean $\pm$ standard deviation and categorical variables as frequencies and percentages. Categorical variables were compared using the chi-square test and continuous variables between the two groups using the unpaired Student's t test. A two-sided p value <0.05 was considered statistically significant. The discriminative ability of serum uric acid for GDM was assessed by ROC analysis, with the area under the curve (AUC) and the sensitivity and specificity at a cut-off of 4.95 mg/dL.

RESULTS

Of the 225 women included, 56 (24.9%) developed GDM and 169 (75.1%) did not (Table 01). All p values below are reported as given in the source thesis.

Table 01: Development of GDM among study participants (N = 225)

GDM developed	Frequency	Percentage
No	169	75.1
Yes	56	24.9

GDM, gestational diabetes mellitus.

Age distribution did not differ significantly between the groups (Table 02). Most women with GDM were aged 20–24 years (53.6%), followed by 25–29 years (23.2%), <20 years (17.9%) and ≥ 30 years (5.3%), and a similar pattern was seen in women without GDM ($p = 0.907$).

Table 02: Age distribution of study participants by GDM status (N = 225)

Age group (years)	GDM (n = 56) n (%)	No GDM (n = 169) n (%)	Total (N = 225) n (%)	p value
<20	10 (17.9)	19 (11.2)	29 (12.9)	0.907
20–24	30 (53.6)	92 (54.4)	122 (54.2)	
25–29	13 (23.2)	46 (27.2)	59 (26.2)	
≥ 30	3 (5.3)	12 (7.1)	15 (6.7)	

Values are n (%). GDM, gestational diabetes mellitus.

Urban residence was more common in both groups (71.4% of women with GDM and 63.3% of those without), and the difference was not statistically significant ($p = 0.583$; Table 03).

Table 03: Residence of study participants by GDM status (N = 225)

Residence	GDM (n = 56) n (%)	No GDM (n = 169) n (%)	Total (N = 225) n (%)	p value
Rural	16 (28.6)	62 (36.7)	78 (34.7)	0.583
Urban	40 (71.4)	107 (63.3)	147 (65.3)	

Values are n (%). GDM, gestational diabetes mellitus.

Socioeconomic class II was the most frequent category in both groups (46.4% and 39.6%). No woman with GDM belonged to class IV, compared with 35 women (20.7%) without GDM. The association was reported as not statistically significant ($p = 0.212$; Table 04).

Table 04: Socioeconomic status of study participants by GDM status (N = 225)

Socioeconomic class	GDM (n = 56) n (%)	No GDM (n = 169) n (%)	Total (N = 225) n (%)	p value
I	10 (17.9)	17 (10.1)	27 (12.0)	0.212
II	26 (46.4)	67 (39.6)	93 (41.3)	
III	20 (35.7)	50 (29.6)	70 (31.1)	
IV	0 (0)	35 (20.7)	35 (15.6)	

Values are n (%). GDM, gestational diabetes mellitus.

Primigravidae formed the majority in both groups (71.4% with GDM; 61.5% without); gravidity was not significantly associated with GDM ($p = 0.471$; Table 05).

Table 05: Gravidity of study participants by GDM status (N = 225)

Gravidity	GDM (n = 56) n (%)	No GDM (n = 169) n (%)	Total (N = 225) n (%)	p value
Multigravida	16 (28.6)	65 (38.5)	81 (36.0)	0.471
Primigravida	40 (71.4)	104 (61.5)	144 (64.0)	

Values are n (%). GDM, gestational diabetes mellitus.

A family history of diabetes mellitus was reported by 13 of 56 women (23.2%) who developed GDM and by 2 of 169 (1.2%) who did not ($p < 0.001$; Table 6). A family history of gestational hypertension was reported by 26 women (46.4%) with GDM and 17 (10.1%) without ($p < 0.001$; Table 07).

Table 06: Family history of diabetes mellitus by GDM status (N = 225)

Family history of diabetes	GDM (n = 56) n (%)	No GDM (n = 169) n (%)	Total (N = 225) n (%)	p value
No	43 (76.8)	167 (98.8)	210 (93.3)	<0.001
Yes	13 (23.2)	2 (1.2)	15 (6.7)	

Values are n (%). GDM, gestational diabetes mellitus.

Table 07: Family history of gestational hypertension by GDM status (N = 225)

Family history of gestational hypertension	GDM (n = 56) n (%)	No GDM (n = 169) n (%)	Total (N = 225) n (%)	p value
No	30 (53.6)	152 (89.9)	182 (80.9)	<0.001
Yes	26 (46.4)	17 (10.1)	43 (19.1)	

Values are n (%). GDM, gestational diabetes mellitus.

No woman who developed GDM reported a previous history of GDM, PCOD or bad obstetric history, whereas 6 (3.6%), 4 (2.4%) and 11 (6.5%) women without GDM did, respectively; none of these differences was statistically significant ($p = 0.440$, 0.530 and 0.268 ; Tables 8–10). A history of macrosomia in a previous pregnancy was reported by 3 women (5.4%) with GDM and 2 (1.2%) without ($p = 0.190$; Table 11).

Table 08: History of GDM in a previous pregnancy by current GDM status (N = 225)

Previous GDM	GDM (n = 56) n (%)	No GDM (n = 169) n (%)	Total (N = 225) n (%)	p value
No	56 (100)	163 (96.4)	219 (97.3)	0.440
Yes	0 (0)	6 (3.6)	6 (2.7)	

Values are n (%). GDM, gestational diabetes mellitus

Table 09: History of polycystic ovarian disease (PCOD) by GDM status (N = 225)

PCOD	GDM (n = 56) n (%)	No GDM (n = 169) n (%)	Total (N = 225) n (%)	p value
No	56 (100)	165 (97.6)	221 (98.2)	0.530
Yes	0 (0)	4 (2.4)	4 (1.8)	

Values are n (%). GDM, gestational diabetes mellitus.

Table 10: Bad obstetric history (BOH) by GDM status (N = 225)

BOH	GDM (n = 56) n (%)	No GDM (n = 169) n (%)	Total (N = 225) n (%)	p value
No	56 (100)	158 (93.5)	214 (95.1)	0.268
Yes	0 (0)	11 (6.5)	11 (4.9)	

Values are n (%). GDM, gestational diabetes mellitus.

Table 11: History of macrosomia in a previous pregnancy by GDM status (N = 225)

Previous macrosomia	GDM (n = 56) n (%)	No GDM (n = 169) n (%)	Total (N = 225) n (%)	p value
No	53 (94.6)	167 (98.8)	220 (97.8)	0.190
Yes	3 (5.4)	2 (1.2)	5 (2.2)	

Values are n (%). GDM, gestational diabetes mellitus.

Mean DIPSI test values were higher in women who developed GDM than in those who did not, both in the first trimester (121.76 ± 8.95 vs 97.99 ± 12.04 mg/dL) and at 24–28 weeks (150.71 ± 5.00 vs 134.23 ± 2.95 mg/dL); both differences were reported as $p < 0.001$ (Table 12).

Table 12: DIPSI test values in the first trimester and at 24–28 weeks by GDM status (N = 225)

DIPSI (mg/dL)	GDM (n = 56) mean $\pm$ SD	No GDM (n = 169) mean $\pm$ SD	p value
First trimester	121.76 ± 8.95	97.99 ± 12.04	<0.001
24–28 weeks	150.71 ± 5.00	134.23 ± 2.95	<0.001

SD, standard deviation; DIPSI, Diabetes in Pregnancy Study Group of India; GDM, gestational diabetes mellitus

Mean serum uric acid at presentation was 5.54 ± 2.23 mg/dL in women who developed GDM and 3.60 ± 1.28 mg/dL in women who did not ($p < 0.01$; Table 13).

Table 13: Serum uric acid at presentation by GDM status (N = 225)

Serum uric acid (mg/dL)	GDM (n = 56) mean $\pm$ SD	No GDM (n = 169) mean $\pm$ SD	p value
At presentation (0–18 weeks)	5.54 ± 2.23	3.60 ± 1.28	<0.01

SD, standard deviation; GDM, gestational diabetes mellitus.

Lower segment caesarean section was more frequent among women with GDM (33 of 56; 58.9%) than among those without (27 of 169; 16.0%; $p < 0.001$; Table 14). Birth-weight distribution differed significantly: 17 neonates (30.4%) of women with GDM weighed more than 4 kg, compared with none in the non-GDM group, whereas no neonate of a woman with GDM weighed less than 2.5 kg compared with 23 (13.6%) in the non-GDM group ($p < 0.001$; Table 15). NICU admission was required for 16 neonates (28.6%) in the GDM group and 10 (5.9%) in the non-GDM group ($p = 0.002$; Table 16). There were no maternal or neonatal deaths in either group (Table 17).

Table 14: Mode of delivery by GDM status (N = 225)

Mode of delivery	GDM (n = 56) n (%)	No GDM (n = 169) n (%)	Total (N = 225) n (%)	p value
LSCS	33 (58.9)	27 (16.0)	60 (26.7)	<0.001
NVD	23 (41.1)	142 (84.0)	165 (73.3)	

Values are n (%). GDM, gestational diabetes mellitus. LSCS, lower segment caesarean section; NVD, normal vaginal delivery.

Table 15: Neonatal birth weight by maternal GDM status (N = 225)

Birth weight (kg)	GDM (n = 56) n (%)	No GDM (n = 169) n (%)	Total (N = 225) n (%)	p value
<2.5	0 (0)	23 (13.6)	23 (10.2)	<0.001
2.5–4	39 (69.6)	146 (86.4)	185 (82.2)	
>4	17 (30.4)	0 (0)	17 (7.6)	

Values are n (%). GDM, gestational diabetes mellitus.

Table 16: Neonatal intensive care unit (NICU) admission by maternal GDM status (N = 225)

NICU admission	GDM (n = 56) n (%)	No GDM (n = 169) n (%)	Total (N = 225) n (%)	p value
Yes	16 (28.6)	10 (5.9)	26 (11.6)	0.002
No	40 (71.4)	159 (94.1)	199 (88.4)	

Values are n (%). GDM, gestational diabetes mellitus.

Table 17: Neonatal and maternal deaths by GDM status (N = 225)

Death	GDM (n = 56) n (%)	No GDM (n = 169) n (%)	Total (N = 225) n (%)	p value
Neonatal	0 (0)	0 (0)	0 (0)	–
Maternal	0 (0)	0 (0)	0 (0)	

No events occurred;

ROC analysis of serum uric acid as a predictor of GDM at 24–28 weeks is shown in Figure 1. At a cut-off of 4.95 mg/dL, serum uric acid measured in early pregnancy predicted GDM with a reported sensitivity of 70.6% and specificity of 83% (AUC 0.770; $p < 0.001$).

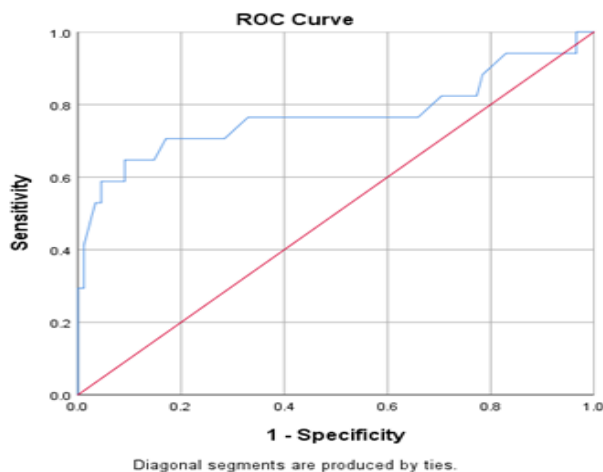


Figure 01: Receiver operating characteristic (ROC) curve of early-pregnancy serum uric acid as a predictor of GDM at 24–28 weeks (N = 225).

DISCUSSION

Principal findings

In this prospective cohort of 225 women booked at 0–18 weeks, GDM diagnosed by the IADPSG one-step OGTT at 24–28 weeks occurred in 24.9%. Serum uric acid at booking was higher in women who went on to develop GDM than in those who did not (5.54 vs 3.60 mg/dL; $p < 0.01$), in keeping with the primary objective. At a threshold of 4.95 mg/dL, discrimination was reported as moderate (AUC 0.770; sensitivity 70.6%; specificity 83%), meaning that uric acid identified a proportion of, but far from all, women who later developed GDM. A family history of diabetes and of gestational hypertension was more frequent among women who developed GDM, whereas age, residence, socioeconomic class, gravidity and previous obstetric history did not differ significantly. GDM was, in turn, associated with more caesarean deliveries, more infants weighing above 4 kg and more NICU admissions. Because all comparisons were unadjusted and observational, they describe associations rather than independent or causal effects.

Comparison with previous studies

Higher early-pregnancy uric acid in women who later develop GDM has been reported by most, though not all, earlier studies. The mean concentrations in our GDM and non-GDM groups (5.54 and 3.60 mg/dL) are close to those of Aker et al. (5.95 vs 3.76 mg/dL; $p < 0.001$) in a retrospective series that included 66 women with GDM [28], and to the two-group comparison of Murthy et al. (4.53 vs 3.13 mg/dL), although the latter enrolled only 30

cases and 30 controls and used DIPSI criteria [34]. Larger cohorts describe graded associations rather than group means. Adjusted risk of GDM increased across uric acid categories in Laughon et al. (highest quartile, >3.57 mg/dL: 3.25-fold, 95% CI 1.35–7.83, adjusted for body mass index and age) [26], in Wolak et al. (GDM prevalence 6.3% to 10.5% across categories; $p < 0.001$) [35], in Zhao et al. (odds ratios 1.11 to 1.70 across quintiles at 13–18 weeks; $n = 85,609$) [36], in Li et al. (OR 1.557, 95% CI 1.055–2.298, highest versus lowest quartile at 16–18 weeks) [37] and in Yue et al. (relative risk 1.43 for 240–300 $\mu\text{mol/L}$ and 1.82 for >300 $\mu\text{mol/L}$) [24]. In a series of 300 women, Ali et al. also reported a significant correlation between first-trimester uric acid and plasma glucose at 24–28 weeks [38], a relationship that was not examined in the present dataset. A dose-response meta-analysis of 23 studies reported a pooled OR of 2.58 (95% CI 1.89–3.52), and 3.26 (95% CI 2.26–4.71) for measurements before 20 weeks, although heterogeneity was very high (I^2 approximately 90%) [39].

Not all studies agree. Maged et al. found no significant difference in uric acid between women who did and did not develop GDM when measured before 15 weeks [32], and Güngör et al. also reported no significant difference (4.42 ± 1.09 vs 4.10 ± 0.84 mg/dL), but measured uric acid at 24–28 weeks rather than early in pregnancy [31]. Such discrepancies plausibly reflect differences in gestational age at sampling, sample size, diagnostic criteria, adjustment for adiposity and the populations studied, and they underline that the timing of measurement matters when comparing series.

The threshold of 4.95 mg/dL used here is higher than those proposed elsewhere: 3.5 mg/dL by Ganta and Kulkarni, in whom 84% of 88 women with GDM exceeded the threshold [30]; 3.6 mg/dL by Amudha et al. [29]; 3.95 mg/dL by Aker et al., with a reported sensitivity of 100%, specificity of 60% and AUC of 0.92 [28]; and 4 mg/dL by El-Gharib et al. [27]. A higher threshold would be expected to trade sensitivity for specificity, which is consistent with the profile reported here (70.6% and 83%). However, the source of the 4.95 mg/dL value is not stated in the thesis, and if it was derived from the same data in which it was evaluated, the reported performance is likely to be optimistic. Thresholds are also not readily transferable between assays, populations and gestational ages at sampling. The AUC of 0.770 is appreciably lower than the 0.92 of Aker et al., whose retrospective, matched-control design differs from the present prospective cohort [28].

The GDM prevalence of 24.9% is higher than the 14.0%, 13.44% and 10.03% reported by Zhao et al., Yue et al. and Maged et al. [24,32,36] and close to the 28% reported by Ganta and Kulkarni [30]. One-step IADPSG criteria generally yield higher prevalence than alternative strategies [19], and a hospital-based sample from a tertiary centre may over-represent higher-risk women; the figure should therefore not be read as a population prevalence.

Interpretation of individual findings

Age, residence, socioeconomic status and gravidity. Age did not differ between groups ($p = 0.907$). Only 15 women (6.7%) were aged 30 years or above, which limits the ability to detect an age effect. The literature is mixed: Fawzy et al. reported markedly older women among those with GDM [40], Rasika et al. found no significant correlation between demographic variables and GDM [41], and age-stratified analyses suggest that uric acid–GDM associations may be

stronger in women aged 35 years or more [36] or, on meta-regression, in younger women [39]. Age-stratified analysis was not possible here. Residence ($p = 0.583$), socioeconomic class ($p = 0.212$) and gravidity ($p = 0.471$) were not associated with GDM; comparable data on residence and socioeconomic class are scarce among the studies reviewed here, whereas Güngör et al. reported differences in gravidity and parity [31]. Notably, no woman with GDM belonged to socioeconomic class IV whereas 35 women without GDM did, and the corresponding p value requires verification.

Family history. A family history of diabetes was reported by 23.2% of women with GDM and 1.2% of those without ($p < 0.001$). A positive family history is an established risk feature for GDM and a criterion for earlier screening [12], and Rasika et al. reported an association between family history of diabetes and the one-step test ($p = 0.048$) [41]. The prevalence of a positive history among women without GDM was, however, strikingly low and rests on only 15 women overall; how family history was defined and ascertained is not described, so the estimate is likely to be imprecise. A family history of gestational hypertension was likewise more frequent in the GDM group (46.4% vs 10.1%; $p < 0.001$). Uric acid has been linked to endothelial dysfunction and oxidative stress in both metabolic and vascular disease [42], so shared pathways are conceivable, but this remains speculative because the variable was not defined in the study and no relationship between uric acid and family history was analysed.

Previous obstetric history. No woman who developed GDM reported previous GDM, PCOD or bad obstetric history, and previous macrosomia was reported by 5.4% of women with GDM and 1.2% of those without; none of these differences was significant. Numbers in these categories were very small (between 4 and 11 women overall, and 5 for macrosomia), so the analyses had little power, and the absence of a significant association should not be read as absence of an effect. Previous GDM, in particular, is a recognised risk factor [12].

Glycaemic values. Women who developed GDM had higher DIPSI values already at booking (121.76 ± 8.95 vs 97.99 ± 12.04 mg/dL), which suggests that glycaemic dysregulation may precede formal diagnosis. The difference at 24–28 weeks (150.71 ± 5.00 vs 134.23 ± 2.95 mg/dL) is largely expected by construction, because GDM was itself defined by glucose values at that gestation. The unusually narrow standard deviations at 24–28 weeks merit checking against source data.

Maternal and neonatal outcomes. The caesarean section rate was 58.9% in women with GDM and 16.0% in those without ($p < 0.001$). Indications for caesarean delivery were not recorded, so it is not possible to say how far this reflects macrosomia, obstetric complications or a lower threshold for intervention in women with GDM. Murthy et al. described macrosomia (13.3%), pre-eclampsia (5%) and polyhydramnios (5%) among GDM pregnancies, conditions that contribute to operative delivery [34]. Macrosomia (>4 kg) occurred in 30.4% of infants of women with GDM and in none of the non-GDM group, a higher proportion than the 13.3% in that series [34]; treatment and glycaemic control in the GDM group were not described, and this is relevant to fetal growth. Birth weight was not related to gestational age, so large- and small-for-gestational-age infants could not be distinguished, and preterm delivery was

not reported; 13.6% of infants in the non-GDM group weighed less than 2.5 kg. NICU admission was more frequent in the GDM group (28.6% vs 5.9%; $p = 0.002$), but indications were not recorded. Pleskacova et al. found that mid-gestational uric acid and xanthine were not associated with adverse perinatal outcomes [43], whereas Yue et al. reported that early uric acid was associated with secondary outcomes including large-for-gestational-age infants [24]. In the present study outcomes were compared by GDM status and not by uric acid concentration, so the data cannot address whether uric acid is associated with adverse outcomes independently of GDM. The absence of maternal and neonatal deaths in a cohort of 225 women cannot be taken as evidence about the quality of antenatal monitoring.

Biological and pathophysiological basis

Uric acid is the end product of purine metabolism, and its serum concentration reflects both production and renal excretion. In normal pregnancy, serum uric acid is lower in early and middle gestation than in non-pregnant women because of enhanced renal urate clearance [44]. A higher-than-expected concentration early in pregnancy could therefore signal altered renal handling or increased production, as suggested in earlier work [24]; these mechanisms are hypotheses and were not examined in this study.

Several pathways could link uric acid to glucose intolerance. Hyperuricaemia has been associated with reduced nitric oxide availability, increased oxidative burden and pro-inflammatory signalling, which may aggravate insulin resistance [24,42]. Xiong et al. reviewed evidence that uric acid induces inflammation, oxidative stress and vascular endothelial injury and is associated with obesity, metabolic syndrome, non-alcoholic fatty liver disease and diabetes [42]. In GDM, Murthy et al. reported higher uric acid together with raised tumour necrosis factor- α and interleukin-8 and reduced antioxidant enzymes [34], and Pleskacova et al. found that uric acid and xanthine correlated with body mass index and glycaemia, with higher uric acid in obese women, in high-risk groups and in those requiring insulin [43]. These observations fit within the broader pathophysiology of GDM, in which inadequate β -cell compensation for progressive insulin resistance is amplified by inflammation, oxidative stress and adipokine dysregulation [9–11].

Our data cannot distinguish whether uric acid contributes causally, or is instead a marker of adiposity, renal handling or other metabolic risk. Adiposity is a particular concern: uric acid rises with body mass index [30,43], and body mass index is not reported in this dataset, whereas the association persisted after adjustment for body mass index and age in Laughon et al. [26]. The observational design and the absence of multivariable analysis preclude any claim that uric acid is an independent predictor.

Future research directions

Larger, multicentre prospective cohorts are needed that record body mass index and gestational weight gain, measure uric acid at defined gestational windows (allowing gestational-age-specific analysis), use a pre-specified threshold, and validate performance in a separate cohort. Studies should report effect sizes with confidence intervals, predictive values and calibration, and should evaluate whether uric acid adds discriminative value to simple clinical risk factors such as family history of diabetes, or to multi-marker models. Standardisation of assay methods and

thresholds across laboratories would facilitate comparison. Finally, if a clinically useful early-risk strategy emerges, its cost-effectiveness and its effect on outcomes should be tested in interventional studies.

STRENGTHS AND LIMITATIONS

Strengths

Serum uric acid was measured before the outcome was ascertained, in a prospective design, which avoids reverse causation. GDM was diagnosed with a standardised, outcome-based one-step 75 g OGTT at a defined gestational window [18]. Women with pre-existing renal, hepatic, thyroid, hypertensive or diabetic disease were excluded, which reduces the influence of conditions that affect uric acid or glycaemia independently of pregnancy. The measurements were made as part of routine antenatal care in a tertiary referral setting, outcome data are presented for all 225 participants, and both maternal and neonatal outcomes were described.

Limitations

The study was conducted at a single tertiary institution, which limits generalisability. The sample of 225 women, with 56 cases of GDM, provided limited power, particularly for uncommon exposures such as previous GDM, PCOD, bad obstetric history and previous macrosomia, and the confidence around estimates such as the family-history associations is likely to be wide. Uric acid was measured once, at a single early visit, and serial measurements were not evaluated; because uric acid varies physiologically across early gestation [44], the 0–18-week sampling window is broad and gestational-age-specific analysis is not available. All comparisons were unadjusted: body mass index, gestational weight gain and other potential confounders are not reported, and no multivariable model was fitted, so independent predictive value cannot be claimed. The origin of the 4.95 mg/dL threshold is not stated, and performance estimates from a data-derived threshold are prone to optimism. Outcome analyses compared women by GDM status rather than by uric acid, and information on GDM treatment, indications for caesarean section and NICU admission, and gestational age at delivery are not reported. Family history and other historical variables were self-reported, and the assay method is not described in the thesis. Finally, no formal sample-size calculation is reported.

CLINICAL IMPLICATIONS

Established practice. The 75 g OGTT at 24–28 weeks remains the reference diagnostic test for GDM [18], and early testing is already advised for women with recognised risk features such as a strong family history of diabetes [12]. Serum uric acid cannot replace the OGTT, and a normal uric acid concentration should not be used to defer or omit it.

Potential applications. Because uric acid measurement is inexpensive, widely available and standardised, it may prove useful as an adjunct for risk stratification at booking, particularly where resources limit early screening, for example by prompting closer follow-up and lifestyle counselling in women with high concentrations. These uses remain hypothetical. The reported discrimination was moderate, the threshold has not been validated, thresholds differ between studies, and the analysis was unadjusted.

Incorporation of uric acid into routine antenatal panels should await confirmation in larger, multicentre cohorts.

CONCLUSION

Among 225 women booked before 18 weeks at a tertiary centre in Kashmir, higher serum uric acid at booking was associated with GDM diagnosed at 24–28 weeks, and a threshold of 4.95 mg/dL showed moderate reported discrimination (AUC 0.770). GDM was associated with higher rates of caesarean delivery, birth weight above 4 kg and NICU admission. These unadjusted, single-centre findings support further evaluation of uric acid as a low-cost adjunct for early risk stratification, but do not justify its use as a stand-alone screening test.

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