



To Evaluate the Predictive Value of Serum Uric Acid Levels in First Trimester for Risk of GDM Later in Low Risk Pregnant Women

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Abstract

Introduction: GDM is reduced glucose tolerance resulting in varied degree of hyperglycemia developing or being recognized first during pregnancy, one of the complications of pregnancy posing not only immediate risk to mother and fetus but also long-term health implications to both.

Compared to European women, south Asian especially Indian females have 11 times increased risk of GDM. However screening and diagnostic tests for GDM are implemented between 24-28 week of gestation resulting in effective loss of period in which insulin resistance secondary to diabetogenic hormones from placenta already initiate metabolic changes leading to adverse fetal and maternal outcome. Association between elevated uric acid levels and adverse pregnancy outcomes like hypertensive disorders of pregnancy, fetal growth restriction is well established however whether hyperuricemia contributes directly to the risk of diabetes mellitus remains largely observational and inconclusive. Elevated uric acid can act as both as a biomarker and a potential mediator of metabolic misregulation during pregnancy.

Objective: Aim of this study was to determine whether elevated uric acid levels in first trimester can serve as a warning signal for development of GDM later in pregnancy thus facilitating timely preventive intervention.

Materials and Methods: This is hospital based prospective observational study, conducted on 200 low-risk pregnant women attending outpatient department of OBG services, AIMS, Faridabad, Haryana over a period of 2 years.

With ethical clearance and patient's consent uric acid levels are obtained in low risk pregnant females of less than 13 weeks gestation. Same patients underwent DIPSI test between 24 to 28 weeks of gestation. Regression analysis employing receiver operating characteristic (ROC) curves and logistic regression was used to evaluate predictability of serum uric acid levels in first trimester for GDM in later part of the pregnancy.

Result: For GDM prediction serum uric acid levels and DIPSI values show strong positive correlation (Pearson correlation coefficient 0.750, $p = 0.0001$).

Conclusion: Elevated serum uric acid levels in first trimester of low risk pregnant females can be considered as independent predictor of GDM later in pregnancy.

Keywords: Gestational Diabetes Mellitus (GDM); Uric Acid

Introduction

Diabetes is emerging as a global pandemic with increasing incidence of obesity, urbanization, sedentary lifestyle influenced with regional and genetic predisposition. To add insult to injury pregnancy predisposes to glucose intolerance due to diabetogenic hormones secreted by placenta. However, this glucose intolerance is overcome by normal function of beta cells of pancreas ramping up insulin production to bridge over state of insulin resistance and inadequate insulin secretion as an underlying mechanism for pathogenesis for GDM [1]. There is a high prevalence of GDM 7 to 25% of all clinically recognized pregnancies worldwide [2]. Indian population reports an incidence rate of 16.55% [3]. GDM is a disease characterized by elevated blood glucose during pregnancy that increases adverse pregnancy outcome for both mother and child [4]. GDM is key risk factor for postpartum type-2 diabetes in pregnant women [5]. Women acquiring GDM have a 10-fold increased risk of developing type-2 diabetes with 50% developing within 10 years of giving birth. Moreover, newborns of these women tend to develop glucose intolerance, obesity and even diabetes during childhood, adolescence, adulthood [6] although early diagnosis and treatment of GDM can reduce risk of adverse pregnancy outcome, many of current diagnostic approaches remain controversial. During pregnancy blood glucose levels are affected by variety of factors like diet, mood, stress, medication, genetics besides the diabetogenic state of pregnancy itself, its diagnosis by single oral glucose tolerance test is subject to some degree of underdiagnosis. Hence need to explore novel biomarkers for early GDM prediction facilitating timely risk stratification and preventive intervention.

Uric acid is one of the most important metabolized substances [7]. Studies have reported that excessive serum uric acid levels are positively associated with insulin resistance and risk of type-2 diabetes, the relation between serum uric acid and risk of GDM has been inconsistent and relatively limited [8]. Uric acid may contribute to insulin resistance by inducing mitochondrial oxidative stress and steatosis in liver. Uric acid can induce local inflammation in adipose tissue leading to reduction in production of adiponectin, an insulin sensitizing adipokine with direct effect on pancreatic islet cells resulting in oxidative stress and islet dysfunction [9].

Uric acid produced from purine metabolism falls by 25-30 % during early gestation with an increase to normal level near term in a healthy pregnancy [10]. Elevated uric acid levels by their inhibitory effect on insulin signaling resulting in insulin resistance as a part of metabolic syndrome [11] high uric acid levels might lead

to endothelial dysfunction leading to decrease in nitric oxide production which is necessary for glucose uptake, its deficiency thus leads to hyperglycemia. Hence hyperuricemia not only worsens the insulin resistance of pregnant state but also predisposes to poor glucose uptake by causing oxidative stress and inflammation. While serum uric acid levels decline from 8th week of gestation up to 24th week due to increased glomerular filtration rate and decreased reabsorption of uric acid from renal tubules [12] i.e. increased renal clearance with hemodilution, abnormal elevations during this period may reflect underlying metabolic dysfunction and impaired glucose homeostasis. Hence this study intends to explore the predictability of increased serum uric acid levels in first trimester to development of GDM subsequently.

Material and Methods

This hospital based prospective study was conducted among low risk pregnant women attending OBG services at Asian Institute of Medical Sciences, Faridabad over a period of 2 years. Inclusion criteria:

- Low-risk antenatal females
- <13 weeks gestation
- Attending OPD services and available for follow-up

Exclusion criteria

- Known pre-gestational diabetes mellitus
- History of GDM in previous pregnancy
- On steroids in any form
- Endocrine disorders
- Known case of gout and hyperuricemia
- Chronic renal disease
- Connective tissue disorders, autoimmune disorders
- Liver diseases and cardio-vascular diseases
- Severe anemia (hemoglobin <7 gm %)

Sample size:

Formula used for calculation of sample size:

$$N = (Z\alpha/2)^2 * (pq) / d^2$$

Where

$Z\alpha/2$ = At 95% confidence interval and 5% α error = 1.96

p= incidence of GDM in pregnant woman= 10.4% according to Sivasarupa I., *et al.* [13]

q=100-p

d= 5% absolute error

$$N = (1.96 * 1.96) (10.4 * 89.6) / (5)^2 N = 143$$

By taking 10% non response rate final sample size came to be = 143+14=157 The final sample size to be taken is 200.

Study Methodology

Approval from the institutional ethics committee taken and informed consent from the patients was obtained before the collection of blood samples.

- Details such as age, demographic data, medical, family, and obstetrical history, immunization history, nutritional supplementation history, and a detailed history of clinical features were recorded on a pre-designed and pre-tested proforma.
- Serum uric acid levels were assessed using an automated photo spectrometric assay and sample taken along with routine antenatal tests at less than 13 weeks gestation.
- GDM was diagnosed using the Oral Glucose Tolerance Test (DIPSI Guideline) between 24 to 28 weeks of gestation in study group. Based on results of hyperglycemia and adverse pregnancy outcome (HAPO) study in 2008, the international association of diabetes and pregnancy study group (IADPSG) new guidelines in 2010 recommended universal one step

screening using 75 gm glucose challenge test (GCT) between 24 and 28 weeks of gestation [13].

Statistical analysis

Data analysis was done using licensed SPSS software version 24.0 (Chicago, Illinois). Univariate analyses were done initially and the results were presented with the help of tables, text, bar-diagrams and pie-charts. Descriptive statistics were used to calculate frequencies of categorical variables, and measures of central tendencies and dispersion were used to describe continuous variables.

Bi-variate analyses was done using the Chi square test/Fisher's exact test for categorical variables and for quantitative variable unpaired student t test was used. ROC curve was depicted to the accuracy of serum uric acid to diagnose the GDM. And Pearson correlation coefficient was calculated between serum uric acid and random blood sugar measured by GCT (75 gm-2hrs) (DIPSI). P value <0.05 was considered as statistically significant.

Results

Table 1: Age (year) distribution of study participants.

Mean	28.705
Median	28.000
Std. Deviation	4.1369
Minimum	21.0
Maximum	36.0

Table 2: Distribution of participants according to gestational age (weeks) at first visit (enrolment visit).

Gestational Age (completed weeks)	Frequency	Percent
5.0	9	4.5
6.0	20	10.0
7.0	58	29.0
8.0	31	15.5
9.0	47	23.5
10.0	6	3.0
11.0	20	10.0
12.0	9	4.5
Total	200	100.0

Table 3: Distribution of participants according to diagnosis of GDM.

GDM	Frequency	Percent
Yes	32	16.0
No	168	84.0
Total	200	100.0

Among the participants, 32 (16.0%) were diagnosed with GDM, while 168 (84.0%) were not. without GDM (3.04 mg/dL, SD 1.24). This difference was statistically significant ($p = 0.0001$), with the median values being 5.40 mg/dL in the GDM group and 3.20 mg/dL in the non-GDM group.

Participants diagnosed with GDM had significantly higher mean serum uric acid levels (5.14 mg/dL, SD 0.65) compared to those The area under the curve (AUC) for serum uric acid as a diagnostic marker for GDM was 0.908 (SE 0.037, $p = 0.000$), with a 95%

Table 4: Comparison of serum uric acid between GDM and without GDM.

GDM	Mean	SD	Median	Minimum	Maximum	p-value
Yes	5.1406	.64501	5.4000	3.80	5.80	0.0001
No	3.0382	1.24038	3.2000	.90	5.20	
Total	3.3746	1.39750	3.5000	.90	5.80	

Table 5: Accuracy of serum uric acid to diagnose the GDM.

Area Under the Curve				
Area	SE	p-value	Asymptomatic 95% Confidence Interval	
			Lower Bound	Upper Bound
.908	.037	.000	.837	.980

confidence interval ranging from 0.837 to 0.980. This indicates excellent diagnostic accuracy. There was a strong positive correlation (Pearson correlation coefficient = 0.750, $p = 0.0001$) between serum uric acid levels and DIPSI glucose values, suggesting that higher uric acid levels are associated with higher glucose levels.

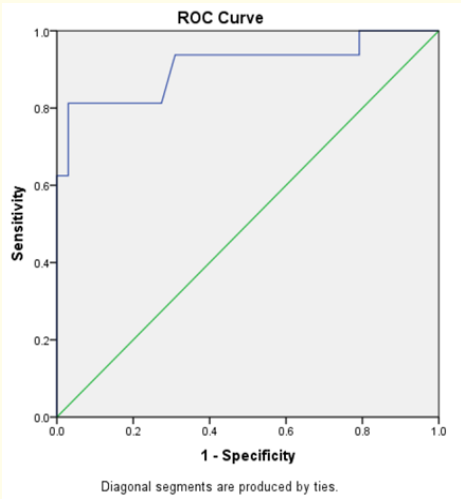


Figure 1

Table 6: Correlation of serum uric acid with random blood sugar measured by DIPSI.

		DIPSI
Serum uric acid	Pearson Correlation	.750
	Sig. (2-tailed)	.0001

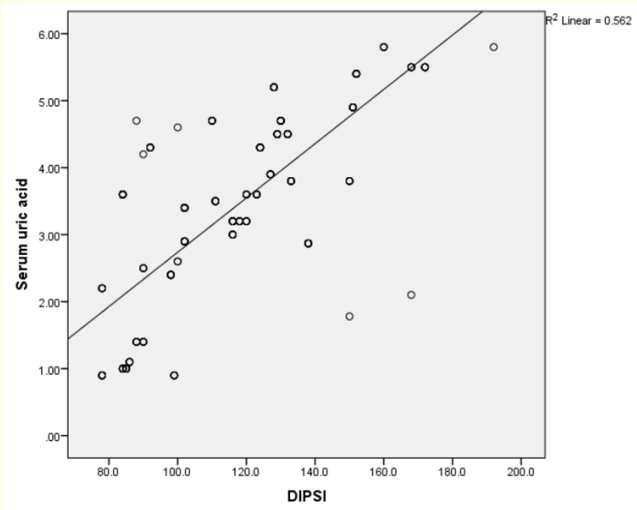


Figure 2

Discussion

Our study shows a significant association between elevated uric acid levels among low-risk pregnant women at less than 13 weeks of gestation and risk of GDM in later pregnancy. Women with elevated levels of serum uric acid in early stages of pregnancy might experience poor maternal physiological adaptation to diabetogenic effects of pregnancy putting them at risk of adverse pregnancy outcomes later [14]. Hence detecting increased uric acid levels might identify women at high risk of developing GDM.

Amudha., *et al.* showed [15] that serum uric acid measured before 14th week of gestation with a cutoff value of more than 3.6 mg/dl had the predictive value for development for GDM within AUC, sensitivity and specificity of 0.914, 92% and 99% respectively. In our study AUC for serum uric acid as a diagnostic marker for GDM was 0.908 indicating excellent diagnostic performance. Furthermore, Zhao., *et al.* [16] in a retrospective cohort study showed that increased serum uric acid levels at 13-18 weeks gestation are significantly associated with increased risk of GDM. Our study focusing on a gestational age of 5-12 weeks confirms this relationship suggesting that elevated uric acid levels are predictive even earlier in pregnancy. Gopalan., *et al.* [17] included women <12 weeks of gestation and found that hyperuricemia significantly

predicted GDM (p = 0.018). The mean UA level in their study (3.81 mg/dL) was slightly higher than ours (3.37 mg/dL). This variation may reflect differences in sample size, dietary patterns, or baseline metabolic profiles. Despite this, both studies support the utility of early UA measurement for GDM prediction.

Pang TT., *et al.* [18] found that hyperuricemia during early pregnancy increased GDM risk (OR 1.250 per SD increase in UA). The prevalence of GDM in their cohort (15.9%) closely matches ours (16%), underscoring the consistency of UA's predictive value. This finding aligns with existing literature, highlighting UA's potential as an early biomarker for GDM. Further research should focus on refining UA thresholds, exploring underlying mechanisms, and validating findings across diverse populations to optimize early GDM prediction and management.

Conclusion

The diagnostic performance of serum uric acid as a biomarker for GDM was excellent in our study, with an area under the curve (AUC) of 0.908, highlighting the potential utility of serum uric acid as an early predictor of GDM, enabling timely risk stratification and intervention to improve maternal and fetal outcomes in presymptomatic low risk antenatal women.

Source of Funding

None.

Conflict of Interest

None.

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