

## To Evaluate the Role of First-Trimester Uric Acid Level in Prediction of Gestational Diabetes Mellitus

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### Abstract

**Objective:** Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy. Objective of this study was to estimate serum uric acid level in first trimester of pregnancy and correlate the first trimester serum uric acid levels and development of GDM.

**Methods:** This prospective observational study was conducted at department of Obstetrics and Gynaecology, SMS medical college and associated hospitals, Jaipur from April 2021 to October 2022. After applying inclusion and exclusion criteria, 70 cases of singleton pregnancy with gestational age <12 weeks were included in this study. Obstetrics, family and personal history was obtained from patient, all routine ante-natal investigations and Hb1Ac was done. Uric acid level was measured using calorimetric assay with detection limit of 10g/dl. The coefficient was 0.9%. All antenatal mothers were followed for around 24-28 weeks for routine GDMs screening. Around at 24-28 weeks, OGCT with 75gm glucose was done irrespective of her fasting status or timing of previous meal (DIPSI). GDM was diagnosed if after 2 hour blood glucose value is  $\geq 140$  mg/dl.

**Results:** In this study we observed that 32.3% patients with elevated uric acid level developed GDM and 9.3% patients with normal uric acid level developed GDM. This difference was statistically significant (p value = 0.001). In this study, elevated uric acid level (>4.2mg/dl) was found a predictor of GDM and has 75% sensitive and 60.7% specific with 32.3% and 90.6% positive and negative predicted values, respectively.

**Conclusion:** Result of this study has suggested that serum uric acid level estimation in first trimester can be used as a marker to predict the GDM in pregnant women.

**Keywords:** Serum uric level, Gestational Diabetes Mellitus (GDM), First trimester pregnancy.

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### Introduction

Gestational diabetes mellitus (GDM) is one of the most challenging medical complications encountered in pregnant

females. WHO and the American diabetic association defines GDM as “any degree of glucose intolerance with onset or first

recognition during pregnancy". [1] GDM has gained utmost importance nowadays because half of GDM women ultimately develop type 2 diabetes mellitus (T2DM) in the ensuing 20 years. In-utero exposure to hyperglycemia can lead to childhood obesity and diabetes.

In India, the prevalence of GDM was 2% in 1982 followed by 7.62% in 1991 and 16.5% in 2003 with expected rate of 79.4 million in 2030 i.e. 15.1% increase from 2000. [2] Compared to European females, the South Asian especially Indian females have 11 fold increased risk for GDM. [3] Women with gestational diabetes mellitus have a 50% chance of developing type 2 diabetes mellitus over the 20 years following their diagnosis of gestational diabetes mellitus. Maternal hyperglycemia leads to an increase in glucose delivery to the fetus, which causes fetal hyperinsulinemia and increased fetal growth.

Early diagnosis of GDM using OGTT is done between 24 and 28 weeks of gestational age. But no tests are available before this gestational age which can predict the development of GDM. GDM is important to be diagnosed early and treated effectively because of its complications in pregnancy. It is associated with various maternal complications like preeclampsia, preterm deliveries, polyhydramnios, still births, increased rates of LSCS and in fetus CNS, cardiac and genitourinary anomalies and NTD, macrosomia, still birth, birth injuries, hypoglycemic episodes, hyperbilirubinemia and RDS. Also these women are at higher risk of developing DM as compared with the normal women.

Uric acid is formed from xanthine by the effect of xanthine oxidase. It is considered the main product of purine metabolism. Nakagawa et al (2007) state that uric acid causes endothelial dysfunction and decreases nitric oxide production. [4] Increased serum uric acid level is

accompanied by hyperinsulinemia, hypertension, dyslipidemia and obesity, supporting that it could be a member of the group of factors of the metabolic syndrome. [5] Normally during pregnancy, the serum uric acid levels decreases significantly from 8th week of gestation up to 24 weeks due to enhancement of renal clearance secondary to increased glomerular filtration rate or reduced proximal tubular reabsorption and due to changes in its production rate.[6] In the first trimester, it likely approximates preconception uric acid level and elevated levels may identify women who are predisposed to metabolic syndrome with an increased risk of developing GDM.

### Material and Methods

This was a prospective observational study, conducted at department of Obstetrics and Gynaecology, SMS medical College, Jaipur from April 2020 to October 2022. Sample size was calculated at 80% study power and 95% confidence limit assuming proportion in group 1 is 3.5% and in group 2 is 18.6%. Sixty four (64) cases were required as sample size which was further enhanced and rounded off to 70 cases as a final size for present study.

**Inclusion criteria:** Singleton live pregnancy <12 week with written & informed consent.

**Exclusion criteria:** 1. Overt Diabetes Mellitus, 2. Patient received steroids in any form, 3. Connective tissue disorder, 4. History of thromboembolism, 5. Liver disease, 6. Cardiovascular disease.

After applying all inclusion and exclusion criteria antenatal women with singleton pregnancy with gestational age <12 weeks, attending ANC OPD were included in study. Obstetrics, family and personal history was obtained from patient, all routine ANC investigations and Hb1Ac was done. Venous sample was withdrawn from study population. The sample was centrifuged. Uric acid level was measured

using calorimetric assay with detection limit of 10g/dl. The coefficient was 0.9%. All antenatal mothers were followed up for around 24-28 weeks for routine GDMs screening. Around at 24-28 weeks, OGCT with 75gm glucose was done irrespective of her fasting status or timing of previous meal (DIPSI). GDM was diagnosed if after 2 hour blood glucose value was  $\geq 140$  mg/dl. This single step procedure had been approved by the Ministry of Health, Govt. of India, WHO and Diabetes in Pregnancy Study group of India (DIPSI) for diagnosis of GDM. Serum uric acid level was correlated with development of GDM. Data thus collected were analyzed statistically.

## Results

In this study 70 antenatal women with singleton pregnancy with gestational age <12 weeks attending antenatal OPD were recruited. The mean age of study participants was  $25.91 \pm 3.86$  years. We observed that 41.4% patients were in age group between 20-24 years followed by 37.2% patients in 25-29 years age group. In this study we found that 42.8% cases were of parity 2 followed by 33.6% patients of parity 1. Out of 70 recruited participants 72.2% patients had no history of casarean section, 22.1% patients had history of one cesarean section and 5.7% had history of two or more casarean sections. We observed that 46.4% patients had elevated serum uric acid ( $>4.2$ mg/dl). The mean serum uric acid was 3.86 mg/dl. (Table: 1)

**Table 1: Demographic and characteristics of the study population**

Characteristics		Percentage
Study subjects distribution according to parity (%)	1 (Primi)	33.6 %
	2 <sup>nd</sup>	42.8 %
	$\geq 3$	23.6 %
Study subjects distribution according to casarean section (%)	Nil	72.2 %
	1	22.1%
	$\geq 2$	5.7%
Study subjects distribution according to serum uric acid (%)	Normal	53.6 %
	Elevated ( $>4.2$ mg/dl)	46.4 %

The study result showed that 48.3% patients between age group 20-24 years, 44.2% between age group 25-29 years, 44.4% patients between age group 30-34 years had elevated serum uric acid level which was not statistically significant (P

value = 1.00). The author also observed that 48.9% primipara and 43.3% parity 2 women's had elevated uric acid which was not statistically significant (P value = 0.816). (Table 2)

**Table 2: Serum uric acid level in relation to age and parity of study subjects**

		Normal uric acid		Elevated uric acid		P value
		N	%	N	%	
Age group(years)	20-24	30	51.7	28	48.3	1.000 (NS)
	25-29	29	55.8	23	44.2	
	30-34	15	55.6	12	44.4	
	35-39	1	33.3	2	66.7	
Parity	1 (primi)	24	51.1	23	48.9	0.816 (NS)
	2	34	56.7	26	43.3	
	$\geq 3$	17	51.5	16	48.5	

The study result revealed that 39.4% with parity-3 patients and 16.7% with parity-2 patients had GDM, which was statistically significant (p value = 0.005). The result showed that 51.9% patients in age group 30-34 years and 100% patients in 35-39 years age group had GDM, which was statistically significant (p value <0.001). (Table 3)

**Table 3: GDM in relation to age and parity of study subjects**

		GDM		No GDM		P Value
		N	%	N	%	
<b>Age group(years)</b>	20-24	3	5.2	55	94.8	<b>&lt; 0.001 (S)</b>
	25-29	8	15.4	44	84.6	
	30-34	14	51.9	13	48.1	
	35-39	3	100	0	0	
<b>Parity</b>	1 (primi)	5	10.6	42	89.4	<b>0.005 (S)</b>
	2	10	16.7	50	83.3	
	≥3	13	39.4	20	60.6	

In our study, 80% of patients had normal DIPSI and 20% of patients had DIPSI greater than 140 mg/dl with a mean 114 mg/dl.

We observed that 32.3% women with GDM had elevated uric acid and 9.3%

women with GDM had normal uric acid level. When we correlated the GDM with serum uric acid level, we found that in majority of GDM patient, uric acid was found elevated, which was statistically significant (p value 0.001). (Table 4).

**Table 4: GDM in relation to Serum uric acid level among study subjects**

	GDM		No GDM		Total
	N	%	N	%	
<b>Elevated uric acid</b>	21	32.3	44	67.7	65
<b>Normal uric acid</b>	7	9.3	68	90.7	75
<b>Total</b>	28	20	112	80	140
Chi-square = 10.096 with 1 degree of freedom; P = 0.001 (S)					

Uric acid level 4.2mg/dl was taken as a standard cutoff for the prediction of GDM. We observed that serum uric acid level was 75% sensitive, 60.7% specific with a positive predictive value of 32.3% and negative predictive value of 90.6% in predicting the development of GDM. It has a diagnostic accuracy of 63.5%. (Table 5)

**Table 5: Diagnostic accuracy of uric acid (at standard cutoff of 4.2mg/dl) for diagnosis of GDM**

Parameter	Value	95% confidence interval
<b>Sensitivity</b>	75%	56.6 – 87.3%
<b>Specificity</b>	60.71%	51.5 – 69.3%
<b>PPV</b>	32.31%	22.2 – 44.9%
<b>NPV</b>	90.67%	81.9 – 95.4%
<b>Diagnostic accuracy</b>	63.57%	55.34 – 71.08%

## Discussion

Gestational diabetes mellitus is a common metabolic disorder during pregnancy which can be attributed to the genetic,

cultural and socio-economic factors; so it is very important to diagnose and treat it effectively at early stage to prevent its complication associated for both mother and fetus. Also these women are at higher

risk of developing DM in the next 2 decades as compared with the normal female population. The prevalence of GDM is rising across the globe and the benefits of broad screening for GDM have not yet been proven. [7,8] Considering that the prevalence of GDM varies greatly between populations, a better risk assessment model could prevent unnecessary oral GCTs for screening of GDM. Studies have shown that early glucose screening is definitely beneficial to patients to reduce the maternal and fetal morbidity. In this tertiary care level hospital based observational study we estimated and correlated first trimester serum uric acid level with development of GDM.

We observed that 46.4% patients had elevated serum uric acid (>4.2mg/dl) and 53.6% showed normal uric acid level. In the present study parity wise differences with serum uric acid was not statistically significant as the p value was 0.816; similar finding was noted in the study by Rasika et al. [9]

In our study, 80% of patients had normal glucose level and 20% of patients had glucose level 140 mg/dl on DIPS test with a mean of 114 mg/dl. A similar study by Ganta S J et al [10] found that out of 312 women, 88 (28.2%) had high OGCT levels.

When we compare the parity and age of participants with GDM, we found significant direct association of increasing age and parity with the development of GDM. Similar finding was noted in the study by Adel T et al. [11]. In 2021, Zhao Y et al [12] also observed that the associations of serum uric acid level with GDM were stronger among pregnant women aged 35 years or older.

We observed that 32.3% women with GDM had elevated uric acid and 9.3% women with GDM had normal uric acid level. When we correlated the GDM with serum uric acid level, we found that in

majority of GDM patient, uric acid was found elevated, which was statistically significant (p value 0.001). A similar finding was observed by Ali O A S et al, [13] who concluded that there is increased risk in development of GDM with the increase in uric acid level at the first trimester. Rasika C et al [9] also concluded that there is increase in the risk of development of GDM with increased levels of serum uric acid in the first trimester. Kapil D et al [14] also observed that out of 8 patients, who developed GDM 4 (50%) had serum uric acid >3.5 mg/dl and 4 (50%) had serum uric levels <3.5 mg/dl.

Uric acid level 4.2mg/dl was taken as a standard cutoff for the prediction of GDM. We observed the sensitivity and specificity of hyperuricemia for prediction of gestational diabetes mellitus were 75% sensitive, 60.7% respectively. We observed the positive predictive value and negative predictive value were of 32.3% and 90.6% respectively. We also noted that it has a diagnostic accuracy of 63.5%. Rehman A et al. [15] observed that the sensitivity and specificity of hyperuricemia for prediction of gestational diabetes mellitus were 91.1% and 95.7% respectively. The positive predictive value and negative predictive value of hyperuricemia were 86.8% and 97.2% respectively. The overall diagnostic accuracy was 94.5%. Amudha P et al. [16] found that the cut off serum uric acid level of 3.6mg/dl was found to have 92% sensitivity; specificity of 99% for the development of GDM. Şahin Aker et al [17] observed first trimester serum uric acid levels had a sensitivity of 100% and specificity of 60% for the prediction of GDM. [18]

### Conclusion

The complications of gestational diabetes mellitus in pregnancy are often diagnosed only after mid-late gestation. By the time the diagnosis of gestational diabetes

mellitus is made, the potential adverse perinatal outcome may become irreversible. Hence, it becomes mandatory to diagnose or predict the gestational diabetes mellitus at the earliest. Though our study results suggest that serum uric acid level estimation in first trimester can be used as a marker to predict GDM in pregnant women, larger studies are required before it can be recommended as a routine first trimester screening test for prediction of GDM, so that its dreadful complications can be avoided in future

#### Authors Contribution

All the authors contributed to the preparation of the final manuscript.

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