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Original Article

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

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## Abstract

**Background:** The aim of this study is to analyze the relationship between first-trimester uric acid levels and the risk of developing gestational diabetes mellitus (GDM).

**Method:** A prospective study was conducted in 100 antenatal women <12 weeks gestation, blood sample for serum uric acid was taken. They were subjected to oral glucose challenge test and oral glucose tolerance test to analyze the association of GDM.

**Results:** GDM complicated 10% of the patients included in the study. Out of 43 patients with serum uric acid with more than 3.6 mg/dl, 13 patients had deranged blood sugar screening, and out of these eight patients developed GDM ($P < 0.05$).

**Conclusion:** This study demonstrates a positive association between elevated first trimester uric acid and GDM.

**Key words:** First trimester, Gestational diabetes mellitus, Uric acid

## INTRODUCTION

Diabetes complicating pregnancy has become more common worldwide, around 3–10% pregnancies.

The reason for this rise in the prevalence of diabetes is mainly change in the lifestyle, dietary habits older age at first conception polycystic ovarian disease and obesity.

Uric acid is associated with insulin résistance in non-pregnant women. In pregnancy, uric acid is correlated with insulin resistance in women with gestational hypertension and gestational diabetes mellitus (GDM). Uric acid is also higher in non-pregnant women with H/O GDM independent of body mass index (BMI).

Since insulin resistance is correlated with elevated uric acid, we can predict the development of diabetes. Pregnancy is a unique physiological condition. It is a diabetogenic condition due to progressive increase in the insulin resistance.

The diabetogenic effects of pregnancy are as follows:
1. Insulin resistance
2. Increased lipolysis
3. Changes in gluconeogenesis
4. Uric acid causing insulin resistance.

Uric acid increase with increased protein intake, alcohol consumption, decreased excretion, or increased endogenous production.

### Aim

The aim of this study is to analyze the relationship between first-trimester uric acid levels and prediction of developing GDM.

Uric acid is the end product of urine metabolism. Uric acid are obtained from both dietary sources and breakdown of body protein liver kidneys. Kidneys excrete two-thirds of the uric acid daily and remaining one-third in the stool.

### Reference values

Adult males: 2.0–7.5 mg/dl

Adult females: 2.0–6.5 mg/dl.

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In early pregnancy, uric acid levels fall by about one-third but rise to non-pregnant levels by the term.

The normal range for urinary uric acid is between 250 and 750 mg over a 24 h period hyperuricemia is seen in gout, renal disease, and renal failure.

Uric acid concentrations decreased significantly by 8 weeks when compared to pre-pregnant values. This level maintained until about 24 weeks.

Then, the concentrations increased such that by the term, they were greater than the pre-pregnancy values in the majority of patients and remain elevated till 12 weeks after delivery.

Uric acid in the first trimester likely approximates preconception uric acid level. Elevated uric acid may identify women who are predisposed to metabolic syndrome with the risk of developing GDM. Lind *et al.* studied the changes in serum uric acid concentrations during normal pregnancy.[1] He found that compared with pre-pregnancy values uric acid concentrations decreased significantly by 8 weeks gestation, and this reduced level was maintained until about 24 weeks. Thereafter, the concentrations increased such that by the term, they were greater than the pre-pregnancy values in the majority of patients and remained elevated until at least 12 weeks after delivery.

| Pregnancy status | Uric acid |
|---|---|
| Non-pregnant adult | 2.5–5.6 |
| First trimester | 2.0–4.2 |
| Second trimester | 2.4–4.9 |
| Third trimester | 3.1–6.3 |

## MATERIALS AND METHODS

A total of 100 antenatal women attending OPD at the first trimester were included in the study after satisfying inclusion and exclusion criteria. Informed consent was obtained from all patients height, weight, and BMI were measured, and gestational age was confirmed by ultrasonography.

### Inclusion Criteria

Antenatal women with gestational age <12 weeks.

### Exclusion Criteria

- Pregnant women >12 weeks
- Overt DM
- Or who received steroids in any form
- Gout
- Other endocrine disorder
- Chronic renal disease
- Connective tissue disorder
- H/O thromboembolism
- Liver disease, cardiovascular disease.

### Measurement of Plasmauric Acid

Venous blood sample was withdrawn from antenatal women with gestational age <12 weeks. The samples were centrifuged and stored at −70°C. Uric acid measured using colorimetric assay with detection limit of 10 mg/dl. The coefficient was 0.9%.

### Screening for GDM

All antenatal mothers were followed up around 24–28 weeks for routine GDM screening with 50 g of oral glucose challenge test (GCT). Those antenatal mothers with plasma glucose level after 1 h ≥140 mg/dl, are considered high risk and are subjected to oral glucose tolerance test.

## RESULT

In our study the frequency is high around above 11 weeks [Figure 1].

Among total 43 patients with elevated uric acid 19 of them from 21 to 25 years of age 15 of them 26–30 years of age [Table 1].

In our study of the total patients 43 with elevated uric acid, 13 patients had positive GCT - constituting 37% and those with normal uric acid of 57 patients 12 were positive for GCT (21%) [Table 2].

In our study among the 43 patients with elevated uric acid, 8 patients were positive for GTT. And the remaining 35 negative for GTT. And among the 57 patients with normal uric acid only 2 were GTT Positive. Hence elevated uric acid in the first trimester strongly associated with GTT ($P < 0.05$) [Table 3].

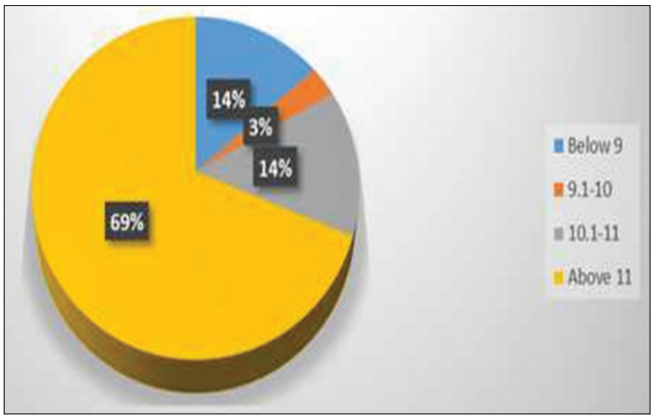


**Figure 1: Gestational age in weeks**

## DISCUSSION

Pregnancy induces progressive changes in maternal carbohydrate metabolism. As pregnancy advances insulin resistance and diabetogenic stress increases due to placental hormones. When this compensation is inadequate gestational diabetes develops.

It is possible that the association of uric acid with insulin resistance is causal. Two mechanisms have been hypothesized by which uric acid can cause insulin resistance. Nakagawa *et al.*[2] proposed that uric acid causes endothelial dysfunction and decreases nitric oxide production by the endothelial cell.[3] Another mechanism by which uric acid may induce insulin resistance may be that uric acid causes inflammation and oxidative stress in adipocytes, which is a contributor to the development of metabolic syndrome.

In our study of the total 100 antenatal, 10 were developed GDM. Out of 10, eight had elevated serum uric acid in first trimester, which constitutes about 16.7%. Moreover, among two GDM mothers with normal serum, uric acid constitute about three with $P < 0.001$. Among those with normal uric acid, GCT was positive among 12 mothers (constituting 21%). Of the elevated serum uric acid, GCT was positive among 13 mothers (constituting 66.7%) with significant $P < 0.001$.

Although uric acid was strongly associated with BMI, the risk of gestational diabetes was increased among women with elevated first-trimester uric acid independent of BMI.

Our findings are consistent with the association of uric acid with insulin resistance in the non-pregnant population.[4] In a large cross-sectional study of 53,477 non-pregnant adults, serum uric acid was positively correlated with fasting serum glucose and insulin resistance, as well as features of the metabolic syndrome, including waist circumference, low HDL cholesterol, hypertriglyceridemia, hypertension, and fasting glucose ≥ 110 mg/dl.

A study by Di Cianni *et al.* in which serum uric acid was measured at a median of 16 months postpartum in women who had pregnancies complicated by gestational diabetes.[4] Uric acid was significantly higher in women with metabolic syndrome (4.8 ± 1.2 mg/dl) versus women without metabolic syndrome (4.1 ± 0.8, $P < 0.01$), independent of BMI, and metabolic syndrome is a known risk factor for developing type 2 diabetes.

According to Dehghan *et al.*, hyperuricemia has also been demonstrated to be a risk factor for developing type 2 diabetes.[5]

This study demonstrates a striking association between first-trimester uric acid and risk of developing gestational diabetes. Women who have a pregnancy complicated by gestational diabetes have up to a 50% chance of developing type 2 diabetes in their lifetime. It would be interesting to know whether these were the women with elevated uric acid in the first trimester.

The relationship of uric acid elevation in early pregnancy does indicate that metabolic state may affect adverse pregnancy outcomes. With the increase in both metabolic syndrome and obesity, more women are entering pregnancy with these conditions. It is possible that of the women who develop GDM, those with elevated first-trimester uric acid are the women who are at risk to develop type 2 diabetes, and this warrants future investigation.

Thus, we postulate that elevated first-trimester serum uric acid helps in the prediction of GDM and also to identify those at risk of developing type 2 DM and follow-up; and to counsel the patient about the short-term and long-term outcomes.

**Table 1: Distribution of maternal age with elevated uric acid**

| Age | Number (elevated uric acid) |
|---|---|
| Upto 20 | 5 |
| 21–25 | 19 |
| 26–30 | 15 |
| >30 | 4 |
| Total | 43 |

**Table 2: Serum uric acid *GCT cross tabulation**

| OGCT | | |
|---|---|---|
| **Uric acid** | **OGCT normal** | **OGCT abnormal** |
| Normal | 45 | 12 |
| Abnormal | 30 | 13 |

OGCT: Oral glucose challenge test

| Uric acid | n | Mean | Standard deviation | Correlations co-efficient | *P* value |
|---|---|---|---|---|---|
| | 100 | 3.50 | 1.21 | 0.209 | 0.036 |
| OGCT | 100 | 114.90 | 31.79 | | |

OGCT: Oral glucose challenge test

**Table 3: Serum uric acid *GTT cross tabulation**

| GTT | | | |
|---|---|---|---|
| **Uric acid** | **Normal** | **Abnormal** | ***P* value** |
| Normal | 55 | 2 | 0.041 |
| Abnormal | 35 | 8 | |

GTT: Glucose tolerance test

## CONCLUSION

The objective of implementing an antenatal screening test for GDM is to identify pre-symptomatic women who will subsequently develop complications of pregnancy and implement efficacious treatment to reduce morbidity and mortality. Currently, complications of pregnancy due to GDM are not diagnosed until mid-late gestation.

Many health professionals advocate the need for an earlier diagnostic/predictive test for GDM, one among them is "the first-trimester serum uric acid."

A pregnant woman with high-risk factors as marked obesity, strong family history of type II DM, previous history of GDM, impaired glucose metabolism or glucosuria, history of neonatal death, history of fetal macrosomia, and along with >3.6 mg/dl is at risk of developing GDM.

The use of first-trimester serum uric acid as a predictor of GDM is simple, inexpensive, non–invasive, and easy to perform. This can be used as a screening test for the prediction of GDM.

Hence, in routine antenatal care with predictive test such as first-trimester serum uric acid can be applied as a screening test for all women, so we can predict GDM and diagnosed in time.

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