



TO STUDY ELEVATED FIRST TRIMESTER SERUM URIC ACID LEVELS AS A PREDICTOR OF GESTATIONAL DIABETES MELLITUS

Gynaecology

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ABSTRACT

Introduction: Gestational diabetes mellitus is one of the most important complications during pregnancy which is associated with both maternal and fetal morbidity and mortality¹. WHO / American diabetes association define GDM as any degree of Glucose intolerance with onset or 1st recognition during pregnancy irrespective of the treatment with diet or insulin². Serum Uric acid is associated with insulin resistance in non-pregnant women³. Uric acid is an independent risk factor for developing type 2 diabetes within 10 years in non-pregnant adults, in pregnancy uric acid is correlated with insulin resistance in women with gestational hypertension¹⁰ and higher at 24-28 weeks gestation in women diagnosed with GDM compared to women without diabetes⁴.

Method: This prospective study was conducted on 154 antenatal women, with singleton pregnancy of gestational age < 15 weeks in first trimester at Rajkiya Mahila Chikitsalaya, JLN Medical College, Ajmer, during Oct 2017 to Sep 2018 after considering all exclusion and inclusion criteria. Obstetric history, family history, and personal history was obtained from patients. Per abdomen examination and USG was done to calculate the gestational age of every patient. Venous blood sample was withdrawn from antenatal women for serum uric acid levels. All antenatal mothers was followed for around 24-28 weeks for routine GDM screening. Association between elevated serum uric acid level in first trimester and GDM was calculated with statistical methods of analysis.

Results: Among the total 154 antenatal patients under study in first trimester, 119 patients (77%) had normal uric acid level and 35 patients (23%) had elevated uric acid level. Out of 35 patients who had elevated serum uric acid level in first trimester, 15(42.85%) had serum uric acid in 1st quartile, 11(31.42%) had serum uric acid in 2nd quartile, 9(25.71%) had serum uric acid level in 3rd quartile. Serum uric acid level of patients under study at 24-28 weeks of gestation, out of 154 patients, 46 (29.87%) had elevated uric acid level and 108 (70.12%) had normal level of uric acid. Out of 154 patients, GCT was negative in 110 (71%) patients, and GGT was positive in 44 (29%) patients. Out of 154 patients, 13 patients (8.5%) had DIPSI positive and 141 patients (91.5%) were negative. DIPSI test is confirmatory test for GDM in patients under study. Out of 13 patients diagnosed GDM 8(61.53%) had family history of GDM and 5(38.46%) had no family history of GDM. Out of 13 patients who had GDM, 10 patients had elevated serum uric acid level, out of them 2(20%) patients had serum uric acid level in 1st quartile, 2(20%) in 2nd quartile and 6(60%) in 3rd quartile.

Conclusion: Hyperuricemia has been demonstrated to be a risk factor for developing type 2 diabetes. In our study, we found that uric acid ≥ 6.5 mg/dl early in pregnancy is associated with increased risk of developing gestational diabetes. Our study demonstrated a striking association between first trimester uric acid and risk of developing gestational diabetes, more than half of the women with uric acid in the highest quartile actually developed the disease. Thus we postulate that elevated 1st trimester serum uric acid helps in the prediction of gestational diabetes mellitus and also identification those at risk of developing type II Diabetes mellitus of follow up.

KEYWORDS

GDM, 1st trimester, DIPSI, GCT, GGT

INTRODUCTION:

Gestational diabetes mellitus is one of the most important complications during pregnancy which is associated with both maternal and fetal morbidity and mortality¹. WHO / American diabetes association define GDM as any degree of Glucose intolerance with onset or 1st recognition during pregnancy irrespective of the treatment with diet or insulin². Serum Uric acid is associated with insulin resistance in non-pregnant women³. Outside of pregnancy hyperuricemia is also associated with the markers of metabolic syndrome including obesity and dyslipidemia⁵⁻⁸. Uric acid is an independent risk factor for developing type 2 diabetes within 10 years in non-pregnant adults, an association that was stronger in women compared to men⁵. Uric acid is also higher in non-pregnant women with history of gestational diabetes, independent of body mass index⁶. Uric acid is associated with insulin resistance and predates development of type 2 diabetes in non-pregnant adults. First trimester hyperuricemia was associated with increased risk of developing GDM. The risk of developing GDM will be 3.25 fold higher if first trimester uric acid was in 4th quartile. Although uric acid was strongly associated with BMI, the risk of GDM was increase among women with elevated first trimester serum uric acid independent of BMI.

Method: This prospective study was conducted on 154 antenatal women, with singleton pregnancy of gestational age < 15 weeks in first trimester at Rajkiya Mahila Chikitsalaya, JLN Medical College, Ajmer, during Oct 2017 to Sep 2018. All exclusion criteria were excluded. Obstetric history, family history, and personal history was obtained from patients. Per abdomen examination and USG was done to calculate the gestational age of every patient. Venous blood sample

was withdrawn from antenatal women for serum uric acid levels measurement by Dynamic extended stability with Lipid clearing agent named as "MODIFIED TRINDER METHOD, END POINT". All antenatal mothers was followed for around 24-28 weeks with proper proforma information for routine GDM screening. Association between elevated serum uric acid level in first trimester and GDM was calculated with statistical methods of analysis.

OBJECTIVE: The aim of the study is to test the association of elevated first trimester serum uric acid as a predictor of gestational diabetes mellitus.

OBSERVATION AND RESULTS: Among the total 154 antenatal patients under study in first trimester, 119 patients had normal uric acid level constituting about 77% and 35 patients had elevated uric acid level constituting about 23%. Out of 35 patients who had elevated serum uric acid level in first trimester, 15(42.85%) had serum uric acid in 1st quartile, 11(31.42%) had serum uric acid in 2nd quartile, 9(25.71%) had serum uric acid level in 3rd quartile. serum uric acid level of patients under study at 24-28 weeks of gestation. Out of 154 patients, 46 (29.87%) had elevated uric acid level and 108 (70.12%) had normal level of uric acid. Out of 154 patients, GCT was negative in 110 (71%) patients, and GCT was positive in 44 (29%) patients.

Table-1 Serum Uric acid level of patients in first trimester

Uric acid	Frequency	Percent	Valid percent	Cumulative percent
Elevated	35	23.0	23.0	23.0
Normal	119	77.0	77.0	100.0
Total	154	100.0	100.0	

Table – 2 Serum Uric acid level in different quartiles in patients who had elevated serum uric acid in first trimester

Serum Uric Acid level in different quartiles in 1st trimester (2 – 4.2) mg/dl	No. of patients	percentage
1st Quartile (4.2-6)	15	42.85
2nd Quartile (6 – 7.5)	11	31.42
3rd Quartile (>7.5)	9	25.71
Total	35	100

Table-3 Glucose Challenge Test as a screening test performed at 24-28 wks of gestation.

GCT	Frequency	Percent	Valid percent	Cumulative percent
Negative	110	71.0	71.0	71.0
Positive	44	29.0	29.0	100.0
Total	154	100.0	100.0	

Out of 154 patients under study, 13 patients had DIPSI positive and constituting 8.5% and 141 patients were negative DIPSI constituting 91.5%. This test is confirmatory test for GDM in patients under study. Out of 13 patients diagnosed GDM 8(61.53%) had family history of GDM and 5(38.46%) had no family history of GDM.

Table-4 DIPSI Test (Diabetes in Pregnancy study group of India) – confirmatory test for GDM (performed at 24-28 weeks of gestation)

GCT	Frequency	Percent	Valid percent	Cumulative percent
Negative	13	8.5	8.5	8.5
Positive	141	91.5	91.5	100.0
Total	154	100.0	100.0	

Out of 13 patients who had GDM, 10 patients had elevated serum uric acid level. Out of them 2 (20%) patients had serum uric acid level in 1st quartile, 2(20%) in 2nd quartile and 6(60%) in 3rd quartile. In our study of the total 35 patients with elevated uric acid, 12 patients (34.28%) had normal GCT and the remaining 23 patients (65.71%) with elevated uric acid had positive GCT. Among 119 patients with normal uric acid, 87 patients (77.5%) had normal GCT and 32 patients (38.5%) was positive for GCT. In our study among the 35 patients with elevated uric acid level, 10 (28.57%) patients were positive for DIPSI and the remaining 25 (71.43%) were negative for DIPSI. Among the 119 patients with normal uric acid level only 3 (2.52%) were DIPSI positive.

DISCUSSION: This study was undertaken to find out the association of elevated first trimester uric acid with development of GDM. In our prospective study 154 antenatal women were included belonging to first trimester, who were attendees of RMC, JLN Medical College, Ajmer during Oct 2017 to Sep 2018. In our study, we measured serum uric acid of patients under study in first trimester and they were follow up at 24-28 wks. At 24-28 weeks of gestation these patients were screened for GDM by GCT and confirmed by DIPSI. Serum uric acid was also measured at 24-28 weeks. In our study 13 total mothers who developed GDM 10 Antenatal mothers had elevated serum uric acid in first trimester, which constitute about 76.92% (% within in DIPSI) and 3 GDM mothers with normal serum uric acid level constitute about 23.08% (% within DIPSI) with p value <0.001. In our study out of 13 patients who developed GDM 6 patients were primigravida i.e. 46%. **Dunlop W et al (2001)** in their study shows that there was no difference detected in the changes seen in serum uric acid levels between primigravida and multigravida.

A study by **Nagalakshmi CS et al (2012)** has shown an increased risk of developing GDM among primigravida. **Al Rowaily CS et al (2010)** have shown in their study that multiparous women were 8.29 times more likely to have GDM than nulliparous women. However they concluded after adjustment of maternal age and history of abortion nulliparous women was 2.95 times more likely to develop GDM than parous women.

In our study all antenatal women undertook glucose challenge test (GCT), more of a screening test. Of the normal uric acid GCT was positive among 32 mothers (constituting 26.6%). Of the elevated serum uric acid GCT was positive among 23 mothers (constituting 66.7%) with significant p < 0.001. In our study out of 35 patients with elevated serum uric acid level 15(42.35%) patients had uric acid level in 1st quartile, 11(37.2%) were in 2nd quartile, 9(25.7%) in 3rd quartile. Out of 13 patients who developed GDM 10 patients had elevated serum uric acid and among them 2(40%) belongs to serum

uric level in 1st quartile, 2(40%) in 2nd quartile and 6(60%) in 3rd quartile.

This results is comparable from study of **Katherine S Laughon, Catovr Janet (2009)** they reported that the subjects with uric acid in the first quartile had a normal one step test value (<120mg/dl). In the second quartile 27.1% had gestational glucose intolerance i.e. one step test of 120 to 140 mg/dl and 5.4% had GDM (>140mg/dl). In the third quartile 81.3% had gestation glucose intolerance and 12.5% had GDM. This distribution has revealed that higher level of serum uric acid in the first trimester were strongly associated with increased levels of one step test (120 to 140mg/dl) i.e. Gestational Glucose Intolerance (GGI) (p<0.001) though only 5.7% were diagnosed to have GDM.

Hyperuricemia has also been demonstrated to be a risk factor for developing type 2 diabetes. In our study, we found that uric acid ≥ 6.5 mg/dl early in pregnancy is associated with increased risk of developing gestational diabetes. Our study demonstrated a striking association between first trimester uric acid and risk of developing gestational diabetes, more than half of the women with uric acid in the highest quartile actually developed the disease and rest did not developed GDM due to different pathways of development of gestational diabetes.

Our findings are consistent with the association of uric acid with insulin resistance in the non-pregnant population and also the early pregnancy uric acid concentrations in our study were similar to those reported by others. Majority of the subjects did not have any changes between serum uric acid levels at <15 weeks and at 24 to 28 weeks of gestation. They either had same levels or slight increase in the level. This could have been due to the normal changes that occur in uric acid levels in pregnancy as stated by **Boyle JA et al.84,(2012)** that the uric acid level fall during the early and mid-trimester rises to normal values in late pregnancy. There was no significant correlation between uric acid levels at 24 to 28 weeks and risk of development of GDM (p=0.094). Though there was a significant correlation between serum uric acid at <15 weeks and at 24 to 28 weeks, serum uric acid at <15 weeks of gestation was a better predictor of GGI and GDM (Pearson's correlation = 0.735). This is due to the fact that serum uric acid levels normally falls in early trimester and mid-trimester and rises to normal values in late pregnancy.

Thus we postulate that elevated first trimester serum uric acid helps in the prediction of gestational diabetes mellitus and also identification those at risk of developing type II Diabetes mellitus of follow up; also to counsel the patient about the short term and long term outcomes.

CONCLUSION: Based on the results and the methodology employed, we have concluded that: There is increase in the risk of development of GDM with increased levels of serum uric acid in the first trimester. This association is independent of age, parity, BMI and family history of DM though there is association of these variables (advanced maternal age, high parity, increased BMI and positive family history) with GDM. Uric acid levels at <15 weeks of gestation is more significantly associated with risk of development of GDM than serum uric acid level at 24 to 28 weeks of gestation. There is no significant changes in the levels of serum uric acid at <15 weeks and at 24 to 28 weeks of gestation.

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 like first trimester serum uric acid can be applied as a screening test for all women then this dreadful Gestational diabetes can be treated in time.

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