



Research Article

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

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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. 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 hypertension 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. Venous blood sample was withdrawn from antenatal women for serum uric acid levels.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 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: 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.

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INTRODUCTION

Gestational diabetes mellitus is one of the most important complications during pregnancy which is associated with both maternal and fetal morbidity and mortality.¹

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 insulin.²

Incidence: It affects 7% of all pregnancy worldwide and in India it ranges from 6-9% in rural and 12-21 % in urban area.³ Serum Uric acid is associated with insulin resistance in non-pregnant women.⁴ Outside of pregnancy hyperuricemia is also

associated with the markers of metabolic syndrome including obesity and dyslipidemia.⁵⁻⁸

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 men.⁹

Uric acid is the end product of purine metabolism catalyzed by enzyme Xanthine oxidase / dehydrogenase. 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 diabetes.¹¹ Uric acid is also higher in non pregnant women with history of gestational diabetes, independent of body mass

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index¹² since uric acid is associated with insulin resistance and predates development of type 2 diabetes in non-pregnant adults, we hypothesize higher serum uric acid in first trimester will be associated with development of gestation diabetes.

Normally during pregnancy, the serum uric acid level decreased significantly from 8th week of gestation upto 24th weeks due to increased glomerular filtration rate and decreased reabsorption of uric acid from renal tubules. In the first trimester it likely approximates preconception serum uric acid level and elevated levels may identify women who are predisposed to metabolic syndrome than increased risk of GDM.

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

This prospective study was conducted at RMC, JLN Medical College, Ajmer during time period Oct. 2017 to Sep. 2018. A total of 154 antenatal women in first trimester were included in the study. The aim of the study will be explained to the antenatal women and informed consent was taken.

Inclusion criteria

Antenatal women with singleton pregnancy with gestational age < 15 weeks

Exclusion criteria

1. Pre-gestational diabetes mellitus
2. Obesity
3. Renal disease
4. Liver disease
5. Cardiovascular disease
6. Gout
7. Smoking
8. Chronic hypertension
9. Multiple gestation

Detailed history regarding present Obstetric history, past obstetric history, family history, and personal history was obtained from the patients. General examination was done. Per abdomen examination was done. USG was done to calculate the gestational age.

METHODOLOGY

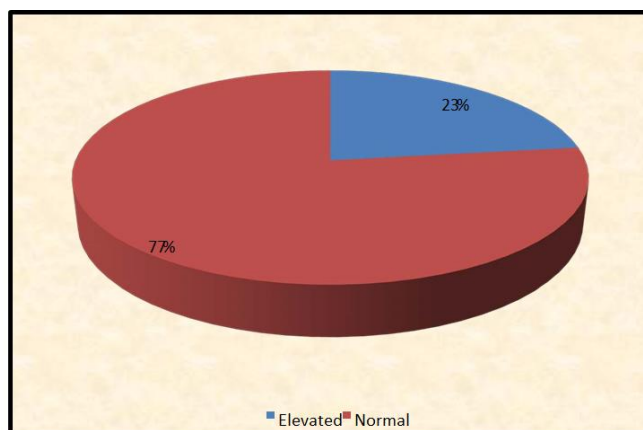
Measurement of plasma uric acid

Venous blood sample was withdrawn from antenatal women with gestational age < 15 weeks. Serum uric acid levels was measured by Dynamic extended stability with Lipid clearing agent named as "MODIFIED TRINDER METHOD, END POINT".

Specimen Collection and Handling

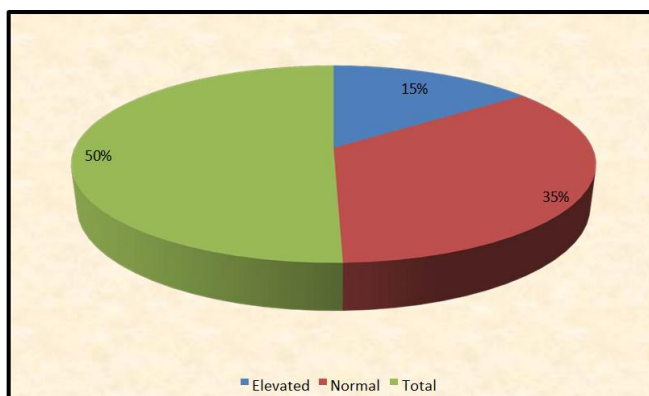
Use non-hemolytic serum or plasma (heparin, EDTA) or urine. It is recommended to follow NCCLS procedures (or similar standardized conditions).

RESULTS



Graph 1 Serum Uric acid level in first Trimester of pregnancy

Graph -1 This graph shows the distribution of serum uric acid level, 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%.



Graph 2 Serum acid level in patients at 24-28 weeks

Above graph 2 shows 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.

Table 1 Serum Uric acid in different quartile in GDM diagnosed patients

Serum Uric acid Level in dif. quartile	No. of GDM patient	%
I quartile	2	40
II quartile	2	40
III quartile	6	60

Following table shows GDM diagnosed patients understudy with elevated serum uric acid level according to different quartile. 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 Ist quartile, 2(20%) in IInd quartile and 6(60%) in IIIrd quartile

Table 2 Serum Uric Acid * GCT Cross tabulation

Serum Uric Acid	Normal	Count	GCT		
			Normal	Positive	
		87	32	119	
		% within Serum Uric Acid	73.4%	26.6%	100.0%
		% within GCT	77.5%	38.5%	61.0%

Elevated	Count	12	23	35
	% within Serum Uric Acid	33.3%	66.7%	100.0%
Total	% within GCT	22.5%	61.5%	39.0%
	Count	89	65	154
Total	% within Serum Uric Acid	57.8%	42.2%	100.0%
	% within GCT	100.0%	100.0%	100.0%

In our study of the total patients (35) with elevated uric acid, 12 patients had normal GCT – constituting 34.28%. And the remaining 23 patients with elevated uric acid had positive GCT constituting 65.71%.

And among those with normal uric acid total (119), 87 patients had normal GCT constituting 77.5% and 32 patients was positive for GCT with 38.5%.

Table 3 Serum Uric Acid * DIPSII Cross tabulation

		DIPSII		Total	
		Positive	Negative		
Serum Uric Acid	Elevated	Count	10	25	35
		% within Serum Uric Acid	28.57%	71.43%	100%
		% within DIPSII	76.92%	17.73%	22.72%
	Normal	Count	3	116	119
		% within Serum Uric Acid	2.52%	97.48%	77.28%
		% within DIPSII	23.08%	82.27%	77.28%
Total	Count	13	141	154	
	% within Serum Uric Acid	8.44%	91.56%	100.0%	
	% within DIPSII	100.0%	100.0%	100.0%	

In our study among the 35 patients with elevated uric acid level, 10

(28.57%) patients were positive for DIPSII. And the remaining 25 (71.43%) were negative for DISPI.

And among the 119 patients with normal uric acid level only 3 (2.52%) were DIPSII positive.

Table 4 Reliability of serum uric acid level as a screening test in prediction of GDM

Sensitivity	specificity	Positive predictive value	Negative predictive value
76.9	82.6	28.57	97.47

Disease Total

Test	Absent
Positive	(c) 25
Negative (b) 3	(d) 116
Sensitivity = a/ a+b X 100	10/10+3 X 100 = 76.9
Specificity = d/c+d X 100	116/25 + 116 X 100 = 82.6

Positive predictive value = a/a+c X 100 = 10/35 X 100 = 28.57

Negative predictive value = d/b+d X 100 = 116/119 X 100 = 97.47

DISCUSSION

This study was undertaken to find out the association of elevated first trimester uric acid with development of GDM. 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 DIPSII. 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 DIPSII) and 3 GDM mothers with normal serum uric acid level constitute about 23.08% (% within DIPSII) with p value <0.001).

In our study out of 35 patients with elevated serum uric acid level 15(42.35%) patients had uric acid level in Ist quartile, 11(37.2%) were in IInd quartile, 9(25.7%) in IIIrd 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 Ist quartile, 2(40%) in IInd quartile and 6(60%) in IIIrd quartile.

In our study, we found that uric acid ≥ 6.5 mg/dl early in pregnancy is associated with a 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.

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 do 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. Elevated or higher normal levels of serum uric acid in the first trimester may be associated with a pre-existing metabolic derangement which leads to poor maternal physiological adaptations and predisposes the pregnant women to development of pregnancy complications like GDM, preeclampsia etc.

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.

Summary

- 35(23%) patients had elevated Ist trimester serum uric acid and 119 (77%) had normal level of serum uric acid in first trimester.
- Out of 35 patients with elevated Ist trimester serum uric acid level 15 (42.85%) patients in Ist quartile, 11 (31.42%) patients in IInd quartile and 9 (25.71%) patients in IIIrd quartile.
- 46 (29.87%) patients had elevated serum uric at 24-28 weeks and 108 (70.12%) patients had normal level of serum uric acid at 24-28 weeks
- Among 35 patients with elevated serum uric acid in Ist trimester.12 (34.28%) patients had normal GCT and 23 (65.71%) patients had positive GCT.

5. Among 35 patients with elevated serum uric acid level in Ist trimester, 10 (28.57%) patients were positive for DIPSI and remaining 25 (71.43%) patients were negative and among 119 patients with normal uric acid level in Ist trimester only 3 (2.52%) patients were DIPSI positive.
6. Reliability of serum uric acid level as a screening test in prediction of

GDM.

Sensitivity – 76.9%

Specificity – 82.6%

Positive predictive value – 28.57%

Negative predictive value – 97.48%

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. 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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