Original Research Article

Increased first trimester serum uric acid as a predictor of Gestational diabetes mellitus

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A R T I C L E   I N F O

A B S T R A C T

Introduction: Women with raised uric acid in pregnancy are interlinked with more incidence of unfavourable outcomes in pregnancy such as gestational diabetes mellitus. The study aims at testing the hypothesis that elevated uric acid in first trimester of pregnancy is associated with subsequent development of gestational diabetes.

Materials and Methods: All pregnant women less than 12 weeks were included in this study after informed consent. Blood samples were collected for serum uric acid analysis and all these patients were followed up with oral glucose tolerance test at twenty-four to twenty-eight weeks of gestation.

Results: The mean age of pregnant women was 29.84 ± 4.94 years. The mean height and weight was 151.52 ± 7.49 cms and 50.60 ± 6.88 kg respectively. The body mass index of patients was 22.13 ± 3.31 kg/m^2. The mean gestational age of pregnant women was 11.14 ± 1.30 weeks. The mean uric acid level was 3.81 ± 1.24 mg/dl. In this study the p value was 0.018 using chi-square test which was significant.

Conclusion: Hyperuricemia in first trimester is a reliable marker for the prediction of gestational diabetes mellitus in later pregnancy.

1. Introduction

Gestational diabetes mellitus is defined as "intolerance of carbohydrates with varying severity with its onset or first detection during the current pregnancy.[1]" Prevalence of GDM ranges between 1 to 14%.[2] The prevalence of GDM is higher in African American and Asian women than in Caucasian women.

GDM is commonly picked up by screening only at 24 to 28 weeks to avoid maternal and fetal complications.[3] Pregnant mothers with GDM have more risk of operative vaginal deliveries and caesarean sections and complications like shoulder dystocia, macrosomia, hypoglycaemia in the newborn.[4]

Women with GDM also have a higher propensity to develop diabetes in later life. The HAPO study states that there is no threshold at which these adverse events occur in the mother or the foetus. The mainstay of treatment remains medical nutrition therapy, glycemic profile or insulin therapy.

Normal value of serum uric acid is between 2 to 6.5 mg/dl.[5] In early pregnancy, there is decreased serum uric acid due to increased GFR. Uric acid is a product of metabolism of purines and is formed by xanthine oxidase enzyme. Hypoxia and ischemia of the placenta and cytokines such as interferon induce the expression of xanthine oxidase and therefore, increase the production of uric acid and also reactive oxygen species. Serum uric acid is interlinked with hypertension, obesity, hyperinsulinemia and dyslipidemia indicating that it could be a part of the group of factors of metabolic syndrome.[6] There is

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strong evidence that hyperuricemia is linked to metabolic syndrome and type 2 DM in the general population. Uric acid produces insulin resistance by causing endothelial dysfunction and by decreasing nitric oxide levels in epithelial cells. Also it causes inflammation as well as oxidative stress in adipocytes.[7]

2. Materials and Methods

This is a prospective cohort study conducted for a period of 18 months which involves 106 antenatal women in first trimester attending OPD in a tertiary care centre. This study was carried out after obtaining ethical clearance from IEC and informed, written consent was obtained from all participants. Sample size was calculated to be 106 based on previous studies.

2.1. Inclusion criteria

1. All non-diabetic antenatal women in their first trimester of pregnancy less than 12 weeks of gestation.

2.2. Exclusion criteria

1. Hypertension
2. Renal disease
3. Liver disease
4. Gout
5. Smoking and alcohol intake
6. Drugs known to cause increased serum uric acid levels. eg: Aspirin, phenothiazines, diuretics

Venous blood sample was taken from antenatal women of less than 12 weeks of gestation. The samples were centrifuged and serum uric acid is measured by colorimetric assay with detection limit of 0.2-20 mg/dl and these women will be followed up at 24-28 weeks to do oral glucose tolerance test. After overnight fasting of 8-10 hours, blood sugar in the fasting state is collected. Later 75 grams oral glucose is given dissolved in plain or lime water to improve patient compliance. Venous sample is measured after fasting, one hour and two hours and assessed for GDM using ADA criteria.

3. Results

Table 1: Age category of the patient

Age Category	Frequency	Percent
20-25	20	18.9
26-30	49	46.2
31-35	22	20.8
36-40	13	12.3
41-45	2	1.9
Total	**106**	**100.0**

3.1. Obstetric code

Among the study population, 57 (53.8%) were Primi. The parity among the study participants is represented in the Table 2.

Table 2: Parity

Obstetric Code Category	Frequency	Percent
Multi	49	46.2
Primi	57	53.8
Total	**106**	**100.0**

3.2. Serum uric acid levels

Among the study population, Elevated (>4.2) uric acid level was present in 42 (39.6%) and Normal (<4.2) uric acid level among 64 (60.4%). The uric acid category is represented in the Table 3.

Table 3: Serum uric acid category

Serum uric acid category	Frequency	Percent
Elevated (>4.2)	42	39.6
Normal (<4.2)	64	60.4
Total	**106**	**100.0**

According to the ADA criteria to interpret the OGTT Values, any two of the high values with fasting $\geq$ 95 mg%, one hour 180 mg% and two hour 155 mg% were considered positive for GTT. According to the above criteria, 11(10.4%) were positive in the study. The GTT results are represented in the Table 4.

Table 4: GTT results

GTT Results	Frequency	Percent
Normal	95	89.6
Positive	11	10.4
Total	**106**	**100.0**

3.3. Association between the serum uric acid level categories and GTT values

Among the elevated serum uric acid category, 8 (19.0%) were positive in GTT and among the normal serum uric acid category, 3 (4.7%) were negative in GTT. The increased proportion of positive GTT among elevated serum uric acid group is statistically significant using chi square test, and represented in the table and bar chart below,

4. Discussion

The main objective in this study is to assess the utility of the 1st trimester uric acid concentrations in predicting the prevalence of diabetes complicating pregnancy. GDM

Table 5: Cross tabulation of serum uric acid category with GTT results

| | | | GTT Results | | Total |
			Normal	Positive	
Serum Uric Acid Category	Elevated	Count	34	8	42
		% within Serum Uric Acid Category	81.0%	19.0%	100.0%
	Normal	Count	61	3	64
		% within Serum Uric Acid Category	95.3%	4.7%	100.0%
Total		Count	95	11	106
		% within Serum Uric Acid Category	89.6%	10.4%	100.0%

Chi-Square – 5.62, P-value – 0.018 (Significant)

treated successfully reduces complications in both mother and the baby.

In our research, mean age of pregnant mothers is 29.8 yrs which is alike to study done by Laughon SK et al.[8] in which mean age was 25.1 yrs and was also similar to a research by Wolak T et al.[9] which was 29.5 yrs.

In this study, mean GA is 11.14 ±1.3 wks which is almost similar to the study by Laughon SK et al. in which the mean gestational age was 8.9 ± 2.5 weeks. In a research by Baliga P et al.,[10] the mean GA was 12 wks plus 3 days which is close to the present study.

In the present study, 53.8% were primi which is identical to research done by Rasika C et al.[11] where primi represented 51.4%. This was also similar to the study by Ganta SJ et al.[12] where primi represented 55.8%. In the research by El-Gharib et al.,[13] 24.8% were primi.

In this study, the mean UA of the participants was 3.81. This was similar to a research done by Aker SS et al.[14] where mean UA level was 3.72 ±1.14 mg/dl. The mean UA in the study conducted by Laughon SK et al. was 3.08 ± 0.85 mg/dl which was similar. The mean UA in a research by Baliga et al. was 2.83 mg/dl which is almost similar.

In this study, according to IADPSG-ADA criteria to interpret the OGTT values, any two of the values with fasting ≥ 95mg%, one hour ≥ 180 mg% and two hour ≥ 155mg% were considered positive for GTT. According to the above criteria, 11(10.4%) were positive in our study. In the study done by Wolak T et al., GDM prevalence was 7.6% which was almost similar. In the research by Laughon SK et al., it was 4.6% and in Baliga P et al., it was 2.28% which were both decreased than the present study. This was also in contrast to a study done by Singh U et al.[15] who observed the GDM prevalence among their study population was 2.66% (8/300) of the pregnancies, using 3 hr glucose tolerance test (Carpenter and Couston criteria) which was lesser than the present study.

In our study, serum uric acid cut-off of 4.2 mg/dl has a positive association with the GTT values with p –value less than 0.05(p=0.018). This was identical to the research by Laughon SK et al. where a UA cut-off of 3.6 mg/dl had a positive interrelation with GDM. In the study by Wolak T

et al., UA cut-off of 5.5 had a greater prevalence of GDM which was similar. This was also in accordance to Rao CN et al. who observed an increased 1st trimester serum UA level had an larger risk for developing diabetes complicating pregnancy among South Indian mothers and that 3.2 mg/dl cut-off point of serum uric acid level predicts gestational diabetes mellitus with a good specificity and sensitivity (p<0.05). This was similar to the cut –off given by El-Gharib et al. which was 4 mg/dl.

In this study, in the raised serum UA category, 8(19%) were positive for GTT and among the normal serum uric acid category, 3(4.7%) were positive for GTT. This was also in contrast to the study by Baliga P et al. where only 2.28% developed GDM in the raised UA category and to a research done by Ganta SJ et al. who studied 312 participants among which 84% with diabetes in pregnancy had UA levels more than 3.5 mg% and 15.9% with diabetes in pregnancy had levels of UA less than 3.5mg%. This decrease in GDM occurrence in our study maybe due to lesser study population.

5. 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 <12 weeks of gestation is more significantly associated with risk of development of GDM.

6. Source of Funding

None.

7. Conflict of Interest

None.

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