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Correlation between first trimester serum uric acid concentration and its association with gestational diabetes mellitus.

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ABSTRACT

Materials and Methods - This is a prospective study conducted in the institute of obstetrics and gynaecology Egmore in 200 antenatal women < 13 weeks of gestation from January 2016 to august 2016. The Women were selected based on inclusion and exclusion criteria. The cut off taken in this study for serum uric acid is 3.6 mg/dl (AJOG, Vol 201, Oct 2009). All women included in the study will undergo Oral GCT with 7g grams of sugar between 22- 24 weeks.

Results – Total of 200 samples were available for analysis. Out of the 200 patients uric acid level <3.6 mg/dl was seen in 99 patients and uric acid >3.6mg/dl in 101 patients. It was noticed that out of 99 patients with normal uric only 13 patients developed GDM (13.1%) and out of 101 patients with raised uric acid 81 women (81.5%) patients developed GDM. Elevated serum uric acid values in first trimester were associated with development of GDM.

Conclusion - A cut off level of 3.4 mg/dL appears to have good sensitivity and specificity in identifying those patients who are most likely to develop GDM later in pregnancy. This, if replicated and confirmed, can have important therapeutic implications in helping identify and manage GDM early, and thus prevent adverse maternal and foetal complications.

KEYWORDS | Serum uric acid, GDM, First trimester screening.

Introduction

GDM is one of the most important complications during pregnancy which is associated with both maternal and fetal morbidity and mortality [1]. World Health Organization and American Diabetes Association define GDM as "any degree of glucose intolerance with onset or first recognition during pregnancy" [2]. The prevalence ranges between 1 and 14 % of all pregnancies [1]

Uric acid is the final oxidation product of purine catabolism. Recent literature suggests a bidirectional causal relationship between hyperuricemia and insulin resistance (3). In fact, hyperuricemia has been found to be a marker and predictor for future development of diabetes and the metabolic syndrome (4)

Serum uric acid is associated with insulin resistance in nonpregnant women [6]. It has been proven that, higher uric acid levels correlates with insulin resistance in women with hypertensive disorders of pregnancy and also higher levels of uric acid levels were noted at 24 to 28 weeks of gestation in women with GDM when compared to women without GDM [7,8]. Normally during pregnancy, the serum uric acid levels decreases significantly from 8th week of gestation up to 24 weeks due to increased glomerular filtration rate and decreased re absorption of uric acid from the renal tubules.

There are two proposed hypothesis by which uric acid acid cac cause endothelial dysfunction and decrease nitric oxide production by endothelial cells. Insulin mediates glucose uptake into the cell depends on nitric oxide. Hence decrease in nitric oxide lead to decrease in glucose uptake and development of insulin resistance. Another mechanism is that uric acid causes inflammation and oxidative stress in adipocytes.

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. Using this concept, we aimed at a prospective analysis of association of first trimester elevated uric acid levels with the development of GDM. This would be useful in predicting GDM at an earlier gestational age, thereby aiding in appropriate management of the same to prevent maternal and fetal morbidity and mortality.

Our study aimed to examine prospectively whether serum uric acid levels in the first trimester is associated with subsequent development of GDM in a random sample of pregnant women attending Antenatal clinics

Material and method

This is a prospective study conducted in the institute of obstetrics and gynaecology Egmore in 200 antenatal women < 13 weeks of gestation from January 2016 to august 2016. The Women were selected based on inclusion and exclusion criteria

Inclusion criteria

Antenatal women in their 1st trimester of pregnancy (<13 weeks of gestation)

Exclusion criteria

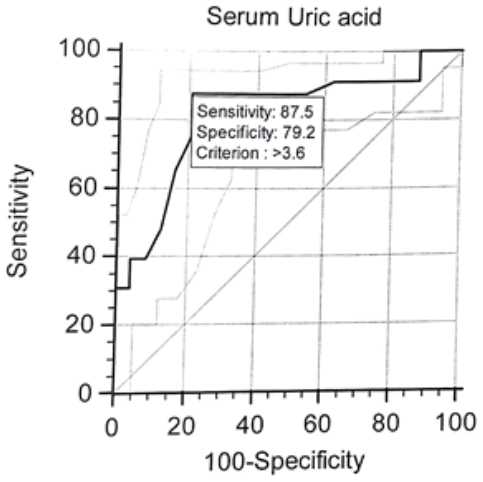
- Renal disease
- Liver disease
- Pregestational diabetes
- Chronic hypertension
- Gout
- Smoking and alcohol intake
- Drugs known to increase uric acid levels in blood eg – Aspirin, Phenothiazine, diuretics.

Informed consent is obtained. The venous blood is drawn and maternal plasma uric acid is measured using colorimetric assay. The cut off taken in this stud is 3.6 mg/dl (AJOG, Vol 201, Oct 2009). All women included in the study will undergo Oral GCT with 7g grams of sugar between 22- 24 weeks. If values >200mg/dl the woman is considered to have GDM. (IADPSG) and if plasma glucose level >140 mg/dl patient is at increased risk of developing GDM will undergo 3 hour oral GTT. Patients are considered to have GDM if more than 2 values exceed the values as in American diabetes association 2009.

Results

Total of 200 samples were available for analysis. Out of the 200 patients uric acid level <3.6 mg/dl was seen in 99 patients and uric acid >3.6mg/dl in 101 patients. It was noticed that out of 99 patients with normal uric only 13 patients developed GDM (13.1%) and out of 101 patients with raised uric acid 81 women (81.5%) patients developed GDM.

(Figure 1)



(Figure 1) The receiver operator curve drawn showed serum uric acid as predictor of GDM with area under curve of 0.819 [95% CI (0.758 – 0.870)] with a sensitivity of 87.5%, specificity of 79.2% at an optimum criterion >3.6mg/dl.

Figure 2

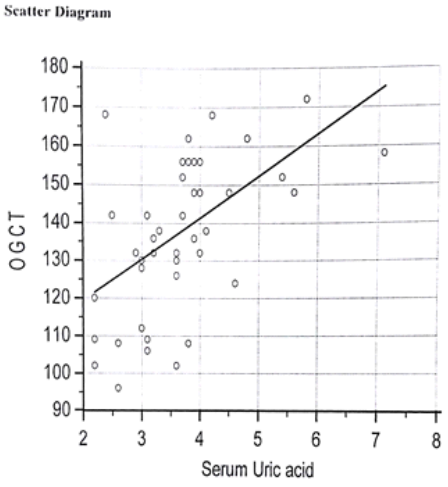


Figure 2 shows linear relationship between serum uric acid and gestational diabetes.

Hence first trimester uric acid concentrations >3.6mg/dl were associated with a trend towards increased risk of developing gestational diabetes (adjusted ODDS RATIO = 5.95% CI 0.759 – 0.870) compared to women with concentrations below this level.

In comparison of baseline variables (age, parity, BMI and family history) with GDM. Age and parity didn't show any significance and there was a significant correlation between the family history and BMI with GDM.

		No GDM	GDM	Total	
Age	Upto 20 years	4 (4.2%)	5(4.8%)	9 (4.5%)	P = 0.882 Not significant
	21-25 years	57 (59.4%)	60 (57.7%)	117 (58.5%)	
	26-30 years	27 (28.1%)	28 (26.9%)	55 (27.5%)	
	31-35 years	6 (6.3%)	6 (5.8%)	12 (6%)	
	36 years above	2 (2.1%)	5 (4.8%)	7 (3.5%)	
	Total	96 (100%)	104 (100%)	200 (100%)	
Obstetric score	Multi para	51 (53.1%)	51 (49%)	102 (51%)	P = 0.564 Not significant
	Primi	45 (46.9%)	53 (51%)	98 (49%)	
	Total	96 (100%)	104 (100%)	200 (100%)	
Family History	No	95(99%)	96 (92.3%)	191(95.5 %)	P = 0.023 Significant
	Yes	1 (1%)	8 (7.7%)	9 (4.5%)	
	Total	96 (100%)	104 (100%)	200 (100%)	

There exists a statistical significance between GDM and Non GDM patients with respect to BMI mean level. The mean BMI for GDM patients were 23.097 whereas mean BMI for Non GDM patients were 22.434.

Discussion

Early intervention and appropriate treatment in patients with GDM or at increased risk for developing of GDM will helpful in preventing the adverse maternal and fetal outcome and also protect them from long term complications. In our study mean age was 25.4 yr without any statistical significance between age of the pregnant women studied. The incidence of GDM with relation to age was low in this study as majority of the subjects were in the low risk age group for the development of GDM and also may be due to the smaller study population. Out of 200 women studied, 49% were primigravida and 51% were multigravida. There was no difference between the parity and GDM (p=0.564). The same has been shown by Dunlop W et al. But this was not correlated with study of nagalakshmi et al (9) with shows increased incidence of GDM in primi. Al-Rowaily et al., have shown in their study that multiparous women were 8.29 times more likely to have GDM than nulliparous women (10) here has also been noted a significant correlation between BMI and risk of development of GDM (p = 0.001). In this showed a risk of development of GDM was directory related BMI. Similar statement was made by Laughon KS et al., [11] Family history has a significant correlation with GDM, this was proved from Ratankar et al study also [12]

The biomarker mean serum uric acid level the subjects developed GDM was 4.275. he results from our study suggest that increasing serum uric acid level was associated with a higher risk of developing GDM. This finding is in keeping with Laughon's 2008 study which also found a dose-related increase in GDM with increases in uric acid levels. It suggests that raised serum uric acid could serve as a marker for subsequent development of GDM. A cut off of 3.4 mg/dL seemed to achieve a good balance of sensitivity and specificity in this population. However, the usefulness and predictive value of this cut-off needs to be piloted and tested in larger sample sizes before it can be widely recommended.Limitations of the study were the study population was small. Influence of diet on serum uric acid was not studied. Other variable like race, ethnicity was not included in the study. Fetal outcome was not studied.

Conclusion

Our study reiterates the association of raised serum uric acid levels in early pregnancy as a risk factor for subsequent development of GDM in an Indian population. A cut off level of 3.4 mg/dL appears to have good sensitivity and specificity in identifying those patients who are most likely to develop GDM later in pregnancy. This, if replicated and confirmed, can have important therapeutic implications in helping identify and manage GDM early, and thus prevent adverse maternal and foetal complications.

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