CO-RELATION BETWEEN FIRST TRIMESTER URIC ACID CONCENTRATION AND DEVELOPMENT OF GESTATIONAL DIABETES MELLITUS

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ABSTRACT: Gestational diabetes mellitus (GDM) is defined by the World Health Organization (WHO) as a carbohydrate intolerance resulting in hyperglycemia of varying severity with onset or first recognition during pregnancy¹ (WHO, 1999). The present study was done to find out the correlation between 1st trimester uric acid concentration and the development of GDM. GDM was diagnosed based on the OGCT and GTT test. Study was done in a total of 1002 patients. Uric acid concentration of >3.6mg/dl was considered abnormal (AJOG, vol201, oct2009). 749 patients had normal uric acid and 253 patients had abnormal uric acid. A total of 65 patients were diagnosed to have GDM (6.48%).

KEY WORDS: Gestational diabetes mellitus, oral Glucose challenge test, oral Glucose tolerance test, uric acid.

INTRODUCTION:

Gestational diabetes (or gestational diabetes mellitus, GDM) is a condition in which women without previously diagnosed diabetes exhibit high blood glucose levels during pregnancy². Gestational diabetes is caused when the body of a pregnant woman does not secrete excess insulin required during pregnancy leading to increased blood sugar levels⁵. Gestational diabetes affects 3-10% of pregnancies, depending on the population studied¹.

Uric acid is the end product of purine catabolism catalyzed by the enzyme xanthine oxidase/dehydrogenase. In non-pregnant women, uric acid is associated with insulin resistance⁶ and is an independent risk factor for development type 2 diabetes within 10 years. Two mechanisms have been hypothesized by which uric acid can cause insulin resistance, the first proposed that uric acid causes endothelial dysfunction and decreases nitric oxide production by the endothelial cell. Insulin action on glucose uptake into cells in the skeletal muscle and adipose tissue is dependent on nitric oxide thus, decreases in nitric oxide lead to decreased glucose uptake and the development of insulin resistance. 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 mice.²

MATERIALS AND METHODS: Prospective study of 1002 patients conducted in the department of obstetrics and gynecology in SRMC, Chennai. Aim of the work explained to all pregnant women.

INCLUSION CRITERIA – antenatal women in their 1st trimester of pregnancy (<12 weeks of gestation)

EXCLUSION CRITERIA – Renal disease, liver disease, pre gestational diabetes, chronic hypertension, gout, smoking and alcohol intake, drugs that increase uric acid level in pregnancy example: Aspirin, diuretics, phenothiazines.
STUDY DESIGN: Maternal plasma uric acid is measured before 13 weeks of gestation from venous sample, it is measured using a calorimetric assay with a detection limit of 10mg/dl. The cut off taken in my study is 3.6 mg/dl (AJOG, vol201, oct2009). Later, screening for GDM is done in these patients. All patients underwent random OGCT (50gms) between 24-28 weeks. If plasma glucose level >140mg/dl then the patient is at increased risk of developing GDM, the patient is then subjected to a oral GTT(100gms).FBS value, 1hr, 2hr, 3hr blood glucose value measured and interpreted according to carpenter and coustan criteria (ADA 2009).

OBSERVATION: The study was conducted in a total of 1002 patients. 365 (36.43%) multigravida and 637(63.57%) primigravida. uric acid >3.6mg/dl was considered abnormal. 749 (74.75%) patients had normal uric acid and 253(25.25%) patients had abnormal uric acid. Spot test was >200 mg/dl in 2 patients (0.2%), 140mg/dl – 200mg/dl in 112 (11%) patients, <140mg/dl in 888(89%) patients. A total of 65 patients were diagnosed to have GDM (6.48%).
Out of the 1002 patients no risk factors for GDM were noted in 714 patients (71.16%) and risk factors were noted in 288 patients (28.84%). Patients with normal uric acid and developing GDM were 24 patients (3.2%). Patients with abnormal uric acid and developing GDM were 41 patients (16.21%).

**DISCUSSION:** GDM is a common medical problem that results from an increased severity of insulin resistance as well as an impairment of the compensatory increase in insulin secretion. Pregnancy in essence serves as a metabolic stress test and uncovers underlying insulin resistance and beta cell dysfunction. GDM is associated with a variety of maternal and fetal complications, most notably macrosomia (fang et al, 2006)

| Uric Acid | <3.6mg/dl | Gestational Diabetes Mellitus |
|-----------|-----------|------------------------------|
| Normal (749) | 725       | 24                           |
| Abnormal (253) | 212       | 41                           |

Therefore it was noticed that out of the 749 patients with normal uric acid 24 patients developed GDM (3.2%) and out of the 253 patients with raised uric acid concentration 41 patients developed GDM (16.21%) $P=0.003$ hence significant.

**SECONDARY OBSERVATION:**

**RISK FACTORS**

Risk factors were present in 288 patients (28.84%)

No Risk factors in 714 patients (71.16%)

Patients with normal and abnormal URIC ACID were studied in relation to their RISK factors and were found that

| RISK ++ | No RISK |
|---------|---------|
| Normal UA | 128 | 621 |
| Abnormal UA | 160 | 93 |

Therefore, patients with normal uric acid and with risk factors developing GDM were 20 patients (15.63%)

$p=0.6$ hence not significant
Therefore, patients with abnormal uric acid and with risk factors developing GDM were 25 patients (15%)  
\[p = 0.008\] hence significant

| RISK FACTOR | NO RISK FACTOR |
|-------------|----------------|
| 288         | 714            |
| GDM (total =49) | 45    | 20   |

DEVELOPMENT OF RISK FACTOR AND GDM

Therefore, 45 patients developed GDM of the 288 patients with risk factors.

| GDM         |         |         |
|-------------|---------|---------|
| NO RISK     | 714     | 20      |
| Both parents DM | 69     | 4       |
| >35 yrs     | 7       | 4       |
| Father DM   | 78      | 2       |
| Mother DM   | 72      | 15      |
| Prev Preg GDM | 32   | 15      |
| Others      | 30      | 5       |
| **Total**   | **65**  |         |

**RISK FACTOR STRATIFICATION IN THE TOTAL POPULATION STUDIED [1002 Patients]**

The main reason for development of GDM as per my study was:
1. History of Diabetes mellitus in mother.
2. History of GDM in previous pregnancy, similar findings were observed in studies done by Torloni Et al, 2009; Proceedings of the 4th international workshop conference on GDM – Chicago, 1998.
   - Advanced maternal age and increased BMI was the main reason for development of GDM
   - PCOS was the main reason for development of GDM according to Toulis Et al, 2009
   - Essential Hypertension was the main reason for development of GDM
   - Monozygotic twins 70% and Dizygotic twins in 20%-30% were the reasons for development of GDM
   - NO Risk factors in 50%
     - Percentage of GDM IS 6.48 %(65 patients) according to the study done in SRMC,
     - The percentage of GDM differs based on the population studied.

4.6% (*Assuit university*)

- Abnormal URIC ACID and GDM in 41 patients (16.205%)
  - \[P = 0.001\] (therefore SIGNIFICANT)
  - *AJOG*, vol 201, issue 4, oct 2009 – showed 46.6% co-relation between abnormal uric acid concentration and GDM
  - *Assuit university* showed 12.6% co-relation
CONCLUSION: My study co-relates in assessing 1st trimester uric acid concentration in pregnant women to predict the development of GDM.

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