قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ

صدق الله العظيم
سورة البقرة الآية رقم (٣٢)

URIC ACID AND BODY MASS INDEX (BMI) IN FIRST TRIMESTER AS PREDICTOR FOR GESTATIONAL DIABETES MELLITUS

Presented By

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Introduction

Definition of Gestational Diabetes Mellitus (GDM)

- Gestational diabetes mellitus (GDM) is defined as glucose intolerance that was not present or recognized prior to pregnancy and it is diagnosed when the pancreatic function in women is not sufficient to control the diabetogenic environment that pregnancy confers (Gilmartin et al., 2008).

Incidence of GDM

- **The incidence of GDM differs among ethnic populations, with higher rates in African American, Hispanic, American Indian, and Asian women than in white women; values range from 1.4% to 14% but overall the condition commonly affects between 2% and 5% of pregnant women (Ben-Haroush et al., 2004).**

Physiopathological mechanisms

- The frequency of GDM varies in direct proportion to the prevalence of type II diabetes in populations, and women who develop GDM during pregnancy have a higher risk of developing type 2 diabetes (T2D) later in their lives. These observations are important for relating the two pathological situations and they probably arise from common physiopathological mechanisms **(Baptiste-Roberts et al., 2009).**

Risk factors

Risk Factor	Odds Ratio
Overweight	2
Obesity	3.7
Severe Obesity	7
Prior Gestational Diabetes	23
Prior Macrosomic Infant	3.3
Maternal Age Greater than 25 y	1.4
Maternal Age Greater than 35 y	2.3
Multiple Gestation	2.2[(a)]
South East Asian	7.6[(a)]
African American	1.8[(a)]
Polycystic Ovarian Syndrome	2.9
Parent with Diabetes	3.2
Sibling with Diabetes	7.1
Periodontal Disease	2.6
Low Maternal Birth Weight	1.9

(a): a Relative risk compared with white race

Uric acid

- Uric acid is the main product of purine metabolism and is formed from xanthine by the action of xanthine oxidase.
- Normal serum uric acid levels are generally 3-7 mg/100 ml for men, and 2-6 mg/100 ml for women, frequently expressed as mg %. The reason is that estrogen promotes excretion of uric acid during the reproductive period.

What happen to serum uric acid level during pregnancy?

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- During pregnancy, maternal serum uric acid levels **initially fall**, with a **subsequent rise** to prepregnancy levels **near term** (Lind et al., 1984). The third-trimester rise in uric acid levels may be related to an increase in fetal uric acid production or a decrease in uric acid clearance (Dunlop et al., 1977).

What are the condition associated with high serum uric acid?

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- High serum uric acid levels are associated with alcohol intake, a purine-rich diet, compromised renal function, and obesity. Insulin increases both sodium and uric acid reabsorption (Alderman 2002). Therefore, increased serum uric acid levels may be an expression of an insulin-resistant state and metabolic syndrome.

What are the condition associated with high serum uric acid?

- This proposition is supported by evidence that higher serum uric acid levels correlate with a lower insulin-stimulated glucose uptake and a higher plasma insulin response to oral glucose loading (Fang et al., 2000).

Is there is association between uric acid and gestational diabetes?

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- The association of high serum uric acid with insulin resistance has been known since the early part of the 20th century, nevertheless, recognition of high serum uric acid as a risk factor for diabetes has been a matter of debate.

Aim of the work

THE AIM OF THIS WORK WAS

TO

Test the hypothesis that increased uric acid levels, and body mass index (BMI) measured in the first trimester of pregnancy, are associated with the subsequent development of GDM.

Patients & Methods

This study was conducted at Damnhour Educational Hospital from November 2014 to June 2015.

It is a prospective observational study which included 520 pregnant women.

Inclusion criteria

Pregnant women with gestational age < 13 weeks.

Exclusion criteria

1. DM before pregnancy
2. Multiple pregnancies
3. Renal diseases
4. Liver diseases
5. Cardiovascular diseases
6. Thyroid diseases
7. Gout
8. Smoking
9. Drugs

History

- Personal history
- Menstrual history
- Obstetric history
- Past history
- Medical history
- Family history

Clinical examination

1 General examination

- Pulse, T, RR and BP
- Body weight
- Height
- BMI
- Chest and heart examination

2 Abdominal examination

$$\frac{Weight(kg)}{height^2(m^2)}$$ (metric)

Clinical examination

1. General examination
2. Abdominal examination

- Inspection
- Palpation
- Auscultation

Ultrasonography

The purpose: Obstetric ultrasound is primarily used to:

- Date the pregnancy (gestational age). The most accurate measurement for dating is the crown-rump length of the fetus, which can be done between 7 and 13 weeks of gestation.
- Confirm fetal viability.
- Determine the site of the fetus (intrauterine or extrauterine).
- Check the site of the placenta.
- Check the number of fetuses.
- Check for any abnormalities.

Investigations

Maternal serum uric acid

Screening for GDM

Measurements of OGTT: Preparation

Screening for GDM

All patients underwent routine GDM screening with 50gm oral glucose-loading test (GLT) between 24-28 weeks gestation. When plasma glucose level after 1hr was >140mg/dl, the patient was considered to be at increased risk for developing GDM and underwent 3hrs oral glucose tolerance test (OGTT).

Measurements of OGTT

Preparation

- The patient is instructed not to restrict carbohydrate intake in the days or weeks before the test.
- The test should not be done during an illness
- A full adult dose should not be given to a person weighing less than 43 kg.
- Performed in the morning
- The patient is instructed to fast (except for water) for 8–12 hours prior to the tests.

Measurements of OGTT

Procedure

- A zero time (baseline) blood sample is drawn.
- The patient is then given 100gm of glucose solution to drink within a 5 minute time frame.
- Blood is drawn after 1, 2 and 3hrs for measurement of glucose.

Measurements of OGTT

Interpretation of OGTT results

- Patients were considered to have GDM if 2 or more of the 4 values exceeded the following (ADA 2009):
  - Fasting blood glucose level ≥95mg/dl
  - 1 hour blood glucose level ≥180 mg/dl
  - 2 hour blood glucose level ≥155 mg/dl
  - 3 hour blood glucose level ≥140 mg/dl

Results

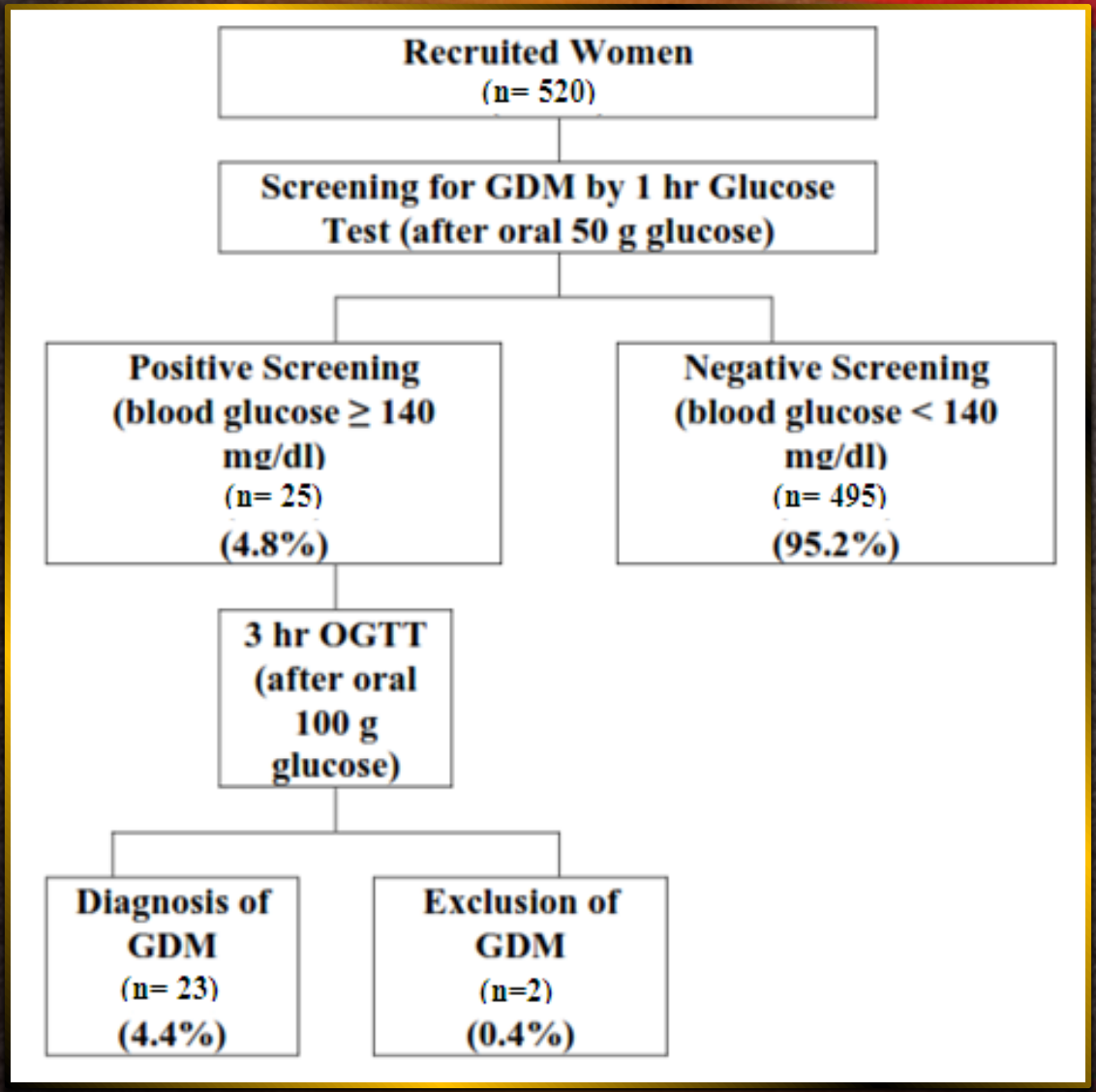
Characteristics of Included Women

Age (Years) Range: Mean ± SD:	 16 – 43 27.55 ± 5.24
BMI (Kg/m^2) Range: Mean ± SD:	 18 – 38.5 26.17 ± 4.21
Parity Range: Median (IQR):	 0 – 8 1 (1 – 2)
No. of Previous Abortions Range: Median (IQR):	 0 – 8 0 (0 – 1)

Gestational Age of Included Women at Recruitment and at Screening for GDM. Serum Uric Acid at Recruitment

Gestational Age at Recruitment(Weeks) **Range:** **Mean ± SD:**	 **10 – 13** **11.01 ± 0.87**
Serum Uric Acid at Recruitment (mg/dl) **Range:** **Median (IQR):**	 **0.4 – 8.2** **2.9 (2.4 – 3.5)**
Gestational Age at Screening for GDM (Weeks) **Range:** **Mean ± SD:**	 **24 – 28** **25.88 ± 1.09**

Study Course



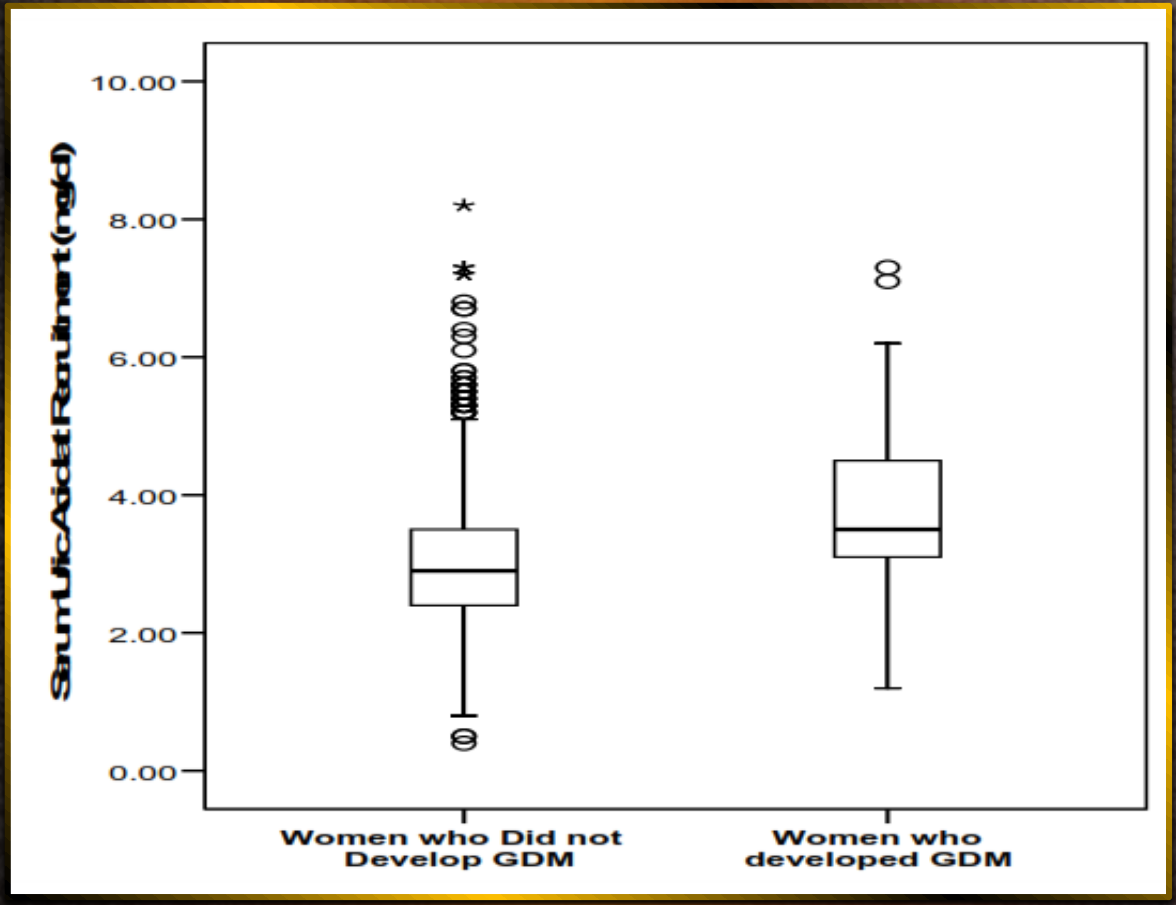
Difference between Women who developed GDM and Women who did not regarding their Characteristics

	Women who developed GDM (n=23)	Women who did not develop GDM (n=497)	P
Age (Years) Range: Mean ± SD:	21 – 39 27.41 ± 4.69	16 – 43 27.55 ± 5.26	>0.05* NS
BMI (Kg/m²) Range: Mean ± SD:	22 – 36 29.02 ± 4.39	18 – 38.5 26.04 ± 4.16	<0.001* HS
Parity Range: Median (IQR):	0 – 4 2 (1 – 2)	0 – 8 1 (1 – 2)	>0.05** NS
No. of Previous Abortions Range: Median (IQR):	0 – 4 0 (0 – 2)	0 – 8 0 (0 – 1)	>0.05** NS

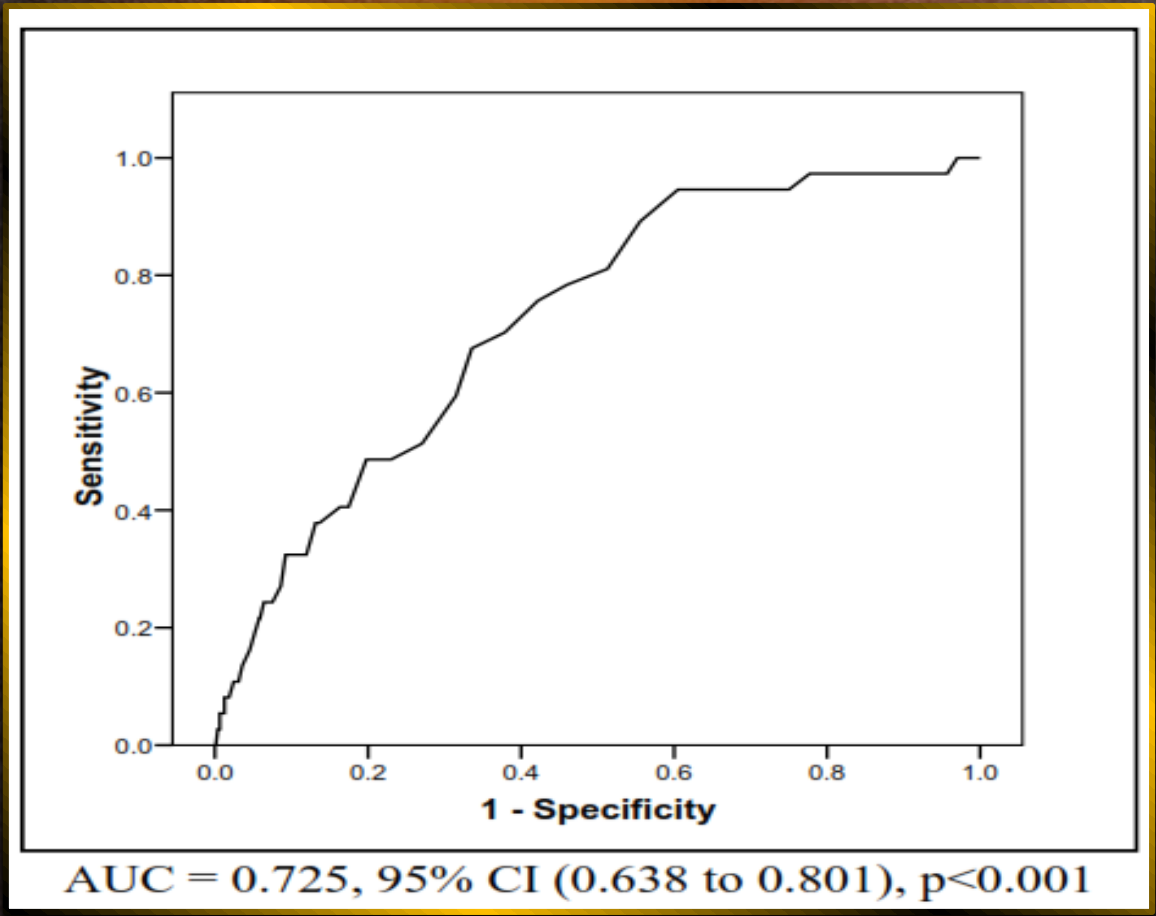
Difference between Women who developed GDM and Women who did not regarding Serum Uric Acid at Recruitment

	Women who developed GDM (n=23)	Women who did not develop GDM (n=497)	P
Serum Uric Acid at Recruitment (mg/dl)			<0.001* HS
Range:	1.2 – 7.3	0.4 – 8.2	
Median (IQR):	3.5 (3.05 – 4.7)	2.9 (2.35 – 3.5)	

Box-Plot Chart showing Difference between Women who developed GDM and Women who did not regarding Serum Uric Acid at Recruitment



ROC Curve for Serum Uric Acid as Predictor of GDM



AUC = 0.725, 95% CI (0.638 to 0.801), p<0.001

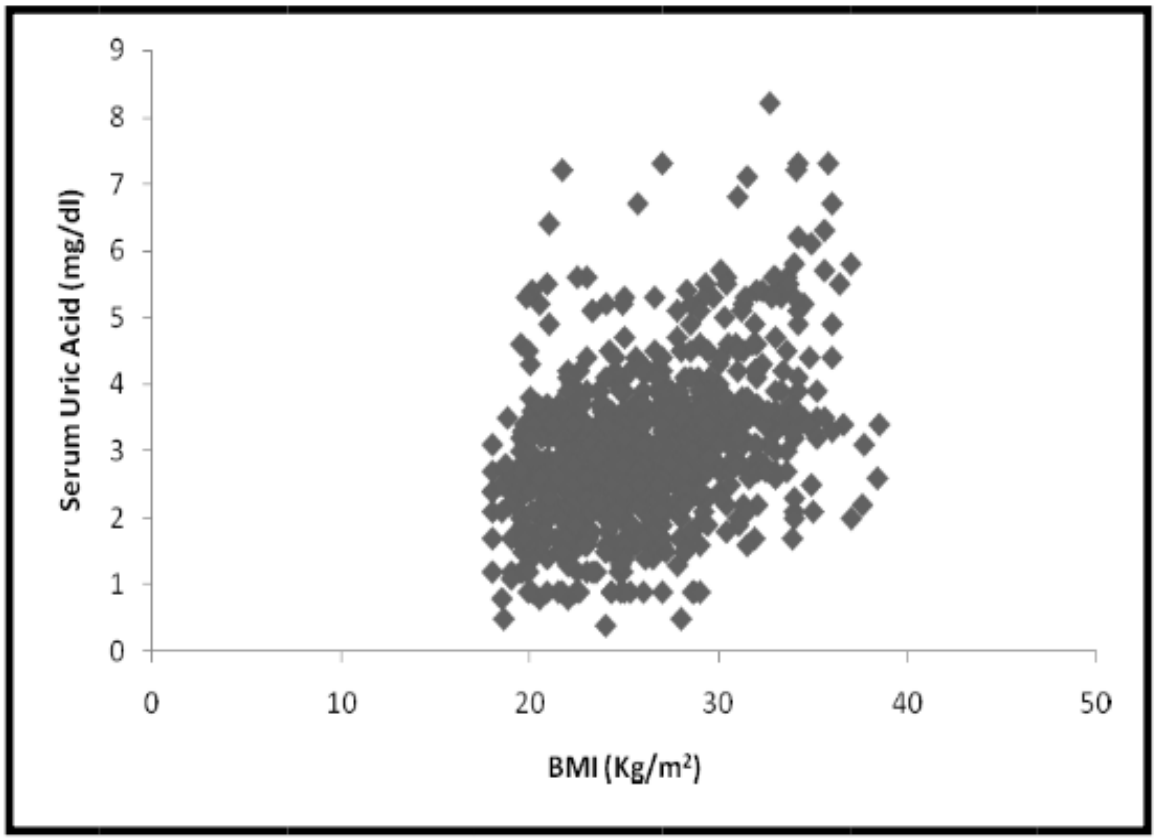
Accuracy of Serum Uric Acid in Prediction of GDM

Serum Uric Acid as Predictor of GDM	Sensitivity	specificity	PPV	NPV	LR+	LR-
≥ 3.05 mg/dl	75.7%	57.8%	7.5%	89.1%	1.8	0.42

Binary Logistic Regression Analysis of Serum Uric Acid as Predictor of GDM

Serum Uric Acid as Predictor of GDM		OR	95% CI	P
≥ 3.05 mg/dl (n=227)	17/210	3.8	1.99 to 9.15	<0.001 HS
< 3.05 mg/dl (n=293)	6/287			

Scatter-Plot showing Correlation between Serum Uric Acid and BMI



r=0.378, p<0.001

Conclusions & Recommendations

In our study, it was found:

Elevated first-trimester uric acid concentration was correlated with an increased risk of developing GDM. The risk of developing GDM was 4-fold higher if first-trimester uric acid was ≥ 3.05 mg/dl [OR 3.8, 95% CI (1.99 to 9.15)].

In our study, it was found:

There was a significant positive correlation between serum uric acid and BMI ($r = 0.378$, $p < 0.001$).

In our study, it was found:

The mean BMI was significantly higher in women who developed GDM when compared to women who did not develop GDM [29.02 ±4.39 Kg/m^2 vs. 26.04 ±4.16 Kg/m^2, respectively, $p<0.001$].

So, we recommend:

Serum uric acid measurement in 1st trimester of pregnancy as a predictor for GDM and screening of GDM at 24-28 weeks gestation.

As regard BMI should be less than 25kg/m for exclusion of obesity as a risk factor for occurrence of GDM.


Thank you