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# CORRELATION BETWEEN SERUM URIC ACID LEVEL AND MATERNAL GESTATIONAL DIABETES

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**Abstract**:
Background: Uric acid is the final oxidative product of purine catabolism. It was being reported that serum uric acid levels are associated with insulin resistance and is considered as a risk factor in the development of glucose intolerance.
Aim of the study: to assess the relationship between maternal serum level of uric acid and Gestational Diabetes Mellitus and its value as diagnostic aid in gestational diabetes.
Patients and methods: A case control study conducted in Al- Imamain Al-Kadhimain medical city during the period from January 2020 to January 2021 , this study included 120 pregnant women in second and third trimester divided into two groups
Case group - 60 pregnant women diagnosed to have gestational diabetes Control group - 60 pregnant women with no gestational diabetes as a control group For all included women 75 g oral glucose tolerance test was performed, Fasting blood sugar 2 hr. blood glucose and HbA1c as parameter of glycemic control were measured and maternal serum uric acid levels were evaluated.
Correlation of uric acid with all parameters and its diagnostic value is evaluated.
Results: Maternal characteristic including age, gestational age, parity and Body mass index showed no statistically significant difference at.
Mean±SEM of fasting blood sugar (mg/dl) in study group was higher in comparison to control group. 2-hour glucose tolerance test blood sugar level was also higher in study group in comparison to control group.
Maternal serum uric acid (Mean±SEM ) was significantly higher in study group than in control group .
Mean ±SEM of HbA1c in gestational diabetes group was significantly higher than level of control group.
Maternal serum uric acid levels were significantly correlated with 2 hr. blood glucose levels of glucose tolerance test in gestational diabetes group.
ROC curve of maternal serum uric acid levels as diagnostic parameter in gestational diabetes revealed Area Under Curve (0.887), Sensitivity (81.7%), Specificity (81.7%), Cut-off value (5.15 mg/dl) at P-value
<0.001.
Conclusion:
• Significantly higher levels of maternal serum uric acid are associated with gestational diabetes.
• Maternal serum uric acid levels are significantly correlated with 2hr glucose tolerance test blood glucose levels and they can be used as diagnostic parameters in gestational diabetes.

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**Keywords**: gestational diabetes, uric acid.

## Introduction

Gestational diabetes mellitus (GDM) is defined as " carbohydrate intolerance of variable degree with onset or first recognition during pregnancy, whether or not insulin is used and regardless of whether diabetes persist after pregnancy"(1). GDM affects ~7% of all pregnancies, resulting in > 200,000 cases per year. (2)

1-6% of women will develop sufficient hyperglycemia to meet the criteria for gestational diabetes mellitus (GDM), of these women between 20% and 50% will develop post-pregnancy type II diabetes mellitus subsequently. (1)

Studies suggest that the prevalence of DM among women of childbearing age is increasing worldwide. This increase is believed to be attributable to more sedentary life, changes in diet, and the virtual epidemic of childhood and adolescent obesity. (3)

Pathophysiology of Diabetes mellitus during pregnancy:

- Pregnancy is a diabetogenic condition characterized by increase in insulin resistance and increased pancreatic insulin secretion as the pregnancy progresses. Skeletal muscle is the body's main site of glucose disposal and becomes insulin resistant during pregnancy. This insulin resistance begins in mid pregnancy and continues until the end of gestation. Placental secretion of hormones, such as progesterone, cortisol, placental lactogen , prolactin, and growth hormone, is a major contributor to the insulin-resistant state seen in pregnancy.(4) Pregnancies are also associated with a 200% to 250% increase in insulin secretion to maintain euglycemia in the mother. These metabolic changes are normal and provide adequate nourishment to the fetus(5).
- GDM have a greater severity of insulin resistance compared to the insulin resistance seen in normal pregnancies. They also have an impairment of the compensatory increase in insulin secretion, particularly first-phase insulin secretion. This decrease in first phase insulin release may be a marker for deterioration of β-cell function.
- It is thought that the cumulative effects of maternal and placental influences result in abnormalities in insulin signaling pathways, which lead to decreased glucose uptake and an increase in insulin resistance. (6)

## 2. Literature Review

Impact of maternal Diabetes on pregnancy and its outcome:

There are both fetal, neonatal, and maternal complications associated with GDM

### Fetal complications:

1.Miscarriages: In all women with preexisting DM, there is a 9%-14% rate of miscarriages. Current data suggest a strong association between degree of glycemic control prior to pregnancy and miscarriage rate. (7)

2.Congenital malformation: approximately 3-8% of infants of diabetic mothers suffer of major congenital abnormalities. (1)

Neural tube defects and cardiac malformations are more common in diabetic population and caudal regression (sacral agenesis) is reported to be 200-400 times more common in infants of women with diabetes.

Other possible malformations are: encephalocele, pre-axial polydactyly, omphalocele and anomalies of the corpus callosum. (8)

3.Fetal growth anomalies: Growth acceleration: between 20%-40% of infants of diabetic mothers have a birth weight that meets the criteria for definition of macrosomia . Excessive body fat stores, stimulated by excessive glucose delivery during diabetic pregnancy often extends to childhood and adult life. Birth injury including shoulder dystocia and brachial plexus injury are more common among macrosomic fetuses.

4.Growth restriction: growth restriction occurs with significant frequency in pregnancies with preexisting type I DM.(8)

5. Long-term complications to the offspring include an increased risk of glucose intolerance, diabetes, and obesity.(2)

**Neonatal complications:**

**1.Hypoglycemia:**

Is a consequence of persistent post natal hyperinsulinaemia when the maternal transfer of glucose has ceased, Which is usually transient. (9)

**2. Hypocalcaemia:**

up to 50% of infants of diabetic mothers have low level of serum calcium that is less than 7mg/dl. These changes appear to be due to a functional hypoparathyroidism. (3)

**3. Polycythemia:**

central venous hemoglobin concentration of greater than 20gm/dl or hematocrit more than 65%. Hyperglycemia is a powerful stimulus to fetal erythropoietin mediated by decreased fetal O2 tension. (3)

**Hyperbilirubinemia:**

It occurs in approximately 25% of infants of diabetic mothers. The causes of hyperbilirubinemia are multiple but predominantly due to prematurity and polycythemia. (3)

**5. RDS:**

The non-diabetic fetus achieves pulmonary maturity at a mean gestational age of 34-35 weeks. However, in a diabetic pregnancy the risk of RDS may pass until after 38.5 weeks of gestation completed. (3)

**Perinatal mortality and birth injury:**

- Stillbirth without an identiiable cause is a phenomenon relatively limited to pregnancies complicated by overt diabetes. These stillbirths are "unexplained" because common factors such as obvious placental insuiciency, placental abruption, fetal- growth restriction, or oligohydramnios are not identified, also fetuses of diadeic mothers often have elevated lactic acid levels, hese fetuses are typically large for gestational age and die before labor, usually late in the third trimester. (10)
- Birth injury: most of birth injuries are associated with difficult vaginal delivery and shoulder dystocia. Common birth injury associated with diabetes is brachial plexus injury, facial nerve injury and cephalohematoma. (3)

**Maternal complications**

**1. Polyhydramnios:**

it occurs when there is suboptimal glycemic control leads, in turn, to fetal hyperglycemia and fetal hyperinsulemia. hyperglycemia, in part through an osmotic action, result in polyurea; this leads to the development of polyhydramnios. (11)

**2. Preeclampsia:**

Preeclampsia developed three to four times more often in women with overt diabetes. The risk of preeclampsia is also related to maternal age and the duration of preexisting diabetes. (12)

**3.Operative delivery:**

Maternal diabetes is a risk factor for caesarian delivery). Reported rates of CS in diabetic women is 50%. (13)

Many factors account for high CS rates as Prematurity, and Macrosomia.

**4. Pelvic floor trauma:**

Macrosomia, nulliparity, episiotomy and instrumental delivery are established isk factors for third- and fourth-degree tears.

Approximately 20% of diabetic women who deliver vaginally suffer second-, third- or fourth-degree tears. Shoulder dystocia is also a risk factor. (1)

**5. Infection:**

Maternal infections are more common in diabetics.

Infection is a risk factor for preterm labor and ketoacidosis and Pyelonephritis.

6. Women with a history of GDM have an increased risk of developing diabetes after pregnancy compared to the general population, with a conversion rate of up to 3% per year. (1)

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**Screening and diagnosis:**

There is no consensus regarding screening and diagnostic methods for GDM. Screening and diagnostic methods can be universal or risk based one step or two step procedure for the diagnoses of GDM in women without pre-existing Diabetes. (14)

One - step procedure: performing OGTT in the morning after overnight fast of ≥8 hours, 75g OGTT with blood glucose measurement fasting , 1- 2 hour at 24-28 weeks in women not having preexisting diabetes , GDM is diagnosed if blood glucose values equals or exceed (15)

- Fasting 92mg\dl (5.1 mmol\l)
- 1-hour 180mg\dl(10.0 mmol\l)
- 2-hour 153mg\dl(8.5 mmol\l)

Two – steps procedures: step one performing 50-g oral glucose challenge test irrespective of last meal at 24-28 weeks in women not having preexisting diabetes ,if blood glucose at 1-hour after load is ≥140g\dl(7.8mmol\l) proceeded to 100g glucose OGTT. GDM diagnosis is made when two or more blood glucose levels equals or exceed (15)

- Fasting95 mg\dl (5.3mmol\l)
- 1-hour 180mg\dl(10.0mmol\l)
- 2-hour 155mg\dl(7.6mmol\l)
- 3-hour 140mg\dl(7.8mmol\l)

Table (1-1) Risk-Based Recommended Screening Strategy for Detecting GDM (16)

| |
|---|
| **GDM risk assessment**: should be ascertained at the first prenatal visit |
| **Low Risk**: Blood glucose testing not routinely required if all the following are present: |
| Member of an ethnic group with a low prevalence of GDM |
| No known diabetes in first-degree relatives |
| Age < 25 years |
| Weight normal before pregnancy |
| Weight normal at birth |
| No history of abnormal glucose metabolism |
| No history of poor obstetrical outcome |
| **Average Risk**: Perform blood glucose testing at 24 to 28 weeks using either: |
| Two-step procedure: 5 0-g oral glucose challenge test (GCT), followed by a diagnostic 100-g OGTT for those meeting the threshold value in the GCT |
| One-step procedure: diagnostic 100-g OGTI performed on all subjects |
| **High Risk**: Perform blood glucose testing as soon as feasible, using the procedures described above, if one or more of these are present: |
| Severe obesity |
| Strong family history of type 2 diabetes |
| Previous history of GDM, impaired glucose metabolism , or glucosuria |
| If GDM is not diagnosed, blood glucose testing should be repeated at 24 to 28 weeks' gestation or at any time symptoms or signs suggest hyperglycemia |

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Table (1-2) The IADPSG and NICE criteria for GDM diagnosis(17)

| | IADPSG criteria | NICE 2015 criteria |
|---|---|---|
| Screening | None | Risk factors at first antenatal clinic<br>BMI >30 kg/m$^2$<br>GDM in a previous pregnancy<br>Previous macrosomic baby ≥4.5 kg<br>Family history (first-degree relative with diabetes)<br>Ethnicity: family origin with a high prevalence of diabetes |
| 75-g OGTT | Universal at 24–28 weeks | Selective testing 26–28 weeks<br>Based on the presence of risk factors |
| Plasma glucose | IADPSG criteria: one or more of the following thresholds be met or exceeded: | NICE 2015 criteria: one or more of the following thresholds be met or exceeded: |
| 0 min | 5.1 mmol/L (92 mg/dL) | 5.6 mmol/L (100 mg/dL) |
| 60 min | 10 mmol/L (180 mg/dL) | |
| 120 min | 8.5 mmol/L (153 mg/dL) | 7.8 mmol/L (140 mg/dL) |

Table (1-3) Diagnosis of overt diabetes in pregnancy(18)

| Measure of Glycemia | Threshold |
|---|---|
| Fasting plasma glucose | At least 7.0 mmollL (126 mg/dL) |
| Hemoglobin Alc | At least 6.5% |
| Random plasma glucose | At least 11. 1 mmol/L (200 mg/dL) plus confirmation |

Apply to women without known diabetes antedating pregnancy. The decision to perform blood testing for evaluation of glycemia on all pregnant women r only on women with characteristics indicating a high risk for diabetes is based on the background frequency of abnormal glucose metabolism in the population and on local circumstance.

**Glucose Monitoring:**

- Assessment of HA1c level every 4-6 weeks during pregnancy is helpful in evaluating overall glycemic control.
- Self-blood glucose monitoring (SBGM) (capillary) has now become the standard of care for monitoring of pregnant women.
- typical schedule involves capillary glucose checks upon awaking in the morning, 1 hour after breakfast, before and after lunch, before dinner, and at bed time, recommend monitoring:

1. Fasting or pre-prandial glucose value between 70 and 95 mg/dl.
2. 1-2 hours post prandial glucose value of 120 mg/dL.
3. 3:00- 4:00 AM glucose value between 70-120mg/dL. (19)

. HbA1c, a measure of glycated hemoglobin which serves as an indicator of blood glucose control in the prior 3–4 months, may be an avenue for earlier identification of women at risk for GDM. However, while

HbA1c is currently used among high-risk women at the first prenatal visit to identify women with overt type 2 diabetes, it is not currently used to screen for GDM.(20)

Table (1-4) HbA1c chart with average blood sugar range.(20)

| A1c (%) | Average Blood Sugar (mg/dL) |
|---|---|
| 4 | 68 |
| 5 | 97 |
| 6 | 126 |
| 7 | 152 |
| 8 | 183 |
| 9 | 212 |
| 10 | 240 |
| 11 | 269 |
| 12 | 298 |
| 13 | 326 |
| 14 | 355 |

**URIC ACID:**

Uric acid (UA) is an endogenously produced water-soluble antioxidant, and it is a heterocyclic compound of carbon, nitrogen, oxygen, and hydrogen. It forms ions and salts known as urates and acid urates such as ammonium acid urate.(21)

Uric acid is created when the body breaks down purine nucleotides. High concentrations of uric acid in blood serum can lead to a type of arthritis known as gout. The chemical is associated with other medical conditions like ammonium acid urate kidney stones.(21)

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- **Chemistry(22)**

Chemical formula is C5H4N4O3

**Figure (1-1) Chemical formula of Uric acid.(22)**

It exhibits greater solubility in hot water than cold allowing for easy recrystallization which is significant in the etiology of gout.

Uric acid is produced by xanthine and hypoxanthine, which in turn are produced from purine.

Uric acid is more toxic to tissues than either xanthine or hypoxanthine. (23)

Uric acid is released in hypoxic conditions. (23)

In humans and higher primates, uric acid is the final oxidation (breakdown) product of purine metabolism and is excreted in urine. (24)

Normal blood plasma uric acid level is 3.6mg/dL- 8.3mg/dL, this plasma uric acid level is variable among different populations and between both sexes, and there are many physiological factors that influence the level of plasma uric acid levels such as:

- Sex: plasma uric acid is higher in males.
- Obesity: plasma uric acid tends to be higher in among obese peoples.
- Social class: the more affluent social classes tend to have higher plasma uric acid level.
- Diet: uric acid rises in individuals taking a high protein diet and among those who consume large amounts of alcohol.
- Genetic factors also are important. (25)
- In humans, about 70% of daily uric acid disposal occurs via the kidneys, and 5-25% of humans' impaired renal excretion leads to hyperuricemia. (26)

Uric acid may be a marker of oxidative stress, and may have a potential therapeutic role as an antioxidant. On the other hand, like other strong reducing substances such as ascorbate, uric acid can also act as a pro- oxidant, particularly at elevated levels. Thus, it is unclear whether elevated levels of uric acid in diseases associated with oxidative stress such as stroke and atherosclerosis are a protective response or a primary cause.(27)

Uric acid synthesis as mentioned above will happen under hypoxic conditions such as hypoxia and ischemia of the placenta and cytokines such as interferon which induce excessive expression of xanthine oxidase and therefore increase the production of uric acid and other reactive oxygen species. (28)

Uric acid is a strong reducing agent (electron donor). It scavenges oxygen radicals, single oxygen, oxo-haemoxidants and the hydroperoxyl radicals. In addition, uric acid can form complexes with iron and inhibits the oxidation of lipids and vitamin C.(27)

Uric acid is strongly connected with cardiovascular events and morality in type II Diabetic patients.(27)

Uric acid possesses antioxidant properties and contributes approximately 60% of the free radical scavenging activity in human serum.(27)

Uric acid and Diabetes in pregnancy

The relationship between a high serum uric acid and insulin resistance has been known since the early 20th century, nevertheless, recognition of high serum uric acid as a risk factor for Diabetes has been a matter of debate. In fact, hyperuricemia has always been presumed to be consequence of insulin resistance rather than its precursor; however, it was shown in a prospective follow-up study that high serum uric acid is associated with higher risk of type II Diabetes independent to obesity, dyslipidemia, and hypertension. (29) Even more some had suggested that uric acid elevation may be a protective response capable of opposing harmful effects of free radical activity and oxidative stress. (30)

Serum uric acid is associated with insulin resistance and several mechanisms have been hypothesized to explain this association. Some studies stated that uric acid causes endothelial dysfunction and decreases nitric oxide production. (31). Insulin mediated glucose uptake into cells in the skeletal muscles and adipose tissue is dependent on nitric oxide. Thus, decrease in nitric oxide leads to decreased glucose uptake and development of insulin resistance. Normally during pregnancy, the serum uric acid level decreases significantly between 8 and 24 weeks of gestation due to increased glomerular filtration rate and reduced re- absorption of uric acid from renal tubules. In first trimester, it likely approximates preconception uric acid levels, and elevated levels may identify women who are predisposed to metabolic syndrome with an increased risk of developing GDM. This concept would be useful in predicting GDM at an earlier gestational age, there by aiding in initiating timely and appropriate management to prevent maternal and fetal morbidity and mortality.(31)

Uric acid is also higher in non-pregnant women with history of gestational diabetes, independent of body mass index.(29)

A remarkable number of changes are observed in the urinary system as a result of pregnancy. A review of the available data would suggest that the glomerular filtration rate and renal plasma flow increase by at least 50% during pregnancy, starting soon after conception and lasting until term.

During normal pregnancy, plasma concentrations of creatinine and uric acid normally decrease as a consequence of their increased glomerular filtration.(32)

Hyperuricemia is considered by some investigators to be a component of the metabolic syndrome that reflects insulin resistance. In several epidemiological studies, correlations between hyperuricemia and obesity, dyslipidemia, and diabetes have been reported.(32)

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Table (1-5) Normal value of S. Uric acid throughout pregnancy (33)

| Serum uric acid units | Non pregnant Female | First Trimester | Second Trimester | Third Trimester |
|---|---|---|---|---|
| mg/Dl | 2.5 - 5.6 | 2 - 4.2 | 2.4 - 4.9 | 3.1 - 6.3 |
| µmol/L | 149 – 333 | 119 – 250 | 143 – 292 | 184 – 375 |

**3. Patients and methods:**

This case control study was carried out in the obstetrics and gynecology outpatient department at AL-Imamain Al-Kadhimain medical city, between January 2020 and January 2021, and it is approved by scientific committee of Iraqi Board of Obstetrics and Gynecology.

This study enrolled 167 pregnant lady GA from(24wk-34wk gestation), before inclusion in this study each women was interviewed and an informed consent was obtained from them.

From these 167 women only 120 patient were eligible for the final analysis, 27 patient were excluded because they met the criteria for DM and 20 were previously defined as exclusion criteria in patient recruiting criteria procedure.

Finaly we analyzed the study group consisting of:

1. Case group – (60) pregnant women who were diagnosed as case of GDM by 75g OGTT.
2. Control group – (60) pregnant women with normal uneventful pregnancy and normal glucose tolerance.

They all were matched in age and gestational age.

Inclusion criteria: include:

1. Pregnancy with single viable fetus.
2. Age range of 20-36 years.
3. Diagnosis of GDM by 75g oral glucose tolerance test.
4. Parity ≤ 5
5. Gestational age range of 24-34 weeks

Exclusion criteria:

1. History of any medical disease as previous diabetes mellitus and hypertension.
2. Taking any vitamin supplement or drugs.
3. Pregnancy with congenital abnormality
4. Smoking.
5. Renal disease.

- Information was recorded for each woman; the weight and height are measured and BMI (Kg/m2) was calculated. gestational age was estimated by the accurate last menstrual period and confirmed or corrected by an early or mid-trimester ultrasonography, parity and age of the patients also recorded.

Oral glucose tolerance test:-

The OGTT was performed for the patients with an overnight fasting of 8 to 14 hours while women was on an unrestricted diet and unlimited physical activity for at least 3 days. A venous blood sample was collected and 75-gm oral glucose load in 300ml of water) administered within 5 minutes. The patients are encouraged to sit throughout the test and to refrain from eating or drinking. additional blood sample were drawn at 1, 2h after the oral glucose load.
Gestational diabetes is diagnosed if one or more reading exceed the following according to IADPSG criteria

- fasting plasma glucose ≥(5.1) mmol\L (92mg\ dl)
- 1-hour plasma glucose ≥(10.0)mmol\L (180mg\dl)
- 2-hour plasma glucose ≥(8.5)mmol\L(153mg\dl)

Measurement of serum Uric acid

- Five millimeters of venous blood (fasting) were drawn from each patients under aseptic precautions and transferred into clean non heparinized tube and waiting for 15 minutes for clotting , then centrifuged at 5000rpm for 10 min.
- the serum was separated for measurement of uric acid by using calometric method.
- HbA1c was measured by using calometric method.

Statistical analysis:
Data were analyzed using SPSS 16 and Microsoft Office Excel 2010. Continuous data were expressed as mean +SEM (standard error of mean), while, nominal variables were expressed as number (%). Student t-test was used to study the relation between numeric data in two groups. Chi- square test and Fischer exact test were used to study association between nominal data. P-value less 0.05 was considered significant.
Questioneer
Patient name:
Age:
Parity:
No. of abortion:
Gestational age GA by LMP and ultrasound History of hypertension in current pregnancy History of pre-pregnancy diabetes
History of GDM in current pregnancy Previous history of GDM
Previous history of IUD or stillbirth History of congenital abnormalities Previous history of big baby Family history of DM
Taking any vitamin supplement Taking any other drugs Smoking
BP
Height WeightBMI FBS
GTT

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## 4. Results

This analysis includes one hundred and twenty pregnant women, and they were divided into two groups:

First group represent sixty pregnant women with gestational diabetes (study group).

Second group sixty pregnant women with normal pregnancy (control group).

The characteristics of women enrolled in this study are shown in table (3- 1) There was no significant differences regarding their age, gestational age, parity and BMI at (P-value 0.22).

Table (3-1) Characteristic of women enrolled in the study

| Characteristic | GDM (n=60) Mean +SEM | Control(n=60) Mean +SEM* | P value |
|---|---|---|---|
| Age (years) | 25.86±0.63 | 26.4±0.49 | 0.221 |
| Gestational age (weeks) | 32.15±0.52 | 31.34±0.52 | 0.273 |
| BMI (Kg/M²) | 27.85±0.31 | 26.23±0.22 | 0.22 |
| Parity | 1.32±0.23 | 1.56±0.36 | 0.370 |

*SEM = standard error of mean

Table (3-2) Shows the risk factors in the study group compared to the control group, they were all with significant value (P<0.001) , where 47 women (78.33%) were obese, (BMI>25) , 25 women (41.67%) have first degree family history of diabetes , 12 women (20%) had history of IUD or stillbirth in previous pregnancy, 27 women (45%) had previous history of abortion and 5 women (8.33%) had previous history of big baby > 4 Kg.

Table (3-2) Risk factors in the study group.

| Characteristic | NO. GDM (n=60) | % |
|---|---|---|
| BMI ≥25 | 47 | (78.33%) |
| Family History of DM | 25 | (41.67%) |
| History of IUD or still birth | 12 | (20%) |
| Previous history ofmiscarriage | 27 | (45%) |
| Previous history of bigbaby | 5 | (8.33%) |

Table (3-3) Shows the glucose tolerance in GDM compared to the control group. The mean fasting, 1 hour and 2hours blood glucose levels, as any two or more abnormal reading are diagnostic of gestational diabetes.

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Table (3-3) Glucose tolerance in GDM and control group (Mean + SEM, mg/dl).

| | Fasting | 1 hour | 2 hour |
|---|---|---|---|
| Study group | 103.98±4.35 | 162.58±28.65 | 155.53±21.7 |
| Control group | 79.00±0.74 | 113±20.3 | 103.75±18.7 |
| P-value | 0.001 | 0.001 | 0.001 |

Figure (3-1) Shows the comparison of fasting blood sugar between the study group and the control group, as it was higher in the study group (103.98) mg/dl compared to (79) mg/dl.

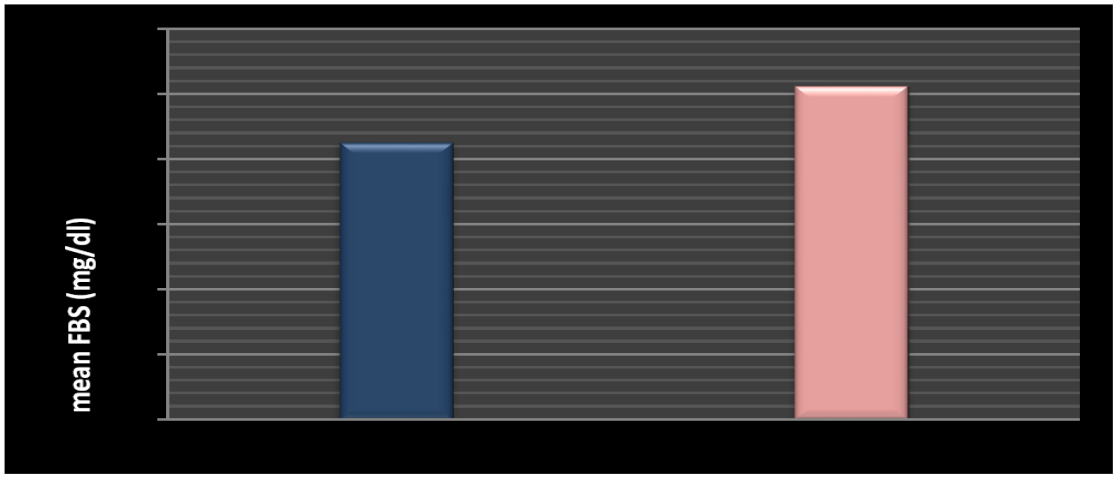


Figure (3-1) Fasting blood sugar in the control and study group

Table (3-4) Shows the serum uric acid in GDM and control groups, where serum uric acid in the study group was (6.71 mg/dl) which is higher than women in the control group (4.56 mg/dl) p value<0.001.

Table (3-4) Serum Uric acid in GDM and control group

| | Group | Mean | SEM | Range | Pvalue |
|---|---|---|---|---|---|
| Uric acid | GDM | 6.71 mg\dl | 0.52 | 3.9-9.2 mg\dl | <0.001 |
| | Control | 4.56 mg\dl | 0.69 | 3.7-6.7 mg\dl | |

Figure (3-2) Shows serum uric acid in GDM and control group, where the level of serum uric acid tended to be significantly higher (p<0.001) in Women in the study group (6.71 mg/dl) than in the control group (4.56 mg/dl) .

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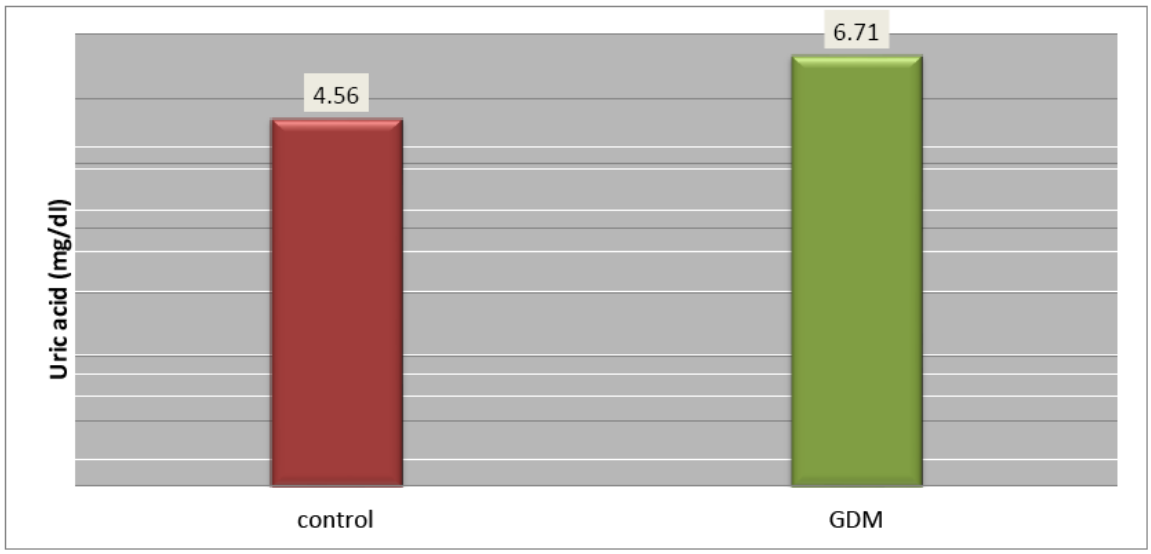


Figure (3-2) Serum Uric acid in GDM and control group
The result are expressed as mean + SEM

Table (3-5) HbA1C values in control and study group

| | Group | mean | SEM | Range | P value |
|---|---|---|---|---|---|
| **HbA 1C** | GDM | 5.8 | 0.57 | 5.1-7.3 | <0.001 |
| | Control | 4.7 | 0.4 | 4.2-5.3 | |

Table (3-6) Pearson correlation between uric acid and other parameters in both groups.

- Maternal serum uric acid level is significantly correlated with 2hr GTT blood glucose level in study group (r=0.261 , p=0.044).

| Parameters | | Uric acid (mg/dl) | |
|---|---|---|---|
| | | Control | Study |
| Age (yr) | r | -0.041 | 0.078 |
| | p | 0.757 | 0.552 |
| Parity * | r | -0.189 | 0.076 |
| | p | 0.148 | 0.562 |
| BMI (kg/m$^2$) | r | 0.074 | -0.073 |
| | p | 0.575 | 0.582 |
| Gestational age (wk) | r | 0.026 | 0.081 |
| | p | 0.844 | 0.539 |
| HbA1c % | r | -0.005 | -0.085 |
| | p | 0.971 | 0.516 |

| | | | |
|---|---|---|---|
| GTT FBS | r | 0.013 | -0.057 |
| | p | 0.919 | 0.665 |
| GTT 1 h | r | 0.110 | 0.197 |
| | p | 0.402 | 0.131 |
| GTT 2 h | r | 0.111 | 0.261 |
| | p | 0.399 | **0.044** |

* Spearman correlation for parity

Figure (3-3) The ROC curve for uric acid as diagnostic aid for glucose intolerance during pregnancy show that (AUC) was 0.887 , p value (0.001) , sensitivity ( 81.7%), specificity (81.7%) cutoff value 5.15 mg \dl

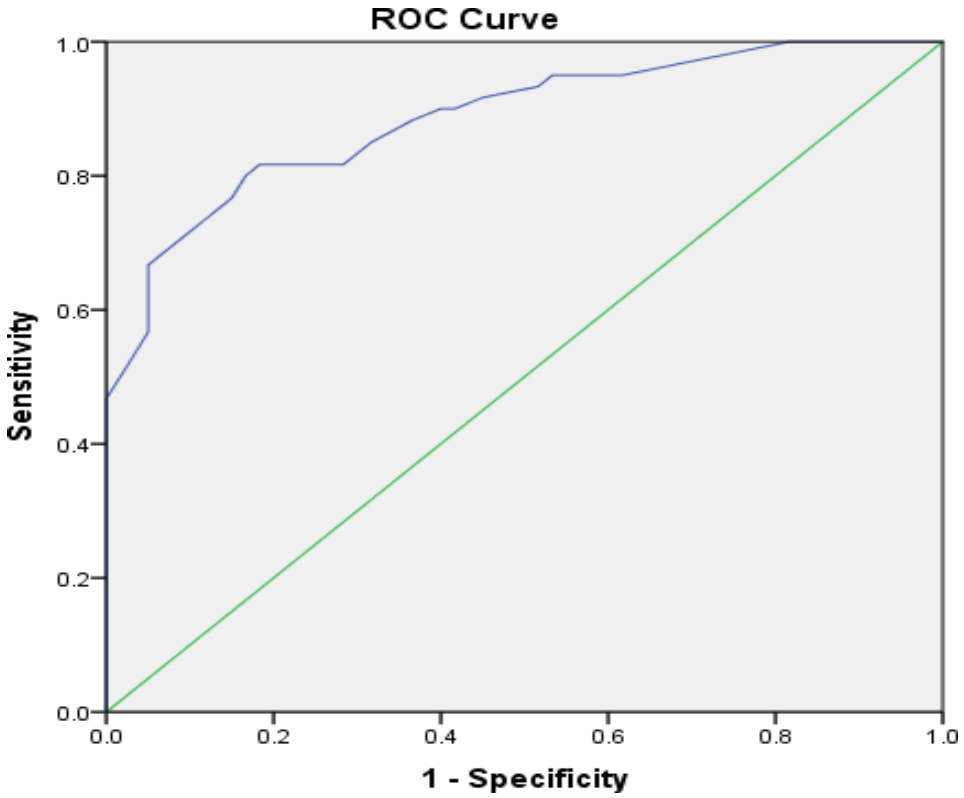


Figure (3-3) The ROC curve for uric acid as diagnostic parameter.

Table (3-7): Area under curve, sensitivity and specificity of uric acid

| Area | P value | Sensitivity | Specificity | Cutoff value (mg/dl) |
|---|---|---|---|---|
| 0.887 | <0.001 | 81.7% | 81.7% | 5.15 |

## 5. Discussion

Uric acids the final oxidation product of purin catabolism . it was being reported that serum uric acid levels are associated with insulin resistance.

The present study evaluated maternal serum uric acid levels in association with gestational diabetes in comparison to women with normal glucose tolerance and found that maternal serum uric acid levels were significantly higher in GDM which was (6.71+ 0.52)mg\dl in comparison to (4.56 + 0.69)in control group(P= <0.001).

In this study the patients were matched in gestational age ,age, parity and body mass index.

This study go with what was found by ( Mishu FA etal ,2019)(34)who concluded that there was distinct alteration of serum uric acid in GDM in comparison to control group of normal pregnancy .the mean level was (4.48+0.4 mg/dl) in GDM in comparison to(3.52±0.74mg\dl) in control group. In addition they reported that estimation of uric acid levels might help in prevention of complication in patient with GDM.

The observed uric acid elevation may be a protective response capable of opposing harmful effect of free radicals activity and oxidative stress.(35)

In addition it is found that gestational hyperuricemia is significantly associated with maternal and fetal complication (Mishu FA)(34)

The finding of the present study also goes with what was found by (Habiba Khudair etal 2018)(36) who assessed serum uric acid level in different gestational ages and found that higher level of serum uric acid are associated with GDM in gestational age >24 week as compared to control group and stated that serum uric (which is a physiological antioxidant) in early pregnancy was associated with higher incidence of GDM

This finding also go with what was found by other studies done by (EL- Gharib MN etal ,2013)(37) and (Wolak T etal,2012)(38)

(Amudha etal ,2017)(39) concluded that elevated or higher normal levels of S.uric acid in first trimester maybe associated with pre-existing metabolic abnormalities which lead to poor maternal physiological adaptation to pregnancy and of pregnancy complications like GDM .

(Anna Pleskacova etal;2018)(40) in their study found that higher uric acid levels were associated with disturbed glucose tolerance.

(Li Yan, Tangwei Yu etal,2020)(41) concluded that higher uric acid levels were positively and independently associated with GDM.

In the present study it is found that maternal serum uric acid levels had significant positive correlation with 2h GTT blood glucose levels.

ROC curve for maternal serum uric acid level as diagnostic parameter in gestational diabetes reviled that AUC was (0.887), sensitivity(81.7%), specificity(81.7%) and cut of value of(5.15mg\dl)at p value <0.001.

(Sed sahin Aker et al ,2016)(42) in their study concluded that serum uric acid has a linear association with the development of GDM and IGT

.ROC curve in their study reviled AUC(0.92)with a diagnostic threshold of (3.95mg\dl) with sensitivity of (100 %) and specificity of (60%).

## 6. Conclusion

- Serum Uric acid is significantly increased in pregnant women with GDM.

- Maternal serum uric acid level is significantly correlated with 2hr GTT blood glucose level and can be used a predictor parameter in gestational diabetes.

**7. Recommendations**

1- Further studies with larger samples to evaluate correlation between uric acid level and GDM are recommended.

2- To evaluate the predictive value of maternal uric acid in GDM and its impact on further development of type II DM.

3.study the impact of maternal uric acid levels on glycemic control in pregnant women with GDM.

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