Assessment of Hyperuricemia in Gestational Diabetes

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ABSTRACT

Introduction: The incidence of gestational diabetes has increased significantly during the last years. Prior studies suggest that GDM is associated with elevated uric acid. **Aim:** To estimate the prevalence of hyperuricemia in gestational diabetes. **Subject and Methods:** This is a cross-sectional study conducted on 221 pregnant females with gestational diabetes mellites underwent a structured interview. **Results:** This study found that the mean serum uric acid of participants is (4.99±0.61) mg/dl with a range (3.6-6.8) mg/dl, with no cases of hyperuricemia. **Conclusions:** This study demonstrated that gestational diabetes mellitus is not associated with hyperuricemia.

Key words: Gestational diabetes, uric acid, hyperuricemia, albumin.

Introduction:

Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance that appears or is for the first time diagnosed during pregnancy (**1**). In recent years, with the delay of child-bearing age and changes in dietary habits and lifestyles, the incidence of GDM has increased significantly (**2**). GDM during pregnancy are considered as predictors for the subsequent development of cardiovascular disease and metabolic syndrome in future non-pregnant life (**3**).

Uric acid is an end product of purine metabolism; elevated plasma uric acid has been associated with many adverse pregnancy outcomes (**3**). One of the problems in dealing with hyperuricemia is that there is no universally accepted definition of hyperuricemia. A practical value would seem to be SUA concentration higher than 405 μmol/L (6.8 mg/dL) as this is urate's solubility point used for measurement in laboratories (**4**). According to American College of Rheumatology, hyperuricemia is defined as serum uric acid (UA) concentration higher than 7 mg/dl (**5,6**).

Gestational hyperuricemia was found to be significantly associated with a high rate of maternal and fetal complications along with proteinuria, hypertension, hyperinsulinemia and in females with pre-eclampsia (**7,8**). GDM is linked to metabolic syndrome and uric acid. UA is known as a marker for metabolic syndrome in non-pregnant subjects**.** Since previous studies on UA metabolism in GDM may indicate a possible link between level of uric acid and pregnancy outcome in females with gestational diabetes (**6,9**).

Subject and methods:

This is a cross sectional study conducted on 221 pregnant females with gestational diabetes mellites aiming to estimates prevalence of hyperuricemia in gestational diabetes. Our study was done at obstetric /family medicine outpatient clinics at Cairo university hospitals.

Pregnant females already diagnosed with gestational diabetes mellitus (by obstetric specialist at 24-28 weeks of gestation) according to American Diabetes Association Guideline criteria for the diagnosis of GDM attending obstetric clinic at Cairo university during the period from October 2020 to June 2022 and who agreed to participate and to be included in the study.

▪ **Inclusion criteria:**

Pregnant females with singleton pregnancy diagnosed with gestational diabetes mellitus by 24-28 weeks of gestation by an obstetric specialist. Agree to participate in the study.

▪ **Exclusion criteria:**

Pregnant females known to have previous diabetes mellitus, chronic hypertension, kidney disease, or other systemic diseases.

A. Sample Size:

Sample size was calculated using Epi info version 7 program based on the previous study of **Amini et al. (10)**, prevalence in hyperuricemia pregnancy was 32.2% and pregnancy with normal uric acid was 16.6%, a minimal sample size of 66 are required to achieve the study objectives under error 1 %, confidence interval 95% by using openepi6 program with power 80%.

B. Data collection tools and technique:

1. The pregnant females were enrolled in the study when they came to the obstetric outpatient clinic, Cairo university and diagnosed with gestational diabetes mellitus diagnosed according to American Diabetic Association (ADA) Guideline criteria for the diagnosis of GDM which recommends the IADPSG criteria ("one-step strategy") for diagnosis of GDM:
2. Any one abnormal value of cut off values after 75- gram oral glucose tolerance test is enough for diagnosis. (Fasting > 92 mg/dl ; 1-hour > 180 mg/dl ; 2-hours > 153 mg/dl). Their blood samples were collected and analyzed for serum Uric acid concentration creatinine, eGFR and albumin.

The following steps were done for cases:

History taking:

1. Personal history: including name, age, address, consanguinity, and special habits as smoking …etc.
2. Menstrual history: The 1st day of the last menstrual period (LMP), regularity of menstrual cycles and history of hormonal medications.
3. Obstetric history: Previous deliveries, mode of deliveries, number and sex of living children, date of last delivery, history of abortions, date of last abortion, puerperium, and history of complications.
4. Past history: Systemic diseases as hypertension, DM, renal diseases, hyperthyroidism, etc.
5. Medical history: Especially of hormonal medications and drugs known to elevate uric acid concentration in the blood such as phenothiazines.
6. Family history: of clinical importance like hypertension, DM, etc.

- **Clinical examination**

    General examination: vital signs (Pulse, temperature, blood pressure, respiratory rate) body weight and chest, abdomen and heart examination, lower limb edema.

- **Ultrasonography:**

    Obstetric ultrasound was used to confirm fetal viability, detect number of fetuses, estimate gestational age, check for other abnormalities.

- **Laboratory tests:**

    Blood samples were taken for assessment serum Uric acid, creatinine, eGFR and albumin concentration.

- **Uric acid level:**

    There is no universally accepted definition of hyperuricemia. A practical value would seem to be SUA concentration higher than 405 µmol/L (6.8 mg/dL) as this is urate's solubility point used for measurement in laboratories (**4**) . According to American College of Rheumatology, hyperuricemia is defined as serum uric acid (UA) concentration higher than 7 mg/dl (**5**).

Sampling technique of Uric acid test:

    A blood sample was taken from all subjects. Three milliliters were collected into sterile plane tubes, centrifuged at 300g (gravitational force) for 5 minutes. Sera were separated immediately and stored at -20 degree Celsius until time of analysis.

Uric acid measurement:

    The Serum uric acid was assayed by commercially available enzymatic, Colorimetric Uric acid L.S kits for the quantitative determination of Uric acid in serum and plasma supplied by BioMed Diagnostic (Authorized Representative in the European Community MDSS GmbH, Germany).

Ethical considerations:

    Ethical approvals were obtained from the research committee in faculty of medicine, Cairo University, and the ethical and research committee of family medicine department. The researcher sit privately the participants who accepted to participate in the study and a written Informed consent was taken (the participant was informed about the objectives, methods, and possible impact of the study.

Statistical Analysis

    All data were collected, tabulated and statistically analyzed using SPSS 26.0 for windows (SPSS Inc., Chicago, IL, USA). Quantitative data were expressed as the mean ± SD & median (interquartile range), and qualitative data were expressed as absolute frequencies (number) & relative frequencies (percentage).

Results

The mean age of the studied group was 32.21±4.98 years; more than half of cases residence (76.9%) was urban. (22.6%) of cases showed positive Consanguinity, (1.4%) were smokers **(Table 1)**.

Mean height of participants was 161.32±3.83 cm ranging from 153 cm to 174 cm, the mean BMI was 31.75±5.20, the antepartum weight was 93.71±15.32 kg and the mean postpartum weight was 82.76±14.58 kg **(Table 2)**.

Regarding obstetric history, the mean gravida was 3.26±1.74 pregnancies, the mean para was 2.70±1.40 deliveries, the mean previous abortions was (0.55±0.73) times, the mean duration since last abortion was (2.90±4.30) years **(Table 3)**.

Regarding blood pressure, the mean systolic blood pressure was 117.43±10.38 mm Hg and the mean diastolic blood pressure was 73.17±8.95 mm Hg, (32.1%) of cases showed positive family history of hypertension. (57.5%) had positive Family history of diabetes. More than half of participants (54.3%) had a history of hormonal medications and majority of cases (89.1%) keep on Regularity of menses.

The mean Random blood sugar was 150.58±31.10 mg/dl. The mean Antepartum Creatinine was 0.59±0.06 mg/dl. The mean Antepartum serum uric acid was 4.99±0.61 mg/dl with no cases of hyperuricemia. The mean Antepartum eGFR was 122.98±5.88. The mean Antepartum albumin was 3.49±0.49 mg/dl **(Table 4)**.

Table (1): basic characteristics of the studied group (n=221):

Variable	cases group (n=221)	
Age (years) Mean±SD Range	32.21±4.98 (20-42)	
Variable	*N*	**(%)**
Residence • Rural • Urban	51 170	23.1 76.9
Consanguinity: • Negative • Positive	171 50	77.4 22.6
Smoking • No • Yes	218 3	98.6 1.4

Table (2): Anthropometric measurements of the studied group (n=221).

Variable	cases group (n=221)
Height Mean±SD Range	161.32±3.83 (153-174)
BMI Mean±SD Range	31.75±5.20 (18.03-51.42)
Antepartum Weight Mean±SD	93.71±15.32

Range	(60-130)

Table (3): Obstetric history of the studied group (n=221)

Variable	cases group (n=221)	
Gravida[] Mean±SD Median (IQR)	3.26±1.74 3 (2-4)	
Para [][] Mean±SD Median (IQR)	2.70±1.40 3 (2-4)	
abortion Mean±SD Median (IQR)	0.55±0.73 0 (0-1)	
Duration since last abortion(years) Mean±SD Median (IQR)	2.90±4.30 0 (0-5)	
SBP Mean±SD Range	117.43±10.38 (80-140)	
DBP Mean±SD Range	73.17±8.95 (0-90)	
Variable	*N*	**%**
History of hormonal medications • No • Yes	101 120	45.7 54.3
Family history of hypertension • No • Yes	150 71	67.9 32.1
Family history of diabetes • **No** • **Yes**	94 127	42.5 57.5
Regularity of menstruation • **No** • **Yes**	24 197	10.9 89.1

[]gravida =number of pregnancies[][] para=number of deliveries

Table (4): laboratory investigations of the studied group (n=221)

Variable	cases group (n=221)
Rondom blood sugar Mean±SD Range	150.58±31.10 (104-279)
Creatinine Mean±SD Range	0.59±0.06 (0.42-0.72)
Uric acid Mean±SD Range	4.99±0.61 (3.6-6.8)

eGFR	
Mean±SD	122.98±5.88
Range	(108-141)
Albumin	
Mean±SD	3.49±0.49
Range	(2.30-4.60)

□Hyperuricemia is defined as serum uric acid more than 6.8 mg/dl.

Discussion

This study finds that the mean age of the studied group was (32.21±4.98) years with mean BMI of (31.75±5.20) and the mean antepartum serum uric acid was (4.99±0.61) mg/dl with a range of (3.6-6.8) mg/dl among the participants.

This is nearly similar to study by **Zhang et al. (11)** who studied Changes in serum adipocyte fatty acid-binding protein in women with gestational diabetes mellitus and normal pregnant women in late pregnancy and found that the mean age of females with GDM was (32.24 ±3.81) and mean BMI (28.91 ± 3.36) with the mean serum uric acid was (5.8±1.6)mg/dl. This is nearly similar to study by **Güngör et al. (12)** who conducted on a total of 112 patients, 56 of whom had gestational diabetes, with mean age group was (29.9 ± 3.9) and the mean uric acid level among women with GDM was (4.37±1.08) mg/dl.

Study by **Kumar et al. (13)** which was a prospective hospital based, case-control study carried on 100 pregnant women aged between 20-35 years attending antenatal clinic, the mean uric acid level among women with GDM was 4.30±0.46 mg/dl and it was 3.037±0.787 mg/dl among healthy pregnant females.

Mishu et al.(14) found that serum uric acid level in GDM group was significantly (p<0.001) higher in third trimesters (4.48 ±0.41 mg/dl) compared to those without GDM (3.52 ±0.74 mg/dl).

This study finds that there were no cases of hyperuricemia(SUA>6.8mg/dl) between participants and this is nearly similar to other studies by **Kumar et al. (13)** and **Pleskacova et al. (15)** who found that there were no cases of antepartum hyperurecemia between females with GDM.

Regarding antepartum creatinine level, this study finds that the mean antepartum creatinine was 0.59±0.06 mg/dl. Several studies had nearly similar results , **Güngör et al. (12)** who studied relationship between serum uric acid, creatinine, albumin and gestational diabetes mellitus found that antepartum creatinine level in females with GDM was (0.6±0.15 mg/dl).

Also, **Erol et al. (16)** who studied evaluation of circulating betatrophin levels in gestational diabetes mellitus found that antepartum creatinine level in females with GDM was (0.6 ± 0.1) mg/dl. **Diboun et al. (17)** who studied metabolic profiling of pre-gestational and gestational diabetes mellitus identifies novel predictors of pre-term delivery, found that antepartum creatinine level in females with GDM was (0.56±0.11)mg/dl.

The mean antepartum albumin was (3.49±0.49) mg/dl which is nearly similar to results of **Güngör et al. (12)** who found that antepartum albumin level was (3.2±.27)mg/dl.

Also**, Diboun et al. (17)** found that antepartum albumin level in females with GDM was (3.5 ± 0.7) mg/dl.

Regarding to estimate GFR during pregnancy, according to **Park et al.(18)** who revealed the optimal gestational eGFR range in their study was 120–150 mL/min/1.73 m^2. This elevation is due to that glomerular filtration rate (GFR) increases 50% and renal plasma flow (RPF) increases up to 80% as compared with nonpregnant levels (**19**) and we find that the antepartum eGFR was(122.98±5.88) mL/min/1.73 m2.

CONCLUSION

Gestational diabetes mellitus is associated with increase level serum uric acid level but it is not associated with hyperuricemia.

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