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ORIGINAL ARTICLE

Diagnostic Accuracy of First Trimester Hyperuricemia for Prediction of Subsequent Gestational Diabetes Mellitus

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ABSTRACT

Background: Gestational diabetes mellitus (GDM) is a condition in which pregnant females develop. GDM causes significant and often potentially maternal and fetal complications. Uric acid is the end product of purine metabolism. Recent literature suggests a bidirectional causal relationship between hyperuricemia and insulin resistance. So we conducted this study.

Objective: To find diagnostic accuracy of first trimester hyperuricemia for prediction of subsequent gestational diabetes mellitus confirmed on oral glucose tolerance test.

Methods: This was a Cross-sectional study conducted at Department of Obstetrics and Gynecology CMH Lahore during time duration 25-4-2017 to 24-10-2017. All females met inclusion criteria were enrolled in this study. Blood samples in first trimester were collected for analysis of serum uric acid. Then after 26-28 weeks of gestation, OGTT was done and presence of GDM was recorded. All the data was collected on proforma. SPSS version 22 was used for data entry and analysis. A 2 x 2 table was generated find the diagnostic accuracy of hyperuricemia taking OGTT as gold standard.

Results: The mean age of females was 26.70±5.21years. The mean height, weight and BMI of females were 1.62±0.07m, 61.07±8.54kg and 23.32±3.72kg/m2. The mean gestational age of females was 9.96±.37weeks at time of enrolment in the study. The mean uric acid level at time of presentation was 4.43±3.61mg/dl. In this study, the sensitivity and specificity of hyperuricemia for prediction of GDM were 91.1% and 95.7%. The PPV and NPV of hyperuricemia were 86.8% and 97.2%. The overall diagnostic accuracy was 94.5%.

Conclusion: Thus the accuracy of hyperuricemia was high and it is now accepted as reliable marker for prediction of GDM in later pregnancy.

Keywords: Diagnostic accuracy, first trimester, hyperuricemia, gestational diabetes mellitus, oral glucose tolerance test, uric acid

INTRODUCTION

Gestational diabetes mellitus (GDM) is a condition in which pregnant females develop; high blood glucose (blood sugar) levels during pregnancy (especially during their third trimester).(1) GDM is the mild form of diabetes mellitus and can be controlled by exercise and carbohydrate diet having low glycemic index.(2)

Glucose is not properly regulated in 3 10% of all pregnancies. GDM is the glucose intolerance of variable degree with onset or first recognition during pregnancy. Annually 21 million people of the world (7% of the population) are reported with some form of diagnosed diabetes; another 6 million people are reported with undiagnosed particularly type 2 diabetes among women of child bearing age.(2)

The prevalence of GDM in the Pakistan is found to be 14.8%.(3) Prevalence of GDM was higher in the elderly multiparous females who were overweight and had family history of diabetes mellitus.(3) GDM causes significant and often potentially maternal and fetal complications including preeclampsia, polyhydramnios, fetal macrosomia, birth trauma, preterm delivery, neonatal metabolic complications and perinatal death.(4)

Uric acid is the end product of purine metabolism and is synthesized by the enzyme xanthine oxidase. Hypoxia and ischemia of the placenta and cytokines such as, interferon induce the expression of xanthine oxidase and therefore, increase the production of uric acid and also reactive oxygen species.(5)

Recent literature suggests a bidirectional causal relationship between hyperuricemia and insulin resistance. In fact, hyperuricemia has been found to be a marker and predictor for future development of diabetes and the metabolic syndrome.(5-7) A study reported that serum uric acid cut-off value 3.4mg/dl (hyperuricemia) had a sensitivity of 90%, specificity of 95% and a negative predictive value of 99% for subsequent development of GDM.(6)

The rationale of this study is to find diagnostic accuracy of first trimester hyperuricemia for prediction of GDM confirmed on oral glucose tolerance test (OGTT). A previous study reported high diagnostic accuracy of uric acid cut-off value 3.4mg/dl (hyperuricemia). As no local study is available and uric acid is considered a novel marker for early prediction of GDM. As GDM is the most common metabolic complications of pregnancy, and causes fetal mortality and morbidity. Therefore, accurate screening and early diagnosis of this condition is very important to allow timely intervention in order to get a satisfactory pregnancy outcome.

MATERIAL AND METHODS

This was a Cross-sectional study conducted at Department of Obstetrics and Gynecology CMH Lahore during time duration 25-4-2017 to 24-10-2017. Non probability consecutive sampling technique was adopted for sample selection. A total of 335 females were included in the study. The sample size is estimated using sensitivity of hyperuricemia 90% with 7% margin of error and specificity of hyperuricemia 95% with 2.5% margin of error(6) and 95% confidence level. We used prevalence of GDM in the Pakistan as 14.8%.(3)

Inclusion criteria for women was all pregnant women aged 18-35 years came for their antenatal checkup in first trimester (gestational age<13 weeks, will be assessed on USG) will be taken in this study. Following women were excluded from the study patients with pre-existing diabetes mellitus, (will be assessed on clinical record), history of hypertension (BP > 120/80), history of connective tissue disorders (will be assessed on available medical record) and females on medications causing hyperuricemia (eg, pyrazinamide, ethambutol, levodopa and theophylline). All females met inclusion criteria after taking informed consent were enrolled in this study. Demographic information like age, name, address and contact details and gestational age at time of enrollment were taken. Blood samples from every female with gestational age < 13 weeks were collected for analysis of serum uric acid. All females were advised for their regular antenatal checkup. All females during 26-28 weeks of gestation were undergone for an OGTT [2 step procedure as described in operational definition]. Frequencies were recorded for GDM by OGTT and hyperuricemia (as per

operational definition). All the data were collected by researcher herself on a prescribed proforma (attached). All patients were managed as per standard protocols.

Data Analysis: SPSS version 22 was used for data entry and analysis. Mean ± S.D were used for quantitative data like age, gestational age at first and third trimester and uric acid level in first trimester. Frequency and % were applied for categorical data like hyperuricemia in first trimester and GDM on OGTT. A 2 x 2 table was generated for GDM by OGTT and hyperuricemia during first trimester (as per operational definition) to find the diagnostic accuracy (sensitivity, specificity, PPV, NPV and likelihood ratio). Data was stratified for age, BMI and parity. Post stratified diagnostic accuracy (sensitivity, specificity, PPV, NPV and likelihood ratio) was found

RESULTS

The mean age of females was 26.70±5.21years. The mean height, weight and BMI of females were 1.62±0.07m, 61.07±8.54kg and 23.32±3.72kg/m2. There were 91 (27.2%) females who were primigravida (parity 0), 74 (22.1%) had parity 1, 60 (17.9%) had parity 2, 67 (20%) had parity 3 while 43 (12.8%) had parity 4. The mean gestational age of females was 9.96±.37weeks at time of enrolment in the study. The mean uric acid level at time of presentation was 4.43±3.61mg/dl. There were 83 (24.8%) females with hyperuricemia while 252 (75.2%) had normal uric acid level. The mean gestational age of females was 30.91±3.18weeks at time of OGTT diagnosis for GDM. There were 79 (23.6%) females positive for GDM while 256 (76.4%) females negative for GDM. In this study, the sensitivity and specificity of hyperuricemia for prediction of GDM were 91.1% and 95.7%. The PPV and NPV of hyperuricemia were 86.8% and 97.2%. The overall diagnostic accuracy was 94.5%. Data was stratified for age of patients. In females aged 18-25years, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of hyperuricemia were 93.8%, 98.3%, 93.8%, 98.3% and 97.3%, respectively. In females aged 26-35years, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of hyperuricemia were 89.4%, 93.6%, 82.4%, 96.3% and 92.5%, respectively. Data was stratified for BMI of patients. In normal BMI females, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of hyperuricemia were 92.8%, 96.7%, 89.7%, 97.8% and 95.8%, respectively. In overweight females, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of hyperuricemia were 93.8%, 90.6%, 75%, 98% and 91.3%, respectively. In obese females, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of hyperuricemia were 71.4%, 100%, 100%, 90.5% and 92.3%, respectively. Data was stratified for parity of patients. In primigravida, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of hyperuricemia were 94.4%, 98.6%, 94.4%, 98.6% and 97.8%, respectively. In primiparous, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of hyperuricemia were 88.9%, 94.6%, 84.2%, 96.4% and 93.2%, respectively. In females having parity 2-4, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of hyperuricemia were 90.7%, 94.5%, 84.8%, 96.8% and 93.5%, respectively.

Table 1: Characteristics of Women

n	335
Age	26.70±5.21 (Min:18 & Max:35)
Height	162±0.07
Weight	61.07±8.54
BMI	23.32±3.72
Gestational Age (Weeks)	30.91±3.18
Uric Acid	4.43±3.61
OGTT	9.96±1.37
Hyperuricemia	83(24.78%)
Gestational Diabetes Mellitus	79(23.58%)

Table 2: Diagnostic accuracy of Hyperuricemia for GDM

		Diabetes on OGTT		Total
		Positive	Negative	
Hyperuricemia	Positive	72(91.14%)	11(4.30%)	83
	Negative	7(8.86%)	245(95.70%)	252
Total		79	256	335

Table 3:

Sensitivity=91.14%	(82.82, 95.64[1])
Specificity=95.7%	(92.47, 97.58[1])
Positive Predictive Value=86.75%	(77.81, 92.44[1])
Negative Predictive Value=97.22%	(94.38, 98.65[1])
Diagnostic Accuracy=94.63%	(91.67, 96.57[1])

Table-4: Diagnostic Accuracy Stratified for Age, BMI and Parity

	Sensitivity	Specificity	PPV	NPV	Diagnostic Accuracy
Age					
18-25 Years	93.80%	98.30%	93.80%	98.30%	97.30%
26-35 Years	89.40%	93.60%	82.40%	96.30%	92.50%
Body Mass Index					
Normal	92.80%	96.70%	89.70%	97.80%	95.80%
Overweight	93.80%	90.60%	75.00%	98.00%	91.30%
Obese	71.40%	100%	100%	90.50%	92.30%
Parity					
Primigravida	94.40%	98.60%	94.40%	98.60%	97.80%
Primiparous	88.90%	94.60%	84.20%	96.40%	93.20%
Parity 2-4	90.70%	94.50%	84.80%	96.80%	93.50%

DISCUSSION

GDM and preeclampsia are two common complications in pregnancy, affecting more than 10% pregnancies worldwide. However, the true underlying causes of these two conditions remain to be fully elucidated. Although both conditions were diagnosed first during pregnancy, it is uncertain whether they originate prior to or during pregnancy.(8)

Several studies have now shown that, compared to their peers, women who go on to develop GDM later in pregnancy have biochemical abnormalities that can be detected in the first trimester including increased levels of uric acid.(9, 10) To date, there has been limited study of pre-gravid function of women who go on to develop GDM. These limited data, however, do support the concept of metabolic dysfunction prior to pregnancy in this patient population.(11, 12)

Many studies have indicated that serum uric acid is associated with hypertension, obesity, hyper-insulinemia and dyslipidemia, suggesting that it could be part of the cluster of factors of the metabolic syndrome.(13)

In this study, the mean uric acid level at time of presentation was 4.43±3.61mg/dl. In this study, the sensitivity and specificity of hyperuricemia for prediction of GDM were 91.1% and 95.7%. The PPV and NPV of hyperuricemia were 86.8% and 97.2%. The overall diagnostic accuracy was 94.5%.

A study reported that serum uric acid cut-off value 3.4mg/dl (hyperuricemia) had a sensitivity of 90%, specificity of 95% and a negative predictive value of 99% for subsequent development of GDM.(6)

While another study demonstrates a striking association between first trimester uric acid and risk of developing GDM, only half of the women with uric acid in the highest quartile actually developed the disease. This finding may be due to different pathways of development of GDM. Women who have a pregnancy complicated by GDM have up to a 50% chance of developing type 2 diabetes in their lifetime. It would be interesting to know whether these were the women with elevated uric acid in the first trimester.(14) This possibility is supported by a study by Di Cianni et al. in which serum uric acid was measured at a median of 16 months postpartum in women who had pregnancies complicated by GDM.(15)

In this study, the mean age of females was 26.70±5.21years. Data was stratified for age of patients. In females aged 18-25years, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of hyperuricemia were 93.8%, 98.3%, 93.8%, 98.3% and 97.3%, respectively. In females aged 26-35years, the sensitivity,

specificity, PPV, NPV and diagnostic accuracy of hyperuricemia were 89.4%, 93.6%, 82.4%, 96.3% and 92.5%, respectively. Table 7

In this study, the mean height, weight and BMI of females were 1.62±0.07m, 61.07±8.54kg and 23.32±3.72kg/m2. Data was stratified for BMI of patients. In normal BMI females, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of hyperuricemia were 92.8%, 96.7%, 89.7%, 97.8% and 95.8%, respectively. In overweight females, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of hyperuricemia were 93.8%, 90.6%, 75%, 98% and 91.3%, respectively. In obese females, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of hyperuricemia were 71.4%, 100%, 100%, 90.5% and 92.3%, respectively.

In this study, there were 91 (27.2%) females who were primigravida (parity 0), 74 (22.1%) had parity 1, 60 (17.9%) had parity 2, 67 (20%) had parity 3 while 43 (12.8%) had parity 4. Data was stratified for parity of patients. In primigravida, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of hyperuricemia were 94.4%, 98.6%, 94.4%, 98.6% and 97.8%, respectively. In primiparous, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of hyperuricemia were 88.9%, 94.6%, 84.2%, 96.4% and 93.2%, respectively. In females having parity 2-4, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of hyperuricemia were 90.7%, 94.5%, 84.8%, 96.8% and 93.5%, respectively.

CONCLUSION

Thus the accuracy of hyperuricemia was high and it is now accepted as reliable marker for prediction of GDM in later pregnancy. Now we can implement the screening of uric acid level in early pregnancy in order to predict GDM in later pregnancy. So that females can be managed early to prevent GDM in later pregnancy which has hazardous consequences at end of pregnancy. This would help us to reduce complications of hyperuricemia and GDM during pregnancy.

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