DIAGNOSTIC ACCURACY OF FIRST TRIMESTER HYPERURICEMIA FOR PREDICTION OF GESTATIONAL DIABETES MELLITUS

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ABSTRACT

Objective: To find the diagnostic accuracy of first trimester hyperuricemia for the prediction of development of subsequent gestational diabetes mellitus.

Study Design: Cross-sectional study.

Place and Duration of Study: Conducted at department of Obstetrics & Gynaecology, Combined Military Hospital Lahore, from Apr 2017 to Oct 2017.

Methodology: All pregnant patients who met the inclusion criteria were enrolled in this study after informed consent. Blood samples in first trimester were collected for analysis of serum uric acid. Then after 24-28 weeks of gestation, Oral glucose tolerance test was done and presence of gestational diabetes mellitus was recorded. All the data were collected on a proforma.

Results: The mean age of females was 26.70 ± 5.21 years. The mean height and weight was 1.62 ± 0.07 meters and 61.07 ± 8.54 kg respectively. Body mass index of patients was 23.32 ± 3.72 kg/m^2. The mean gestational age of females was 9.96 ± 0.37 weeks at time of enrolment in the study. The mean uric acid level at time of presentation was 4.43 ± 3.61 mg/dl. In this study, the sensitivity and specificity of hyperuricemia for prediction of gestational diabetes mellitus were 91.1% and 95.7%. The positive predictive value and negative predictive value of hyperuricemia were 86.8% and 97.2% respectively. The overall diagnostic accuracy was 94.5%.

Conclusion: Hyperuricemia in the first trimester is a reliable marker for prediction of gestational diabetes mellitus in later pregnancy.

Keywords: Diagnostic accuracy, First trimester, Gestational diabetes mellitus, Hyperuricemia, Oral glucose tolerance test, Uric acid.

INTRODUCTION

Gestational diabetes mellitus is defined as any degree of glucose intolerance with onset or first recognition during pregnancy[1]. Globally 21 million people (7% of the population) are reported annually with some form of diagnosed diabetes. Another 6 million people are reported with undiagnosed diabetes, particularly type 2 diabetes among women of child bearing age[2].

The prevalence of gestational diabetes mellitus in Pakistan is 14.8%. Higher prevalence of gestational diabetes mellitus is seen in elderly, multiparous women who have a family history of diabetes mellitus or are overweight[3]. Gestational diabetes mellitus causes significant maternal and fetal complications. These include but are not limited to: polyhydramnios, preeclampsia, fetal macrosomia, preterm delivery, birth trauma, neonatal metabolic complications and perinatal death[4].

The enzyme xanthine oxidase synthesizes uric acid, which is the end product of purine metabolism. Cytokines such as interferon, along with hypoxia and ischemia of the placenta, induce the expression of xanthine oxidase. This increases 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

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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 gestational diabetes mellitus[6].

Women with gestational diabetes mellitus have a 50% chance of developing type 2 diabetes mellitus over the 20 years following their diagnosis of gestational diabetes mellitus. Maternal hyperglycemia leads to an increase in glucose delivery to the fetus, which causes fetal hyperinsulinemia and increased fetal growth. Excessive fetal growth can lead to increased cesarean deliveries, birth trauma, and long-term risk of obesity and glucose intolerance. Immediate fetal complications include hypoglycemia, cardiomyopathy, respiratory distress syndrome, hyperbilirubinemia and hypocalcemia. This abundance of complications show the significance of early risk stratification with suitable screening and diagnosis, and of therapeutic interventions that maintain optimal glycemic control[8].

The rationale of this study was to find the diagnostic accuracy of first trimester hyperuricemia for prediction of development of gestational diabetes mellitus which was confirmed later on oral glucose tolerance test. As gestational diabetes mellitus is one of the most common metabolic complications of pregnancy, and has a significant association with fetal mortality and morbidity. Accurate screening and early diagnosis of this condition is, therefore, of immense importance in order to allow timely intervention with the goal of achieving a satisfactory pregnancy outcome.

METHODOLOGY

A cross sectional study was conducted at the department of Obstetrics & Gynaecology, Combined Military Hospital Lahore, from April 2017 to October 2017. Institutional Ethics Review Board approval certificate reference number is 413/ERC/CMHLMC .

A total of 335 womenbetween 18-35 years of age who were in first trimester were taken in this study after informed consent. The sample size was calculated by using WHO sample calculator. We used prevalence of gestational diabetes mellitus in the Pakistan as 14.8%[3]. Non probability consecutive sampling technique was used.

Patients with pre-existing diabetes mellitus, history of hypertension, connective tissue disorders and on medications causing hyperuricemia (eg, pyrazinamide, ethambutol, levodopa and theophylline) were excluded from the study.

Demographic information like age, name, address and contact details and gestational age at the 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 between 24-28 weeks of gestation underwent oral glucose tolerance test. Frequencies were recorded for gestational diabetes mellitus by oral glucose tolerance test and hyperuricemia. All the data were collected by researcher herself on a prescribed proforma. The serum uric acid level of 3.4 mg/dl was considered as hyperuricemia.

American College of Obstetricians and Gynecologists has recommended a two-step procedure for screening & diagnosis of gestational diabetes mellitus. Firstly, a 50g glucose challenge test should be performed. If a blood glucose level of more than 7.8 mmol/L (140 mg/dL) was obtained, it is followed by a 100 gram glucose dose. The diagnosis of gestational diabetes mellitus is then defined by a blood glucose level exceeding the cutoff value on at least two intervals.

- Fasting: 5.3mmol/L (95 mg/dL)
- 1 hour after drinking the glucose solution: 10 mmol/L (180 mg/dL)
- 2 hours: 8.6 mmol/L (155 mg/dL)
- 3 hours: 7.8 mmol/L (140 mg/dL)

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 percentage were applied for categorical data like hyperuricemia in first trimester and gestational diabetes mellitus on oral glucose tolerance test .

A 2x2 table was generated for gestational diabetes mellitus by oral glucose tolerance test and hyperuricemia during first trimester to find the diagnostic accuracy (sensitivity, specificity, positive predictive value and negative predictive value. Data was stratified for age, body mass index and parity. Post stratified diagnostic accuracy was found.

RESULTS

The mean age of females was 26.70 ± 5.21 years. The mean height, weight and Body mass index of females were 1.62 ± 0.07 meters, 61.07 ± 8.54 kg and 23.32 ± 3.72 kg/m^2 respectively. There were 91 (27.2%) females who were primigravida, 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 ± 0.37 weeks 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 26.31 ± 1.18 weeks at time of oral glucose tolerance test for diagnosis for gestational diabetes mellitus. There were 79 (23.6%) females positive for gestational diabetes mellitus while 256 (76.4%) females negative for gestational diabetes mellitus. The overall diagnostic accuracy was 94.5% as shown in table.

Table: Accuracy of hyperuricemia for gestational diabetes mellitus.

		Diabetes on Oral Glucose Tolerance Test	
		Positive n (%)	**Negative n (%)**
Hyperuricemia	Positive	72 (21.5%)	11 (3.3%)
	Negative	7 (2.1%)	245 (73.1%)
Total		79 (23.6%)	256 (76.4%)

Sensitivity=91.1%, Specificity=95.7%, Positive Predictive Value=86.8%, Negative Predictive Value=97.2% Diagnostic accuracy=94.6%

DISCUSSION

Gestational diabetes mellitus is defined as two or more elevated glucose values obtained during a 3-h oral glucose tolerance test. It has been linked with adverse pregnancy outcomes and increased perinatal complications even with milder degrees of carbohydrate intolerance. In a study by Ali El- Shabrawy *et al*, first trimester serum uric acid levels were shown to be associated with subsequent development of impaired glucose tolerance and gestational diabetes mellitus. Testing serum uric acid in first trimester has shown to have good predictive value for the diagnosis of gestational diabetes mellitus and it can be used as a risk assessment tool[9].

In a study by Ali *et al*, the patients with uric acid >3.5, 79.7% had plasma glucose levels of 120 to 140 mg/dl and 12.5% had plasma glucose levels of ≥140mg/dl[10]. The prevalence rate of gestational diabetes mellitus in the population having high serum uric acid was between 50-51% in a study by Ismail *et al*[11]. while our study showed diagnostic accuracy of 94%.

Several studies have now shown that, compared to their peers, women who go on to develop gestational diabetes mellitus later in pregnancy have biochemical abnormalities that can be detected in the first trimester including increased levels of uric acid[12].

Al-Sadda *et al*[13] showed that women who developed gestational diabetes mellitus were significantly older, with higher BMI. Fawzy *et al*, also confirmed in their study that the risk of developing gestational diabetes mellitus was higher if first-trimester uric acid level of 3.15mg/dl was taken as cut off point with a sensitivity of 77.8% and specificity of 66.5%[14].

Numerous studies have demonstrated that serum uric acid is associated with hypertension, obesity, hyperinsulinemia and dyslipidemia, indicating that it could be part of the group of factors of the metabolic syndrome[15].

In a study by Ganta *et al* 84% women with gestational diabetes mellitus had uric acid levels above 3.5 mg/dl and 15.9% with gestational diabetes mellitus had uric acid levels below 3.5 mg/dl. Women with higher body mass index showed high uric acid levels[16].

A study reported that serum uric acid cut-off value 3.4mg/dl had a sensitivity of 90%, specificity of 95% and a negative predictive value of 99% for subsequent development of gestational diabetes mellitus[6].

Laughon *et al* demonstrated in their study that first-trimester uric acid concentrations in the highest quartile (>3.57-8.30mg/dL) were seen in 46.6% of the women with gestational diabetes mellitus[17]. This was not consistent with our study where the diagnostic accuracy was 94%. In a study by Aker *et al*, at a diagnostic threshold of 3.95 mg/dL, uric acid levels predicted development of gestational diabetes mellitus with 60% specificity and 100% sensitivity[18].

Thus the accuracy of hyperuricemia was high and it is now accepted as a reliable marker for prediction of gestational diabetes mellitus in later pregnancy. Now we can recommend the screening of uric acid level in early pregnancy in order to predict gestational diabetes mellitus in later pregnancy. So that females can be managed early in pregnancy to reduce complications.

The limitation of this study was that 12 patients were excluded during the study because they had excessive vomiting after drinking glucose solution.

CONCLUSION

Hyperuricemia in the first trimester is a reliable marker for prediction of gestational diabetes mellitus in later pregnancy.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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