Original Article

Diagnostic Accuracy of Serum Uric Acid in First Trimester of Pregnancy for the Diagnosis of Gestational Diabetes Mellitus

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ABSTRACT

Objective: To assess the diagnostic accuracy of elevated uric acid in the first trimester of pregnancy for the diagnosis of gestational diabetes mellitus (GDM) keeping the oral glucose tolerance test as the gold standard.

Methodology: This cross-sectional study was done at the Department of Gynaecology & Obstetrics, Islamabad Medical Complex, NESCOM, Islamabad after ethical approval. A total of 455 booked pregnant females presenting within the first trimester were enrolled using non-probability convenience sampling technique. All participants were included after taking informed consent. Their blood sample was taken for uric acid analysis. Females were labeled as having normal (≤3.4 mg/dL) and high uric acid (>3.4 mg/dL). During 22-24 weeks of pregnancy, an oral glucose tolerance test (OGTT) was performed for diagnosing GDM. Data was analyzed using the Statistical Package for the Social Sciences (SPSS) version 25.

Results: In our study, 198(43.5%) pregnant females had GDM. Among the patients with GDM, 147(74.2%) of them had high uric acid level, with a significant association (p-value=0.00001). Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+), negative likelihood ratio (LR-), and diagnostic accuracy of first trimester high uric acid keeping OGTT as the gold standard were 74.24%, 87.94%, 82.58%, 81.59%, 6.2, 0.29, and 81.98%, respectively.

Conclusion: The high uric acid level in the first trimester is a significant predictor of gestational diabetes mellitus with a diagnostic accuracy of 81.98%.

Keywords: *Gestational diabetes mellitus. Uric acid. Oral glucose tolerance test.*

INTRODUCTION

Gestational diabetes mellitus (GDM) has gained utmost importance owing to its adverse effects on maternal and child health. It is a condition of glucose intolerance that occurs in pregnancy when insulin is insufficient to combat the diabetes-inducing effects of various pregnancy hormones.[1] Most of the pregnancies are complicated by GDM, affecting approximately 14% of the females.[2] The chances of gestational hypertension and pre-eclampsia increase in pregnant females with GDM and the majority of them are delivered through caesarean section.[3] Both the mother and child are affected by GDM with a predisposition to coronary artery disease and type 2 diabetes mellitus. It is also a leading cause of financial constraints particularly in developing countries.[4]

Pathogenesis of GDM is still not clear. Genetic, environmental, and metabolic factors are involved in the disease pathogenesis.[5] Insulin resistance, induced by various placental hormones, is the key factor in the causation of disease. In addition, decreased secretion of insulin to meet the body's requirements also plays a role in causing the disease.[6] The pregnant females are screened for GDM after 20 weeks using oral glucose tolerance test (OGTT). Those having GDM are treated with dietary modification, physical activity, and drug therapy.[7]

Hyperuricemia is a predisposing factor for metabolic syndrome and GDM. High levels of uric acid damage endothelial cells, hence reducing their generation of nitric oxide (NO). Nitric oxide promotes the uptake of glucose by body tissues mediated by insulin. The decreased production of NO disturbs this normal phenomenon, leading to insulin resistance. Hyperuricemia also induces inflammation and oxidative stress, which also attributes to GDM.[8] There is a considerable reduction in serum uric acid in the first trimester owing to an increase in glomerular filtration rate and a decrease in the reabsorption of uric acid. Hyperuricemia in the first trimester can recognize pregnant females that have a strong predisposition to develop metabolic syndrome like GDM.[9]

Our study was designed to determine the relation of high uric acid in the first trimester of pregnancy with gestational diabetes mellitus. Our study also evaluated the diagnostic accuracy of first trimester high uric acid, comparing it to the gold standard oral glucose tolerance test for diagnosing GDM in our population. An oral glucose tolerance test is done between 22 to 24 weeks of gestation to diagnose GDM. High levels of uric acid in early pregnancy can be used for screening for GDM. Pregnant women with first trimester hyperuricemia can be considered a high-risk group for GDM and target groups for early prevention & treatment.

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METHODOLOGY

This cross-sectional study was done at the Department of Gynaecology & Obstetrics, Islamabad Medical Complex, NESCOM, Islamabad from 30th November 2021 to 29th May 2022 after ethical approval. After obtaining informed consent, 455 pregnant females were enrolled using non-probability convenience sampling technique. Booked cases of pregnant females with the age range of 18-40 years presenting within 12 weeks of gestation were included. Pregnant females with a history of diabetes mellitus, hyperlipidemia, coronary artery disease, hypertension or underlying chronic inflammatory conditions were excluded.

Demographic details like name, age, contact details, parity, and gestational history were taken. Their gestational age was confirmed on antenatal ultrasound and a blood sample was taken for uric acid analysis. Females were labeled as having normal (≤3.4 mg/dL) and high uric acid (>3.4 mg/dL). The patients were followed till 22-24 weeks of gestation. During 22-24 weeks of gestation, OGTT was done with 75 g of glucose for diagnosing GDM. Gestational diabetes mellitus was labeled based on the National Institute for Health and Care Excellence (NICE) criteria. Pregnant females with a fasting glucose level ≥5.6 mmol/L and 2-hour postprandial glucose level ≥7.8 mmol/L on OGTT with 75 g of glucose were diagnosed as having GDM.[10]

STATISTICAL ANALYSIS

The data was analyzed using the Statistical Package for the Social Sciences (SPSS) version 25. Mean and standard deviation (SD) were applied for quantitative data. Frequency and percentage were used for qualitative data. Chi-square test was applied to determine the relation between high uric acid & GDM and comparison of high uric acid with OGTT based on demographic variables. A p-value of ≤0.05 was considered statistically significant. A 2x2 table was made to estimate the measures of diagnostic accuracy taking OGTT as a gold standard. The measures of diagnostic accuracy were also stratified for age and parity.

RESULTS

The age of the pregnant females ranged from 18-40 years with a mean of 30.12±5.3 years. Most of them [232(50.99%)] were between 31 to 40 years of age. The mean gestational age was 9.24±1.8 weeks. Most of the patients had a parity of 3-5(54.51%) (Table 1). In our study, 198(43.5%) pregnant females had GDM. The mean level of serum uric acid was 6.21±1.54 mg/dL. Serum uric acid levels were high in 178(39.1%) females. Among the patients with GDM, 147(74.2%) had high uric acid level. Out of 455 females, 178(39.1%) had high serum uric acid and 277(60.9%) had serum uric acid within the normal range. Among 178 females with high serum uric acid, 147[True Positive (TP)] had GDM and 31[False Positive (FP)] had no GDM on OGTT. Among 277 females with normal serum uric acid, 51[False Negative (FN)] had GDM on OGTT, whereas 226[True Negative (TN)] had no GDM on OGTT. The association of high uric acid with GDM was statistically significant, with a p-value of 0.00001 (Table 2). This association was significant (p-value <0.00001) in pregnant females of all age groups and parity. Table 3 shows the comparison of high uric acid with GDM based on demographic variables of pregnant females. Overall sensitivity, specificity, PPV, NPV, LR+, LR-, and diagnostic accuracy of high uric acid in the first trimester keeping the actual OGTT as a gold standard were 74.24%, 87.94%, 82.58%, 81.59%, 6.2, 0.29, and 81.98%, respectively. Poststratified measures of diagnostic accuracy were also calculated for age and parity. The diagnostic accuracy of high uric acid was good in all age groups. The diagnostic accuracy was high in females with a parity of 1-2(90.82%). These results are shown in Table 4.

DISCUSSION

The frequency of gestational diabetes mellitus is increasing continuously on a global scale because of various epidemiological factors such as maternal obesity and increased age. Greater than 90% of cases of GDM are reported in developing countries.[11] It is of

Table 1: Study Variables of the Pregnant Females

Variables		Descriptive Statistics
Age (Years)	**Mean±SD**	30.12±5.3
	18-30	223(49.01%)
	31-40	232(50.99%)
Parity (Frequency & Percentage)	**1-2**	207(45.49%)
	3-5	248(54.51%)
Gestational Diabetes (Frequency & Percentage)	**Present**	198(43.5%)
	Absent	257(56.5%)
Serum Uric Acid (Frequency & Percentage)	**High**	178(39.1%)
	Normal	277(60.9%)

Table 2: Relation of High Uric Acid in the First Trimester with GDM

Uric Acid	GDM (Oral Glucose Tolerance Test)		Total	Chi-Square Statistic	p-value
	Positive	Negative			
High	147(TP)	31(FP)	178	188.55	0.00001*
Normal	51(FN)	226(TN)	277		
Total	198	257	455		

**Significant p-value*

Table 3: Comparison of High Uric Acid with OGTT Based on Demographic Variables

Study Variables		Level of Uric Acid	GDM		Chi-Square Statistic	p-value
			Positive	Negative		
Age Groups (Years)	**18-30**	**High**	62(TP)	18(FP)	93.96	<0.00001*
		Normal	18(FN)	125(TN)		
	31-40	**High**	85(TP)	13(FP)	87.36	<0.00001*
		Normal	33(FN)	101(TN)		
Parity	**1-2**	**High**	83(TP)	08(FP)	137.39	<0.00001*
		Normal	11(FN)	105(TN)		
	3-5	**High**	64(TP)	23(FP)	55.05	<0.00001*
		Normal	40(FN)	121(TN)		

**Significant p-value*

Table 4: Diagnostic Accuracy of First Trimester High Uric Acid Stratified on Demographic Variables

Study Variables		Sensitivity	Specificity	PPV	NPV	LR+	LR-	Diagnostic Accuracy
Age Groups (Years)	**18-30**	87.41%	77.50%	87.41%	77.50%	3.76	0.16	83.86%
	31-40	75.37%	86.73%	88.60%	72.03%	5.68	0.28	80.17%
Parity	**1-2**	88.30%	92.92%	91.21%	90.52%	12.47	0.13	90.82%
	3-5	61.54%	84.03%	73.56%	75.16%	3.85	0.46	74.60%

utmost significance to determine the risk factors and predictors of gestational diabetes to scale up its prevention at an early stage.[12]

In our study, pregnant females had a mean age of 30.12±5.3 years. The study participants had a mean age of 26.70±5.21 years in a study by Rehman et al. and 26.4±4.9 years according to Palaniappan et al.[13,14] Majority of the females (50.99%) were above 30 years of age in our study. Another study reported that most of the women (46.2%) were in the 26-30 years age group.[15] The average gestational age was 9.24±1.8 weeks in our study and 9.96±.37 weeks in another study.[13]

Our results revealed that the mean level of first trimester uric acid was 6.21±1.54 mg/dL. The mean uric acid level was 4.43±3.61 mg/dL in a study.[13] A study reported a mean uric acid of 2.9±0.9 mg/dL in the first trimester.[14] In our study, 43.5% females had GDM and among them, 74.2% had high uric acid. In another study, 39.6% of pregnant females had high uric acid in the first trimester and 19% of them developed gestational diabetes. On the other hand, only 4.7% of the women with normal uric acid had GDM.[15] A study demonstrated that 50-51% of pregnant females with high uric acid levels developed gestational diabetes.[16] A meta-analysis revealed a significant relation between high uric acid and GDM.[17] Another study reported that the chances of GDM increase with high uric acid in pregnancy particularly in the first trimester.[18] A study conducted in China found that a higher level of uric acid in early pregnancy is linked with greater chances of developing gestational diabetes, premature delivery birth, and low birth weight.[19]

A retrospective cohort study was conducted to determine the association between serum uric acid and the risk of GDM. They observed adverse pregnancy outcomes like GDM with preeclampsia, GDM requiring pharmacotherapy, large for gestational age infant, and preterm delivery. The study concluded that a high uric acid level before 24 weeks of gestation is strongly associated with the subsequent development of GDM. Increased uric acid has also a similar association with GDM requiring pharmacotherapy,

GDM with preeclampsia, and preterm delivery. They recommended that the best time for screening of serum uric acid is before 18 weeks of gestation.[20] Our results showed that the sensitivity, specificity, PPV, NPV, and diagnostic accuracy of first trimester high uric acid keeping the OGTT as a gold standard were 74.24%, 87.94%, 82.58%, 81.59%, and 81.98%, respectively. A study conducted in India reported that the sensitivity of serum uric acid in the diagnosis of GDM was 50% and its specificity was 67%.[21] Palaniappan et al. observed 100% sensitivity and 84.2% specificity of high uric acid levels.[14] Another study reported that hyperuricemia has a sensitivity of 77.8% and a specificity of 66.5%.[22]

CONCLUSION

The high uric acid level in the first trimester is a significant predictor of gestational diabetes mellitus with a diagnostic accuracy of 81.98%. It can be used as a screening tool for early diagnosis of GDM to reduce the morbidity & mortality of both mother & fetus.

LIMITATIONS & RECOMMENDATIONS

This study recommends that serum uric acid is simple, non-invasive, economical, and easily available investigation. So, it should be used as a screening tool for early prediction and management of gestational diabetes. The study determined the diagnostic accuracy of high uric acid to diagnose GDM at a cutoff of 3.4 mg/dL. Further studies should be conducted that measure the diagnostic accuracy at two or more cutoff values and construct a receiver operating curve (ROC) which can accurately select the optimal cut-off value.

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