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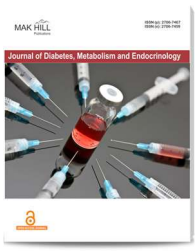

Research Article

Prediction of Gestational Diabetes Mellitus by Estimation of Serum Uric Acid in First Trimester of Pregnancy in Women Attending OPD-A Prospective Study

K. Madhavi[1*], Y. Aruna[2], Madhavi Latha[3], Bujjaiah[4], A. Divya[5], A.S. Beaulaw[6] and P. Madhusudhana[7]

[1]Professor, Department of OBG, S.V. Medical College, Tirupathi, India
[2]Assistant Professor, Department of OBG S.V Medical College Tirupati, India
[3]Professor, Department of Biochemistry S.V Medical College, Tirupati, India
[4]Associate Professor, Department of General Medicine, S.V. Medical College, Tirupati, India
[5,6]Student, Department of OBG, S.V Medical College, Tirupati, India
[7]Scientist B, MRU

***Corresponding Author**
Dr. K. Madhavi
(dr.madhavi.tagore@gmail.com)

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Abstract: Background: Gestational Diabetes Mellitus (GDM) is an important metabolic complication of pregnancy associated with adverse maternal and fetal outcomes. Early identification of women at increased risk of GDM may facilitate timely intervention and reduce associated morbidity. Serum uric acid, a product of purine metabolism, has been proposed as a potential marker of metabolic disturbances associated with GDM. This study was undertaken to evaluate the role of first-trimester serum uric acid in predicting abnormal glycemic parameters during pregnancy. **Aim:** To estimate serum uric acid levels in early pregnancy and evaluate its association and predictive ability for subsequent abnormal glycemic parameters and gestational diabetes mellitus. **Materials and Methods:** A prospective observational study was conducted among 170 pregnant women with gestational age less than 12 weeks attending the antenatal outpatient department at Government Maternity Hospital, Tirupati. Serum uric acid was estimated during the first trimester. Glycemic parameters were subsequently assessed, including GCT, fasting blood sugar, 1 and 2 hour blood glucose values. Statistical analysis was performed using descriptive statistics, Spearman correlation, Mann-Whitney U test and Receiver Operating Characteristic (ROC) curve analysis. **Results:** The median serum uric acid level was 3.5 mg/dL (IQR 2.9-3.9). Serum uric acid demonstrated a significant positive correlation with GCT ($\rho = 0.61$), FBS ($\rho = 0.38$), 1 hour blood glucose ($\rho = 0.38$) and 2 hour blood glucose ($\rho = 0.50$), with $p<0.001$ for all correlations. Women with abnormal glycemic values had significantly higher median serum uric acid levels (4.5 mg/dL vs. 3.3 mg/dL; $p<0.001$). ROC analysis showed excellent discriminatory ability, with AUC values of 0.96 for GCT, 0.97 for FBS, 0.96 for 1 hour blood glucose and 0.92 for 2 hour blood glucose. **Conclusion:** First-trimester serum uric acid showed a significant positive association with subsequent glycemic abnormalities and demonstrated excellent discriminatory ability in this study population. Serum uric acid may therefore have potential as an early biochemical marker for identifying pregnant women at increased risk of GDM. Larger multicentric studies are required to validate the observed cutoff values and establish its role in routine clinical screening.

Keywords: Gestational Diabetes Mellitus, Serum Uric Acid, First Trimester, Pregnancy, Glycemic Parameters, GCT, Fasting Blood Glucose, ROC Curve, Early Prediction, Biomarker

INTRODUCTION

Gestational Diabetes Mellitus (GDM) is defined as carbohydrate intolerance of variable severity, with an onset or first recognition during pregnancy, whether diet modification or insulin is used for treatment and whether or not the condition persists after pregnancy [1-3].

Globally, prevalence of GDM is on the rise. In India, the prevalence of GDM was 2% in 1982 followed by 7.62% in 1991 and 16.5% in 2003 with expected rate of 79.4 million in 2030 i.e., 15.1% Increase from 2000.

Compared to European females, the South Asian especially Indian females have 11 fold increased risk for GDM. GDM is important to be diagnosed early and treated effectively because of its complications in pregnancy. It is associated with various maternal complications like preeclampsia, preterm deliveries, polyhydramnios, still births, Increased rates of LSCS and in fetus CNS, cardiac and genitourinary anomalies and NTD, macrosomia, still birth, birth injuries, hypoglycemic episodes post-delivery, hyperbilirubinemia and RDS. Also these women are at higher risk of developing DM in the next 2 decades as compared with the normal female population. Studies have shown that early glucose screening is definitely beneficial to patients to reduce the maternal and fetal morbidity [4].

The earliest screening for GDM for a low risk pregnant woman is done only at 24-28 weeks. The prevalence of GDM in low risk population is about 7-10%, any test which gives us an indicator of impending GDM will be of great help to advise the patient about life style and dietary modifications. Also early detection and treatment of morbidity will also ease the disease burden [5].

Uric acid is the end product of purine metabolism and is synthesized by the enzyme xanthine oxidase. More number of evidence suggests that uric acid could be an important risk factor for the development of diabetes in women [6]. " A study explored the relationship between beta cell function and uric acid. Insulin secretion was stimulated with L-arginine and it was observed that the islet beta-cell function in hyperuricemic patients increases compensatively. Thus concluding that the serum uric acid level is positively correlated with insulin resistance. In normal pregnancy, there is a decrease in the serum uric acid levels in the first trimester due to the increased GFR or reduced proximal tubular reabsorption [7].

But as the pregnancy progresses the uric acid levels rise because of the increased fetal production, decreased clearance and decreased binding to albumin [8]. High levels of uric acid in the early pregnancy may be an indicator of the existing metabolic disturbance which will hinder the maternal physiological adaptations generally seen in pregnancy and thus making the pregnant women more vulnerable to the development of gestational diabetes mellitus.

Early screening and accurate diagnosis of GDM is very important for timely intervention and optimal outcome both for the mother and the baby. This necessitates the search for a reliable indicator in the early gestation where we could educate the pregnant women about the developing GDM and prevention of maternal and fetal morbidity [9-12].

Objectives

Aims and Objective of the Study:

- To Estimate the level of serum uric acid in early pregnancy
- To identify Gestational diabetes mellitus among pregnant women
- To predict the development of Gestation diabetes mellitus in women having raised Serum uric acid levels

Need for Study

Early detection of GDM in the first trimester can reduce maternal and fetal complications.

MATERIALS AND METHODS

Type of Study

Prospective Observational study.

The prospective observational study was conducted in Government Maternity hospital, Tirupati from Pregnant women of gestational age less than 12 weeks who attending antenatal outpatient department on Friday for regular antenatal check up were enrolled in this study.

Demographic information, obstetrical, medical and family history was obtained. Height, weight, BMI were measured. Gestational age is calculated from the LMP and further confirmed by ultrasonography. Blood samples were collected for estimation of serum uric acid, GTT along with other routine serological investigation. At 24-28 weeks of gestation, one step test (DIPSI) to detect GDM using 75 g of oral glucose was done irrespective of the last meal of the patient. Those antenatal mothers with plasma glucose level of >140 mg/dl after 2 hours were diagnosed as GDM.10 [2].

Study Population

All the pregnant women in their first trimester who are residing at Tirupati attending antenatal OPD on Friday and who have given written informed consent at GMH, Tirupati.

Duration of Study

One year from the scientific and ethics committee approval.

Sample Size

Sample size calculation for a cross sectional study with qualitative outcome at 95% confidence interval is:

$$N = \frac{(Z_{\alpha/2})^2 PQ}{L^2}$$

Where

N = Sample size

$Z_{\alpha/2}$ = Standard normal variate at 95% confidence interval =1.96 (from Z table)

P = Prevalence of Gestational diabetes in India = 13% (***Mantri, N., Goel, A.D., Patel, M. et al. National and regional prevalence of gestational diabetes mellitus in India: a systematic review and Meta-analysis. BMC Public Health 24, 527 (2024). https://doi.org/10.1186/s12889-024-18024-9***)

Q = 100-P = 100-13% = 87%

L = Absolute precision of 5%

Substituting the values

$$N = \frac{(1.96)^2 \times 13 \times 87}{5 \times 5}$$

N =170

Inclusion Criteria

- All patients who come for antenatal check up (<12 weeks)
- Those who have given consent for participation in study

Exclusion Criteria

- Multiple pregnancies
- Chronic hypertension
- Overt diabetes
- Gout
- Renal disease
- Smoking

Sample Collection for Serum Uric Acid

Informed consent will be taken from the pregnant women participating in the study:

- 3 mL of venous blood will be drawn under strict aseptic precaution into a vacutainer (Red cap) from the subjects selected for the study
- Collected blood will be centrifuged at 3000rpm for 10-15 minutes and the separated serum will be used for investigations
    - Fully automated analyzer Transasiaerba xl 600

Expected Values

Serum uric acid levels:

- **Adults Male:** 3.5-7.2 mg/dl
- **Adults female:** 2.5-5.6 mg/dl

Pregnant female:

- **First trimester:** 2.0-4.2 mg/dl
- **Second trimester:** 2.4-4.9 mg/dl
- **Third trimester:** 3.1-6.3 mg/dl

Brief Procedure

Brief Procedure is shown in Figure 1.

Statistical Analysis

- EPI INFO 7.2.6.0
- Descriptive quantitative statistics represented as MEAN±SD.
- Descriptive qualitative statistics represented as percentages.
- Interferential statistics will be tested using t-test and Chi-square test

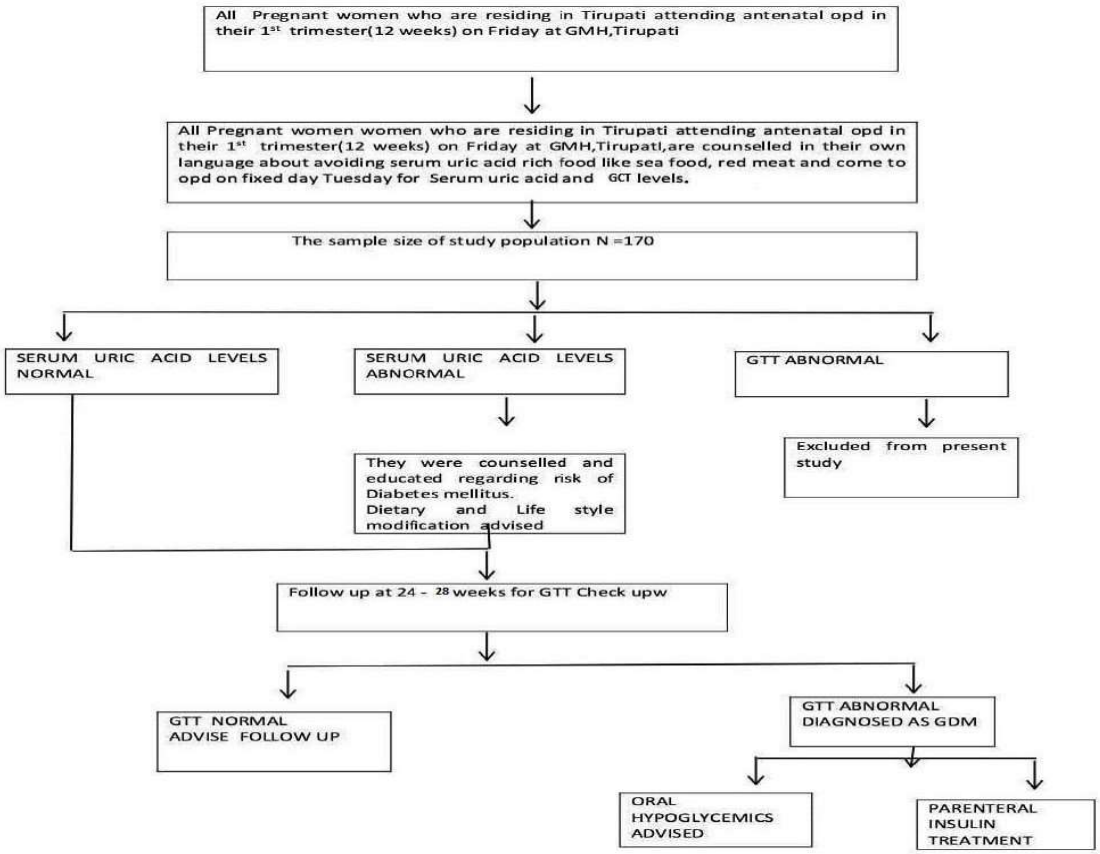

Figure 1: Brief Procedure

Table 1: Distribution of Study Parameters (n = 170)

Parameter	Median	Interquartile range	Minimum	Maximum
Serum uric acid (mg/dl)	3.5	2.9-3.9	2.2	4.9
GCT (mg/dl)	126	121-136	104	188
FBS (mg/dl)	79	72-86	62	105
1 hour blood sugar (mg/dl)	153	145-159	128	199
2 hours blood sugar (mg/dl)	127.5	121-135	106	175

Table 2: Correlation of Study Parameters with Uric Acid Levels (n = 170)

Parameters	Spearman correlation (ρ)	p-value
GCT	0.61	<0.001*
FBS	0.38	<0.001*
1 hour blood sugar	0.38	<0.001*
2 hours blood sugar	0.50	<0.001*

*Statistically significant

Table 1 presents the descriptive statistics for serum uric acid and all glycemic parameters in the study population. Data of all the parameters show non normal distribution. The median serum uric acid level was 3.5 mg/dL, with an interquartile range of 2.9-3.9 mg/dL. Among the glucose parameters, the median GCT was 126 mg/dL, FBS was 79 mg/dL, 1-hour blood sugar was 153 mg/dL and 2-hour blood sugar was 127.5 mg/dL.

Table 2 demonstrates the strength and direction of the relationship between serum uric acid and each glycemic parameter using Spearman's rank correlation coefficient. All four parameters-GCT, FBS, 1 hour blood sugar and 2 hour blood sugar-showed a statistically significant positive correlation with uric acid levels ($p < 0.001$ for all). The strongest correlation was observed with GCT ($\rho = 0.61$), indicating a moderate-to-strong positive association, while FBS and 1 hour blood sugar showed weaker but still significant correlations ($\rho = 0.38$ each). The 2 hour blood sugar also demonstrated a notable correlation ($\rho = 0.50$). These findings suggest that higher blood glucose levels across all time points are consistently associated with elevated serum uric acid. The significance of all correlations supports the potential role of uric acid as a metabolic marker linked to glucose dysregulation (Figure 2).

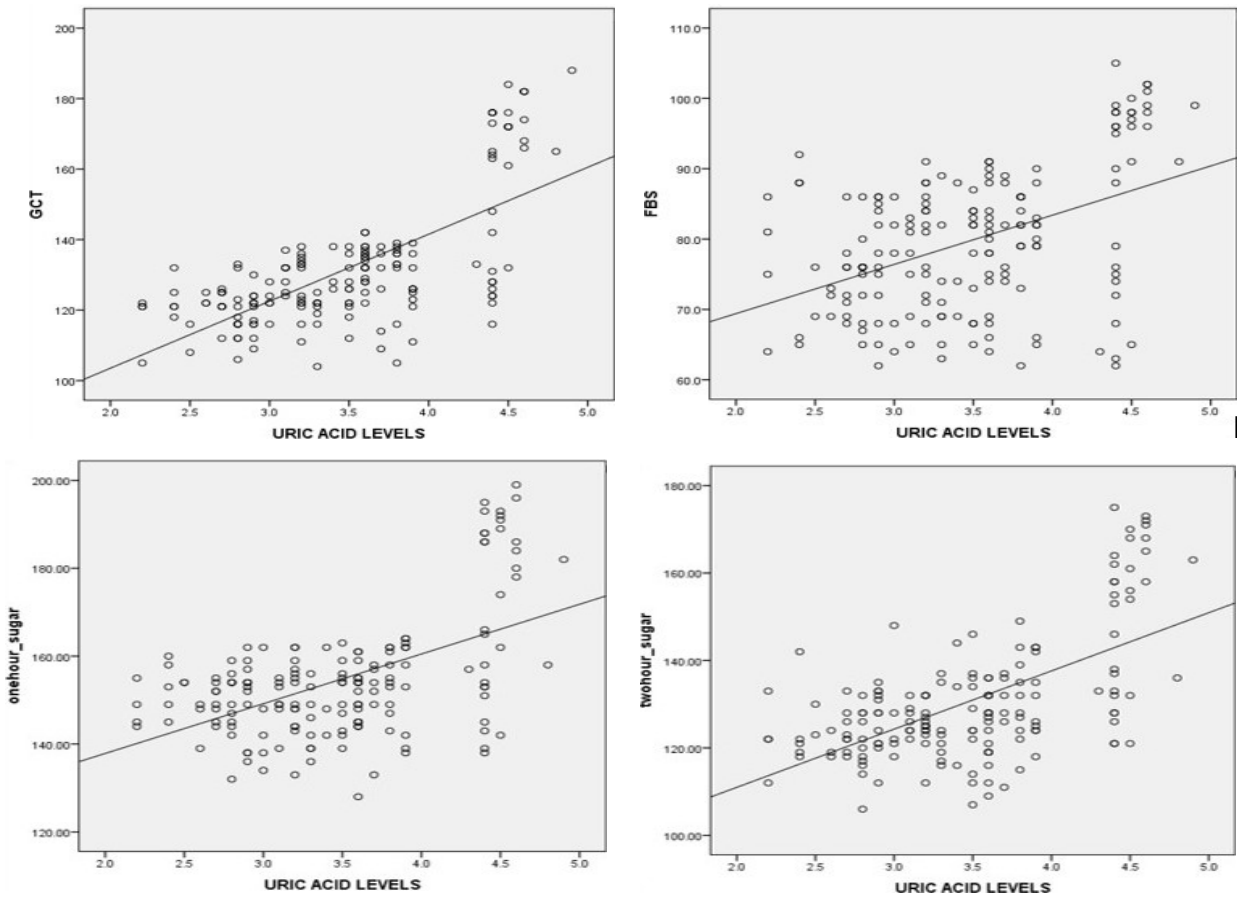

Figure 2: Scatter Plot Distribution of the Parameters (n = 170)

Table 3: Comparison of Serum Uric Acid Levels Across the Groups by Mann-Whitney U-test

Parameter		Median	Mean rank	p-value
GCT (mg/dl)	≥140(n = 25)	4.5	152.5	<0.001*
	<140(n = 145)	3.3	73.9	
FBS (mg/dl)	≥95(n = 19)	4.5	157.2	<0.001*
	<95(n = 151)	3.3	76.4	
1 hour blood sugar (mg/dl)	≥180(n = 16)	4.5	157.2	<0.001*
	<180(n = 154)	3.3	78.0	
2 hours blood sugar (mg/dl)	≥145(n = 23)	4.5	147.5	<0.001*
	<145(n = 147)	3.3	75.8	

Table 4: ROC Analysis of Uric Acid for Predicting GCT, FBS and OGTT Thresholds

Parameter	Uric acid cutoff value	Area (95% confidence limits)	p-value	Sensitivity	Specificity
GCT (≥140)	3.6	0.96(0.92-0.99)	<0.001*	92.0%	75.2%
FBS (≥95)	4.3	0.97(0.95-0.99)	<0.001*	100.0%	91.4%
1 hour blood sugar (≥180)	4.3	0.96(0.94-0.99)	<0.001*	100.0%	89.6%
2 hours blood sugar (≥145)	3.8	0.92(0.85-0.98)	<0.001*	87.0%	84.4%

Table 3 compares median serum uric acid levels between two groups-those above and below the specified diagnostic cutoffs for each glycemic parameter. For GCT (≥140 mg/dL), the uric acid median was 4.5 mg/dL in the high group versus 3.3 mg/dL in the normal group, with a marked difference in mean ranks (152.5 vs. 73.9). Similarly, for FBS ≥95 mg/dL, 1-hour blood sugar ≥180 mg/dL and 2-hour blood sugar ≥145 mg/dL, the high groups consistently showed a median uric acid of 4.5 mg/dL, while the normal groups had a median of 3.3 mg/dL across all parameters. The mean rank differences were large and highly significant ($p < 0.001$ for all comparisons), indicating that participants with abnormal glucose values had substantially higher uric acid levels.

Table 4 evaluates the diagnostic performance of serum uric acid in predicting abnormal glycemic thresholds using receiver operating characteristic (ROC) curve analysis. The area under the curve (AUC) for all four parameters was remarkably high, ranging from 0.92 to 0.97, indicating excellent discriminatory ability. The optimal uric acid cutoff values

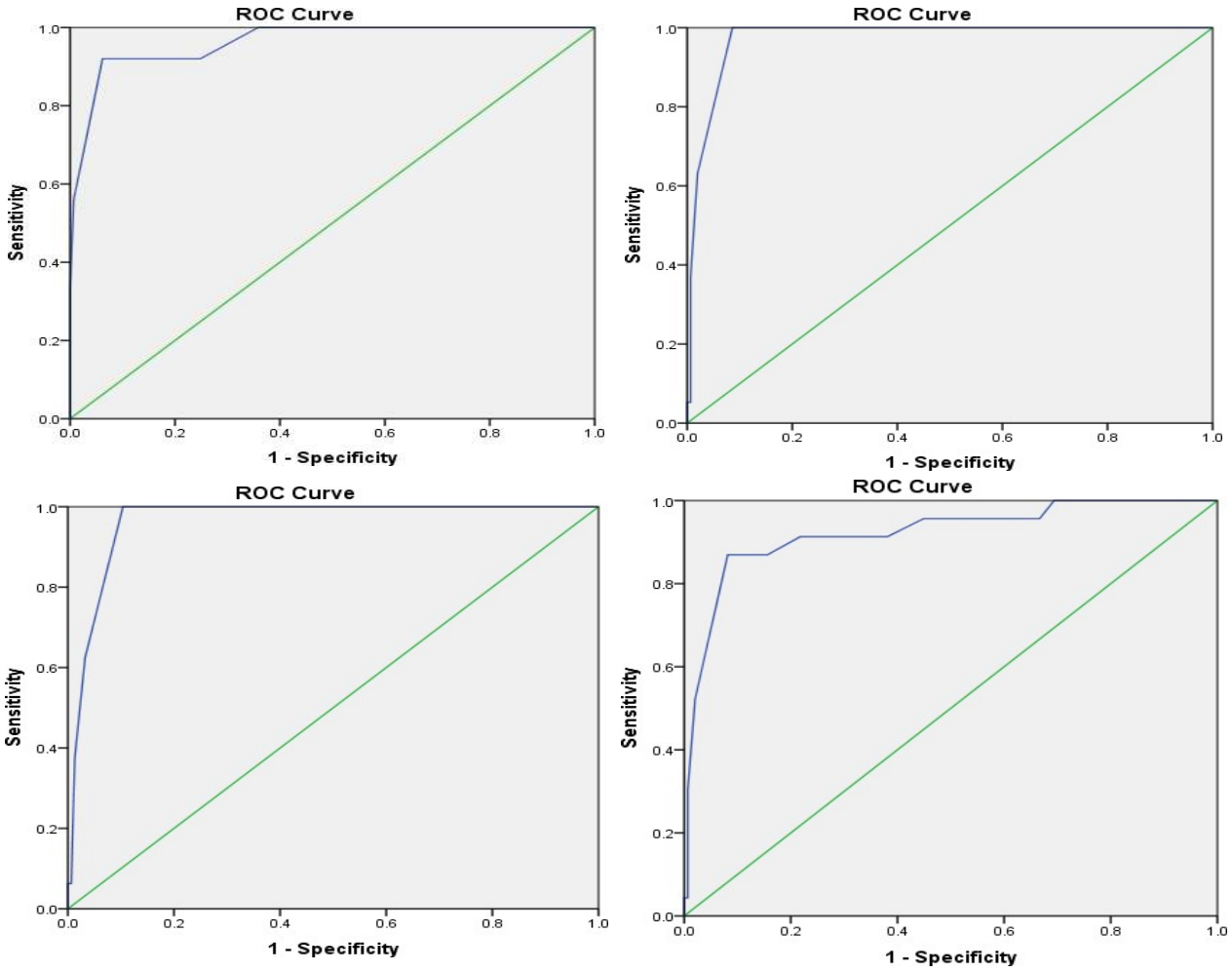

Figure 3(a-d): ROC Analysis of Uric Acid for Predicting (a) GCT Threshold (≥140), (b) FBS threshold (≥95), (c) 1 hour blood sugar (≥180) and (d) 2 hour blood sugar (≥145)

varied across parameters: 3.6 mg/dL for GCT (≥140), 4.3 mg/dL for both FBS (≥95) and 1-hour blood sugar (≥180) and 3.8 mg/dL for 2-hour blood sugar (≥145). The AUC for FBS was the highest at 0.97 (95% CI: 0.95-0.99), while 2-hour blood sugar had the lowest but still excellent AUC of 0.92 (95% CI: 0.85-0.98). All ROC analyses were statistically significant with $p < 0.001$. Sensitivity was highest for FBS and 1-hour blood sugar (both 100.0%), followed by GCT (92.0%) and 2-hour blood sugar (87.0%). Specificity ranged from 75.2% for GCT to 91.4% for FBS, with 1-hour blood sugar and 2-hour blood sugar showing intermediate values of 89.6% and 84.4%, respectively (Figure 3-6).

DISCUSSION

Gestational diabetes mellitus is an important metabolic complication of pregnancy and is associated with adverse maternal and fetal outcomes. Since routine screening is generally performed during the later part of pregnancy, identification of an early biochemical marker that could indicate an increased risk of GDM may facilitate earlier recognition and intervention. The present study evaluated the association between first-trimester serum uric acid levels and subsequent glycemic abnormalities in 170 pregnant women [13].

The present study demonstrated a median first-trimester serum uric acid level of 3.5 mg/dL. Serum uric acid showed a statistically significant positive correlation with all the glycemic parameters assessed. The correlation was strongest with GCT ($\rho = 0.61$), followed by 2 hour blood glucose ($\rho = 0.50$), while FBS and 1 hour blood glucose demonstrated correlations of $\rho = 0.38$ each. All correlations were statistically significant with $p<0.001$.

These findings suggest that increasing serum uric acid levels are associated with increasing glucose levels. The positive association observed across different glycemic measurements supports the possibility that serum uric acid may reflect underlying metabolic disturbances associated with abnormal glucose regulation [14-16].

The biological rationale for this association is supported by the background of the study. Uric acid is the end product of purine metabolism and is influenced by renal handling and metabolic factors. During normal pregnancy, serum uric acid generally decreases during the first trimester because of increased glomerular filtration and altered tubular handling. Therefore, a relatively higher uric acid concentration during early pregnancy may reflect an altered metabolic state [17].

In the present study, women with abnormal glycemic values consistently had higher serum uric acid levels. The median serum uric acid was 4.5 mg/dL in women with abnormal GCT, FBS, 1 hour and 2 hour glucose values, compared with 3.3 mg/dL in their respective normal groups. These differences were highly statistically significant ($p<0.001$).

The ROC analysis further strengthened these observations. Serum uric acid demonstrated excellent discriminatory ability, with AUC values between 0.92 and 0.97. The highest AUC was observed for FBS (0.97), followed by GCT and 1 hour blood glucose (0.96 each) and 2 hour blood glucose (0.92).

For FBS ≥95 mg/dL and 1 hour blood glucose ≥180 mg/dL, a serum uric acid cutoff of 4.3 mg/dL demonstrated 100% sensitivity, indicating that the marker identified all women in the study who crossed these specified glucose thresholds. The corresponding specificity was 91.4% for FBS and 89.6% for 1 hour glucose. For GCT ≥140 mg/dL, a cutoff of 3.6 mg/dL demonstrated 92% sensitivity and 75.2% specificity, while a cutoff of 3.8 mg/dL for 2 hour glucose ≥145 mg/dL showed 87% sensitivity and 84.4% specificity.

The findings of the present study are in agreement with the concept explored in previous studies cited in the project, which have investigated first-trimester hyperuricemia as a potential marker for the development of GDM. The project references include studies by Rehman *et al*. [7], Singh *et al*. [9], Kappaganthu *et al*. [10] and Şahin Aker *et al*. [16], which evaluated the relationship between serum uric acid and gestational diabetes.

The major strength of the present study is the prospective assessment of serum uric acid in early pregnancy followed by evaluation of glycemic parameters later in pregnancy. The consistent association between elevated uric acid and abnormal glucose measurements, together with the high AUC values on ROC analysis, suggests that serum uric acid may have potential as an early biochemical marker for identifying pregnant women at increased risk of abnormal glucose regulation [18].

However, the findings should be interpreted within the context of the study design and sample size. The study was conducted in a single tertiary-care setting and included 170 participants. Further studies involving larger and more diverse populations would be useful to validate the identified uric acid cutoff values and determine their applicability in routine clinical practice [19,20].

Overall, the present study provides evidence that first-trimester serum uric acid is significantly associated with subsequent abnormal glycemic parameters and demonstrates excellent discriminatory performance in this study population.

CONCLUSION

The present prospective observational study demonstrates a significant positive association between first-trimester serum uric acid levels and glycemic parameters in pregnant women.

Higher serum uric acid levels were significantly associated with higher GCT, FBS, 1 and 2 hour blood glucose levels. Women with abnormal glycemic values had significantly higher median serum uric acid levels than those with normal values.

ROC analysis demonstrated excellent predictive performance of serum uric acid, with AUC values ranging from 0.92 to 0.97. The highest discriminatory ability was observed for FBS, with an AUC of 0.97.

These findings suggest that first-trimester serum uric acid may serve as a useful early biochemical marker for identifying pregnant women at increased risk of abnormal glucose regulation and possible GDM. Early identification could potentially allow closer surveillance and timely lifestyle or dietary interventions.

However, serum uric acid should not be considered a replacement for established diagnostic testing based on the findings of this study alone. Larger, multicentric prospective studies are required to validate the proposed cutoff values and establish the clinical utility of serum uric acid as an early screening marker for GDM.

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