ISSN: 2581 – 3633
PubMed - National Library of Medicine - ID: 101745081

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at:www.ijmacr.com

Volume – 8, Issue – 4, July - 2025, Page No.: 212 – 218

Association between Mid-Trimester Serum Uric Acid Levels and the Risk of Developing GDM: A Prospective Study

[1]Dr. Shifa Khanam, 3rd Year Postgraduate, Department of Obsteterics and Gynecology, SSMC, Tumakuru

[2]Dr. Indira H, Professor & HOD, Department of Obsteterics and Gynecology, SSMC, Tumakuru

[3]Dr. Girish B.L, Professor, Department of Obsteterics and Gynecology, SSMC, Tumakuru

Corresponding Author: Dr. Shifa Khanam, 3rd Year Postgraduate, Department of Obsteterics and Gynecology, SSMC, Tumakuru

How to citation this article: Dr. Shifa Khanam, Dr. Indira H, Dr. Girish B.L, "Association between Mid-Trimester Serum Uric Acid Levels and the Risk of Developing GDM: A Prospective Study", IJMACR- July - 2025, Volume – 8, Issue - 4, P. No. 212 – 218.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background: Gestational diabetes mellitus (GDM) is glucose intolerance that is primarily detected during pregnancy. The present study was conducted to assess the role of serum uric acid as a predictor of gestational diabetes mellitus.

Materials & Methods: 90 antenatal women in first trimester were enrolled. Venous blood sample was taken from all patients and serum uric acid was measured by colorimetric assay with detection limit of 0.2- 20 mg/dl and patients were followed up at 24-28 weeks to do oral glucose tolerance test.

Results: The outcome of the study was found be that, among study participants during 13-20 weeks of gestation, 77.7% had normal uric acid level, 14.44% had uric acid level more than normal and after a follow up till 24- 28 weeks Oral Glucose Tolerance Test (Oral GTT) and the results identified that, among our study participants who were diagnosed with GDM (20 participants) 13 out of 20(45%) had raised uric acid levels.

Conclusion: This study showed a positive association between uric acid levels and the risk of GDM. Also, our results indicate that measuring uric acid levels before 20 weeks of gestation can potentially predict GDM.

Keywords: Dyslipidemia, Gestational Diabetes Mellitus, Hyperuricemia, Uric Acid

Introduction

Gestational diabetes mellitus (GDM) is a metabolic disorder of glucose intolerance and hyperglycemia first time diagnosed during gestational period. Gestational diabetes mellitus (GDM) is one of the most common pregnancy complications, with adverse effects on both the mother and the fetus. Besides the traditional risk

factors of GDM, for example, maternal obesity, advanced maternal age, and family history of diabetes, some new risk factors have also been gradually discovered and paid attention to period. Onset of GDM is common in the middle to late trimester but continues till term. Prevalence of GDM is estimated at 1-14%.

Occurrence of GDM is reported in 7% of pregnancies, and this accounts for >0.2 million diseased cases each year. Gestational diabetes mellitus (GDM) is a common and important complication of pregnancy, affecting 7−25% of all clinically recognised pregnancies worldwide. The high prevalence of GDM has raised substantial concerns because it is not only associated with adverse perinatal outcomes but also related to increased long-term risks of cardiovascular and metabolic diseases in both mothers and their offspring. It is therefore crucial to identify potential modifiable risk factors of GDM and implement early prevention.

Uric acid (UA) is a xanthine derivative of purine catabolism. A previous study reported uric acid is a pro-oxidant hence may be used as a biomarker of oxidative stress, but it also showed antioxidant potential. Soluble form of uric acid; the urate is a potent scavenger of superoxide (O) and hydroxide (-OH) radicals and is capable of chelating the transition metals. Elevated serum uric acid level is termed the hyperuricemia that has been linked to metabolic syndrome of insulin resistance, hyperinsulinemia, diabetes mellitus, etc. 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. Serum uric acid is interlinked with hypertension, obesity, hyperinsulinemia and dyslipidemia indicating that it could be a part of the group of factors of metabolic syndrome.

Hyperinsulinemia may contribute to hyperuricemia through activation of sympathetic nervous system that reduces the urinary excretion of uric acid. Hyperuricemia in GDM reflects the metabolic syndrome of insulin resistance. Hyperuricemia has been closely correlated with obesity, hyperlipidemia and dyslipidemia and DM.

Materials and Methods

Prospective Observational Study was conducted to assess uric acid levels in 13-20 weeks of pregnancy to predict gestational diabetes mellitus. The pregnant women who attended the OPD in department of Obstetrics and Gynecology, at Sri Siddhartha Medical College, Tumakuru, for an antenatal checkup, who fulfil the required criteria was included in this study. After obtaining the ethical clearance from the Institutional Ethical Committee (IEC) of Sri Siddhartha Medical College, the study was conducted. After proper counselling, written informed consent was taken from all the selected patients. A detailed history, thorough clinical examination, including BMI and routine investigations was carried out. The study was conducted for a period of 8 months.

Ninety pregnant women who reported to the antenatal OPD at 13-20 weeks of period of gestation and who fulfilled the inclusion criteria and were willing to participate in the study were enrolled, upto the period of initial 7 months of the study and were followed up upto next 5 months of the study period so that the last enrolled patient can complete the followup process as per methodology. Detailed obstetric and menstrual history, past history of hypertension, diabetes and family history of hypertension and diabetes was taken and detailed general physical examination was conducted. This was followed by serum uric acid levels. Rest of the

investigation structure were as per the protocol. All the enrolled patients were followed up every month till 28 weeks of gestation and fortnightly after that upto 36 week and weekly thereafter until delivery. OGCT was done at first visit and repeated at 24-28 weeks.

Inclusion Criteria

1. All pregnant woman of age between 18-35 years
2. Serum uric acid levels assessment at 13 to 20 weeks of all pregnant woman of age between 18-35 years
3. No h/o GDM and Overt diabetes
4. No existing obstetrical morbidity

Exclusion Criteria

1. Pregnant women with comorbidities.
2. Patient who refuse to participate or consenting for the study
3. Patients who are lost to follow up

Study analysis

The data will be collected and entered in MS Excel sheet and Data analysis will be done using SPSS version 24.0 software. Descriptive Statistics like proportion, mean, standard deviation will be calculated. Categorical variables will be assessed using Chi-Square Test. A p-value less than 0.05 will be taken as statistically significant.

Results

Table 1: Distribution of subjects based on age:

Age (Years)	Number	Percentage (%)	p value
Less than 20	6	6.67	0.01
21-30	62*	68.89	
31-40	22*	24.44	
Total	90	100.00	

(*p<0.05 significant)

Table 1 Shows significant distribution og GDM in young group between 21-30yrs, around 62 among 90 had higher incidence of GDM.

Graph 1: Distribution of subjects based on age

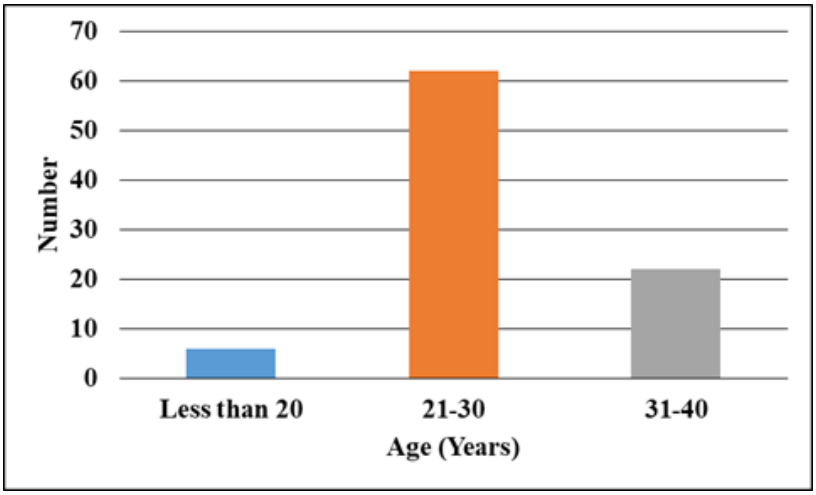

Table 2: Distribution of subjects based on parity

Parity	Number	Percentage (%)	p value
Parity	2*	2.22	0.03
G2A1	8*	8.89	
G2P1L1	36	40.00	
G3P2L2	10	11.11	
G4P2L2A1	2*	2.22	
Primi	32	35.56	
Total	90	100.00	

(*p<0.05 significant)

Table 2 shows incidence of GDM is significant in primigravida than multigravida, 10 out of 90 had GDM with significant p value of 0.03.

Table 3: Mean BMI

Observation	MEAN±SD
BMI	24.09±1.87

Table 3 shows the incidence of GDM among study participants was around 24kg/m^2 which indicates normal BMI.

Table 4: Distribution of subjects based on GA weeks

GA weeks	Number	Percentage (%)	p value
12-14	10*	11.11	0.04
15-16	44	48.89	
17-18	24	26.67	
19-20	12*	13.33	
Total	90	100.00	

(*p<0.05 significant)

Graph 2: Distribution of subjects based on GA weeks

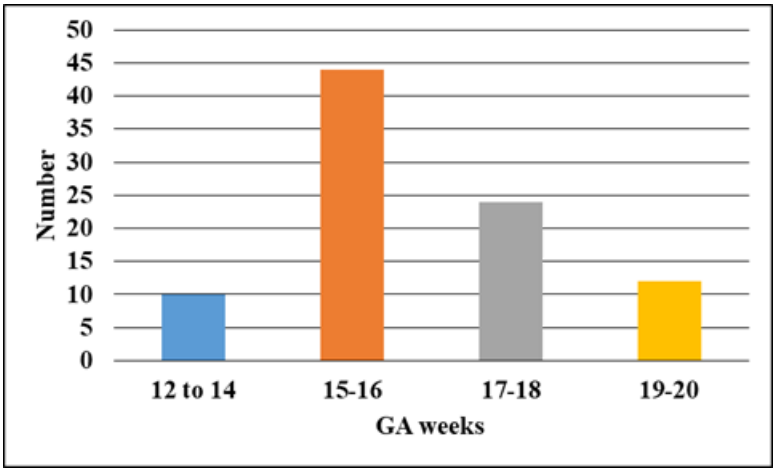

Table 5: Mean values of biochemical values

Observation	MEAN±SD
Ist trimester Fasting blood glucose	89.85±3.56
Ist trimester HbA1C	5.04±2.01
Serum uric acid	3.44±1.37

Table 5 shows reference range taken for HbA1C; Serum Uric acid taken in this study.

Table 6: Risk of gestational diabetes by first trimester uric acid quartile

Uric acid quartile	GDM (n=20)		Adjusted OR
	Number	Percentage (%)	
1st (2.1)	6	30.00	Ref
2nd (2.7)	5	25.00	1.45 (0.59-4.78)
3rd (3.2)	7	35.00	3.76 (0.84-6.19)
4th (4.2)	2	10.00	4.89 (1.34-8.21)

Table 7: Distribution of subjects based on GDM

GDM	Number	Percentage (%)	p value
Yes	20	22.22	0.03
No	70*	77.78	
Total	90	100.00	

(*p<0.05 significant)

Discussion

The risk factors that have been implicated in the development of GDM are similar to the factors associated with overt diabetes and include increased maternal age, obesity, ethnic background, family history of T2DM and a previous history of GDM. Other risk factors include previous history of a macrocosmic baby, previous adverse pregnancy outcome, glycosuria, polyhydramios or large foetus in present pregnancy.

Among these risk factors, increased maternal weight is the most commonly evaluated reversible risk factor.

Wang *et al*. showed that an independent significant relationship between reduced intake of polyunsaturated fat and development of GDM. The meta-analysis, including 23 studies and 105,380 women, aimed to determine the prognostic role of maternal uric acid during gestation in women with GDM. Their study showed a significant association between elevated uric acid levels among pregnant women and the risk of GDM. Despite the importance of universal screening for GDM at 24–28 weeks of gestation based on the American Diabetes Association recommendations, it seems that early diagnostic tests assessing metabolic markers are necessary to prevent APOs, including pregnancy-induced hypertension, GDM and small for gestational age.

During normal pregnancy, the serum uric acid levels fall considerably until around the 20th week of gestation due to increased glomerular filtration rate and decreased reabsorption of uric acid from the renal tubules, although it gradually increases toward normal concentrations by the end of pregnancy. It seems that women with elevated levels of blood serum uric acid in the early stages of

pregnancy might experience poor maternal physiological adaptation to this process, which could put them at risk of adverse pregnancy outcomes(APOs).

The current study identified among our study participants are 70(44%) of antenatal mothers had normal uric acid level (2.6 – 6.0 mg/dl), 13(45%) had uric acid level more than normal (>6.0 mg/dl) and 7(10%) had uric acid level less than normal (<2.6 mg/ dl). (Table:6). In present study out of twenty patients who developed GDM patients (45%) had serum uric acid >3.5 mg/dl and four patients (55%) had serum uric levels <3.5 mg/dl.

In our study the mean uric acid in patients with GDM is 3.8 mg/dl. And the sensitivity of serum uric acid was 45% and specificity was 55%. The outcome of the study was found be that, among study participants during 13-20 weeks of gestation, 77.7% had normal uric acid level, 14.44% had uric acid level more than normal and after a follow up till 24- 28 weeks Oral Glucose Tolerance Test (Oral GTT) and the results identified that, among our study participants who were diagnosed with GDM (20 participants) 13 out of 20(45%) had raised uric acid levels. We found that age group 21-30 years had 62, 31-40 years had 22. Parity was multipara in 36 and primi in 32. Serum uric acid was elevated (>3.8) in 20 and normal (<3.8) in 70. GTT result was normal in 70 and positive in 20 patients.

In a study conducted by Laughon et al total of 1570 samples were available for analysis with a mean gestational age at sampling of 8.9 ± 2.5 weeks and uric acid concentration of 3.08 (± 0.85) mg/dl. Using a cut point of 3.6 mg/dl yielded a positive predictive value (PPV) of 9.0% and negative predictive value (NPV) of 96.7% for development of GDM.

Conclusion

The main purpose of implementing an antenatal screening test for GDM is to rule out pre-symptomatic women who develop pregnancy complications and to promote efficacious treatment protocol to decease the morbidity and mortality. Presently, pregnancy complication that arise due to GDM are not ruled out until mid-late gestation.

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