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ASSOCIATION BETWEEN ELEVATED SERUM URIC ACID LEVELS IN EARLY PREGNANCY AND DEVELOPMENT OF GESTATIONAL DIABETES MELLITUS

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ABSTRACT

Background: Gestational Diabetes Mellites is a form of hyperglycaemia that develops or is first recognized during pregnancy and poses risks to both mother and foetus. It is one of the commonest complications of pregnancy, with a prevalence of about 11.7% South East Asian Countries. Women with gestational diabetes are at an increased risk of complications during pregnancy and at delivery. **Objective:** To determine the association between elevated Serum uric acid levels in early pregnancy and development of gestational diabetes mellitus. **Material and Methods:** This hospital based prospective cohort study was conducted among pregnant women coming for routine antenatal care to Outpatient Department of Obstetrics and Gynecology at S. Nijalingappa Medical College, Bagalkot. Duration of Study was from June 2023 to December 2024. **Result:** A statistically significant association was found between Serum uric acid levels and development of GDM. Risk ratio showed a higher odds ratio of developing GDM among cases with Raised uric acid level (SUA >4.2mg/dl). **Conclusion:** Elevated serum uric acid levels, traditionally considered in the context of hypertensive disorders, also emerged as an independent predictor of GDM, likely due to their role in oxidative stress and metabolic dysfunction.

INTRODUCTION

Gestational Diabetes Mellites (GDM) is a fairly common metabolic disorder in pregnant women. GDM is a growing public health concern in lieu of its higher prevalence and ever increasing burden on health care.[1] The International Diabetes Federation estimates that one in six live births (16.8%) are to women with some form of hyperglycemia in pregnancy. While only 16% of these cases may be due to pre-existing diabetes either known previously or detected for first time, the majority (84%) of them are GDM.2 Indian population reports an incidence rate of 16.55%.[3]

GDM is associated with a spectrum of maternal complications such as hypertensive disorders of pregnancy, increased risk of caesarean section, and long-term risk of type 2 diabetes mellitus (T2DM). For the foetus, it poses risks of macrosomia, neonatal hypoglycaemia, shoulder dystocia, and predisposition to obesity and glucose intolerance later in life. This huge disease burden necessitates universal screening and diagnosis of GDM using glucose tolerance tests between 24 and 28 weeks of gestational age, though reports suggestive of earlier diagnosis are available.[4]

Currently, most screening protocols for GDM are implemented between 24–28 weeks of gestation, a period by which metabolic changes and insulin resistance may have already led to adverse fetal development. Consequently, there is a growing emphasis on identifying predictive biomarkers and risk factors in early pregnancy that can facilitate timely risk stratification and preventive intervention. Among the various metabolic indicators being investigated, the triglyceride-glucose (TyG) index and serum uric acid (SUA) levels have emerged as promising, accessible, and non- invasive predictors of GDM.

Elevated uric acid is associated with both cardiovascular disease events and risk factors, such as hypertension, metabolic syndrome, chronic kidney disease, obesity, and diabetes in nonpregnant adults.5 All of these are known to increase the risk of pre-eclampsia and gestational diabetes. Association between elevated first trimester uric acid and increased risk for development of gestational diabetes has been well established.6 Elevated serum

uric acid is a feature of hyperinsulinemia and insulin resistance, thus hypothesizing that raised levels of serum uric acid in pregnancy can be indicator of gestational diabetes. However, availability of evidence from North Karnataka is limited in this regard.

Hence, this study intended to explore the utility of this invaluable index and asses if the same can be used for early detection of GDM. Since serum uric acid levels and plasma glucose levels are easily accessible, available, acceptable and affordable investigations compared to other lab investigations. In present dissertation, the correlation between GDM and serum uric acid levels was studied.

MATERIALS AND METHODS

This hospital based prospective Cohort study was conducted among Pregnant women coming for routine antenatal care to Outpatient Department of Obstetrics and Gynecology at S. Nijalingappa Medical College, Bagalkot. Duration of Study was from June 2023 to December 2024

Inclusion Criteria
- Antenatal mothers enrolled in early pregnancy i.e. at <20 weeks period of gestation and are available for follow up.

Exclusion Criteria
- Known pregestational diabetes mellitus
- Receiving steroids in any form
- Known cases of Gout and hyperuricemia
- Mothers with known renal disease
- Severe anemia (Hb < 7g%)
- Known haemoglobinopathies.

Sample Size Estimation
According to the study conducted by Sánchez-García A et al,[7] the prevalence of GDM was found to be 10-14.3%=10
The Relative risk for GDM with Triglycerides index levels in first trimester was found to be 1.03.
α (two-tailed) =0.050 and at 95% confidence level. β =0.200 and 80% of power of the study.
The standard normal deviate for $\alpha = Z\alpha = 1.960$ The standard normal deviate for $\beta = Z\beta = 0.842$ Sample size estimated is 262-270 pregnant women.
Sampling method: Purposive sampling method.

Method of collection of data
A detailed history and complete clinical examination of patients was done to rule out the exclusion criteria. The aim and objectives of the intended study was properly explained to the subjects and informed consent was taken on the proforma sheet. The preliminary data regarding the age, parity, history of GDM, history of DM in family, history of macrosomia in previous pregnancy, weight and height were collected.

Blood sample collected for routine antenatal check-up during the first antenatal visit was utilized for measuring the serum uric acid, fasting plasma triglyceride and fasting plasma glucose values.

Serum uric acid levels was measured by enzymatic uricase method, fasting plasma glucose was measured using the glucose oxidase assay and fasting triglycerides was analyzed by the glycerol phosphate oxidase method in the laboratory of S. Nijalingappa medical college.

Diagnosis of GDM: All Antenatal mothers during their follow up visit between 24-28 week period of gestation were subjected to glucose challenge with 75grams of glucose irrespective of the fasting state as is routinely done in our OPD. GDM was diagnosed using DIPSI criteria8 i.e., plasma glucose >/= 140mg/dl after 2h of glucose challenge is diagnostic.

Timing of the tests
After a fasting period of 12 hours; serum uric acid, fasting plasma triglyceride and fasting plasma glucose values are measured in early pregnancy i.e. at <20weeks period of gestation. During follow up, Glucose challenge with 75gram glucose is given at 24 to 28 weeks of gestation to diagnose GDM.

Based on S. uric acid levels, the patients were divided into two groups i.e. between the levels of <4.2mg/dl and >4.2 mg/dl. Calculated triglyceride glucose indices were divided into quartiles. These groups were then analysed for the risk of development of GDM and their role as screening tests. The relation of S. uric acid levels and triglyceride glucose index in early pregnancy (<20weeks) with the development of GDM will be studied as the primary outcome. Their role as early predictors of GDM will be studied as secondary outcome.

Statistical Analysis: Data analysis was done using IBM SPSS version 24.0 Statistical analysis was done using SPSS software 24.0. Data obtained were tabulated in the Excel sheet and analysed. Quantitative data were expressed as mean±standard deviation and nonparametric data were expressed as median and min-max values. Percentages were used for representing qualitative data. Relative risk, Absolute risk and Attributable risk were calculated. Chi-square test for proportions in Qualitative data and Student's unpaired t – test for Quantitative data. Women were categorized by tertiles of the triglyceride glucose index to compare GDM case distribution and the risk of developing GDM, using the lowest tertile as reference.

RESULTS

The mean age of the study participants was 25.91 ± 4.57 years. Participants belonged to age group 18-36 years.

Table 1: Obstetric score of study

	Frequency	Percent
Gravida		
1	95	35.2
2	81	30.0

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3	73	27.0
4	10	3.7
5	11	4.1
Total	270	100.0
PARITY		
0	107	39.6
1	99	36.7
2	62	23.0
4	2	0.7
Total	270	100.0
LIVE BIRTHS		
0	107	39.6
1	99	36.7
2	62	23.0
4	2	0.7
ABORTION		
0	213	78.9
1	36	13.3
2	20	7.4
3	1	0.4
Total	270	100.0

Table 2: Gestational age of study subjects

Gestational age	Frequency	Percent
≤12 WEEKS	141	52.2
>12 WEEKS	129	47.8
Total	270	100.0

Mean BMI of the study participants was 25.78 ± 3.68. Majority of the study participants were in the Obese category (48.9%).

Table 3: Body Mass Index categories of Study subjects

Body Mass Index Categories	Frequency	Percent
Underweight	2	0.7
Normal range	63	23.3
Over weight	73	27.0
Obese 1	105	38.9
Obese 2	27	10.0
Total	270	100.0

Table 4: Family History of Diabetes Mellitus among study participants

Family history	Frequency	Percent
NO	176	65.2
YES	94	34.8
Total	270	100.0

The mean Fasting Blood Sugar values was 80.61 ± 12.08mg/dL

Uric acid

The mean uric acid level 3.23±1.22 mg/dL The table 5 compares two groups based on their uric acid levels: Uric acid ≤4.2 mg/dL (229 participants) and Uric acid >4.2 mg/dL (41 participants).

Table 5: Assessment of study subject characteristics based on uric acid levels

	Uric acid ≤4.2 (229/270)	Uric acid >4.2 (41/270)
Mean Age	25.57±4.69	27.80±3.34
BMI	25.29±3.02	28.49±5.49
Fasting Blood Sugar	80.28±11.54	82.41±14.80
Triglyceride	106.32±48.08	114.77±54.73
Family history of DM	78 (34.1%)	16 (39.0%)
History of Macrosomia	3(1.3%)	1(2.4%)
GDM Diagnosis	5(2.2%)	29(70.7%)
Abortion	4(1.7%)	1(2.4%)

Table 6: Association of Serum Uric Acid with Gestational Diabetes Mellitus among the study subjects

URIC ACID LEVEL	GDM negative	GDM positive	P value
≤ 4.2 mg/dl	215 (97.7%)	5 (2.3%)	0.00*
>4.2 mg/dl	11 (27.5%)	29 (72.5%)	

Total	226 (86.9%)	34 (13.1%)	

A significant association (p < 0.05) was found between uric acid level diagnosis of Gestational Diabetes Mellitus

Table 7: Risk Estimate between gestational Diabetes mellitus and Uric Acid level

Risk Estimate			
	Value	**95% Confidence Interval**	
		Lower	**Upper**
Odds Ratio for URIC ACID RECODED (</= 4.2 / >4.2)	113.364	36.767	349.529
For cohort GDM DIAGNOSIS BY DIPSI = negative	3.554	2.148	5.880
For cohort GDM DIAGNOSIS BY DIPSI = positive	.031	.013	.076
N of Valid Cases	260		

On assessment of risk ratio, it was found that A very high odds ratio (113.364) for the recoded variable suggests a strong association. GDM-negative individuals have higher odds compared to the reference group, while GDM-positive individuals have significantly lower odds for having uric acid level >4.2mg/dl. Confidence intervals indicate statistical significance.

Table 8: Risk Estimate between gestational Diabetes mellitus and Uric Acid level

Variable	Odds Ratio (OR)	95% Confidence interval	P value
Uric Acid > 4.2	128.992	38.660 - 430.392	**.000**
Elevated TyG index	18.601	1.934 - 178.878	**.011**

Regression analysis shows that the odds of developing Gestational Diabetes mellitus in cases with uric acid > 4.2mg/dl is 128.992 times compared to ≤ 4.2mg/dl category.

DISCUSSION

The statistically significant association observed between serum uric acid level and Gestational diabetes mellitus underlines its utility in diagnosis of GDM. Many observational studies support a positive correlation between serum UA levels and diabetes risk as well as GDM. Rasika et al reported that the risk of GDM in pregnant women increases as serum UA levels rise in the first trimester.[9] A systematic review and meta-analysis by Su S et al showed that elevated UA levels are positively related to the risk of GDM, especially in early pregnancy.[10] In a prospective study, Duo et al. demonstrated that elevated serum UA levels were positively associated with the development of GDM, and the association was enhanced when serum UA exceeded 240 μmol/L.[11]

The results of the current study showed a higher odd of developing GDM (p<0.05) among cases with elevated GDM. Serum UA concentration in the first trimester was significantly higher in women with gestational diabetes mellitus (GDM) than in women with normal glucose tolerance (NGT). Our findings are consistent with those of Laughon et al, who reported that higher first-trimester UA levels were associated with an increased risk of GDM independent of maternal BMI and age.6 Similarly, a cohort study by Yan Zhao et al confirmed that elevated serum UA in early pregnancy significantly increases the risk of developing GDM later in gestation.[12]

Serum uric acid, a routinely measured biochemical parameter, holds substantial promise as a predictive and diagnostic tool, particularly in pregnancy-related complications like GDM. SUA can improve early risk stratification and patient outcomes.

The present study indicates that Serum uric acid, predicts GDM with an AUC of 0.928 (95% CI: 0.863–0.994). In a study by Rehman A et al, it was found that the mean SUA level was significantly higher in women who developed GDM (3.73 ± 0.43 mg/dL) compared to controls (3.19 ± 0.49 mg/dL). The AUC for SUA predicting GDM was 0.92 (95% CI: 0.87–0.97). A SUA cutoff value of 3.91 mg/dL yielded a sensitivity of 69.7% and specificity of 96.4%.[13]

A comprehensive meta-analysis by Su S et al, which included 11 studies with a total of 80,387 pregnant women revealed that elevated SUA levels were significantly associated with an increased risk of GDM (OR = 1.670, 95% CI: 1.184–2.356). Subgroup analysis indicated that this association was particularly strong when SUA was measured during the first trimester (OR = 3.978, 95% CI: 2.177–7.268).[10]

A systematic review and meta-analysis by Shaofei Su evaluated multiple studies to assess the relationship between SUA levels and GDM risk. The analysis concluded that elevated SUA levels were significantly associated with an increased risk of developing GDM, reinforcing the potential role of SUA as a predictive marker.[10] These studies collectively suggest that elevated SUA levels in early pregnancy are associated with a higher risk of developing GDM. The high AUC values reported indicate that SUA could serve as a valuable early biomarker for GDM prediction. However, variations in cutoff values and sensitivities across studies highlight the need for standardized thresholds and

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further large-scale prospective studies to validate these findings.

CONCLUSION

Elevated serum uric acid levels, traditionally considered in the context of hypertensive disorders, also emerged as an independent predictor of GDM, likely due to their role in oxidative stress and metabolic dysfunction. Serum uric acid levels, being cost-effective and derived from routine laboratory investigations, should be considered for inclusion in early antenatal screening protocols to identify women at risk for developing GDM before 20 weeks of gestation.

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