Study the Effect of Uric Acid level in Gestational Diabetes Women and Relationship with other Biochemical Parameters

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ABSTRACT

Gestational diabetes (GDM) is a type diabetes mellitus that first appears or is identified during pregnancy. It plays a significant role in the transmission of diabetes from generation to generation and is a leading source of morbidity in mothers and infants. The purpose of this study was to compare and analyze the impact of uric acid as a clinical predictor of GDM in pregnant women in the first, second, and third trimesters of pregnancy. Ninety Iraqi women with gestational diabetes, aged between (20-45) years participated in the study. All patients were divided into three groups: 30 women (G_1) first trimester (≤12 weeks), 30 women (G_2) second trimester (≥13-28 weeks), and 30 women (G_3) third trimester (≥29-40 weeks). All women underwent clinical and biochemical examinations, including glucose monitoring, uric acid, blood urea, serum creatinine, and liver function tests [alkaline phosphate, aspartate aminotransferase and alanine aminotransferase]. The results of the study indicate a highly significant increase in FBS, urea, ALP, SGOT in the comparison groups (P < 0.001). A significant difference increases at (P< 0.05) for the groups participating in the study such as HOMA-IR%. While uric acid had a significant increase difference at (P< 0.05) between the participating groups. Moreover, the results have been varied in between a negative and positive relationship for uric acid and other measured parameters. Increased uric acid levels in the first trimester until the third trimester of pregnancy is associated with risks of developing GDM.

Keywords*: *Gestational Diabetes Mellitus, Insulin resistance, Serum uric acid, Liver function tests.

INTRODUCTION

During pregnancy, the metabolism of some nutrients (such as glucose) changes to ensure their proper delivery across the placenta to the fetus. Some cases of pre-gestational diabetes may be discovered during pregnancy and may be called GDM. Thus, any kind of carbohydrate intolerance, regardless of severity, that initially manifests during pregnancy is referred to as gestational diabetic mellitus (GDM)[1]. Both the mother and the fetus are at risk from GDM, and some of these dangers last throughout the mother and child's lifetimes. The high prevalence of GDM is of great concern because it is not only associated with adverse perinatal outcomes but also is also linked to a higher lifetime risk of metabolic and cardiovascular disorders. It is therefore important to identify the potential risk factors, modifiable treatment of GDM and implementation of early prevention[2]. This concept is true whether the course of treatment involves oral hypoglycemic medications, pharmaceutical insulin, or just changing one's lifestyle. During this period, metabolic processes are reorganized according to the fetus's need for growth. Insulin resistance increases, especially in the third trimester due to a combination of increased maternal obesity and the effects of placental hormonal products[3]. The enzyme xanthine oxidase produces uric acid, the end result of purine metabolism. Numerous studies indicate that uric acid may be a significant risk factor for women's diabetes development. A study looked into the relationship between uric acid and the function of cells[4]. Insulin release was boosted by L-arginine, and it was seen that in hyperuricemic patients' islet beta-cell activity increased compensatively[5]. It may be concluded that there is a positive correlation between insulin resistance and blood uric acid levels. In a typical pregnancy, either decreased proximal tubular reabsorption or an increase in Glomerular Filtration Rate (GFR) causes a drop in serum uric acid levels in first trimester[6,7].

ric acid levels rise as pregnancy goes on due to increased fetal synthesis, decreased clearance, and lowered binding to albumin[8], High uric acid levels in the early stages of pregnancy could be a sign of an ongoing metabolic disorder that will impair the physiological changes that pregnant women typically experience, increasing their risk of developing gestational diabetes mellitus[9,10]. Many investigations have been carried out to evaluate the relationship between hyperuricemia and GDM, demonstrating that in women with gestational diabetes, insulin resistance and uric acid were correlated[11]. those with GDM have greater serum uric acid levels at 24-28 weeks gestation than those without the disease[12]. Regardless of body mass index (BMI), uric acid levels are elevated in non-pregnant women with a genetic history of GDM[13]. Higher uric acid in the first trimester may be linked to the development of GDM since it is linked to insulin resistance and occurs before the onset of type 2 diabetes in non-pregnant persons[14].

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PATIENTS AND METHODS

Ethical and scientific committee approval was obtained for the study. Ninety Iraqi women diagnosed as gestational diabetes mellitus their age range was (20-45) years, BMI (18-25 Kg/m^2). A study was done at National Diabetes Center/ Mustansiriyah University, Baghdad, Iraq during the period from November 2023 to April 2024. All patients were categorized to three groups: 30 women (G1) first group (≤12) weeks), 30 women (G2) second group (≥13-28 weeks), and 30 women (G3) third group (≥29-40 weeks).

All women underwent clinical and biochemical examinations. Fasting venous blood samples were collected from all patients. Laboratory evaluations consisted of glycemic control including fasting serum insulin, blood urea, serum creatinin and liver function test [(Alkalin pfosphates(ALP), Aspartate Aminotransferase (AST/GOT) and Alanine Aminotransferase (ALT/GPT)] was measured in Cobas (e111) /Germany. Insulin levels: Serum insulin levels were determination by the DRG insulin ELISA kit, and calculated insulin resistance from equation: [HOMA-IR= [fasting glucose mmol/l * fasting insulin µU/ml]/22.5].

Statistical analysis: The Mean ±SD of the data was show using a significant threshold of (P <0.05), the One-way ANOVA test was used to assess the differences between all studied groups with the using of Tukey's Least Significant Difference (LSD) test as a post-hoc test for pairwise comparisons of the studied groups. The SPSS software (SPSS, Chicago, IL, USA) version 22 was utilized.

Inclusion criteria

Singleton pregnancy and pregnant women with diabetes.

Exclusion criteria

• Obese
•Chronic medical illnesses (hypertension, gout, blood disorders, liver diseases, renal disease)
• Smoking.

RESULT

Table 1 shows the incidence rate according to family history of the disease. There is a significant difference (P-value ≤0.05) between the percentage of patients with family history of DM (54 %) and those without family history (46%.)

Table 1. Family history of diabetes mellitus

p-value	Percentage%	Frequency	Family History
\	54	51	Present
\	46	39	Absent
0.05	100.0	90	Total

p-value≤0.05 indicates significance

Table 2 shows the distribution percentage % according to parity. There is a significant difference between the percentage of primigravida and multigravida (P- value ≤0.05)

Table 2. Parity distributions of diabetic patients

p-value	Percentage%	No. of patients	Parity
\	36	32	Primigravida
\	64	58	Miltigravida
0.05	100.0	90	Total

p-value≤0.05 indicates significance

Table 3 shows the comparison (Mean ±SD) of different biochemical Parameters among study groups. The data showed that there was a highly significance difference in FBG (p≤0.01) for both (G1 vs G2) and (G1 vs G3). While the value of HOMA-IR% had recorded significance increasing at (p <0.05). Other parameters of kidney and liver function tests, statistical significances were included and an increasing significance was found (P≤0.05) among the three comparison groups.

Table 4 shows uric acid level measurements in different groups ,there is a significant difference among the three groups

Table 5 refers to discrepancy in the results between a negative and positive relationship for uric acid and other measured parameters. The correlation coefficient for uric acid shows that, there is a positive

Table 3. Comparison (Mean ±SD) of Biochemical Parameters among study groups

Parameters	first group (≤12) weeks)	second group (≥13-28 weeks)	third group (≥29-40 weeks)	P- value (G_1) Vs (G_2)	P- value (G1) Vs (G3)	P- value (G_2) Vs (G_3)
	Mean ± SD (G1)	Mean ± SD (G2)	Mean ± SD (G3)			
	N=30	N=30	N=30			
FBG (mg/dl)	179.33±14.10	184.76±6,54	196.80±16.50	0.01**	0.01**	0.02**
Insulin (ng/dl)	16.21±2.27	10.02±1.23	9.31±2.22	0.560	0.592	0.124
HOMA IR%	4.58±1.63	5.82±1.01	6.42±2.36	0.05*	0.05*	0.05*
B.urea (mg/dl)	28.80±7.91	36.63±7.58	41.16±6.00	0.001**	0.03**	0.01**
S.creatinin (mg/dl)	0.73±0.24	0.75±0.82	0.74±0.32	0.651	0.628	0.643
ALP (mg/dl)	55.43 ± 11.04	94.80± 1.86	105.23± 18.73	0.001**	0.001**	0.005**
GOT (mg/dl)	7.70 ±0.39	8.59± 4.60	15.46 ± 3.87	0.003**	0.005**	0.001**
GPT (mg/dl)	7.83± 0.57	8.83± 1.63	9.54± 1.26	0.60	0.68	0.06

p-value≤0.05 indicates significance, whereas p-value≤0.01 indicates high significance.

Table 4. Uric acid level among study groups.

Parameters	G_1 (≤12) weeks) Mean±SD (G_1) N=30	G_2 (≥13-28 weeks) Mean±SD (G_2) N=30	G_3 (≥29-40 weeks) Mean±SD (G_3) N=30	P-value (G_1) Vs (G_2)	P-value (G_1) Vs (G_3)	P-value (G_2) Vs (G_3)
Uric acid (mg/ml)	4.20±0.91	5.75±0.73	6.21 ±1.11	0.05	0.05	0.05

p-value≤0.05 indicates significance, whereas p-value≤0.01 indicates high significance.

Table 5. Correlation coefficient of uric acid level with clinical variables among study groups.

Variables	Correlation coefficient		
	First group (≤12) weeks)	second group (≥13-28 weeks)	third group (≥29-40 weeks)
	r	r	r
UA vs FBG(mg/dl)	0.470*	0.260*	0.316*
UA vs Insulin (ng/dl)	0.168	-0.116	0.139
UA vs HOMA-IR%	0.221*	0.205*	0.522**
UA vs B.urea (mg/dl)	0.111	-0.116	0.568**
UA vs S.creatinin (mg/dl)	-0.056	-0.153	0.891
UA vs ALP (mg/dl)	0.363*	0.397*	0.725**
UA vs GOT (mg/dl)	0.272*	0.347*	0.467*
UA vs GPT (mg/dl)	0.130	0.115	0.105

**At the 0.01 levels, correlation is significant.
*At the 0.05 levels, correlation is significant.

statistically significant relationship with both FBS, ALP, and GOT. Also a highly significant correlation with HOMA-IR, urea, and ALP at third trimester.

DISCUSSION

Large amount of glucose reach the fetus which leads to fetal hyperinsulinemia, although insulin does not cross the placenta but high concentrations of insulin have been shown to increase lipid accumulation. So the placenta responds to insulin by expressing insulin receptors and ignoring lipid metabolism[15]. When the insulin hormone receptors on cell membranes do not react appropriately to insulin, glucose from the blood cannot enter the cells, a condition known as insulin resistance (IR), a form of biological misinformation in the body[16] .The pancreas attempts to transfer glucose from the blood into the cells in this state by producing large amounts of insulin[17]. In the current study, obesity was excluded from the study because prepregnancy BMI is directly correlated with the risk of GDM and increases insulin resistance[18]. In this Iraqi study there is a significant association of family history and GDM and this concurrent with astdy done by Zhang M ..etc. he concluded that a family history of diabetes considered as an independent risk factor for GDM[19].

When the regulatory and signaling ability of the insulin hormone decreases, blood glucose levels change and IR[20] occurs. Glucose is taken into the fetus' body through the placenta, which promotes fetal growth and increases the rate of Macrosomia. In addition, hyperglycemia excites fetal islet beta cells, which become larger than before insulin secretion, resulting in higher blood insulin levels[21]. Significantly high insulin hormone and glucose levels increase the incidence of fetal hyperactive metabolism, leading to increased fetal peripheral hematopoiesis and neonatal polycythemia[22]. Severe disruption of glucose absorption after birth causes neonatal hypoglycemia, which leads to permanent damage to brain cells[23].

The relationship between the development of T2DM or pre-diabetes after giving birth and inadequate glycemic management during a GDM has been explained by two theories. First, the degree of the symptoms may have an impact on this[24].Chronic insulin resistance and β-cell dysfunction, manifested as hyperglycemia during pregnancy and leading to persistent glycemic abnormalities (pre-diabetes and T2DM) in the postpartum or subsequent period[25]. The second theory holds that pancreatic islets are exposed to long-term increased blood sugar levels throughout pregnancy. Oxidative stress exerts toxicity on β cells, causing further β cell dysfunction[26]. Cell death and resulting pre-diabetes or T2DM after pregnancy. The cascade phenomenon has been shown in multiple studies that discovered decreased β-cell mass in T2DM patients compared to non-diabetic subjects[27].

Asymptomatic elevated levels of uric acid in adults cause increased inflammatory cytokines and Oxidative stress create insulin resistance, which in turn raises blood glucose levels[28]. Increased uric acid may play a protective role and cause resistance to the harmful effects of oxidative stress and free radical activity. Elevate uric acid levels in the blood can also predict the development of hypertension in the future[29]. Elevated uric acid levels in GDM are important metabolic factors. In terms of clinical practice, hyperuricemia is a risk factor for renal illness, metabolic syndrome, cardiovascular disease, and diabetes as well as a significant contributor to higher death rates[30]. According to earlier research, hyperuricemia is primarily associated with women and is associated with an increased risk of developing diabetes and insulin resistance within ten years.Insulin resistance is caused by the same mechanism among women who are pregnant and those who are not[31]. Raising plasma insulin concentrations triggers the sympathetic nervous system. This has a separate correlation with decreased uric acid excretion from the kidneys. The two hypotheses that underlie the incremental alterations in glucose metabolism and insulin resistance in hyperuricemia are the excretion of uric acid from adipose tissue[32] and estimations of nitric oxide release in endothelial cells (linked to glucose uptake in skeletal muscle).

A study conducted by (Sautin et al.) ,which revealed that elevated serum uric acid causes endothelial dysfunction and is responsible for a subsequent decrease in endothelial cell nitric oxide production. Nitric oxide is involved in insulin's function in absorbing glucose into fat in animal tissue and skeletal muscle. Therefore, due to reduced nitric

oxide levels, glucose uptake decreases, leading to the development of insulin resistance[33]. Among other processes, uric acid can induce insulin resistance through adipose inflammation and oxidative stress. Hyperuricemia-induced tissue growth contributes to the development of metabolic syndrome in mice[34]. Insulin resistance will increase rapidly as part of the physiological state changes of the second trimester of pregnancy. Once the fetus is born, maternal physiological status will eventually return to normal. A homeostatic model of insulin resistance was used to calculate the rise in insulin resistance. Other risk factors for this condition include hyperuricemia, maternal obesity, and the presence of diabetes hormones[35]. Hypertension and hyperuricemia during pregnancy were found to be strongly linked with higher insulin resistance[36] in a study conducted by Wise et al. Other risk factors for insulin resistance during pregnancy include the presence of diabetogenic hormones during the middle of pregnancy. Elevated insulin resistance, hyperuricemia, and gestational hypertension during pregnancy[37] were found to be significantly correlated in Weisz et al. study.

It has been determined that hyperuricemia is a separate risk factor for diabetes, metabolic syndrome, and cardiovascular disease[38]. In non-pregnant women, hyperuricemia without symptoms exacerbates insulin resistance because it causes oxidative stress and the production of inflammatory cytokines, which ultimately raises blood glucose levels[28]. In a similar vein, it is a major risk factor for insulin resistance during pregnancy and increases the incidence of GDM[39]. Insulin resistance is associated with elevated uric acid levels during pregnancy.

CONCLUSION

Elevated serum uric acid since the 1st trimester until 3rd trimester would appear and this increase can be linked to several factors, including (parity, and family history). It was also found that the correlation coefficient between high uric acid and biometrics of individuals participating in the study raises concerns that the risk of developing GDM is increased.

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