



Evaluation of uric acid levels as antioxidant during normal pregnancy and pregnancy with complication (diabetes and hypertension)

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ABSTRACT

The uric acid is a waste product of the living cell, produced by xanthine oxidase, which contributes up to 60% of the total plasma antioxidant activity in healthy subjects. The study provides data relating serum uric acid, glucose levels and blood hypertension. Seventy nine patients with pregnancy diabetes mellitus, 25 normal healthy with pregnancy, 25 DM patients, and fifty normal healthy persons, where seen from February till July 2017, in Al-Semawa General Hospital, were participated in the study. The results revealed a highly significant difference ($P < 0.001$) in uric acid, glucose level and hypertension in almost pregnancy diabetic patients and DM patients when compared to control group. In conclusion, this study found that pregnancy women at the early development stage of glucose disorders had a significantly of hyperuricemia and in clinical practices, measurement of serum uric acid level may help to identify the risk of hypertension.

Keywords: uric acid, waste product, xanthine oxidase, plasma antioxidant activity, pregnancy, diabetes mellitus

INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. The chronic hyperglycemia of diabetes is associated with long-term damage and dysfunction of Kidneys, nerves, heart, and blood vessels (1). There are four etiological types of DM: Diabetes mellitus type 1 (DMT1), Diabetes mellitus type 2 (DMT2), other specific types, and gestational diabetes (GDM) that in same way divide to gestational diabetes with impaired tolerance (IGT) and impaired Fasting glucose (IFG) as stages in the natural history of disordered carbohydrates metabolism (2). Gestational diabetes mellitus is a condition in which women without previously diagnosed diabetes exhibit high blood glucose levels during pregnancy (especially during third trimester of pregnancy), and it generally has few symptoms and it is most commonly diagnosed by screening during pregnancy (affects 3–10% of pregnancies (3). Women with GDM are at increased risk of developing DMT2 (or, very rarely, latent autoimmune diabetes or Type 1) after pregnancy, as well as having a higher incidence of pre-eclampsia and Caesarean section (4). Their offspring are prone to developing childhood obesity, with DMT2 later in life.

Insulin resistance pregnancy hormones and other factors are thought to interfere with the action of insulin as it binds to the insulin receptor (5). Insulin resistance is a normal phenomenon emerging in the second trimester of pregnancy, which progresses thereafter to levels seen in non-pregnant patients with DMT2. It is thought to secure glucose supply to the growing fetus. Women with GDM have an insulin resistance they cannot compensate with increased production in the β -cells of the pancreas. Placental hormones, and to a lesser extent increased fat deposits during pregnancy, seem to mediate insulin resistance during pregnancy. Cortisol and progesterone are the main culprits, but human placental lactogen, prolactin and estradiol contribute too (6).

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Table 1: Bio statistical calculation for glucose level mm/L in serum of GDM patient with different durations and Normal healthy (controls)

Glucose mm\L	12> Weeks	12-24 Weeks	24< Weeks
Sample size	20	32	27
Mean \pm SD	10.005 \pm 3.099	13.331 \pm 4.961	15.587 \pm 4.765
Range	13.7 – 6.8	24.1 – 6.5	26.3 – 6.7
SE	0.693	0.877	0.917
T – test	2.684		4.566
Probability	0.0098 (Significant)		<0.0001(Highly significant)

Hypertensive disorders of pregnancy are the most common medical disorders of pregnancy and are associated with increased maternal and perinatal risks. In a subset of pregnancy women's with gestational hypertension, blood pressure remains elevated after delivery, leading to the diagnosis of chronic hypertension. These women have a tendency not only for hypertension in subsequent pregnancies but for chronic hypertension later in life (7).

Uric acid is a waste product of the living cell, produced by xanthine oxidase, which contributes up to 60 % of the total plasma antioxidant activity in healthy subjects due to its wide distribution and relatively high concentration, and it is more toxic to tissues than either xanthine or hypoxanthine and it released in hypoxic conditions (8). In high concentrations, uric acid may act as a pro – oxidant and hyperuricemia has been suggested to be a risk factor for oxidative stress associated disorders (9). The association of high serum uric acid with insulin resistance has been known since the early part of the 20th century, high serum uric acid as a risk factor for diabetes and the associated with higher risk of DMT2, independent of obesity, dyslipidemia, and hypertension (11).

The aim of this study is to examine and measure potential clinical application of uric acid & hypertension in the evaluation of pregnancy women with GDM syndrome, and study the possible correlation between serum uric acid with hypertension.

MATERIALS AND METHODS

Patients Samples

Seventy nine patients with pregnancy diabetes mellitus, 25 normal healthy with pregnancy, 25 DM patients, and fifty normal healthy person were considered as controls groups, where seen from February till July 2017, in Al-Semawa General Hospital. The diagnosis was done by clinical examination.

Blood Sampling

The blood was allowed to coagulate at room temperature and centrifuged for 10 min .The resulting serum were separated. The serums were stored at -20 °C. The stability studies showed that the following parameters (Glucose, Uric acid) were constant under these conditions, for up to three months (10). Blood pressure is measured using a device called asphygmomanometer; this apparatus measures the pressure in the machine's cuff when it's inflated.

Statistical Analysis

Statistical analysis was done by using student t-test. All the data were presented as mean \pm standard deviation. P-values <0.05 were considered significant.

RESULTS

Table 1 depicts all the biochemical parameters which used in this study in patients of DM and control group. There is a highly significant increase in glucose level in pregnancy diabetic patients and DM patients with duration of the pregnant less than 12, between 12 – 24 and more than 24 weeks as compared to the control group (P < 0.0001). There is no significant correlation between glucose levels in pregnancy diabetic patient with duration of the pregnant between 12–24 weeks & patients with duration of the pregnant more than 24 weeks as shown in **Table 2**.

Table 2: Biostatistical calculation and study t-test for glucose level mm/L in serum of GDM patients that have duration(12-24 weeks) and (24<weeks) compared with GDM (<12 weeks)

Glucose mm\L	Controls	12> Weeks	12-24 Weeks	24< Weeks
Sample size	50	20	32	27
Mean \pm SD	4.954 \pm 0.911	10.005 \pm 3.099	13.331 \pm 4.961	15.587 \pm 4.765
Range	6.1 – 3.4	13.7 – 6.8	24.1 – 6.5	26.3 – 6.7
SE	0.129	0.693	0.877	0.917
T – test	10.535		11.674	15.349
Probability	<0.0001 (Highly significant)			

Table 3: Bio statistical calculation for Uric acid level nm/L in serum of GDM patient with different durations and Normal healthy (controls)

Uric Acid un/L	12> Weeks	12-24 Weeks	24< Weeks
Sample size	20	32	27
Mean \pm SD	276.95 \pm 87.467	359.187 \pm 75.006	404.814 \pm 81.085
Range	188 – 451	199 – 447	456 – 220
SE	19.558	13.259	15.604
T – test	3.608		5.170
Probability	0.0007 (Significant)		<0.0001(Highly significant)

Table 4: Biostatistical calculation and study t-test for Uric acid level un/L in serum of GDM patients that have duration(12-24 weeks) and (24<weeks) compared with GDM (<12 weeks)

Uric Acid un/L	Controls	12> Weeks	12-24 Weeks	24< Weeks
Sample size	50	20	32	27
Mean \pm SD	343.56 \pm 71.248	276.95 \pm 87.467	359.187 \pm 75.006	404.814 \pm 81.085
Range	436 – 201	188 – 451	199 – 447	456 – 220
SE	10.076	19.558	13.259	15.604
T – test	3.307		0.949	3.429
Probability	0.0015 (Significant)		0.3454(No Significant)	0.0010(Significant)

Table 5: The statistical calculation and students t-test for hypertension level of GDM with all duration of study and Uric Acid levels

Uric Acid Un/L Hypertation&	Hypertation <12 Weeks	<12 Weeks Uric Acid	12-24 Weeks Uric Acid	>24 Weeks Uric Acid
Sample size	8	20	32	27
Mean \pm SD	13.125 \pm 0.353	276.95 \pm 87.467	359.187 \pm 75.006	404.814 \pm 81.085
Range	13 – 14	188 – 451	199 – 447	456 – 220
SE	0.125	19.558	13.259	15.604
T – test	8.434		12.923	13.520
Probability	<0.0001 (Highly significant)		<0.0001 (Highly significant)	<0.0001 (Highly significant)

Table 3 shows that there is a significant increase in Uric Acid level in GDM patients with duration of the pregnant less than 12 weeks and more than 24 weeks as compared to the control. There is no significant difference between patients with duration of the pregnant between 12–24 weeks as compared to the control group. Also there is a significant difference between patients with duration of the pregnant less than 12 weeks & patients with duration of the pregnant between 12 – 24 weeks and patients with duration of the pregnant more than 24 weeks. There is a significant correlation between Uric Acid levels in GDM patient with duration of the pregnant between 12–24 weeks & patients with duration of the pregnant more than 24 weeks.

In **Table 5**, there is a highly significant increase in hypertension and Uric Acid levels in GDM patients with duration of the pregnant less than 12 weeks as compared to the control group ($P < 0.0001$), and in GDM with duration of the pregnant between 12–24 weeks there is a significant difference between DM patients & control group and a significant difference between GDM with duration of the pregnant more than 24 weeks & control group as shown in table 6. There is a highly significant difference between hypertension level of patients with different durations of the pregnant & Uric Acid levels, **Table 7** and **8**.

Table 6: The statistical calculation and students t-test for Hypertension level of GDM patient with duration (<12 weeks) and Uric Acid levels of GDM patients with different durations

Uric Acid un/L & Hypertension	Controls Uric Acid	Hypertension <12 Weeks	Hypertension 12-24 Weeks	Hypertension >24 Weeks
Sample size	50	8	24	20
Mean ± SD	343.56±71.248	13.125 ±0.353	13.083 ±0.282	13.2 ± 0.410
Range	436 – 201	13 - 14	13 – 14	13 - 14
SE	10.076	0.125	0.057	0.091
T-test		13.020	22.642	20.645
Probability		<0.0001 (Highly significant)	<0.0001 (Highly significant)	<0.0001 (Highly significant)

Table 7: The statistical calculation and students t-test for Hypertension level of GDM patient with duration (12-24 weeks) and Uric Acid levels of GDM patients with different durations

Uric Acid Un/L& Hypertation	>24 Weeks Hypertension	<12 Weeks Uric Acid	12-24 Weeks Uric Acid	>24 Weeks Uric Acid
Sample size	20	20	32	27
Mean ± SD	13.2 ± 0.410	276.95 ±87.467	359.187 ± 75.006	404.814±81.085
Range	13 - 14	188 – 451	199 – 447	456 – 220
SE	0.091	19.558	13.259	15.604
T – test		13.485	20.552	21.537
Probability		<0.0001 (Highly significant)	<0.0001 (Highly significant)	<0.0001 (Highly significant)

Table 8: The statistical calculation and students t-test for Hypertension level of GDM patient with duration (>24 weeks) and Uric Acid levels of GDM patients with different durations

Uric Acid Un/L Hypertation &	Hypertation 12-24 Weeks	<12 Weeks Uric Acid	12-24 Weeks Uric Acid	>24 Weeks Uric Acid
Sample size	24	20	32	27
Mean ± SD	13.08333 ± 0.2823299	276.95 ± 87.46758	359.1875 ± 75.00642	404.8148 ± 81.08544
Range	13 – 14	188 – 451	199 – 447	456 – 220
Standard error of mean	0.05763034	19.55834	13.25939	15.6049
T – test		14.814	22.553	23.641
Probability		<0.0001 (Highly significant)		<0.0001 (Highly significant)

DISCUSSION

The untimely interference and suitable management in female with GDM will be cooperative in preventing the adverse maternal and prenatal outcome and as well protect them from long term consequences. Several studies have shown the association of hyperuricaemia in the first trimester with development of GDM later in life. In current study, Uric acid levels in serum of GDM patients that have different durations in pregnancy seemed to be significantly differences ($P < 0.01$), this results suggested that increased serum uric acid (a physiological antioxidant) in early trimester was associated with higher incidence of GDM. This finding is in accordance with that of Fawzy *et al.* (11), El-Gharib *et al.* (22), Aparna K *et al.* (13), Sujata Maitra *et al.* (15), Nagalkshmi CS *et al.* (16), Talya Wolak *et al.* (19) and Zhou J *et al.* (2012) who demonstrated that the first trimester hyperuricemia is associated with an increased risk of developing GDM. The elevation in serum uric acid level may be a protective response which is capable of opposing harmful effects of free radical and oxidative stress seen in GDM as uric acid possesses antioxidant properties, and contributes about 60% of free radical scavenging activity in human serum. Elevated serum uric acid can predict the development of diabetes and hence can be considered as an early sign of peripheral insulin resistance syndrome. Elevated or high normal levels of serum uric acid in first trimester may be associated with a preexisting metabolic derangements which lead to poor maternal physiological adaptations and predisposes the pregnant women to development of pregnancy complication like GDM (14).

The finding results were consistent with Yoo *et al.* (23), when they found in a huge cross-sectional study of 53,477 non-pregnant females, that serum uric acid was positively correlated with fasting serum glucose and insulin resistance, as well as features of the metabolic syndrome, including hypertension and fasting glucose.

Hypertensive disturbances are the most common medical disorders of pregnancy and are associated with increased maternal and perinatal risks. In this study we observed the strong positive association between hyperuricemia and hypertension. There was a highly significant difference ($P < 0.0001$) in hypertension level of GDM patient and uric acid levels with different durations. Garrick *et al.* (25) found that 31% of their patients had hyperuricemia with hypertension. Significant high serum uric acid level in hypertensive patients were also observed by Eisen *et al.* (26) and Grayson *et al.* (27). The serum level of uric acid was associated with the incident of hypertension and may be important of developing hypertension (24).

In conclusion, we found that pregnancy women at the early development stage of glucose disorders had a significantly of hyperuricemia and in clinical practices, measurement of serum uric acid level may help to identify the risk of hypertension.

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