Gestational Diabetes Mellitus and Hormonal Alteration

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Abstract

Gestational Diabetes Mellitus is known as carbohydrate intolerance first detected during pregnancy. Pregnancy is periods of intense hormonal changes. The aim of the present study was to investigate a possible relation between the changes in serum hormones such as Luteinizing hormone (LH) , follicle stimulating hormone(FSH), Progesterone, and Prolactin with gestational diabetes mellitus. Thirty patients with gestational diabetes mellitus aged (22 -40) year attending the national center for treatment and research of diabetes/ AL-Mustansiriya University in Baghdad and 29 controls aged (20-39) year were participated. Hormonal tests including, FSH, LH, Progesterone, and Prolactin were detected by using Enzyme Linked Fluorescent Assay (ELFA) kits. The demographic characteristics of gestational diabetes mellitus indicated that the most commonly affected age at (20-29) year (50%) ,60% of patients had Body Mass Index(BMI) at $\geq 30 kg/m^{2+}$, 76.6% of patients at first trimester of pregnancy, 23.3% had previous abortion,60% at the first pregnancy ,and 46.6% of patients had urine protein with one plus. A highly significant increase ($p \leq 0.001$) in Fasting serum glucose(FSG), LH, FSH, progesterone, and prolactin were observed in sera of gestational diabetes mellitus patients in comparison to that of control pregnancy group. A non-significant correlation of FSG with age, BMI, LH, FSH, and progesterone were demonstrated. While a significant positive correlation of FBS with prolactin was found. It is conclude that higher prolactin level in pregnancy possibly played a role in gestational diabetes mellitus partly by impairing the functions of insulin, and result in hyperglycemia.

Keyword: Gestational diabetes, FSH, LH, Progesterone, Prolactin.

داء السكري الحملي والتغيرات الهرمونية

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الخلاصة

ان داء السكري الحملي وكما هو معروف بعدم التحمل الكربوهيدراتي اكتشف لأول مرة خلال فترة الحمل الذي يمثل دورة من التغيرات الهرمونية المكثفة. تهدف الدراسة الحالية الى الكشف عن وجود علاقة محتملة بين التغيرات الهرمونيه في الدم مثل الهرمون اللوتيني ،الهرمون المحث للجريب، البروجسترون، والبرولاكتين مع مرض السكري الحملي. ضمت هذه الدراسة ٣٠ من المريضات اللواتي يعانين من داء السكري الحملي وحضروا المركز الوطني لعلاج وابحاث السكري في الجامعة المستنصرية ببغداد بمدى عمري تراوح بين (٢٢ -٤٠) سنة و٢٩ من الحوامل غير المصابات بالسكري بمدى عمري تراوح بين (٢٠-٣٩) سنة . تضمنت الفحوصات الهرمونية الهرمون اللوتيني ،الهرمون المحث للجريب، البروجسترون، والبرولاكتين باستخدام عدة الالفا (ELFA).اظهرت نتائج الدراسه الديموغرافية لداء لسكري الحملي أن الأكثر تأثرا عادة تكون في سن (٢٠-٢٩) سنة (٥٠٪)، وكتلة الجسم ل ٦٠٪ من المرضى≤ ٣٠ و ٧٦.٦٥% من المريضات هن في الأشهر الثلاثة الأولى من الحمل، ٢٣.٣٪ لديهم اجهاض سابق، ٦٠٪ هو الحمل الأول، وكان بروتين البول ل ٤٦.٦٪ من المريضات بقيمة زائد واحد. بينت النتائج وجود زيادة معنوية عالية ($p \leq 0.001$)في مستوى كل من سكر الدم الصيامي ، الهرمون اللوتيني، الهرمون المحث للجريب، البروجسترون، والبرولاكتين في مصل دم الحوامل المصابات بداء السكري مقارنة مع تلك لمجموعة الحوامل غير المصابات بداء السكري. في الوقت نفسه تم اثبات عدم وجود علاقة معنويه لسكر الدم الصيامي مع العمر ، الهرمون اللوتيني، الهرمون المحث للجريب،و البروجسترون ، في حين تبين وجود علاقة معنويه موجبة بين سكر الدم الصيامي وهرمون البرولاكتين. نستنتج أن ارتفاع مستوى البرولاكتين في الحمل له دور الى حد ما في الاصابة بداء السكري الحملي من خلال التعطيل في وظائف الأنسولين، مما يؤدي إلى ارتفاع السكر في الدم.

الكلمات المفتاحية: سكر الحمل ، الهرمون المحث للجريب ،الهرمون اللوتيني ، البروجستيرون ، البرولاكتين.

Introduction

Gestational Diabetes Mellitus (GDM) is known as carbohydrate intolerance first revealed during pregnancy [(1)]. It is the most public metabolic disturbance of pregnant women, involves between 2% and 5% of pregnant women [(2)]. Diabetes Mellitus type1 and type 2 could be diagnosed newly or secondary to metabolic changes related to pregnancy [(3)].Gestational diabetes mellitus accounts for ninety percent of cases of diabetes

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mellitus in pregnancy, however eight percent of cases are preexisting type 2 [4]. GDM reveals usually between 24 and 28 weeks of gestation [5].A large number of risk factors related to GDM increase have been fixed, including history of macrosomia, strong family history of diabetes, ethnicity, metabolic syndrome and obesity [2,6].Pregnancy is periods of intense hormonal changes[1]. Women at risk for gestational diabetes have insulin resistance before conception. Insulin resistance during pregnancy stems from a variety of factors, including alterations in growth hormone and cortisol secretion , human placental lactogen secretion , and insulinase excretion which is produced by the placenta and facilitates metabolism of insulin[7]. Moreover, the steroid hormones such as progesterone and the estrogens have been shown to be involved in β-cell physiology and disturbance of the glucose insulin balance [8,9] .

Luteinizing hormone (LH) and follicle-stimulating hormone (FSH) are omit gonadotropins are secreted from gonadotrophs cells in the anterior pituitary. Most gonadotrophs secrete only LH or FSH, but some time both hormones[10]. In female, LH stimulates secretion of sex steroids from the gonads progesterone and estradiol [10]. Progesterone is necessary for pregnancy reservation, and, in most mammals, LH is required for function and growth of corpora lutea[10]. LH levels will decrease if pregnancy occurs, and luteal function will instead be maintained by the action of human chorionic gonadotropin, which is similar to LH and secreted from the new placenta [11].

The prolactin(PRL), is major stimuli for the adaptation of the endocrine pancreas during gestation [12]. Prolactin is a polypeptide originally known as a pituitary hormone for its ability to promote lactation in response to the breast feeding [13]. Besides its well-known lactogenic properties, prolactin is also a highly versatile hormone whose functions are related to reproduction, growth and development, metabolism, immune regulation, brain function, and behavior [14,15]. Maternal prolactin increases synchronously to insulin during the second half pregnancy and stimulates β-cell proliferation, insulin production, and insulin secretion [16,17]. Moreover, it is known that the glucose metabolic regulation impact of prolactin is not close to the period of pregnancy [15,18,19].

The aim of the present study was to investigate a possible correlation between the changes in serum hormones such as LH, FSH, Progesterone, and Prolactin with gestational diabetes mellitus.

Materials and Methods

Case control study was used in the present where 30 women with gestational diabetes mellitus aged (22 -40) years as case and 29 age-matched of pregnant women aged (20-39) years as control attending the national center for treatment and research of diabetes/ AL-Mustansiriya University in Baghdad. Exclusion criteria were: age <20 years, diabetes diagnosed before pregnancy, physical disability, medications like oral corticosteroids and metformin, and multiple pregnancies.

Five milliliters of venous blood samples were collected from the gestational diabetes mellitus and the healthy pregnant as controls group then immediately transferred into plane tube and allowed to coagulate at room temperature then centrifuged at 3000 rpm for 5 min. The resulting serum was separated and stored at (-20°C) until use. BMI is being calculated directly as weight (in kilograms)/ height^2 (in meters). Hormonal tests including, FSH, LH, Progesterone, and Prolactin were detected by using Enzyme Linked Fluorescent Assay (ELFA) kits in Mini Vidas system and performed according to the manufacturer's instructions.

Statistical Analysis

The statistical software (SPSS v 15; Chicago, IL, USA) was used. The data were analyzed using unpaired *t*-test and person correlation coefficients. Differences were considered significant when $P< 0.05$.

Results and Discussion

Table 1 show the baseline characteristics of gestational diabetes mellitus where it was found that the most commonly affected age at (20-29) year(50%) ,60% of patients had BMI at $\geq$ 30kg/m^{2+}, 76.6% of patients at first trimester of pregnancy, 23.3% had previous abortion,60% at the first pregnancy ,and 46.6% of patients had urine protein with one plus.

Table (1): Baseline characterization of gestational diabetes mellitus.

Category	Number (%)
Age in year	
20-29	15(50%)
30-39	14(46.6%)
40-49	1(3.33%)
BMI	
≤19	0(0%)
20-24	1(3.33%)
25-29	11(36.66%)
≥30	18(60%)
Trimester	
First	23(76.66%)
Second	6(20%)
Third	1(3.33%)
Pregnancy history	
Previous abortion	7(23.3%)
No abortion	23(76.66%)
First pregnant	18(60%)
Urine protein	
Trace	5(16.66%)
+	14(46.66%)
++	9(30%)
+++	2(6.66%)

Meanwhile a highly significant increase of BMI values was observed in gestational diabetes mellitus patients in comparison to that of control group (p=0.00) as shown in Table 2. This result was in line with Torloni MR *et.al* who reported that the GDM is positively associated with prepregnancy BMI where for every 1 kg/ m^2 increase in BMI, the prevalence of GDM increased by 0.92%[20].

The results represented in Table 2 indicated highly significant increases (p=0.00) in FSG, LH, FSH, progesterone, and prolactin in sera of gestational diabetes mellitus patients in comparison to that of control pregnancy group.Insulin secretion in women with GDM is defective and, therefore, is unable to rise adequately to compensate for the insulin resistance; the result is hyperglycemia [21].

LH and FSH play central roles in the hypothalamic-pituitary-gonadal axis, and, thus, conditions related to LH and FSH increases can be caused by pathology of either the hyperthalamus or pituitary [22]. LH increases almost always occurs in conjunction with follicle-stimulating hormone (FSH) increases because LH and FSH are secreted by the same pituitary gonadotrope cells.

Table (2): Mean values of BMI, F.S.G, LH, FSH, Progesterone, and Prolactin levels in sera of patient and control groups.

Parameters	group	Range (min-max)	Mean	SD	P value
BMI (kg/m^2)	Control	19.00-28.40	23.5724	1.9063	0.00
	Patients	21.90-35.50	29.8967	3.0337	
FSG (mg/dl)	Control	65.00-100.00	84.5172	32.6097	0.00
	Patients	130.40-260.00	180.0900	32.6097	
LH (pg/ml)	Control	9.10-17.10	14.3966	1.8084	0.00
	Patients	9.70-30.10	19.6633	4.6668	
FSH(pg/ml)	Control	8.80-18.70	15.8138	1.9913	0.00
	Patients	10.10-34.20	20.1533	5.3723	
Progesterone(pg/ml)	Control	10.20-104.00	44.7276	19.7237	0.00
	Patients	35.40-92.50	75.3533	12.7009	
Prolactin(pg/ml)	Control	13.70-42.10	27.2414	8.0499	0.00
	Patients	38.00-80.10	52.9900	12.2372	

Though a highly significant increase of progesterone level((p=0.00) was observed in the present study in sera of gestational diabetes mellitus in comparison to that level in control group (Table 2), we demonstrated a non-significant correlation ((p>0.05) of progesterone with FBS as shown in Table 3. In previous studies of progesterone conflict data was reported where one of them has found association of progesterone with the development of gestational diabetes due to the enhancement of insulin resistance [23,24], while another group did not find a correlation between progesterone level and an increasing risk of gestational diabetes mellitus [25]. In diabetes, the death of insulin-producing β-cells by apoptosis leads to insulin deficiency. The lower prevalence of diabetes in females suggests that female sex steroids protect from β-cell injury [26]. In addition Straub *et al*. suggested that the progesterone, might contribute to the poor adaptation of insulin secretion and action to the increased requirements during pregnancy [27].

Table (3): Correlations of FSG with age, BMI, and hormonal parameters.

Parameters	r value	P value
Age	0.302	0.105
BMI	0.252	0.179
LH	-0.151	0.424
FSH	-0.148	0.434
Progesterone	0.173	0.360
Prolactin	0.427	0.019

The present study indicated a highly significant increase in progesterone level in sera of gestational diabetes mellitus in compression to that of control group. This result was in agreement with Guyton & Hall who's reported that no significant difference in plasma prolactin in normal or diabetic pregnant in fact it level might be lower in the pregnant with GDM [28]. While this result was in disagreement with the results of Milasinovic L. *et.al* who reported that there were no significant differences in the level of plasma prolactin in normal or diabetic pregnancies; in fact its level might be lower in the pregnancies with gestational diabetes mellitus and, prolactin might have no effect on glucose intolerance during pregnancy [29]. Arumugam R *et al* reported that PRL up-regulates β-cell glucose uptake and employment, whereas glucose increases islet PRL receptor expression and more effects of PRL on cell cycle gene expression and DNA synthesis [30].

The results presented in Table 3 indicated a non-significant correlation of FSG with age, BMI, LH, FSH, and progesterone. On the other hand it was observed a significant positive correlation of FSG with prolactin. This result was in disagree with previous study which demonstrated that there is no correlation between the prolactin concentrations and the impairment of glucose tolerance and as a result the abnormal prolactin levels are not of pathophysiologic importance for the development of GDM [31].

Conclusion

In the light of the present results the findings confirmed that higher prolactin level in pregnancy possibly played a role in gestational diabetes mellitus partly by impairing the functions of insulin, and result in hyperglycemia.

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