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RESEARCH ARTICLE

Association of Placental Lactogen and Prolactin with Insulin Resistance in Gestational Diabetes Mellitus in Mosul City

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ABSTRACT

One common pregnancy problem is gestational diabetes mellitus (GDM), which is characterized by the onset or recognition of glucose intolerance during pregnancy. Pregnancy-related insulin resistance gives rise to it in women whose pancreatic function is inadequate, resulting in elevated blood sugar levels. Between 2 and 38% of pregnancies globally are affected by GDM. One hundred and twenty pregnant women, aged between twenty and thirty-nine, took part in this study. As a control group for the study, fifty healthy women were involved. On the other hand, seventy women who had already received a diagnosis of gestational diabetes were part of the second group. The results of this study investigated that there was a significant increase in the concentration of fasting glucose in pregnant women with gestational diabetes mellitus in the 2nd and 3rd trimester of each groups (20-29) and (30-39) years at the probability level (P≤0.05) as a compared with control group. As the result showed a significant increase in the concentration of insulin hormone, humane placental lactogen (HPL) (Lactogenic hormone) and prolactin (PRL) in pregnant women with gestational diabetes in the 2nd and 3rd trimester of each groups as a compared with control group. Also Insulin resistance (IR) increased significantly in in the women with gestational diabetes in the 2nd and 3rd trimesters of each groups. (GDM), refer to abnormal glucose tolerance with first recognition during the pregnancy, (GDM) associated significantly with increased of insulin hormone, human placental lactogen and prolactin hormones, GDM also associated with insulin resistance in the 2 nd and the 3rd trimester of pregnancy.

INTRODUCTION

One of the most prevalent pregnancy complications is gestational diabetes mellitus (GDM) , which is typified by the onset or identification of carbohydrate intolerance during pregnancy. It occurs in pregnant women whose pancreatic activity is inadequate to reverse pregnancy-related insulin resistance, resulting in elevated blood sugar levels. Globally, GDM affects 2 to 38% of pregnancies [1,2].

A family history of diabetes of any kind, advanced maternal age, and being overweight or obese are risk factors for gestational diabetes. However, the mother's metabolic incapacity to maintain a normal blood sugar level affects about 1 in 6 births globally. Insulin resistance and inadequate insulin production combine to cause gestational diabetes mellitus [3].

Normal insulin concentrations are insufficient to elicit the proper physiologic response from the insulin receptor, a condition known as insulin resistance. In order to control the mother's blood sugar levels, beta cells must secrete more insulin than usual. Placental hormones, which make sure the fetus gets enough nutrition for optimal growth and development, cause the mother to gradually become insulin resistant during a healthy pregnancy. Maternal beta cells correct for insulin resistance via increasing total cell number, insulin synthesis, and insulin secretion to maintain glucose homeostasis [4].

The primary cause of GDM's development is caused by hormones like human placental lactogen, estrogen, and cortisol. Insulin resistance is mediated by these hormones, which are secreted by the placenta during pregnancy. The second trimester of pregnancy is characterized by a progressive development in insulin resistance. GDM occurs in women who do not produce enough Insulin to overcome this Insulin resistance. Consequently, it is advised to have a GDM screening between weeks 24 and 28 of pregnancy [5].

Human placental lactogen (HPL) and prolactin (PRL) are two examples of lactogenic hormones that are often disregarded in relation to maternal metabolism and glucose homeostasis throughout pregnancy and, in the case of PRL, after delivery. These hormones also have potential use in diagnosis and treatment [6].

During pregnancy, elevated levels of placenta-derived human placenta lactogen (HPL) and PRL, two lactogenic hormones, may be linked to decreased insulin binding and systemic insulin resistance, but they also directly or indirectly support the parallel process of maternal pancreatic beta cell proliferation. A common ancestral gene gave rise to the members of the placental lactogenic growth hormone family, including prolactin. Prolactin has been linked to over 300 distinct functions, the majority of which are related to lactation and reproduction, hence secretion increases during pregnancy. These functions include growth, development, reproduction, metabolism, water and electrolyte balance, brain and behavior, and immune system regulation [7].

While prolactin stimulates beta cells to secrete more insulin in response to glucose, elevated insulin resistance results in decreased inhibition of hepatic gluconeogenesis, decreased inhibition of lipolysis in adipose tissue, and decreased peripheral glucose absorption [8].

Adiponectin deficiency in adipose tissue contributes to adiponectin-mediated dysregulation of glucose homeostasis in hyperprolactinemia by reducing muscle fatty acid oxidation and hepatocyte fatty acid uptake, both of which impair insulin sensitivity [9].

Aim of the Study

The aim of this study to investigate the relationship between placental lactogen and prolactin with insulin resistance in gestational diabetes mellitus compare with control groups.

MATERIAL AND METHOD

In this study, 70 blood samples were collected from pregnant women with gestational diabetes mellitus (GDM), whose ages ranged from (20-39) years. They were diagnosed by female doctors specializing In gynecology, obstetrics, and Infertility at Al-Wafa Health Center, Al-Batoul Hospital, Mosul General Hospital, and Educational Specialist In Nineveh Governorate, based on clinical examination In addition to biochemical tests for the period from October (2023) to February (2024), and 50 blood samples were taken from healthy pregnant women who did not suffer from gestational diabetes and of the same ages and were considered a control group. Relying on collecting information according to the questionnaire form, and after collecting venous blood from patients after abstaining from food (fasting) for a period of (12-14) hours from the patient and control group, it was placed in plastic Jell Tube tubes free of any anticoagulant material with clean, sterile covers. It was left at room temperature for 20 minutes until the blood coagulated, and the blood was separated

using a centrifuge for 5 minutes at a speed of 3000 rpm to obtain the blood serum, If it was drawn using a micropipette, and the serum was divided Into dry, sterile plastic Eppendorf tubes (after Measure both Insulin and glucose concentrations until the required biochemical and hormonal tests are performed [10].

Experimental Design:

Control group

This group include a pregnant woman (healthy women who do not suffer from gestational diabetes). This group was divided into two parts based on the Age as follows:

A- Group of healthy, pregnant women: Includes 25 pregnant women with age (20-29) years.

B- Group of healthy pregnant women: Includes 25 pregnant women with age (30-39) years. Group of women with gestational diabetes

This group include 70 pregnant women with gestational diabetes. This group was divided into two parts based on the Age:

A-The group of pregnant women with gestational diabetes include 35 women with age (20-29) years.

B- The group of pregnant women with gestational diabetes include 35 women age (30-39) years.

Hormonal and Biochemical Tests:

The following laboratory tests were performed: Body mass Index (BMI) determined by summing weight and height of individual. The formula is BMI= Kg/m2, glucose concentration using a ready-made test kit by using an optical extinguisher Device Spectrophotometer from the EMCLAB company (German), and insulin concentration in the blood serum using a ready-made test kit from the Roche company (German). Estimation of insulin resistance was determined by using the insulin resistance assessment guide according to the following equation: HOMA-IR = Glucose × Insulin /405. The ELISA Kit manufactured by the Sunlong Biotech Company (Chines) to estimate blood serum placental lactogen. Estimating the concentration of the prolactin hormone by using a ready-made analysis kit from the Mindray Company (Chinese).

Statistical Analysis:

The IBM SPSS statistical software program was used to gather, examine, record, and enter data. The means, standard deviations, and ranges were shown when it was established that the quantitative data distribution was parametric. A straightforward experimental setup and a fully randomized design were employed to evaluate the data after Duncan's multiple range test revealed that distinct alphabetic letters significantly differed between various parameters at the probability level ($P \leq 0.05$) [11].

RESULTS

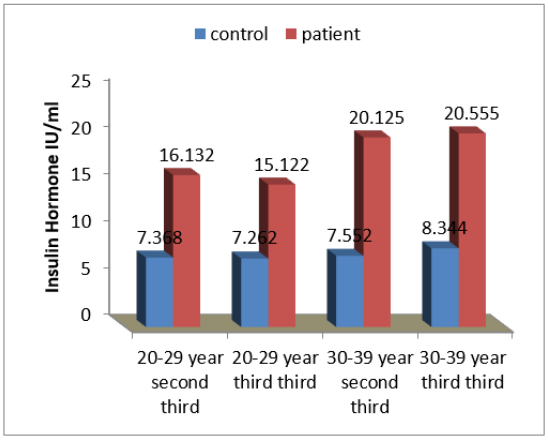
The results of the current study, as shown in the table, showed that there was a significant increase in the concentration of fasting glucose (FBS) in pregnant women with gestational diabetes in the age group (20-29) and in the 2nd and 3rd trimesters, at the level of probability ($P \leq 0.05$), as the concentration reached glucose in women with gestational diabetes in the 2nd and 3rd trimesters were (121.10, 120. 90) mg/100 ml, respectively, compared to the control group (84.80, 86.80) mg/100 ml. While the glucose concentration in the age group (30-39) and in the second and third trimesters of women with gestational diabetes reached (114.10, 111.70) mg/100 ml, respectively, compared to control (86.80, 81.40) mg/100 ml, respectively.

Table 1:The value of study parameters

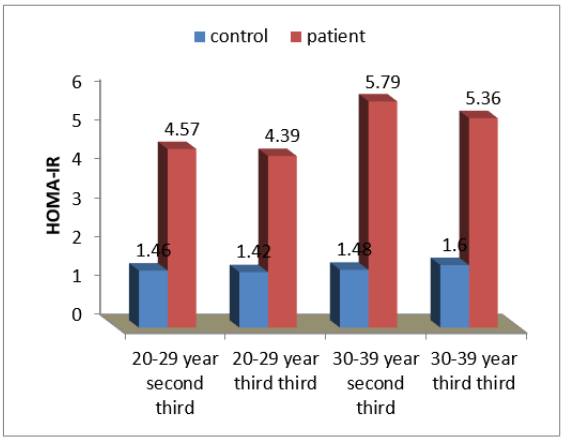
Group / Parameter	Control		Patients		Control		Patients	
	20-29 years		20-29 years		30-39 years		30-39 years	
	2nd Trimester	3rd Trimester	2nd Trimester	3rd Trimester	2nd Trimester	3rd Trimester	2nd Trimester	3rd Trimester
Glucose mg/100ml	84.80±11.69 bc	86.80±13.84 bc	121.10±21.22 a	120.90±24.93 a	86.80±15.38 bc	81.40±15.70 c	114.10±30.50 ab	111.70±31.59 ab
Insulin IU/ml	7.36±1.44 b	7.26±1.22 b	16.13±6.48 a	15.12±5.70 a	7.55±1.37 b	8.34±1.52 b	20.12±6.36 a	20.55±8.27 a
Insulin Resistance	1.46±0.27 b	1.42±0.33 b	4.57±1.99 a	4.39±2.16 a	1.48±0.31 b	1.60±0.15 b	5.79±2.62 a	5.36±2.04 a
HPL ng/ml	11.46±4.61 c	12.33±2.06 c	23.92±2.62 b	25.98±1.77 ab	11.92±3.75 c	13.26±3.23 c	27.63±1.64 a	28.61±1.06 a
PRL ng/ml	55.03±17.76 e	139.81±34.09 bc	105.61±25.81 cd	200.22±36.56 a	75.89±23.15 de	162.05±39.08 b	127.88±33.63 bc	206.11±33.09 a

The no. followed by different letters means there is a significant change. The values are means ± standard deviation SD.

The table (1) and figure (1.a) also shows that the concentration of the Insulin hormone increased significantly in the age group (20-29) and in the 2nd and 3rd trimesters at the level of probability (P≤0.05), as the concentration of the hormone insulin in women with gestational diabetes and in the second and third trimesters reached (16.13, 15.12) IU/ ml. Respectively compared to the control (7. 36, 7.26) IU/ ml, respectively. As for the age group (30-39), the Insulin concentration in women with gestational diabetes reached (20.12, 20.55) IU/ ml, respectively, compared to control (7.55, 8.34)



fig(1.a)



fig(1.b)

fig (1.a) fig(1.b)

Fig (1.a) and Fig (1.b) show the relationship between Insulin resistance and HOMA-IR

The results in the table(1) and figure(2.a) also showed a significant Increase in the concentration of Human placental lactogen (HPL) in the age group (20-29) in women with gestational diabetes in the 2nd and 3rd trimesters of pregnancy at the probability level (P≤0.05), as It reached (23.92, 25.98) ng /ml compared to the

control (11.46, 12.33) ng/ml, respectively, while in the age group (30-39) in the second and third trimesters it reached (27.63, 28.61) ng/ml, respectively, compared to the control (11.92, 13.26) ng/ml respectively.

The results in the table (1) and figure (2.b) also show a notable rise in the concentration of the prolactin hormone in the age group (20-29) and in the second and third trimesters at the probability level (P≤0.05), as it reached (105.61, 200.22) ng/ml, respectively, in women with gestational diabetes, compared to control (55.03, 139.18) ng/ml, respectively. As for the age group (30-39), the concentration of the prolactin hormone in women with gestational diabetes in the 2nd and 3rd trimesters reached (127.88, 206.11) ng/ml, respectively, compared to the control (75.89, 162.05) ng /ml respectively.

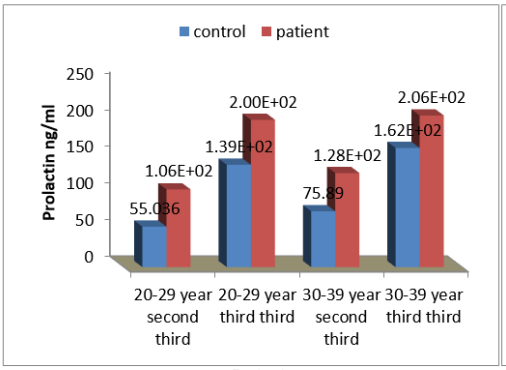


fig (2.a)

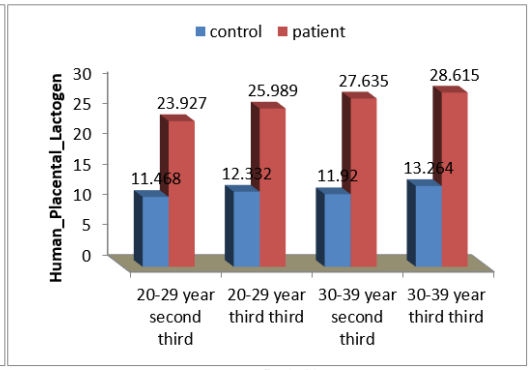


fig (2.b)

fig (2.a) fig (2.b)

DISCUSSION

The results in this study demonstrated a significant increase in the concentration of glucose, the hormone insulin, and the indicator of Insulin resistance HOMA-IR in the blood serum of pregnant women with gestational diabetes in both age groups (20-29) and (30-39) and in the 2 nd and 3 rd trimesters. In pregnant women with gestational diabetes compared with control at the level of probability (P≤0.05).

The results of this study were consistent with the fact that Insulin resistance is a hallmark of progression to GDM [12]. The results of this study were consistent with the findings of [13].

The reason for this is either inadequate beta cell growth and concurrent insulin shortage, or hyperglycemia brought on by an exceptionally high level of insulin resistance (IR), maybe as a result of insulin resistance that was there before in overweight women [14].

Insulin resistance develops while a pregnancy goes on because insulin sensitivity decreases with time. The primary causes of this insulin resistance condition include decreased plasma adiponectin and increased levels of cortisol, progesterone, tumor necrosis factor-α (TNF-α), placental growth hormone, and other anti-insulin hormones in the mother and placenta. Increased human placental lactogen (hPL) and prolactin enhance maternal beta cell mass and glucose-stimulated insulin production while insulin sensitivity decreases, maintaining steady glucose control homeostasis [15].

Increased insulin resistance causes beta cell function to become inadequately regulated, which leads to GDM [16].

Insufficient insulin secretion results from beta cells' inability to respond appropriately to changes in blood glucose levels. Insulin resistance (IR) exacerbates pancreatic beta cell dysfunction by excessively stimulating insulin production in response to elevated blood sugar [17].

The results in the table showed a significant increase in the concentration of placental growth hormone lactogen (HPL) in the blood serum of pregnant women with gestational diabetes in both age groups (20-29) and (30-39) and in the second and third trimesters in pregnant women with

diabetes. Pregnancy compared with control at the level of probability (P≤0.05). The results of this study were consistent with his findings [18,19].

This is explained by the fact that PL controls the maternal pancreatic beta cells' pregnancy adaptations, which can stop the onset of glucose intolerance during pregnancy [20,21].

Gestational diabetes occurs when a diabetic patient becomes pregnant or when a glucose tolerance disorder develops during pregnancy. In the second trimester, under the influence of hormones produced in the placenta, pronounced insulin resistance develops. At the same time, placental lactogen stimulates increased capacity of beta cells in the mother's pancreas with increased insulin production. Placental size and function influence metabolic conversion. If the mother has underlying Insulin resistance or poor ability to increase insulin secretion, gestational diabetes develops. The placentas of diabetic women show structural changes in all forms of the disease. These placentas are often larger and show changes in villous vascularity and maturation [22].

HPL is the main pro-diabetic hormone that is synthesized by the fetal unit and the placenta [23]. Because HPL promotes lipolysis, there are more free fatty acids in the blood. It gives the mother a variety of fuels to help save glucose and amino acids for the developing fetus. Consequently, the rise in the levels of free fatty acid immediately obstructs the uptake of glucose into cells that is initiated by insulin [24]. As a result, HPL is regarded as a potent inhibitor of the effects of insulin during pregnancy

The results in the table showed a notable rise in the concentration of the hormone prolactin (PRL), in the blood serum of pregnant women with gestational diabetes in both age groups (20-29) and (30-39) and in the 2nd and 3rd trimesters in pregnant women with gestational diabetes compared with control at the level of probability (P≤0.05). The results of this study were consistent with the findings of [25]. This is because, during pregnancy, prolactin is crucial in stimulating beta cell growth and insulin secretion [26].

During pregnancy, the concentration of prolactin rises, under the influence of rising levels of estrogen and progesterone [27]. Plasma prolactin levels steadily increase five to ten times.

Prolactin's effects on glucose metabolism differ depending on the physiological state. Increased prolactin levels exacerbate insulin resistance in patients, such as those with diabetes mellitus or pituitary prolactinoma [28].

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