

Evaluation of maternal serum prolactin in pregnant women with gestational Diabetes mellitus

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Abstract

Maintenance of normal glucose metabolism during pregnancy is of particular importance. Prolactin may be a mediator in pathogenesis of impaired glucose metabolism. This study aimed to assess the levels of maternal serum prolactin in pregnant women with gestational Diabetes mellitus (GDM).

This prospective observational study was done at AL– Emammain AL- Kadhemain Medical City/ Department of Obstetrics and Gynecology in Baghdad/ Iraq during the period from 1st March to 1st October 2018 on 150 pregnant women who were referred for OGTT for different indications. For all included women, maternal serum prolactin level and 75 gm OGTT was performed.

The results showed that the mean±SD of maternal serum prolactin levels for all included women was (135.14±22.67) ng/ml and there was significantly negative correlation with (1hr) and (2hr) blood glucose levels of 75 gm OGTT at p value (0.027), (0.003) respectively. Out of 150 women included in the study (52) women diagnosed to have GDM and (98) women to have normal glucose tolerance. The mean±SD of maternal serum prolactin level was (123.6±13.7) ng/ml in GDM group which is significantly lower in comparison with mean ±SD (141.3±24.1) ng/ml in normal group at p value (0.0001).

It can be concluded that women with GDM showed significantly lower serum prolactin levels in comparison with levels in women with normal glucose tolerance.

Keywords Prolactin, Glucose tolerance, GDM.

1. Introduction

Prolactin hormone is mainly synthesized and secreted by lactotrophs cells in the pituitary gland but is also produced at sites outside the pituitary gland such as mammary gland ovary, uterus, prostate, lymphocyte and brain. Prolactin plays an essential role in lactation, gonadal function, metabolism and regulation of the immune system [1].

Prolactin controls milk production (lactogenesis) but not the milk-ejection reflex; the rise in prolactin fills the breast with milk in preparation for the next feed, in usual circumstances, in the absence of galactorrhea, lactation ceases within one or two weeks following the end of breastfeeding. Levels can rise after exercise, high-protein meals, minor surgical procedures [2].

Prolactin deficiency occurs as a result of general pituitary hormone deficiency, which is characterized by the deficiency of other pituitary hormones in addition to prolactin. A primary cause of pituitary hormone deficiency is a pituitary tumour. The most striking example of prolactin deficiency is that of Sheehan syndrome, in which the anterior pituitary gland of pregnant women is partly or totally destroyed during or shortly after giving birth. This syndrome tends to occur more frequently in women who have excessive bleeding during delivery. Affected women do not produce breast milk and cannot nurse their infants [3].

Physiological changes in circulating prolactin have been associated with pregnancy, lactation, physical activity, sleep, and stress [4]. During the pregnancy period maternal prolactin increases concurrently with the increased demand for insulin to stimulate β -cell proliferation, insulin production and secretion in order to accommodate the growing fetal compartment as well as the substantial increase in insulin resistance [5,6].

Gestational diabetes mellitus is defined as impaired carbohydrate tolerance resulting in hyperglycemia which first develops or becomes diagnosed during pregnancy (46). Screening for GDM in pregnancy offers an opportunity for target surveillance and early intervention.

The risk factors for GDM include BMI >30 kg/m², GDM in previous pregnancy, Previous macrosomic baby ≥ 4.5 Kg, Family history (first degree relative with diabetes) and Family ethnic origin with a high prevalence of diabetes (47).

Glucose tolerance test is a medical test in which glucose is given and blood samples taken afterward to determine how quickly it is cleared from the blood. The test is usually used to test for diabetes, insulin resistance, impaired beta cell function and sometimes reactive hypoglycemia and acromegaly. The OGTT should be done after an overnight fasting of between 8 and 14 hours. During the previous 3 days, there must be an unrestricted diet. The patient must be seated throughout the test and not smoke [9].

2. Patients and Methods

This prospective observational study was conducted at AL-Imamain AL-Kadhmain medical city during the period from 1st march to the 1st October 2018. The study protocol was approved by the scientific council of Obstetrics and Gynecology/Iraqi Board for medical specialization and agreement of department of Obstetrics and Gynecology of AL- Imamain AL- Kadhmain medical city.

This study included 150 pregnant women in their 3rd trimester (28-36) weeks who were referred for OGTT for different indications. Verbal consents were taken from all included women and maternal characteristics were evaluated including age, parity, gestational age and body mass index. For each included women, serum prolactin level was estimated and 75g oral GTT was performed.

Maternal age (20-30) years, parity (0-6), gestational age (28 and above) weeks with a single viable fetus and BMI (21.5-30) kg/m² were included in our study, while the past medical history of pituitary disease, past medical history of thyroid disease, using some medications such as corticosteroid, beta-blockers, diuretics, antidepressant, history of chronic renal disease and women who are lactating while they are pregnant were excluded from the study.

Evaluation of all included women were done including obstetric and U/S examination. Confirmation of gestational age was done by LMP and corresponding early pregnancy ultrasound scan.

BMI was calculated by dividing body weight (kg)/ height (M)².

On the day of the test blood sample for fasting serum prolactin level and fasting blood glucose level were taken.

To all studied women, 75grams of sugar in 8 ounces equal to cup of water were given to drink. 1hr and 2 hr blood glucose levels were estimated. If a patient lost the glucose by vomiting the test was discontinued.

Gestational diabetes mellitus is diagnosed if one or more reading exceeded the following according IADPSG criteria: Fasting plasma glucose \geq (5.1) mmol/L (92mg/dL), 1-hour plasma glucose \geq (10.0) mmol/L (180 mg/dL) and 2-hour plasma glucose \geq (8.5) mmol/L (153 mg/dL).

From each women (5) ml venous blood sample was taken, and serum samples were obtained after centrifugation to estimate S. prolactin levels by using ELFA technique (Enzyme Linked Fluorescent Assay).

Statistical Analysis

Analysis of data was carried out using (Statistical Packages for Social Sciences-version 25).

The significance of difference of different means (quantitative data) were tested using Students-t-test to compare between two independent means. The significance of difference of different percentages (qualitative data) were tested using Pearson Chi-square test (χ^2 -test) with application of Yate's correction or Fisher Exact test whenever applicable. Statistical significance was considered whenever the P value was equal or less than 0.05.

3. Results

Table (1) showed maternal characteristics in all the study cases. Regarding maternal age, the Mean±SD was 27.3±4.8 and range was (20-38), for parity the Mean±SD was (1.8±1.2) and range was (0-6), and for gestational age, the Mean±SD was (31.8±2.5), and range was (28-36), while for BMI, the Mean±SD was (26.88±1.70) and range was (21.5-30.0).

Table 1. Maternal characteristics in all study cases

		No	%
Age (years)	<20y	-	-
	20---24	49	32.7
	25---29	47	31.3
	30---34	38	25.3
	=>35y	16	10.7
	Mean±SD (Range)	27.3±4.8 (20-38)	
Parity	Primi	20	13.3
	Para 1	45	30.0
	Para 2	51	34.0
	Para 3	26	17.3
	Para 4 & more	8	5.3
	Mean±SD (Range)	1.8±1.2 (0-6)	
Gestational age (weeks)	28---	39	26.0
	30---	33	22.0
	32---	34	22.7
	34---	44	29.3
	Mean±SD (Range)	31.8±2.5 (28-36)	
BMI (Kg/m2)	Normal (18.5-24.9)	13	8.7
	Overweight (25.0-29.9)	131	87.3
	Obese (=>30.0)	6	4.0
	Mean±SD (Range)	26.88±1.70 (21.5-30.0)	

Table (2) showed that the mean \pm SD of prolactin distribution was (135.14 \pm 22.67) ng/ml, and the range was (90-199).

Table 2. Distribution of prolactin levels in all study cases

		No	%
Serum prolactin (ng/ml)	<100	2	1.3
	100---	11	7.3
	110---	12	8.0
	120---	46	30.7
	130---	27	18.0
	140---	25	16.7
	150---	2	1.3
	160---	6	4.0
	170---	8	5.3
	180---	7	4.7
	190---199	4	2.7
	Mean\pmSD(Range)		135.14\pm22.67(90-199)

Table (3) showed the 75g OGTT results (mmol/L) in all study cases. At (0 hr), the Mean±SD was (4.85±0.28) and the range was (3.9-5.7). At 1hr, the Mean±SD was (9.22±0.61) and the range was (7.5-10.0). At 2hr, the Mean±SD was (8.26±0.79) and the range was (7.0-11.0).

Table 3. 75g OGTT results (Mmol\L) in all study cases

GTT Results	Mean±SD	(Range)
0 hour	4.85±0.28	(3.9-5.7)
1 hour	9.22±0.61	(7.5-10.0)
2 hours	8.26±0.79	(7.0-11.0)

Out of 150 women included in the study, (52) women were diagnosed to have GDM and (98) women to have normal GTT.

Table (4) showed comparison of maternal characteristics and serum prolactin levels in GDM group and normal group. In GDM group, the mean±SD of maternal age was (26.6±4.3), with a range of (20-35), while in normal GTT group, the mean±SD was (27.6±5.0), with a range of (20-38) at p value = (0.239). In the GDM group, the mean±SD of parity was (1.6±0.96), with a range of (0-4), while in normal GTT group the mean±SD was (1.8±1.3), with a range of (0-6) at p value = (0.248). In the GDM group, the mean±SD of gestational age was (32.0±2.4), with a range of (28-35) and in normal GTT group, the mean±SD was (31.7±2.5), with a range of (28-36) at p value = (0.385). The mean±SD of BMI in the GDM group was (27.3±1.7), with a range of (24-30), while in normal GTT group, the mean±SD was (26.6±1.7), with a range of (21.5-30) which is significantly higher in GDM group at p value = (0.019). Concerning maternal serum prolactin levels (ng/ml) in the GDM group, the mean±SD was (123.6±13.7), with a range of (99-170). While in the normal group, the mean±SD was (141.3±24.1), with a range of (90-199) at p value = (0.0001), which is significantly lower in the GDM group.

Table 4. Comparison of maternal characteristics and serum prolactin in GDM group and normal group

		GDM No. (52)	Normal No. (98)	P value
Age (years)	Mean±SD(Range)	26.6±4.3(20-35)	27.6±5.0(20-38)	0.239
Parity	Mean±SD(Range)	1.6±0.96(0-4)	1.8±1.3(0-6)	0.248
Gestational age (weeks)	Mean±SD(Range)	32.0±2.4(28-35)	31.7±2.5(28-36)	0.385
BMI (Kg/m ²)	Mean±SD(Range)	27.3±1.7(24-30)	26.6±1.7(21.5-30)	0.019#
Serm prolactin	Mean±SD(Range)	123.6±13.7(99-170)	141.3±24.1(90-199)	0.0001#
*Significant difference between proportions using Pearson Chi-square test at 0.05 level.				
#Significant difference between independent means using Students-t-test at 0.05 level.				

Table (5) showed comparison of GTT results between GDM and normal group. At 0 hr in GDM group, the mean±SD was (4.92±0.34), while in the normal group, the mean±SD was (4.82±0.23), p value was (0.029), which is significantly higher in the GDM group. At 1hr in GDM group, the mean±SD was (9.60±0.44). In the normal group, the mean±SD was (9.02±0.59), p value was (0.0001) which was significantly higher in the GDM group. At 2hr in GDM group, the mean±SD was (9.02±0.77), while in normal group, the mean±SD was (7.85±0.39), which was significantly higher in GDM group at p value =0.0001.

Table 5. Comparison of GTT results between GDM and normal group

	GDM	Normal	P value
GTT 0hour (Mmol/L)	4.92±0.34	4.82±0.23	0.029#
GTT 1hour (Mmol/L)	9.60±0.44	9.02±0.59	0.0001#
GTT 2hours (Mmol/L)	9.02±0.77	7.85±0.39	0.0001#
#Significant difference between independent means using Students-t-test at 0.05 level.			

4. Discussion

The present study evaluated the association between maternal serum prolactin levels in the 3rd trimester of pregnancy and glucose tolerance in 150 pregnant women at risk of gestational diabetes.

(Ekinici EL et al, 2017) [10], in their study, also found that there is significant correlation between maternal serum prolactin levels and 2hr blood glucose levels of GTT, but they demonstrated that higher maternal serum prolactin levels were associated with glucose intolerance which did not coincide with the results of the present study as we found that out of 150 included women, (52) were diagnosed to have gestational diabetes with mean \pm SD of maternal serum prolactin level (123.6 \pm 13.7) ng/ml, and (98) women have normal GTT with mean \pm SD of serum prolactin (141.3 \pm 24.1) ng/ml, which is significantly lower in comparison with gestational diabetes at (p=0.0001).

(Mohammed H. Shalayel et al, 2010) [11], in their study, compared serum prolactin levels between women with gestational diabetes and healthy control group and found that maternal prolactin levels were recorded to be higher in the control group but the results were statistically not significant; they also found that prolactin increased progressively as pregnancy advanced and its peak levels were demonstrated in the 3rd trimester, they attributed the decrease in prolactin level in gestational diabetes to decrease in insulin secretion since insulin stimulates both acute secretion and de novo synthesis of decidual prolactin.

(Makoto Daimon et al, 2017) [12] Stated that studies on serum prolactin levels within the physiological range showed conflicting results. In this study, the range of prolactin levels in all included women were found to be within the normal physiological range which was (90-199), and it was (99-170) for GDM group and (90-199) for normal group.

The role of prolactin on glucose metabolism and insulin resistance depends on its circulating concentrations. Physiologically elevated levels help normal adaptive increase in insulin secretion through expanding B-cell mass and improvement of insulin sensitivity, while pathological levels could be different as they exacerbate insulin resistance and are associated with higher risk of hyperglycemia and obesity [13].

(Deepti Shroff Karhade and David C. Wang, 2016) [14] found that high intra partum fasting serum prolactin levels are associated with decrease risk of postpartum

pre diabetes and diabetes, and they performed OGTT for included women 3 months postpartum and concluded that significantly higher prolactin levels are associated with normal postpartum glucose tolerance.

The same result was found by (Ravi Retnakarn et al, 2016) [15] who concluded that serum prolactin in pregnancy can provide insight in to postpartum diabetes risk. In our study, higher prolactin levels were associated with normal antepartum glucose tolerance. Lactogens including human placental lactogen and prolactin, are major stimuli for adaptation of the endocrine pancreas during gestation and the hormone control of lactation led by prolactin may cause regulation of adipocyte biology and metabolism of glucose and lipids [16].

During pregnancy, levels of prolactin and prolactin receptors elevate in parallel with the increase of β -cell mass and glucose-stimulated insulin secretion to up regulate islet cell function and maintain normal glucose homeostasis [17].

Banerjee RR et al, 2016) [18], in their study, showed that loss of (PRLR) signaling in B-cells results in gestational diabetes and failure to expand B-cell mass during pregnancy and this is another explanation of the association of gestational diabetes with lower serum prolactin levels.

Li J et al, 2018) [19] concluded that normally high circulating total prolactin concentrations are associated with a lower risk for type 2 Diabetes and a biologically normal range of prolactin may play a protective role in the pathogenesis of this condition.

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