

## Estimation of Prolactin Level in Iraqi Diabetic Women of Menopause

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### ABSTRACT

**Background:** Menopause is the stage of a woman's life when her menstrual cycles cease for good. In the early stages of menopause, cardiovascular risk significantly rises, primarily as a result of the loss of estrogen's protective effects. **Objective:** The objective of the current study was to measure the prolactin level in menopausal diabetic Iraqi women as well as the correlation between prolactin levels and other biochemical markers. **Methods:** This study was carried out on fifty patients women with diabetes type 2 during menopause aged (40–48 years) who visited the National Diabetes Center/AL-Mustansiriya University, Baghdad-Iraq. On the other hand, forty healthy women without diabetes aged (40–48 years) were recruited as control. The study included measurements of the biochemical parameters such as, glyated hemoglobin HbA1c by using (Bio-Rad device, France), Prolactin (PRL) estimated by using (minividas device, Biomerieux-France). Fasting blood sugar (FBS), total cholesterol (TC), triglycerides TG, and high-density lipoprotein HDL were evaluated enzymatically by an auto-analyzer (Kenza 240 TX analyzer) (Biolabo, France). **Results:** The clinical biochemical markers showed that the serum levels of prolactin, fasting blood sugar (FBS), body mass index (BMI), HBA1c, TC, TG, low-density lipoproteins LDL and very low-density lipoproteins (VLDL) were increased significantly, while the decreased level of serum (HDL) in diabetic women of menopause as compared with healthy women (P=0.0001). **Conclusion:** As a result of the considerable changes in prolactin levels and altered serum lipid profiles associated with menopause, cardiovascular disease development is at increased risk on its own.

### Introduction:

In the majority of women's lives, menstruation ends permanently during the menopause. The menopausal age indicator may significantly impact women's health due to various hormonal settings[1]. Early menopause is referred to as such a condition if it affects women before age 45 [2]. Cardiovascular risk significantly rises during early menopause, primarily as a result of the loss of estrogen's protective effects [3]. Due to decreased ovarian activity, menopause has been linked to an increase in belly obesity. In postmenopausal women, these modifications to body composition may result in issues with insulin sensitivity and glucose metabolism [4].

Type 2 diabetes risk and early menopause have not always been linked by study [5]. One of the biggest issues affecting public health in the twenty-first century is diabetes. A startling 537 million persons globally were estimated to have diabetes in 2021. The International Diabetes Federation (IDF) predicted the number would rise to 643 million by 2030[6].

According to estimates from the World Health Organization, there were 422 million cases of diabetes worldwide in 2014, up from 108 million cases in 1980[1]. Aging, modern lifestyle, obesity epidemic, insulin resistance, and illnesses including sleep problems and depression that each individually increase the risk of T2DM put midlife women at substantial risk for the condition[7]. A peptide hormone called prolactin is released by the anterior pituitary gland to regulate glucose metabolism and insulin sensitivity. It is associated with some conditions correlated with

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atherosclerosis [8][9]. Its receptors are found throughout the body in many different tissues and organs, including fat, the liver, and the pancreas . PRL can increase insulin production, encourage beta cell growth, and participate in the regulation of glucose metabolism, by stimulating the peroxisome proliferator-activated receptor. PRL can also promote adipocyte growth and reduce lipolysis [10]. Despite this, there is mounting evidence that it is a pleiotropic factor with more than 300 biological roles that have been identified thus far [11]. Additionally, it has a variety of roles in metabolism, milk secretion, and the stimulation of breast growth. According to experimental investigations, PRL affects food intake, body weight gain, and insulin resistance by preventing the generation of adiponectin and IL-6 in adipose tissue, which may result in type 2 diabetes mellitus. However, experimental studies have also shown that PRL influences pancreatic cell development and lowers the threshold for glucose-stimulated insulin release [12]. Ages 30 to 50 seem to have higher levels in women than in males [13]. The lack of estrogen during menopause directly impacts CVD risk factors such as dyslipidemia, diabetes mellitus, obesity, or hypertension, raising the risk of CVD in menopausal women [14]. An atherogenic lipid profile, including an increase in T.C, LDL-C, TG, apolipoprotein B (apoB), and maybe lipoprotein (a) Lp(a), a reduction in HDL-C, and obesity are linked to the menopause transition[15][16]. After the loss of ovarian hormone secretion, alterations in the size and density of these lipoprotein particles are anticipated to occur in addition to these significant lipid abnormalities. This explains a portion of postmenopausal women's higher cardiovascular risk, especially in those whose menopause began sooner [17].

## Materials and Methods:

### Population and study design

This cross-sectional study was conducted on fifty patient's women with diabetes type 2 during menopause aged (40–48) years. This study also included forty healthy women as control aged (40–48) years. The data for this study was collected and analyzed completed from 2018 to 2023. Five milliliters (5 mL) of venous blood were collected from all patients enrolled in this study. Each patient had blood drawn in the morning 8.00-8.30 Am ) after the patient's psychological

condition had stabilized over the fasting interval of 10 to 12 hours. The blood was separated into small amounts, (2 ml) were utilized to assay glycated hemoglobin (HbA1c), and (3 ml) were held in simple tubes until coagulation was completed. The serum was subsequently separated by centrifugation for 10 minutes at a speed of 3000 revolutions per minute, and it was then stored frozen (-20 °C) for analysis.

### Biochemical Measurements

glycated hemoglobin (HbA1c) concentration was determined by A bio-Rad device from a French company. Prolactin was estimated by using minivans (Biomérieux company).Fasting blood sugar FBS, total cholesterol T.C ,triglycerides TG and High-density lipoprotein HDL were assessed enzymatically and photometrically by an auto-analyzer (Kenza 240 TX analyzer) supplied by (Biolabo company,France), while low-density lipoprotein cholesterol LDL-c and very low-density lipoprotein VLDL-c were calculated as described by the Friedewald equation.

$$\text{VLDL-c (mg/dL)} = \text{TG}/5$$

$$\text{LDL-c (mg/dL)} = \text{T.C} - (\text{HDL-c} + \text{TG}/5)[18].$$

The medical staff assessed anthropometric measures including waist, hip, height, and body weight to determine body mass index (BMI) using this equation :  $\text{BMI} = (\text{weight}/\text{kg}) / (\text{height m}^2)$ [13]. Date of birth, gender, and history information including duration of diabetes was also requested and documented.

### Statistical Analysis

Statistical analysis was performed using software SPSS 26.0 and all experimental values were analyzed and presented as means  $\pm$  standard deviation (SD), where Student's t-test was used to compare the difference in the mean values of any two groups. In addition, the Pearson correlation coefficient was used to describe the status and strength of association between prolactin and other factors, the results were considered statistically significant if ( $P \leq 0.05$ ).

### Results:

The anthropometric information for the control group and the diabetic women in menopause is shown in Table (1). The mean levels of weigh ( $88.56 \pm 14.3$  kg),

body mass index ( $31.72 \pm 4.1 \text{ kg/m}^2$ ), waist ( $106.3 \pm 10.07 \text{ cm}$ ) and Hip ( $106.5 \pm 9.24 \text{ cm}$ ) increased in women patients compared with control group ( $79.85 \pm 15.40 \text{ kg}$ ), ( $27.83 \pm 4.84 \text{ kg/m}^2$ ), ( $84.4 \pm 8.31 \text{ cm}$ ) and ( $98.52 \pm 11.1 \text{ cm}$ ) respectively, with high significant differences ( $P \leq 0.05$ ), while the level of height ( $166.49 \pm 9.94 \text{ cm}$ ) a less compared with healthy women ( $169.2 \pm 6.04 \text{ cm}$ ) with no significant difference ( $P \geq 0.05$ ).

**Table 1: (Mean ±SD) anthropometric characteristics of the studied groups**

Parameter	Mean±SD		p-value
	Control (n=40)	patients (n=50)	
Weight(kg)	79.85 ±15.40	88.56±14.3	0.007
Height(cm)	169.2±6.04	166.49±9.94	0.18
BMI (kg/m <sup>2</sup> )	27.83±4.84	31.72±4.1	0.0001
Waist(cm)	84.4±8.31	106.3±10.07	0.0001
Hip(cm)	98.52±11.1	106.5±9.24	0.0001

For the clinical characteristics shown in Table (2) it found serum levels of prolactin ( $30.40 \pm 10.31 \text{ ng/ml}$ ), FBS ( $196.9 \pm 54.1 \text{ mg/dl}$ ), HbA1c ( $8.52 \pm 1.48\%$ ), TC ( $226.2 \pm 51.98 \text{ mg/dl}$ ), TG ( $207.7 \pm 77.7 \text{ mg/dl}$ ), LDL ( $146.3 \pm 53.23 \text{ mg/dl}$ ), and VLDL ( $41.41 \pm 15.64 \text{ mg/dl}$ ) increased with a high significant difference ( $P=0.0001$ ) in diabetic women of menopause compared with healthy women ( $25.9 \pm 4.6 \text{ ng/ml}$ ), ( $88.12 \pm 7.18 \text{ mg/dl}$ ), ( $4.81 \pm 0.32\%$ ), ( $146.8 \pm 21.6 \text{ mg/dl}$ ), ( $92.47 \pm 8.14 \text{ mg/dl}$ ), ( $75.6 \pm 23.4 \text{ mg/dl}$ ), and ( $18.49 \pm 1.62 \text{ mg/dl}$ ) respectively, while decreased level of serum (HDL) in patients group ( $38.54 \pm 4.64 \text{ mg/dl}$ ) compared with control ( $52.7 \pm 5.53 \text{ mg/dl}$ ) with high significant difference ( $P=0.0001$ ).

**Table 2: (Mean ±SD) clinical characteristics of the studied groups**

Parameter	Mean±SD		p-value
	Control (n=40)	patients (n=50)	
Prolactin (ng/ml)	25.9±4.6	30.40±10.31	0.007
FBS (mg/dl)	88.12±7.18	196.9±54.1	0.0001
HbA1c (%)	4.81±0.32	8.52±1.48	0.0001
TC(mg/dl)	146.8±21.6	226.2±51.98	0.0001

TG(mg/dl)	92.47±8.14	207.7±77.7	0.0001
HDL(mg/dl)	52.7±5.53	38.54±4.64	0.0001
LDL(mg/dl)	75.6±23.4	146.3±53.23	0.0001
VLDL (mg/dl)	18.49±1.62	41.41±15.64	0.0001

Table (3) measured the strength of the association between prolactin and the other elements in postmenopausal Iraqi women with diabetes, where it was found a weak positive correlation with each (weight, BMI, waist, Hip, TC, TG, LDL, and VLDL) while appearing the prolactin weak negative correlation with (HDL, FBS, and HbA1c).

**Table 3: Correlation between prolactin and different parameters in group patients**

parameters	Prolactin	
	r	p-value
Weight (kg)	0.267	0.06
Height(cm)	0.179	0.214
BMI (kg/m <sup>2</sup> )	0.176	0.22
Waist (cm)	0.259	0.06
Hip(cm)	0.257	0.07
FBS (mg/dl)	-0.229	0.109
HbA1c(%)	-0.198	0.169
TC (mg/dl)	0.087	0.55
TG (mg/dl)	0.060	0.67
HDL (mg/dl)	-0.117	0.41
LDL (mg/dl)	0.085	0.55
VLDL (mg/dl)	0.034	0.812

**Discussion:**

In this study, there is a significant increase in serum levels of (FBS and HbA1c) in diabetic women menopausal compared with healthy women, this is consistent with the previous study done by *Ajam et al* [19] and *Hussein S Z and Al- Samarrai A H* [20]. The increase in abdominal fat buildup that occurs with aging is a key factor in the relationship between diabetes and age. In addition, the loss of muscular mass and strength important components for glucose metabolism causes older persons to engage in less physical exercise. Finally, these modifications increase insulin resistance. Therefore, the aberrant glucose metabolism seen in

elderly persons is largely explained by the interaction between increasing insulin resistance and decreased insulin production, which is also caused by several anomalies in beta-cell islets and insulin secretion[4]. The findings supported a recent study by [21] and showed that diabetic women in menopause had higher prolactin levels than the control group [21]. The pituitary hormone prolactin is required for the start and maintenance of lactation as well as many other physiological functions in the body. In addition to metabolism, immunological control, brain activity, behavior, and osmoregulation [18].

Previous small-scale studies linked the hyperprolactinemia with atherosclerosis and cardiovascular disease risk factors such as insulin resistance, Low-grade inflammation, deteriorated endothelial function, elevated thrombosis risk, dyslipidemia. Furthermore, individuals with acute coronary syndrome, myocardial infarction, and stroke had considerably higher serum prolactin concentrations than did healthy controls [22][23]. In line with [21], the current data showed that diabetic women had higher body mass indices (BMI) than healthy women, as indicated in table (1), we discovered a substantial rise in the mean values of (waist and hip) in these patients when compared with control. A challenge for postmenopausal women is obesity. This is a result of estrogen loss and growth hormone reduction. The quick increase in fat may be explained by the drop in these two hormones [20]. Therefore, it is plausible that BMI has an impact on reproductive hormones in a way unrelated to how it affects metabolic syndrome [24]. The strongest predictor of coronary heart disease and type 2 diabetes, regardless of BMI>30, is abdominal obesity. Prior research revealed that abdominal obesity, high BMI and large waist circumference are a major risk factors for diabetic, atherogenic, prothrombotic, inflammatory disorders and cardiovascular disease [25]. Analysis of lipid profiles in groups studied showed interesting results. Except for HDL cholesterol, which fell in comparison to control groups as indicated in table (2), all lipid profile measures increased in diabetic patients women going through menopause. These results were somewhat consistent with[26] and a prior study conducted by[27][15][28][29] as well, which demonstrate a substantial difference between

postmenopausal individuals and premenopausal (control group). Numerous epidemiological studies suggest menopause-associated changes in the lipid profile [30]. Menopause causes lipid profile alteration by increasing the levels of T.C, TG, LDL, and VLDL. Therefore the risk of cardiovascular disease after menopause will be higher, due to the change in their lipid pattern, loss of ovarian function, and loss of estrogen effect in protecting the cardiovascular system [29][31]. Changes in lipid metabolism and an abundance of adipose tissue have a significant impact on the production of extra fatty acids, adipocytokines, proinflammatory cytokines, and reactive oxygen species that cause lipid peroxidation and result in the development of insulin resistance, abdominal adiposity, and dyslipidemia [32]. Diabetes is another contributory factor of dyslipidemia due to insulin resistance[28]. Lack of estrogen results in higher levels of total cholesterol and lipoproteins, which create a lipid profile that is extremely favorable to atherogenic potential [33]. The level of LDL-C in women also tends to rise in the same proportion as it does in men after menopause due to the absence of estrogen, which also causes an increase in hepatic cell surface LDL-C receptors and a quick elimination of LDL-C particles in premenopausal women. However, its clearance is decreased during menopause due to low estrogen synthesis [34]. Additionally, according to Shende S et al., increasing serum triglyceride levels in this study may be caused by an estrogen-related decline in lipoprotein lipase (LPL) activity following the loss of ovarian function [35]. Low levels of HDL in diabetic women in postmenopause might not result from the loss of female sex hormones, but from the aging process[36].

## **Conclusion**

As a result of the altered serum lipid profile associated with menopause, cardiovascular disease development is at increased risk on its own. The physiological changes that occur during menopause are diabetic females due to reduced estrogens which lead to a shift towards a more atherogenic lipid profile. In this study, we found dyslipidemia common in menopausal and demonstrated that cardiovascular risk factors like TC, LDL, VLDL, and TG were increased progressively with the duration of menopause while HDL was decreased. Our study also found a significant increase in



levels of (prolactin, HbA1C, and FBS) during the menopausal transition. According to the study, prolactin plays a significant role in the pathophysiology of insulin resistance and diabetes mellitus. Furthermore, we recommended that the measure of (lipid profile, prolactin, HbA1C, and BMI) should be done routinely for menopausal diabetic females to correct their condition.

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Nil

#### Conflicts of interest

The authors declare that they have no conflicts of interest.

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#### Abbreviations

Fasting blood sugar (FBS), Total cholesterol (TC), Triglycerides TG, High-density lipoprotein (HDL), Glycated hemoglobin (HbA1), Prolactin (PRL). Body mass index (BMI)

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## تقدير مستوى البرولاكتين لدى النساء العراقيات المصابات بداء السكري في مرحلة سن اليأس

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### الخلاصة :

الخلفية النظرية: سن اليأس هو الوقت الحرج في حياة معظم النساء عندما تتوقف فترات الحيض بشكل دائم، ففي سن اليأس المبكر تزداد مخاطر الإصابة بأمراض القلب والأوعية الدموية بشكل كبير ، ويرجع ذلك أساساً إلى فقدان الآثار الوقائية لهرمون الاستروجين. الهدف من الدراسة: هدفت الدراسة الحالية إلى تقييم مستوى البرولاكتين في مصل الدم لدى النساء العراقيات المصابات بداء السكري في سن انقطاع الطمث، وكذلك لإيجاد علاقة بين مستوى البرولاكتين والمتغيرات البيوكيميائية الأخرى. المواد وطرائق العمل: أجريت هذه الدراسة على خمسين مريضة مصابة بالسكري من النوع الثاني في مرحلة سن اليأس تتراوح أعمارهن بين (40-48 سنة) قاموا بزيارة المركز الوطني للسكري / الجامعة المستنصرية ، بغداد ، العراق. من ناحية أخرى ، تم تجنيد أربعين امرأة سليمة تتراوح أعمارهن بين (40-48 عامًا) كمجموعة تحكم. تضمنت الدراسة قياس المتغيرات الكيميائية الحيوية الآتية: تقدير الهيموغلوبين السكري (HbA1c) باستخدام جهاز الفرنسي الميثا (Bio-Rad)، كما تم تقدير البرولاكتين مناعياً باستخدام جهاز (minividas) المجهز من شركة (Biomerieux) الفرنسية، في حين تم تقييم سكر الدم، الكوليسترول الكلي (TC)، والدهون الثلاثية (TG)، والبروتين الدهني عالي الكثافة (HDL) إنزيمياً بواسطة جهاز المحلل التلقائي (Kenza 240 TX analyzer) المجهز من شركة (Biolabo) الفرنسية. النتائج: أظهرت الدراسة ان الاختبارات السريرية لكل من (البرولاكتين، سكر الدم الصائم (FBS)، مؤشر كتلة الجسم (BMI)، السكر التراكمي (HbA1c)، الكوليسترول الكلي (TC)، الدهون الثلاثية (TG)، البروتينات الدهنية منخفضة الكثافة (LDL) والبروتينات الدهنية منخفضة الكثافة جداً (VLDL) قد زادت معنوياً وبشكل ملحوظ ، بينما انخفض مستوى (HDL) لدى النساء المصابات بالسكري في سن اليأس مقارنة بالنساء الأصحاء (P=0.0001). تم قياس قوة الارتباط بين البرولاكتين والمتغيرات السريرية الأخرى في النساء المرضي، حيث وجد هناك ارتباط إيجابي ضعيف بين البرولاكتين مع كل من (الوزن، مؤشر كتلة الجسم، الخصر، الورك، TC ،TG ،LDL وVLDL)، بينما أظهرت النتائج وجود ارتباط سلبي ضعيف بين البرولاكتين مع (HDL وFBS وHbA1c). الخلاصة: يرتبط انقطاع الطمث بتغيرات كبيرة في مستويات البرولاكتين وتغير مستوى الدهون في الدم وبالتالي تعتبر عامل خطر مستقل للإصابة بأمراض القلب والأوعية الدموية.

الكلمات المفتاحية : صور الدهون ، البرولاكتين ، داء السكري من النوع الثاني، سن اليأس، الهيموغلوبين السكري.