

Serum Adiponectin Marker in Women with Polycystic Ovary Syndrome

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Abstract

Background: One of the leading causes of female infertility is polycystic ovarian syndrome (PCOS). Adiponectin is one of many adipokines adipose tissue releases that affect insulin resistance (IR).

Objective: To measure PCOS participants' IR, adiponectin, and serum insulin levels.

Materials and procedures: a case-control study involving 80 patients with PCOS (40 obese and 40 nonobese) and 80 controls (40 obesity and 40 nonobese). Adiponectin was measured using an enzyme-linked immunosorbent assay, while serum levels of insulin and FBS were measured using a chemiluminescent automated immunoassay system (ECL).

Results: Regardless of body mass index and PCOS, women had lower levels of adiponectin and higher levels of blood fasting glucose, insulin, and IR compared to the relevant with a p-value of ≤ 0.001 for controls.

Conclusion: According to weight, blood adiponectin levels inversely correspond to IR. It can, therefore, act as an indicator in PCOS-affected women.



مؤشر الأديبونيكتين في مصل الدم لدى النساء المصابات بمتلازمة تكيس المبايض

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الخلاصة

المقدمة: أحد الأسباب الرئيسية للعقم عند النساء هو متلازمة المبي

ض المتعدد الكيسات (PCOS). الأديبونيكتين هو واحد من العديد من الأديبوكينات التي تفرزها الأنسجة الدهنية والتي تؤثر على

مقاومة الأنسولين (IR).

الهدف: قياس مستويات مقاومة الانسولين والأديبونيكتين

والأنسولين في الدم لدى المشاركين في متلازمة تكيس المبايض.

المواد والإجراءات: دراسة الحالات والشواهد التي تشمل ٨٠ مريضاً يعانون من متلازمة تكيس المبايض (٤٠ يعانون من السمنة المفرطة و ٤٠ من غير المصابين بالسمنة) و ٨٠ من الضوابط (٤٠ من السمنة و ٤٠ من غير المصابين بالسمنة). تم قياس الأديبونيكتين باستخدام مقايصة الامتصاص المناعي المرتبط بالإنزيم، في حين تم قياس مستويات مصل الأنسولين ومستويات سكر الصيام باستخدام نظام المقايصة المناعية الآلي الكيميائي (ECL)

النتائج: بغض النظر عن مؤشر كتلة الجسم ومتلازمة تكيس المبايض، كان لدى النساء مستويات أقل من الأديبونيكتين ومستويات أعلى من الجلوكوز في الدم أثناء الصيام، والأنسولين، ومقاومة الانسولين مقارنة مع القيمة الاحتمالية ٠,٠٠١ ≤ للضوابط.

الاستنتاج: وفقاً للوزن، فإن مستويات الأديبونيكتين في الدم تتوافق عكسياً مع الأشعة تحت الحمراء. وبالتالي يمكن أن يكون بمثابة مؤشرات لدى النساء المصابات بمتلازمة تكيس المبايض.

1. Introduction

The majority frequent reason for hyperandrogenism and anovulatory infertility in women of reproductive age is polycystic ovary syndrome (PCOS), a common heterogeneous condition. In addition to impaired ovarian steroidogenesis, complicated pathogenesis includes: (a) hypothalamic-pituitary gonadotropin secretion disruptions in particularly elevated levels of LH; (b) diminished ovarian steroidogenesis; and (c) compensatory hyperinsulinemia brought on by insulin resistance (IR), which increases androgen production and decreases the synthesis of sex hormone-binding globulin (SHBG), contributing to PCOS-associated (Khan, Stas and Kurukulasuriya, 2006). Women with PCOS have a five to ten times higher than average chance of developing type 2 diabetes mellitus. (Ovalle and Azziz, 2002). Within the etiology of PCOS-related hyperandrogenism, insulin has both direct and indirect functions. LH (luteinizing hormone) and insulin work together to increase the production of androgen in theca cells. (Ehrmann *et al.*, 2005). Both thin and fat women with PCOS have IR, however, obesity and PCOS may have an independent

impact on IR (Dunaif *et al.*, 1989). Target tissues include skeletal muscles and adipose tissue, as well as the liver fails to respond appropriately to normal plasma insulin concentrations in IR (Longo, 2012). In industrialized nations, obesity is a disease that is spreading quickly and causes both adipocyte hyperplasia and hypertrophy (Kahn and Flier, 2000). Women with PCOS are more likely to have central obesity (50%) and more elevated peripheral IR. Several adipokines, including leptin, adiponectin, resistin, and vaspin, are released by visceral adipose tissue (Fukuhara *et al.*, 2005). A protein known almost solely as adiponectin produced via adipocytes, is thought to have insulin-sensitizing, anti-inflammatory, anti-diabetic, and anti-atherogenic effects at high levels, whereas low amounts are linked to obesity, insulin resistance, metabolic syndrome, type 2 diabetes, and cardiovascular disease (CVD) (Toulis *et al.*, 2009). In the current study, we compare obese and non-obese PCOS patients with the corresponding controls in terms of blood adiponectin levels, insulin, and IR.

2. Material and Methods

From November 2022 to April 2023, a case-control study was conducted in the Chemistry and Biochemistry Department at Kerbala College of Medicine, Iraq. It included 80 PCOS women with a diagnosis (40 obese and 40 non-obese) and 80 controls (40 obese and 40 non-obese) between the ages of 18 and 40.

Women who are younger than 18, those with any known illnesses, infections, or inflammatory problems, Cushing's syndrome, hyperprolactinemia, and congenital adrenal hyperplasia, or who were any of the medication had been prohibited from participating in the current investigation. The institutional ethics committee received permission from the ethical committee. Participants' informed consent was acquired. Each subject underwent a physical examination. Each person's height and weight were recorded. By using kg/m², the body mass index (BMI) was computed.

According to the Rotterdam ESHRE (European Society of Human Reproductive Medicine) updated consensus 2003 (Fauser *et al.*, 2012), PCOS was diagnosed.

Each participant in the trial provided a fasting blood sample of 6 ml. A chemiluminescent automated immunoassay system (ECL) (Cobas e 411, Roche Diagnostic, Germany) was used to test fasting serum glucose and insulin. The enzyme-linked immunosorbent test was used to quantify serum adiponectin. The following formula was used to calculate IR by the homeostasis model assessment (HOMA): Fasting insulin (μIU/ml) × fasting glucose (mg/dl)/405 (Nestler *et al.*, 2002).

Statistic evaluation

An SPSS (Statistical Package for the Social Sciences) Statistics student t-test software, version 28.0 (IBM, SPSS, Chicago, Illinois, USA), was used to compare the mean and SD. The p values of ≤ 0.05 and ≤ 0.001 are regarded as statistically significant and highly significant, respectively.

3. Results

Glucose levels were higher in obese PCOS women (93.06 ± 9.51) and non-obese PCOS women (93.61 ± 10.48) when compared with controls (87.20 ± 4.65 and 84.6 ± 84.43), with a p-value of < 0.001 (**Table 1**).

IR in obese PCOS patients 3.81 ± 0.94 and non-obese PCOS 2.06 ± 0.76 were high when compared with controls 1.54 ± 0.26 and 1.28 ± 0.27 , with p values of < 0.001 , 0.002 respectively (**Table 1**). Serum insulin concentration in obese PCOS females (15.71 ± 4.56) and in non-obese women with PCOS (13.21 ± 8.10) were high when contrasted to their controls (7.29 ± 1.31 and 7.13 ± 1.62), as appropriate, with a p-value of < 0.001 .

With a p-value of ≤ 0.001 , obese PCOS females (7.87 ± 2.50) and non-obese females (9.40 ± 2.56) had lower serum levels of adiponectin than their respective controls (11.86 ± 3.59 and 11.71 ± 3.33 , respectively) (**Figure 1**).

Table 1: Characteristics of Obese and non-obese PCOS and Control

Variables	Non-obese		P-value	Obese		P-value
	Case	Control		Case	Control	
BMI	24.77 ± 2.34	23.71 ± 1.69	0.02*	33.40 ± 3.71	33.77 ± 3.52	0.64
Insulin ($\mu\text{U/ml}$)	13.21 ± 8.10	7.13 ± 1.62	<0.001*	15.71 ± 4.56	7.29 ± 1.31	<0.001*
FBS (mg/ml)	93.61 ± 10.48	84.68 ± 4.43	<0.001*	93.06 ± 9.51	87.20 ± 4.65	<0.001*
HOMA-IR	2.06 ± 0.76	1.28 ± 0.27	0.002*	3.81 ± 0.94	1.54 ± 0.26	<0.001*

Data expressed as mean \pm SD. BMI= body mass index; FBS= fasting blood sugar; HOMA-IR= homeostasis model assessment-estimated insulin resistance. Statistical significance is defined as * $p \leq 0.05$.

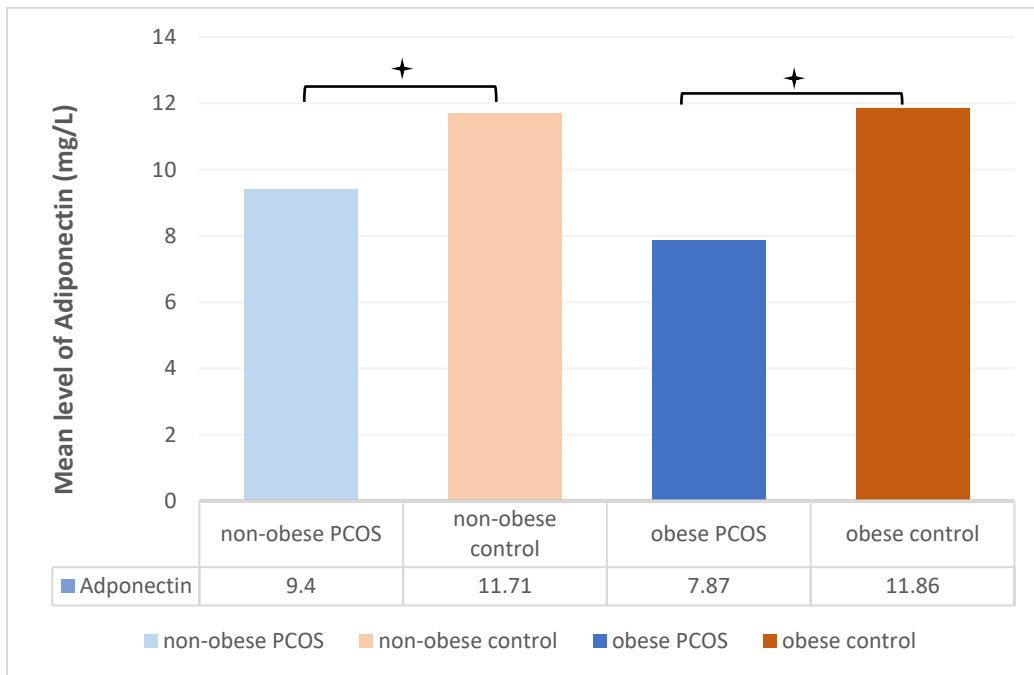


Figure 1: Comparison of Adiponectin in Non-Obese PCOS, Non-Obese Controls, Obese PCOS and Obese Controls. Statistically Significant at * $p \leq 0.001$

4. Discussion

In our investigation, both obese and non-obese PCOS subjects had significantly higher mean fasting blood glucose levels compared to controls, combined with significantly higher serum levels of insulin and IR. Zuo et al. reported making comparable findings (Zuo, Zhu and Xu, 2016). The primary mechanism in the etiology of PCOS in both obese and non-obese people is thought to be hyperinsulinemia and IR, Yun et al (Yeon Lee et al., 2010) have demonstrated that obese PCOS women with elevated blood glucose and BMI of over 27 develop diabetes. The percentage of obese PCOS patients was 31% compared to 10.3% of thin PCOS patients and 7.5% compared to 1.5% of PCOS patients who are slim, respectively.

In PCOS patients, insulin signalling that is mediated by a protein tyrosine kinase receptor has been studied; Dunaif and his team (Dunaif et al., 1989) revealed increased insulin receptor serine phosphorylation in insulin-resistant PCOS patients, which prevents insulin receptor tyrosine kinase function. It also influences the P450c17 enzyme's activity, which in women with PCOS results in hyperandrogenism. Additionally, hyperinsulinemia amplifies the actions of LH on theca interstitial cells, increasing the synthesis of androgen (Yeon Lee et al., 2010).

Patients with PCOS have an IR rate between 50% and 70%. IR promotes Oxidative stress because reactive oxygen species (ROS) are produced due to hyperglycemia and increased levels of free fatty acids. According to several studies, the degree of clinical presentation and hyperinsulinemia severity are associated (Yeon Lee et al., 2010).

Patients with PCOS have shown signs of oxidative stress brought on by hyperglycemia, IR, and ongoing inflammation. Due to the excess generation of ROS caused by hyperglycemia and more significant amounts of free fatty acids, IR increases Oxidative stress. By causing multinucleated cells to produce tumour necrosis factor (TNF α), hyperglycemia also contributes to inflammation. Excess testosterone enhances the production of ROS from leukocytes, the expression of the p47phox gene, and the development of MDA, according to studies done on lean, healthy women of reproductive age who also had hyperglycemia. It's possible that diet-induced Oxidative stress, with hyperandrogenism as the progenitor, is the cause of OS being present in the lack of obesity. Chronic inflammation is exacerbated by Oxidative stress and vice versa (Deba et al., 2017).

Independent of IR, the current investigation demonstrated that adiponectin levels were considerably lower in obese and not obese women with PCOS than in their controls, showing a negative connection between adiponectin and obesity indexes (BMI). Vardhana et al. reported making comparable observations (Vardhana et al.,

2009). Nevertheless, several research studies have indicated the opposite (Spranger *et al.*, 2004), and Lewandowski *et al.* said variable adiponectin levels (Lewandowski *et al.*, 2005).

A 247 amino acid polypeptide called adiponectin, mainly released by adipose tissues, has an antagonistic relationship with obesity, metabolic syndrome, and IR (Shin, Lee and Lee, 2011). Adiponectin is recognized to play essential roles in the control of lipid and glucose metabolism through the promotion of oxidation of fatty acids, inhibition of liver glucose production, and increased skeletal muscle and liver insulin sensitivity. Women with PCOS who are lean or obese possess a larger ratio of trunk to peripheral fat than those who are not. The absence of a correlation between insulin sensitivity and body weight may be explained by this effect (Svendsen *et al.*, 2008). According to Groth (Groth, 2010), IR may not be the only possible answer. High androgen levels could be a contributing factor.

In obesity, the expression of adiponectin receptors (adipo R1 and 2) is reduced (Kadowaki and Yamauchi, 2005). Such receptors are, however, both visceral and subcutaneous fat tissue, which are upregulated in PCOS patients. AdipoR1 expression is favourably connected with insulin, testosterone/SHBG (Sex hormone binding-globin) 100, and the androgen index in both forms of fat in all women but negatively correlated with SHBG (Kalish *et al.*, 2003). According to a previous study (Sir-Petermann *et al.*, 2007), It's probable that PCOS-related metabolic problems existed before hyperandrogenism, and adiponectin may be employed as a susceptibility biomarker for females who are in danger of developing PCOS.

5. Conclusion

Within the current study, women with PCOS, regardless of BMI, had decreased adiponectin levels in serum. However, the values in PCOS patients who were obese were lower than those in PCOS patients who were not obese. Fasting insulin and HOMA-IR were negatively correlated with adiponectin. Therefore, regardless of BMI status, it can become a biomarker for women at risk of developing PCOS.

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Compliance with Ethical Standards

Conflict of Interest

The authors warrant that they don't have any competing interests to declare.

Ethical Approval

All procedures involving human subjects in research projects were carried out by Kerbala University's research committee's ethical standards, the 1964 Helsinki Declaration, and any updates or additional ethical guidelines deemed equivalent.

Informed Consent

Each participant in the study gave their consent in writing.

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