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Association between Insulin Resistance and Lipid profile in a Sample of Iraqi Polycystic ovary syndrome Patients

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Received: 2 May 2023 **Accepted: 6 July 2023**

DOI: https://doi.org/10.24237/ASJ.02.02.756C

Abstract

A common metabolic disorder in women with polycystic ovarian syndrome (PCOS) is dyslipidemia. Since insulin resistance is a major pathophysiology of PCOS, dyslipidemia in PCOS-affected women may be consistent with that of insulin resistance. This study was planned to determine insulin level in PCOS patients, and interpretation of Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) with lipid profile level. Fifty eight patients and thirty controls were involved for this study. All subjects' lipid profiles, FBS, and insulin levels were examined. Patients with PCOS had significantly higher serum insulin levels than the healthy control group (p 0.05). Insulin resistance in PCOS is significantly higher than in healthy controls. In PCOS patients, there is a negative connection between HOMA-IR and HDL-C. HOMA-IR was found to positively correlate with TG and TC in the patient group where the person coefficient values for (TG,TC and HDL-C) : 0.4486, 0.405 and 0.3109 respectively . Conclusion: dyslipidemia and insulin resistance both lead to the development of atherosclerosis in PCOS patients

Keywords: Serum insulin, HOMA-IR, lipids profile, polycystic ovarian syndrome

Academic Science Journal

العلاقة بين مقاومة الأنسولين والدهون في عينة من مرضى متلازمة تكيس المبايض العراقيات

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الخلاصة

اضطراب التمثيل الغذائي الشائع لدى النساء المصابات بمتلازمة تكيس المبايض هو اضطراب شحميات الدم . نظرًا لأن مقاومة الأنسولين هي فيزيولوجيا مرضية رئيسية لمتلازمة تكيس المبايض ، فقد يكون عسر شحميات الدم لدى النساء المصابات بمتلازمة تكيس المبايض متسقًا مع مقاومة الأنسولين. تم التخطيط لهذه الدراسة لتحديد مستوى الأنسولين لدى مرضى متلازمة تكيس المبايض ، وتفسير تقييم نموذج التماثل الساكن لمقاومة الأنسولين بمستوى ملف الدهون .شارك في هذه الدراسة ثمانية وخمسون مريضًا وثلاثون عنصر تحكم. وجد أنه تم قياس الأنسولين ونسبه السكر في الدم ونسبة الدهون لجميع الأشخاص. المرضى الذين يعانون من متلازمة تكيس المبايض لديهم مستويات أنسولين مصل أعلى بكثير من مجموعة التحكم الصحية. تكون مقاومة الأنسولين في متلازمة تكيس المبايض أعلى بكثير منها في مجموعه الضوابط الصحية. في مرضى متلازمة تكيس المبايض ، هناك علاقة سلبية بين مقاومه الانسولين والكوليسترول واطئ الكثافة بينما كانت هناك علاقه ايجابيه بين مقاومه الانسولين والدهون الثلاثية ومستوى الكوليسترول الكلي حيث كانت قيم معامل بيرسون (0.3109 , 0.405 , 0.4486) على التوالي. يؤدي كل من عسر شحميات الدم ومقاومة الأنسولين إلى تطور تصلب الشرايين لدى مرضى متلازمة تكيس المبايض.

الكلمات المفتاحية : مصل الانسولين، HOMA-IR، الدهون، متلازمة تكيس المبايض.

Introduction

A kind of hormonal condition called polycystic ovarian syndrome (PCOS) affects roughly 5-20% of females worldwide who are of age to become pregnant (1). Patients with PCOS produced more male hormones, which leads to an imbalance in hormone levels (2). As a result, menstrual cycles are impacted, so becoming pregnant is more challenging than in healthful females (3). There is currently no treatment for PCOS (4). A significant number of metabolic variables change in conjunction with the onset of PCOS (5,6). Increased lipid profiles, hypertension, and an increase in the metabolic disorder (a group of risk factors for cardiovascular diseases)(7,8) are among the increasing risk factors for type 2 diabetes mellitus

and cardiovascular disease (CVD), as well as weakening glucose tolerance or type II diabetes, which adds to the risk potential of cardiovascular disease (9). Additionally, recent research has established that elevated androgen production, hyper insul1nemia, and insulin resistance may all have an impact on PCOS etiology (10, 11). While the results of the other research indicate that PCOS is caused by both hereditary and natural factors (12). Raised insulin levels and increased blood pressure, which lead to T2DM and cardiovascular disease, respectively, are serious issues brought on by IR (13). While the measurement of waist circumference is a common diagnostic tool and frequently results in missed diagnoses, IR is not commonly examined by measuring fasting insulin levels. A diet with a typical quantity of carbs can be challenging for individuals with insulin resistance to lose weight (14).

Materials and methods

1. Subjects

Fifty eight PCOS sufferers (from Iraq) with ages ranging from 18 to 39 years of age. Obesity, metabolic syndrome, and pregnant women, Thyroid disorders, and cardiovascular problems were all excluded from this study even though every individual had lipid profile abnormalities. Thirty appeared volunteers were used in the study as controls, and their Ages ranges between (18–39) were comparable to those of PCOS patients. Based on the following physician criteria, the controls were selected .The investigation group included (88) women of reproductive age and (58) polycystic ovary syndrome patients who did not have diabetes or heart disease and had not had their fallopian tubes removed or one of their ovaries removed. According to their atherogenic index of plasma (AIP), the PCOS group of patients is classified into two subgroups: - The first group consists of obese women with PCOS with AIP $\geq$ 0.5 and the second group consists of PCOS patients AIPI<0.5 and a control-freak female of 30. Women with PCOS are referred to as the first group (G1). Women with PCOS who are at risk of developing (CVD) are referred to as the second group (G2). The blood was drawn in the morning after an overnight fast and on days 3-5 of the early follicular phase of the menstrual cycle. The serum was separated after centrifugation and divided into five Eppendorf tubes to prevent repeated

freezing and thawing, and maintained frozen until the end of analysis. Blood samples were obtained in clot activator tubes.

Measurements of anthropometry

For each study group, the age and Body Mass Index (BMI) were calculated. A formula that uses the fundamental equation of weight divided by the square of height is used to calculate BMI. It is seen as a sign of cardiovascular and metabolic illness. Due to an increase in abdominal fat tissue, women with PCOS exhibit a marked rise in obesity and body weight.

Homeostasis Model Assessment (HOMA-IR)

A number of methods were used to measure insulin resistance (IR). According to the equation below, fasting insulin (U/ml) and glucose (mg/dl) are used to compute the homeostasis model assessment (HOMA). Given that it affects the harmony of numerous metabolic pathways, insulin resistance is an important topic for research (15).

HOMA-IR= [g**lucose**(mg\dl) × **fasting insulin**(μU/ml)] /405

2. Statistical analysis

The statistical analyses were carried out using the SPSS version 25 computer program (Statistical Package for Social Sciences), and the ANOVA test was used to confirm that the disparity in median between more than two groups was considered statistically significant. The data were entered into the computer database structure. BMI, FBS, lipid profile, and serum insulin. The independent t-test (analysis of variance) was the basic statistical method used to examine the significance of the difference in averages between two groups.

Results and discussion

1. Characteristics of PCOS patient groupings and Normal Subjects

Anthropometries factors between the studied groups. The age distributions of PCOS patients on average G1, G2 (27.70 ±1.18, 26.13 ±1.40) respectively and healthy subjects (25.26 ±1.73)

. Poly cystic ovary syndrome patients G1, G2 had a BMI of (29.64±1.1,28.05±4.03) kg/m2 respectively, which was close to healthy people's (28.3±2.0). The BMI was used to calculate overall adiposity. Higher BMI was discovered to be directly and inversely connected to HDL. Insulin resistance, hypertension, diabetes, and increased atherosclerosis due to dyslipidemia (16) were proposed causes of the cardiac events in obese patients. It is believed that elevated TC (17) and LDL cholesterol (18) are the main factors contributing to dyslipidemia's effect on cardiac events. However, recent data reveals that the widely held belief that there is a direct correlation between BMI and LDL cholesterol is oversimplified. In reality, the "obesity conundrum" (19) has been dubbed a weaker-than-expected connection between LDL and BMI. However, it is undeniable that visceral fat, rather than subcutaneous abdominal fat, is more closely associated with insulin resistance, and that central fat, rather than peripheral fat, is linked to insulin resistance as shown Table 1.

Table 1: PCOS patient groups' anthropometry measures in comparison to the healthy population

Age (years)	Control (30)		G1(38)		G2(20)		P value
	Number	%	Number	%	Number	%	
17-19	13	43.3	13	34.2	2	10.0	0.013*
20-29	10	33.3	14	36.8	13	65	
30-39	7	23.3	11	28.9	5	25	
Mean	25.26 ±1.73		27.70 ±1.18		26.13 ±1.40		0.282
BMI(Kg/m^2)							
Normal(18-24.9)	10	33.3	6	15.7	5	25	0.012
Overweight (25- 29.9)	17	56.6	16	42.1	5	25	
>30) = Obese	3	10.1	16	42.1	10	50	
Mean ±SE	28.3±2.0		29.64±1.1		28.05±4.03		0.202
a:refer to significant different between G2and C , b: refer to significant different between G1and C c: refer to significant different between G1and G2							

2. Groupings of PCOS patients and healthy subjects by their metabolic factors

In comparison to controls (982.4 mg/d L), patients had significantly higher mean FBS in G1 and G2 (1043.4 and 1081.4 mg/d L, respectively). There was statistical significance (at P 0.05)

between PCOS patients and controls groups despite the fact that insulin serum levels were significantly higher in PCOS patients in G1, G2 (34.60 4.07, 43.02 5.49 U/ml) and HOMA-IR (8.88 2.01, 11.47 5.09) than in the control group (6.05 1.09) (Table 2).

Table 2: Means ±SE for FBS, Insulin, HOMA-IR level

PARAMETER	CONTROL GROUP MEAN	G1MEAN N(38)	G2MEAN N(20)	LEAST SIGNIFICANT DIFFERENCE (LSD)	P-VALUE
FBS (m g l/dl)	98±2.4	104±3.4	108±1.4	5.23	0.061
Insulin (µ U/ml)	25.01±2.25	34.60±4.07 (b) (c)	43.02±5.49 (a)	14.808 *	0.0496
HOMA-IR	2.2±1.09	8.88±2.01 (c)	11.47±5.09 (a)	13.21*	0.032
Values are expressed as means ± SE, *P < 0.05 is significant , **P < 0.001 is highly significant					
a:refer to significant different between G2 and C , b: refer to significant different between G1and C c: refer to significant different between G1and G2					

Both PCOS and Type 2 diabetes (T2D) are prevalent disorders connected to IR and compensatory hyper 1nsulinemia. Women with PCOS are known to frequently have poor glucose tolerance, and women with T2D have been observed to have an increased chance of having polycystic ovaries compared to the general population. Endocrine and reproductive issues can be normalized by increasing insulin sensitivity. Metformin and inositol's, two insulin sensitizing medications, have been observed in clinical studies to enhance PCOS women's endocrine and metabolic profiles (20).

3. PCOS Lipid Profile in Groups of Patients and Healthy Subjects

The lipid profile of (TC, TG, LDL, VLDL, HDL,) showed in the PCOS patients G1,G2 (146.53 ±5.51, 169.67 ±4.38, 41.93 ±4.08 , 14.88 ±1.21, 58.78 ±5.64) respectively,(157.93 ±7.33 , 175.60 ±5.44, 51.43 ±6.39 , 22.83 ±2.07 , 43.17 ±2.58) respectively than control group (139.43 ±6.99, 114.26 ±10.37 , 39.99 ±5.35, 12.80 ±1.18, 65.41 ±4.50) However, when compared to the control group, they demonstrated different significant in the p-value (p0.05, P0.01)Table (3).

Table 3: Mean and standard error for the lipid profile of PCOS patient and healthy subject groups

PARAMETER	CONTROL	G1	G2	LSD	P-VALUE
TC(mg/dl)	139.43 ±6.99	146.53 ±5.51	157.93 ±7.33 (a)	20.396*	0.0466
TG(mg/dl)	114.26 ±10.37	169.67 ±4.38 (b)	175.60 ±5.44 (a)	24.032**	0.0003
LDL-C(mg/dl)	39.99 ±5.35	41.93 ±4.08	51.43 ±6.39 (a)	16.571*	0.308
VLDL-C(mg/dl)	12.80 ±1.18	14.88 ±1.21	22.83 ±2.07 (a)	5.052**	0.0002
HDL-C(mg/dl)	65.41 ±4.50	58.78 ±5.64 (c)	43.17 ±2.58 (a)	13.696 **	0.0009
Mean ± SE with a significant difference (*p<0.05) with a highly significant difference (**P≤0.01)					
a:refer to significant different between G2 and C , b: refer to significant different between G1and C c: refer to significant different between G1and G2					

Table 4: Atherogen1c index of Plasma for the research groups

PARAMETER	CONTROL GROUP MEAN	G1 MEAN	G2 MEAN	LSD	P-VALUE
AIP	0.2± 0.03	0.460±0.04	0.609±0.043 (a)	0.52**	0.0002
Values are expressed as means ± SE, *P < 0.05 is significant , **P < 0.001 is highly significant					
a:refer to significant different between G2 and C , b: refer to significant different between G1and C c: refer to significant different between G1and G2					

Around 70% of PCOS individuals experience the metabolic abnormality known as dyslipidemia. Unusually, PCOS is linked to an atherogenic lipid profile with higher triglycerides, higher LDL, and lower HDL values. Clinical data show a connection between dyslipidemia and poor glucose in PCOS (21). In PCOS individuals with type 2 diabetes or impaired glucose, the prevalence of abnormal lipids was higher (88%), compared to 58% in PCOS patients with normal glucose. In addition, 81% of PCOS individuals had abnormal lipid levels (22). Hyperinsulinemia and hyperandrogenemia may be the causes of dyslipidemia in people with PCOS. As a result, catecholamine-induced lipolysis in adipocytes increased, releasing free fatty acids into the bloodstream (23).

4. Relationship between HOMA-IR and Lipid Profile in PCOS Patients

The relationship between TG, TC, and HDL and HOMA-IR insulin resistance is depicted in Figures (1, 2, and 3) the p value for HOMA –IR were 0.032:

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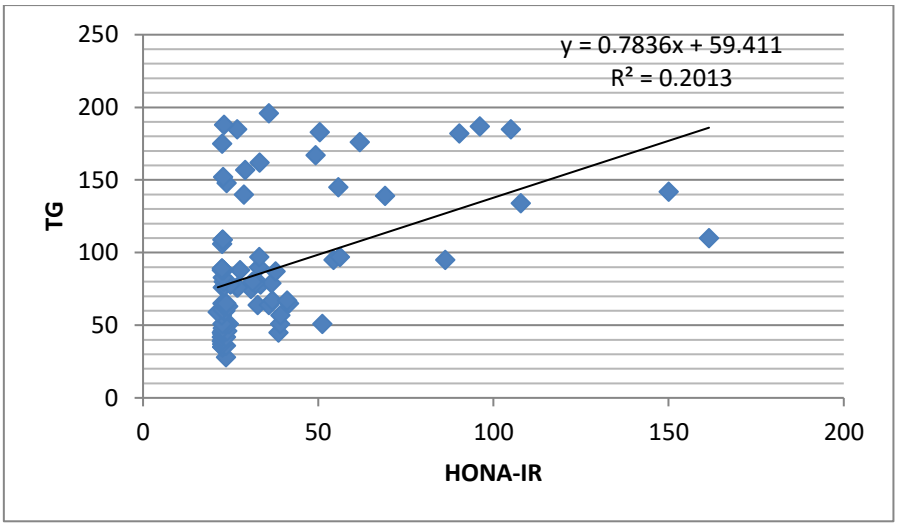

Figure 1: Association between insulin resistance (HOMA-IR) and TG

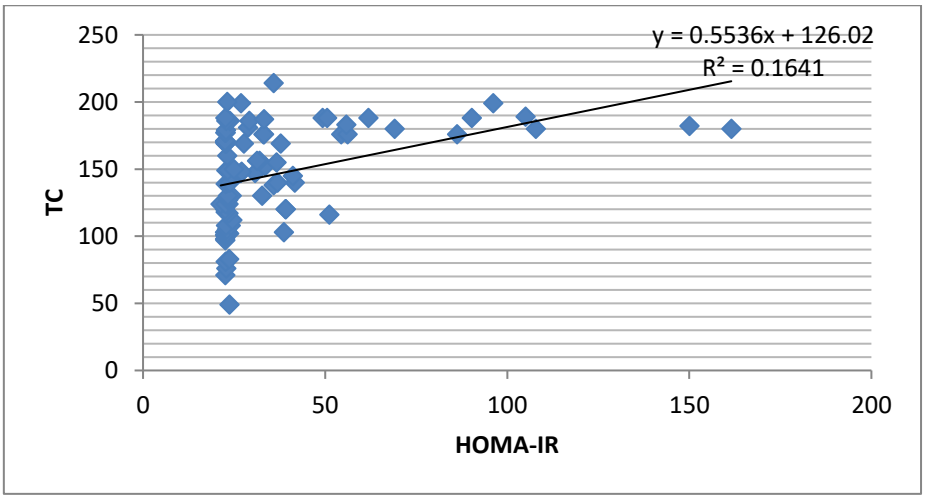

Figure 2: Association between insulin resistance (HOMA-IR) and TC

We have shown a strong positive correlation between insulin resistance (HOMA-IR) and both TG and TC in a large population of PCOS patients, as shown in the figures (1&2), and a significant inverse association with HDL, as shown in the figure (3).

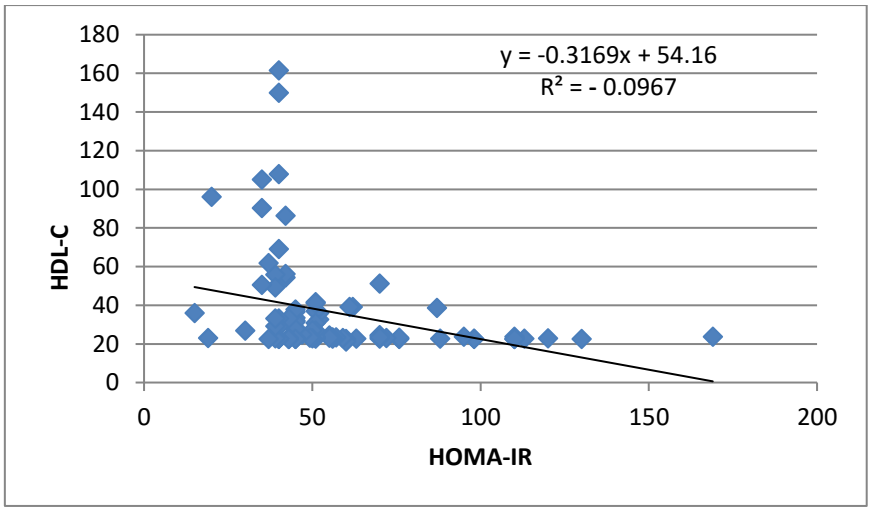

Figure 3: Association between insulin resistance (HOMA-IR) and HDL-C

Conclusions

Patients with PCOS who also have insulin resistance are more likely to develop atherosclerosis. Despite the fact that a lot of study has been done to unravel the intricate causes of this dyslipidemia.

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