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Leptin–Adiponectin Imbalance as a Predictive Biomarker for Polycystic Ovary Syndrome in Overweight Iraqi Women: A Case-Control Study – Review

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Abstract
Polycystic ovary syndrome (PCOS) is a multifactorial endocrine disorder frequently associated with obesity and metabolic dysfunction. Adipokines, particularly leptin and adiponectin, play key roles in regulating insulin sensitivity, lipid metabolism, and reproductive function, and their dysregulation may contribute to PCOS pathogenesis. This case-control study investigated serum leptin, adiponectin, and lipid profile levels in 120 Iraqi females aged 18–44 years, including 60 overweight PCOS patients and 60 age-matched healthy controls. Blood samples were collected during days 2–5 of the menstrual cycle, and biochemical parameters were analyzed using ELISA and spectrophotometry. PCOS patients exhibited significantly elevated leptin levels and reduced adiponectin concentrations compared to controls ($P<0.05$). The leptin/adiponectin ratio demonstrated strong diagnostic performance, with an AUC of 0.80, 80% sensitivity, and 73% specificity at a cutoff value of 0.03. Leptin showed a significant positive correlation with BMI, triglycerides, and VLDL, indicating its involvement in metabolic disturbances associated with PCOS. These findings suggest that disrupted adipokine balance contributes to metabolic and reproductive abnormalities in overweight women with PCOS and highlight the potential of the leptin/adiponectin ratio as a supportive biomarker for disease detection.
Keywords: adiponectin, Adipokines, leptin, Poly Cystic Ovarian syndrome (PCOS)

1. Introduction

Three criteria are used in the field to diagnose PCOS (polycystic ovarian syndrome), an endocrinopathy of early reproductive age in females: the Androgenetic Association (AE-PCOS) criteria in 2006, the Rotterdam (ROT) criteria in 2003, and the criteria developed by the National Institutes of Health in 1999 [1]. These factors include the growth of male hormones like testosterone, the emergence of hair in undesirable places like the face and chest, or irregular menstrual cycles in females (lack of ovulation), which results in larger ovaries [2]. PCOS affects 2% to 26% of people worldwide [3], [4], with obese patients having a high frequency of roughly 73%. PCOS is closely linked to obesity, which is characterized by an android body, a high waist-to-hip ratio, and anterior abdominal wall fat [5]. PCOS is caused by environmental, genetic, and behavioral variables that combine ineffectively. The most common clinical manifestation of PCOS is the release of more androgenic substances than normal theca cells. Increase production of enzymes in the steroid synthesis pathway leads to increased androgen secretion [6]. The combination of abdominal obesity and insulin resistance causes an increase in the amount of androgen in the blood because elevated insulin levels in obese females may directly boost androgen manufacturing in the cell, which affects fatty acid metabolism along with lipids building up in the liver, subsequently leading for decreased SHBG production [7].as shown in figure 1.

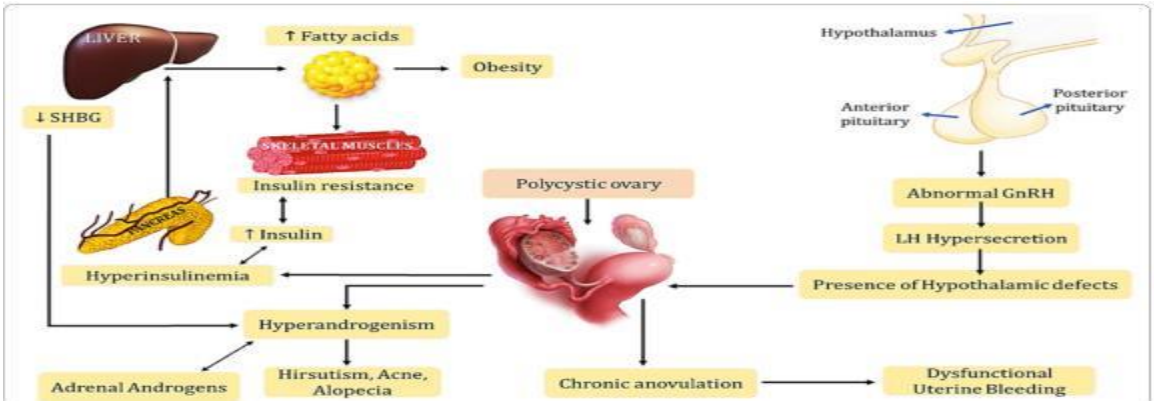

Figure 1: Polycystic ovarian syndrome and obesity [8]

Symbols: Luteinizing hormone (LH), gonadotropin-releasing hormone (GnRH), polycystic ovarian syndrome (PCOS), and sex hormone binding globulin (SHBG).

Adipokines, also referred to as adipocytokines, are endocrine chemicals secreted by adipose tissue. Adipocytes produce leptin and adiponectin [9]. [10], and the hormone leptin, which is produced from adipose tissue, controls neuroendocrine function and energy balance through its brain receptor [11].Leptin, which is produced by white adipocytes, is secreted into the blood and transported to the brain by an appropriate mechanism [12], where it operates to release or suppress proteins that ultimately result in a decrease in food intake, an upsurge in energy consumption, and an increase in physical activity.It also affects reproductive processes in a number of ways, such as inhibiting folliculogenesis [13]. Hyperleptinemia and obesity are related, and the condition in obese PCOS is more complex [14–16]. As seen in figure 2, insulin controls circulating leptin concentrations [17], which can reach their receptors at the level of the arcuate nucleus through the blood brain barrier. Their plasma levels are proportionate to body fat [11].

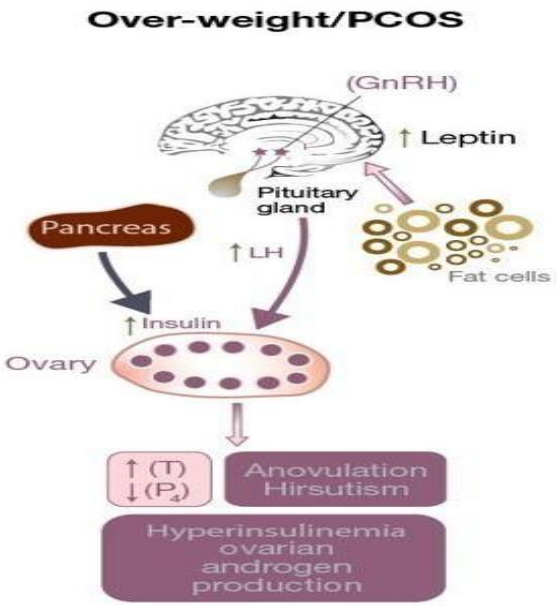

Figure (2) Effect of leptin on females with polycystic ovarian syndrome [11]

This study looked at blood leptin and adiponectin levels in females with PCOS and how they related to lipid profiles and anthropometric obesity indicators.

Design of the study
This study was planned as a case-control study with overweight Iraqi PCOS patients in order to test leptin and adiponectin levels and examine the type of relationship that exists between these hormones and lipid profile as variables contributing to the development of PCOS.

2. Materials and Techniques

2.1 Gathering Samples

A study sample of 120 independent females with ages ranging from 18 to 44 and body mass indices greater than 25 was gathered from patients who visited private clinics in the Babylon region of Iraq. The participants were split into two groups:

1. Control groups: comprised sixty females of normal weight (BMI 20–25) who appeared to be in good health.
2. Patient groups: comprised sixty overweight (BMI >25) girls with PCOS. Blood samples were taken from females between the second and fifth day of the cycle. Three milliliters of the blood were drained into a plain tube gel to prepare the serum, which was then employed in the testes after separation and centrifuged at 3000 Xg for five to ten minutes.

2.2 Biochemical Analysis

While the lipid profile (triglycerides, cholesterol, HDL, LDL, and VLDL) was evaluated using a spectrophotometer with a wave length of 520 nm, adiponectin and leptin were assessed using an ELISA kit (enzyme-linked immunosorbent assay).

2.3 Calculation Result

Instead of concentrating on the x-axis and displaying the best fit curve across the point on the graph as shown in figures (3), (4), the standard curve was displayed by drawing the OD of every standard on the y-axis.

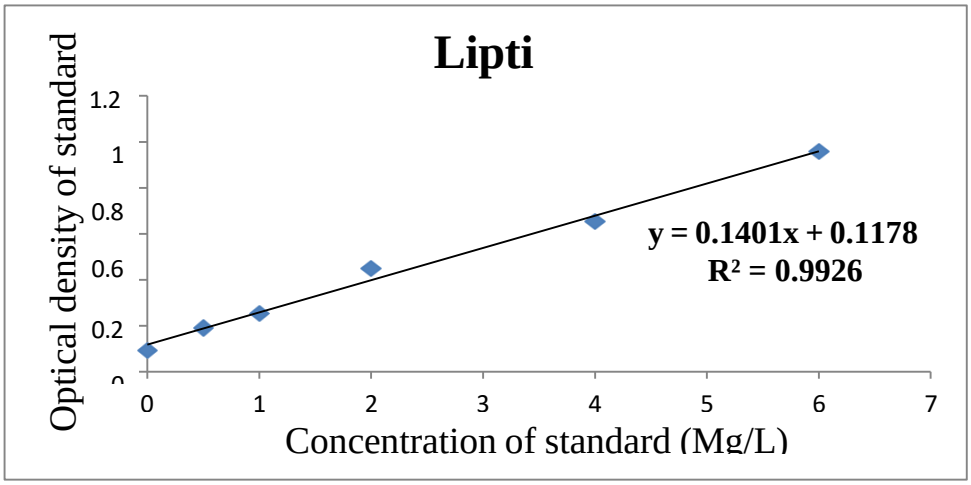

Figure 3: The standard curve for leptin concentration

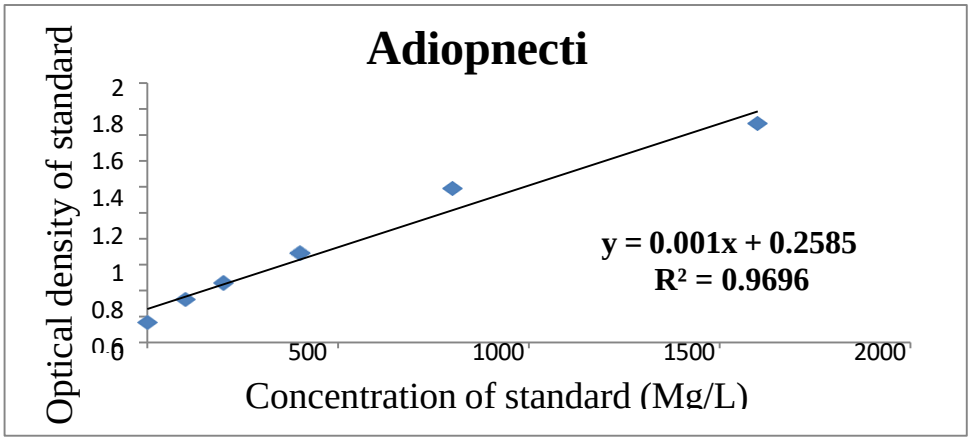

Figure 4: The standard curve for adiponectin concentration

2.4 Statistical Analysis

In this study, statistical software SPSS version 23 was utilized. All descriptive data were continuous (scale) variables, given as mean ± standard error (mean ± SE). scale factors such as BMI and age. The parametric tests adhered to the statistical normal distribution. The studied parameters were compared between the examined groups using the student's t test for two groups.

The correlation coefficient (r) was used to compare two continuous variables, and a P-value of 0.05 or less was considered significant.

3. Results

Table 1 summarizes the demographic information of the groups under study. The BMI was significant, however the P-value for age between the patient and control groups was not.

Table 1 Demographic data of patient and control groups

Variable	Study groups	No.	Means ±SD	P- value
Age (years)	PCOS-Patient	60	25.13 ±2.2	0.23
	Control	60	25.58 ±1.8	
BMI Kg/m^2	PCOS-Patient	60	27.59 ±0.69	<0.00
	Control	60	25.68 ±1.28	

The following criteria were used to assess PCOS (polycystic ovarian syndrome), BMI (body mass index), and SD (standard deviation): P-values more than 0.05 were not significant, but P-values less than 0.05 were.

Table 2 summarizes the hormonal variables. When comparing patients and controls, the P-values for leptin, adiponectin, and the leptin/adiponectin ratio were substantially different.

Table 2: Hormonal variables between patient and control groups

Variable	Study groups	No.	Means ±SD	P- value
Leptin (µg/L)	Patient	60	2.80 ±0.5	0.025
	Control	60	2.53 ±0.7	
Adiponectin (µg/L)	Patient	60	74.3 ±14.5	<0.00
	Control	60	103.9 ±15.0	

Leptin/Adiponectin Ratio	Patient	60	0.04 ±0.01	<0.00
	Control	60	0.029±0.01	

SD (standard deviation), PCOS (polycystic ovarian syndrome), and P-values 0.05 were deemed significant; P-values greater than 0.05 were not.
When comparing the patient and control groups, the lipid profiles were significantly different, as Table 3 illustrates.

Table 3: Lipid profile data between patient and control groups

Variable	Study groups	No.	Means ±SD	P- value
TG (mg/dl)	Patient	60	294.1 ±20.3	<0.00
	Control	60	148.03 ±14.8	
CHO (mg/dl)	Patient	60	224.8 ±16.6	<0.00
	Control	60	166.8 ±14.4	
HDL (mg/dl)	Patient	60	16.7 ±2.0	<0.00
	Control	60	29.0 ±3.5	
LDL (mg/dl)	Patient	60	149.2 ±17.8	<0.00
	Control	60	108.2 ±7.7	
VLDL (mg/dl)	Patient	60	58.8 ±10.8	<0.00
	Control	60	29.6 ±2.05	

SD (standard deviation), TG (triglyceride), CHO (cholesterol), HDL (high density lipoprotein), LDL (low density lipoprotein), and VLDL were all regarded as significant when P-values were less than 0.05. (extremely low-density lipoprotein) were all regarded as noteworthy. Furthermore, as Table 4 illustrates, the current study found favorable relationships between BMI and leptin in overweight patients (P-value <0.001, r = 0.83). In contrast, Table 4 shows a positive correlation coefficient between leptin and patients' leptin/adiponectin ratio (P-value<0.001, r = 0.051) and a positive correlation coefficient between leptin and TG and VLDL (P<0.001, r = 0.60, 0.631, respectively).
While the distribution of leptin and adiponectin levels directly affects the regulation of gonadotrophic hormone and results in PCOS symptoms, the amount of leptin increases with BMI, which raises the ratio of leptin to adiponectin in females with PCOS.

Table 4: Correlation between variables within patient

		Leptin	Lep/ADP Ratio	TG	VLDL
BMI	r	.843**	.213	.613**	.603**
	Sig.	.000	.103	.000	.000
Leptin	r	1	.511**	.601**	.631**
	Sig.		.000	.000	.000
Lep/ADP Ratio	r	.511**	1	.370**	.370**
	Sig.	.000		.004	.004
TG	r	.601**	.370**	1	1.000**
	Sig	.000	.004		.000
VLDL	r	.631**	.370**	1.000**	1
	Sig.	.000	.004	.000	

** indicators that indicate the correlation is significant at the 0.01 level include TG (triglyceride), VLDL (very low-density lipoprotein), Lep/ADP Ratio

(leptin/adiponectin ratio), and r (Pearson Correlation).

Operating Characteristic of the Receiver with an AUC (area under the curve) of 0.80 (P-value <0.001) and sensitivity of 80% and specificity of 73% at a cutoff value of 0.03, the analysis of the leptin/adiponectin ratio demonstrated a good ability to predict PCOS caused from overweight vs. normal weight control females. This suggests it may be a better tool for confirming the diagnosis of PCOS, as shown in figure (5).

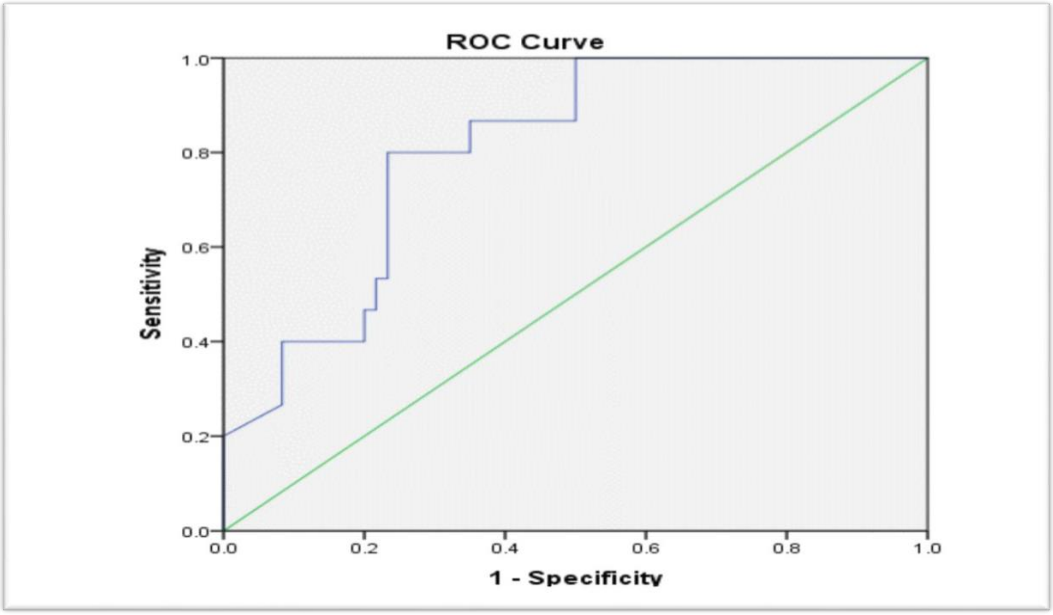

Figure 5: Leptin/adiponectin ratio receiver operating characteristic (ROC) curve for PCOS patients under management; AUC stands for area under the curve

4. Discussion

In order to prevent differences in parameter outcomes that might have resulted from the significant age variance, the age-matched technique was applied in this study between the patient and control groups. When evaluating obesity, BMI is regarded as an anthropometric measure [18]. PCOS is strongly correlated with obesity, which raises leptin levels and lowers adiponectin in comparison to controls. Because of this, obese females have higher levels of leptin synthases in their adipose tissue than females of normal weight. Similar to some research [19], [20–22], our study demonstrates a positive correlation between leptin and BMI in females with PCOS. The results of this study show that compared to age-matched controls, all plasma lipid levels were significantly higher in the PCOS group. Leptin, triglycerides, and VLDL are strongly correlated, according to several studies [23]. Similar studies demonstrate that dyslipidemia, which is common in females experiencing PCOS, is characterized by high VLDL-C in addition to low HDL-C and higher triglycerides [24], [25]. Abdominal adipose tissue grows due to high levels of androgen generated by the ovary's theca cells; the tissue underneath the skin develops insulin resistance because and insulin prevents protein kinase C from absorbing glucose [26]. Leptin's impact on female PCOS patients: A high level of focus results in

1. Granulosa cells produce and store leptin, and a high concentration of it inhibits the expression of aromatase, which affects a dominant follicle's capacity to produce adequate amounts of estrogen, leading to androgen accumulation and the conversion of androgenic substances to estrogen [27], [28].
2.The lack of folliculogenesis is associated with elevated leptin levels [29].
3.High amounts of adiponectin cause inadequate amounts of gluconeogenesis and FFA uptake. Additionally, it impacts ovulation, the production of progesterone and estrogen, and the pituitary's decreased secretion of GnRH and LH.

5. Conclusion

This study demonstrates that overweight Iraqi women with PCOS exhibit pronounced alterations in adipokine profiles, characterized by elevated leptin levels and markedly reduced adiponectin concentrations. The strong association between leptin, BMI, triglycerides, and VLDL highlights its central role in metabolic dysfunction accompanying PCOS. Moreover, the leptin/adiponectin ratio showed high diagnostic value, indicating its potential utility as a complementary biomarker for identifying PCOS in overweight females. Given the significant dyslipidemia observed in affected patients, routine assessment of lipid profiles, particularly triglycerides and VLDL is recommended to reduce long-term cardiometabolic risks. Overall, the findings support the role of adipokine imbalance in the development and progression of PCOS and emphasize the importance of monitoring metabolic indicators alongside hormonal markers in clinical evaluation.

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