Hilla University College Journal For Medical Science

Manuscript 1076

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ORIGINAL STUDY

Hilla Univ Coll J Med Sci

Study the Metabolic and Hormonal Changes in Obese and Non-Obese Women with Polycystic Overy syndrome: Case-Control Study

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Abstract

Background: Women with PCOS experience pathological symptoms like diabetes and insulin resistance (IR), obesity and being overweight, infertility, and irregular menstruation due to hormonal abnormalities.

Objectives: Study the association between metabolic and hormonal changes in PCOS.

Materials and methods: Forty-five Iraqi women with newly diagnosed PCOS, aged between 20–40 years, were divided into two groups X Obese Women with PCOS, Y Non-Obese PCOS. The samples were collected from private labs, Al-Sadr Teaching Hospital, and Al-Zahraa Hospital in the Najaf Governorate. Each was tested using an enzyme-linked immunosorbent assay (ELISA) for the subject's reproductive hormones and by colorimetric methods used to determine (Fasting serum glucose (FSG), triglycerides (TG), (Total cholesterol (TC), and high-density lipoprotein (HDL-C).

Results: Compared to healthy fertile women, PCOS patients had considerably lower levels of SHBG and HDL-C, while PCOS women had significantly higher levels of LH, TC, LH/FSH ratio, LDL-C, TT, FAI, FINS, FSG, TG, and HOMA-IR. Obese women with PCOS had a significantly higher serum level of LH than healthy women, especially in obese PCOS women compared to non-obese women with Pcos Furthermore, PCOS patients in this research had significantly elevated levels ($P = 0.0001$). The influence of obese and non- obese hormones levels on the biochemical parameters in women patients with PCOS,evaluated by the correlation coefficient.

Conclusion: The present study had a beneficial effect on inflammatory and endothelial dysfunction markers in overweight and obese patients with PCOS, Since hepatic IR is only seen in obese women with PCOS, the combined detrimental impact of obesity and PCOS on insulin action is well known.

Keywords: PCOS, LH, FSH, Free androgen index, Obesity

1. Introduction

Up to 15% of women of reproductive age have polycystic ovarian syndrome, a common endocrine disorder. Notably, a noteworthy association has been observed in recent decades between an increased frequency of PCOS and the rising incidence of obesity. Despite PCOS's high incidence and high cost, the condition's cause is still unknown [1]. PCOS is the most severe endocrinopathy among fertile women. It is a complicated, multidimensional illness. Chronic anovulation, an excess of testosterone, and a changed cardiometabolic profile are its distinguishing characteristics. When comparing women with PCOS to those without, the former are more likely to have (T2DM) type 2 diabetic mellitus when matched for age and (BMI) body mass index, insulin resistance (IR), central obesity, nonalcoholic fatty liver disease (NAFLD), and hyperinsulinemia. The impairment of adipose tissue (AT) physiology has been associated with PCOS. Adipocyte hypertrophy in PCOS appears to be caused by a combination of hyperandrogenemia and hyperinsulinemia. Adipose tissue produces adipocytes, which exude proinflammatory

Received 2 July 2025; accepted 19 July 2025.
Available online 31 December 2025

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https://doi.org/10.62445/2958-4515.1076

chemicals called adipokines in response to variations in adipocyte activity. These compounds increase sensitivity to low-grade inflammation [2].

Diabetes mellitus, dyslipidaemia, obesity, hypertension, anxiety, and depression are further public in women who have PCOS. Health issues affect women with PCOS at every stage of life, including the years after menopause and before conception. The circle depicts the life cycle of a woman with PCOS [3]. If you have Acne (83%), hirsutism (60–92%), acne (45% in women with acne as the lone symptom) or oligomenorrhea (65–87% exhibited evident polycystic ovaries on ultrasound), the usual ultrasound features of the polycystic ovary are certainly the utmost established detectable signals related to any of the normal symptoms. The use of an ultrasonic scan as a fundamental component of the investigation is becoming increasingly warranted due to the well-known heterogenicity, unexpected character, and consistency in the clinical and endocrinological components of the condition, particularly in the reproductive age group [4]. The existence of 12 or more follicles in ovaries that range in diameter from 2 to 9 mm, or at least one ovary's ovarian volume increasing by more than 10 cm3, were the criteria for using ultrasound to detect polycystic ovarian alterations. This "string of pearls"-like arrangement of follicles along the ovary's border is one of the basic characteristics of PCOS ultrasonography [5]. Numerous studies have shown that individuals with PCOS have increased levels of antral and pre-antral follicle cells. Additionally, an overly high number of produced follicles is caused by the defective apoptotic activity of mature follicular cells. This abnormal development is further linked to the presence of ovarian cysts in the patients [6, 7].

Insulin resistance (IR)refers to the reduced sensitivity of target organs (liver, skeletal muscle, and adipose tissue) to insulin, resulting in a decrease in the efficiency of insulin in promoting glucose utilization and uptake. The body compensates for excessive insulin secretion, forming hyperinsulinemia to maintain blood sugar stability. One of the characteristic features preceding PCOS is persistent hyperinsulinemia. Burghen first proposed the involvement of IR in the pathogenesis of PCOS in 1980, and subsequent studies demonstrated that IR was the core initiating factor in the occurrence of PCOS [8].

2. Materials and methods

A case - control study The 90 subject included volunteers women with in the age 20–40 years were included to 45 newly diagnosed PCOS women divided to:25 Obese PCOS women and 20 Non-Obese women with in the age 20–40 years old. that was carried out between October 2024 and march 2025 at the facility in Al- Sadder Medical City in Najaf, Iraq, and the Al-Zahra'a Teaching Hospital for Gynecology and Obstetrics. Women with PCOS were diagnosed using the Rotterdam ESHRE / ASRM (2003) criteria [9] by the Gynecologest in order to compare them with 45 non-PCOS women who appeared to be Fertile in good health with age-matched PCOS women unpaid helper as control group. The University of Kufa's Faculty of Science Ethics Committee and the Najaf Health Directorate of the Administration of Gynecology and Obstetrics Hospital gave their approval to the study (33552 /2024/10/1). Informed consent was signed by each subject.

Excluded Criteria: Women with PCOS who were receiving concurrent clomiphene treatment and had hormonal imbalances, such as hyperprolactinemia or thyroid dysfunction, those who had damaged or blocked fallopian tubes, were not included. As well as those who used supplements or any other ovulation induction therapy, as well as those who were pregnant while participating in the study were also excluded. For each individual patient, comprehensive anthropometric measurements—including the circumference of the waist (WC), which was assessed at the midpoint between the costal margin and the iliac crests—were conducted for the purpose of calculating the body mass index (BMI) by dividing the weight in (kg) kilograms by the square of the height in meters (m) which is the ratio of weight (Kg) to height squared (m^2). The blood samples were collected a 12-hour fast, five milliliters of venous blood were drawn on cycle day two in all of women volenteers. Until analysis time, the serum was kept at –20°C after being separated.

High-density lipoprotein cholesterol (HDL-C), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and (TC) total cholesterol were measured via colorimetric techniques using commercially available test kits. To assess the amount of free testosterone in the serum, ELISA kits were utilized (Monobind,USA). ELISA kits (ELabscience/USA) were utilized to quantify fasting insulin (FINS) and sex hormonebinding globulin (SHBG). (Minividas, Biomerieux, France) The immune-fluorescence technique was employed to measure luteinizing hormone (LH), follicle stimulating hormone (FSH), and total testosterone (TT). The homeostatic model assessment (HOMA-IR) was used to determine insulin resistance. It was calculated using a conventional formula as follows: Fasting insulin (IU/L) divided by fasting glucose (mmol/L) is known as HOMA-IR, and the cutoff value is > 2.5 [10]. Additionally, the conventional formula FAI = total testosterone (TT)/SHBG × 100

Table 1. Comparison of Anthropometric, Hormonals and metabolic parameters between the control group and the patients.

Parameters	PCOS Patients group Mean ± SD	Healthy control group Mean ± SD	P-value
n.	45	45	–
Age (Years)	20.24 ± 4.93	20.17 ± 4.25	0.339
BMI (kg/m^2)	27.93 ± 5.33	22.33 ± 2.40	0.01
WHR	1.04 ±0.27	0.71 ± 0.18	0.014
LH (IU/L)	10.43 ± 2.11	5.30 ± 1.58	0.0001
FSH (IU/L)	7.06 ± 1.42	6.00 ± 1.49	0.0008
LH/FSH	1.51 ± 0.40	0.83 ± 0.22	0.0001
TT (n mol/L)	3.09 ± 0.91	1.25 ± 0.32	0.01
FT (p mol/L)	13.18 ± 1.13	2.69 ± 0.74	0.0001
SHBG (n mol/L)	1.02 ± 0.01	7.38 ± 3.88	0.0001
FAI	3.14 ± 1.62	0.18 ± 0.02	0.001
FSG (mg/dL)	102.22 ± 10.43	82.89 ± 8.35	0.001
Insulin (m IU/L)	11.76 ± 1.55	6.44 ± 1.35	0.0001
HOMA-IR	3.64 ± 1.09	1.37 ± 0.49	0.0001
HOMA%S	66.14 ± 22.26	80.96 ± 20.65	0.0001
TC (mmol/L)	5.12 ± 2.03	3.26 ± 1.11	0.001
TG (mmol/L)	2.01 ± 0.57	0.78 ± 0.09	0.0001
HDL-C (m mol/L)	1.13 ± 0.48	2.07 ± 0.51	0.001
VLDL (m mol/L)	0.51 ± 0.06	0.18 ± 0.01	0.0001
LDL-C (mmol/L)	5.12 ± 1.89	1.11 ± 0.76	0.0001

N; number, Standard Deviation (SD): Waist-to-Hip Ratio (WHR), Body Mass Index (BMI) Fasting Serum Glucose (FSG), A measure for insulin sensitivity, or HOMA%S HOMA-IR: Insulin Resistance Homeostatic Model Assessment FSH: follicular stimulating hormone, LH: luteinizing hormone, and FAI: fasting insulin FAI stands for free androgen index, TT for total testosterone, FT for free testosterone, Total cholesterol (TC) Triglycerides (TG) Both HDL-C and LDL-C are high-density lipoproteins that include cholesterol.

Table 2. Comparison between obese and non-obese PCOS women with Obese and Non-Obese healthy control groups.

Parameters	PCOS obese Patients group Mean ± SD	PCOS non-obese Patients group Mean ± SD	P-value
n.	25	20	–
Age (Years)	28.75 ± 4.57	27.84 ± 5.25	0.001
BMI (kg/m^2)	33.01 ± 2.306	22.17 ± 5.09	0.0001
WHR	1.60 ± 0.20	1.31 ± 0.25	0.049
LH (IU/L)	13.49 ± 2.38	11.38 ± 1.91	0.01
FSH (IU/L)	7.011 ± 1.587	7.102 ± 1.311	0.18
LH/FSH	1.505 ± 0.44	1.237 ± 0.48	0.047
TT (n mol/L)	4.07 ± 0.68	2.76 ± 0.89	0.01
FT (p mol/L)	14.13 ± 1.02	12.96 ± 0.91	0.01
SHBG (n mol/L)	1.01 ± 0.01	0.87 ± 0.03	0.001
FAI	4.11 ± 0.97	3.01 ± 0.92	0.01
FSG (mg/dL)	110.31 ± 7.28	98.67 ± 10.03	0.0001
Insulin (m IU/L)	11.881 ± 1.655	11.672 ± 1.488	0.04
HOMA-IR	4.62 ± 1.04	3.65 ± 1.23	0.04
HOMA%S	65.17 ± 19.28	70.19 ± 23.24	0.02
TC (mmol/L)	7.09 ± 3.36	4.84 ± 1.13	0.01
TG (mmol/L)	3.02 ± 0.62	2.19 ± 0.42	0.04
HDL-C (m mol/L)	1.079 ± 0.34	1.42 ± 0.57	0.03
VLDL-c (m mol/L)	0.613 ± 0.26	0.45 ± 0.44	0.01
LDL-C (m mol/L)	5.43 ± 1.37	3.12 ± 0.96	0.01

N: number, SD: Standard deviation, WHR: Waist-to-hip ratio, Fasting serum glucose (FSG) Insulin Sensitivity HOMA%S Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) FAI stands for Fasting Insulin. Follicle stimulating hormone (FSH), luteinizing Hormone (LH), TT stands for total testosterone, FT for Free Testosterone, and FAI for Free Androgen Index. TC: total cholesterol levels, Triglycerides, or TG LDL-C: low density lipoprotein-cholesterol, and HDL-C: High-density Lipoprotein-cholesterol.

was used to construct the free androgens index (FAI) [11].

2.1. Statistical analysis

The program utilized for statistical analysis was SPSS (Statistical Package for the Social Sciences; version 26.0, SPSS Inc., Chicago, IL, USA). When the distribution is normal, analysis Each result's mean and SD was noted. The study's groups' statistical significance was assessed using an unpaired Student's t-test. T - tests were used to evaluate two separate samples. The link between variables examined using Pearson's correlation analysis for comparing parameters of PCOS-afflicted women; a P-value of <0.05 was considered statistically significant.

3. Results

3.1. Demographic characteristics of patients and control groups

In Table 1 displays the study groups' baseline characteristics. 45 people with PCOS to compare with 45 fertile. The control group consisted of women in good health. Between the study groups, there is no appreciable difference in the age variables. PCOS patients exhibit higher levels of Body mass index (BMI), Central adiposity (WHR), Androgens (TT, FT, FAI), LH and LH/FSH ratio, Glucose and insulin levels, Lipid markers (TC, TG, VLDL, LDL-C), Insulin resistance (HOMA-IR).

PCOS patients show lower levels of SHBG, Insulin sensitivity (HOMA%S), HDL-C.

3.2. Comparison of hormonesand metabolic parameters obese PCOS and non-obese

The study groups' obese and non-obese PCOS women were compared, as shown in Table 2. The outcome shows that, in comparison to the healthy control group.

3.3. Correlation analysis between hormones levels with other anthropometric and biochemical parameters

Table 3 examines how the Pearson correlation coefficient (r) assesses the impact of obese and non-obese hormones levels on biochemical indicators in women patients with PCOS.

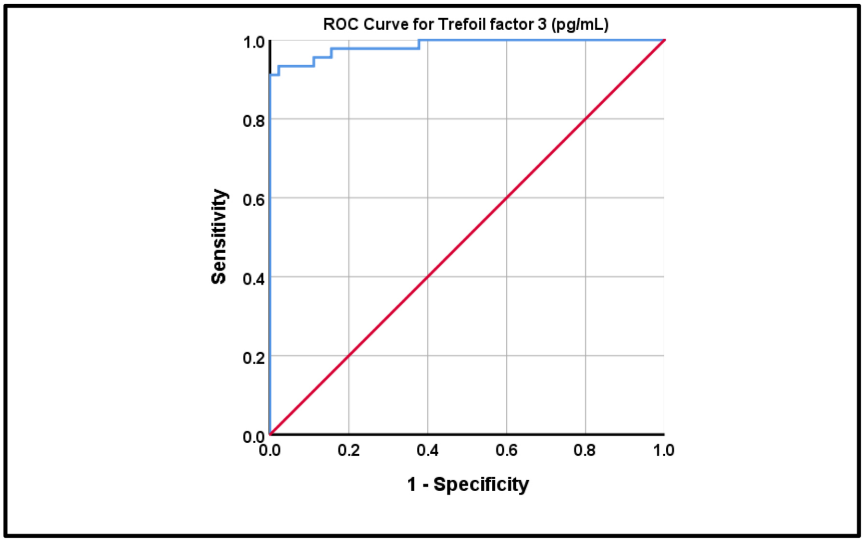

Fig. 1. Analysis ROC curve of LH levels as discriminators of PCOS obese patients.

Table 3. Data of correlation analysis between HOMA-IR with clinical Biochemical parameters in patients group.

Parameters	r	p-value
Age (year)	0.080	0.451
WHR	0.261	0.013
FSH (IU / L)	0.599	0.0001
LH / FSH	0.547	0.0001
SHBG (n mol / L)	–0.392	0.001
TT (n mol / L)	0.364	0.001
FT (p mol / L)	0.413	0.001
FAI	0.462	0.001
FSG (mg / dL)	0.273	0.01
Insulin (m IU/L)	0.713	0.0001
HOMA-IR	0.695	0.0001
HOMA%S	–0.586	0.0001
TC (m mol / L)	0.273	0.01
TG (m mol / L)	0.261	0.02
LDL-C (m mol / L)	0.317	0.01
HDL-C (m mol / L)	–0.336	0.001
VLDL-C (m mol / L)	0.295	0.01

r: pearson correlation WHR: Waist-to-hip ratio, SHBG: Sex Hormone binding Globulin blood test, HOMA-IR: Homeostatic Model Assessment for Insulin Resistance, Focal stimulating hormone (FSH), free testosterone (FT), and free androgen index (FAI) TC stands for total cholesterol. total testosterone (TT), TG: triglycerides, The acronyms HDL-C and LDL-C stand for high-density lipoprotein and cholesterol, respectively.

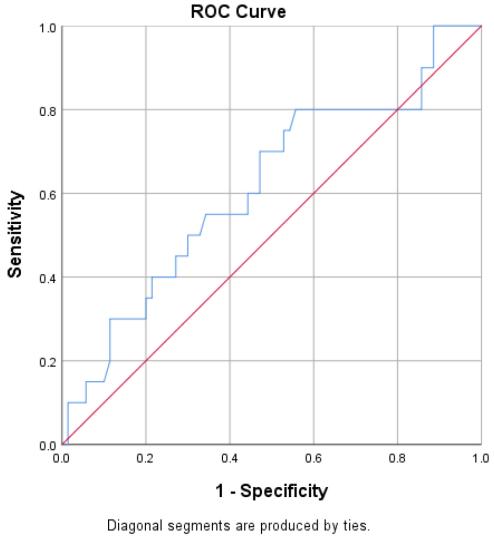

Fig. 2. Analysis ROC curve of FSH levels as discriminators of PCOS obese patients.

3.4. Receiver operating characteristic (ROC)

4. Discussion

In the study show in the One of the most recognizable hormonal traits is abnormal gonadotropin production, which is connected to PCOS women's continued anovulatory status [12].

In Iraq, women with PCOS are frequently obese. Obesity increases the likelihood that PCOS will worsen its effects. It makes metabolic disorders more likely. The presence of fat exacerbates insulin resistance. Although many PCOS patients have normal BMIs, the prevalence of obesity in these women varies. It is not necessary to be obese to diagnose PCOS [13]. Scientists consider PCOS to be one of the main causes of infertility, obesity and it has many dimensions, including in addition to genetic causes, environmental and social causes. Regular PCOS is associated with elevated blood levels of androgens, including testosterone. This may result in acne and hirsutism (excessive facial and body hair) [14] Compared to the irregularly menstruating group, the regularly menstrual group was significantly older, had a higher basal FSH concentration, and had fewer

Table 4. Area under the curve analysis of the observed biomarkers for PCOS diagnosis is the receiver operating characteristic.

Variables	Cut-off concentration	Sensitivity%	Specificity%	AUC	95% CI of AUC	P-value
LH (IU/l)	9.4800	75%	78.6%	0.813	0.722–0.903	<0.0001
FSH (IU/L)	6.7650	60%	55.7%	0.615	0.472–0.759	0.117
BMI (kg/m^2)	24.9550	100%	98%	0.995	0.984–1.000	<0.0001
HOMA-IR	2.6500	70%	74.3%	0.798	0.690–0.905	<0.0001

AUC: Area under the curve, CI: Confidence interval.

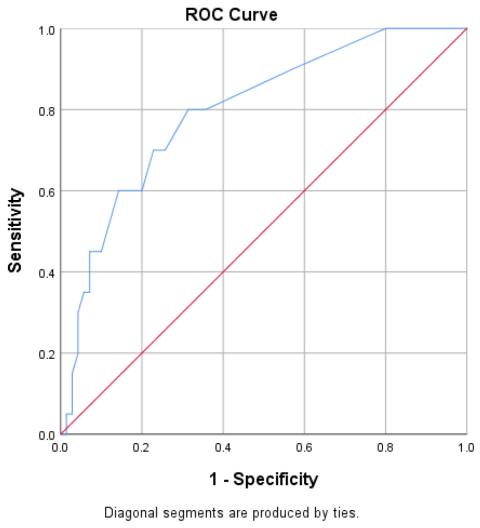

Fig. 3. Analysis ROC curve of HOMA-IR levels as discriminators of PCOS obese patients.

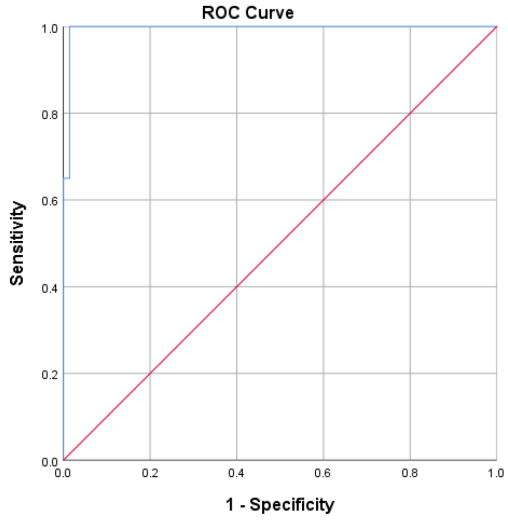

Fig. 4. Analysis ROC curve of BMI levels as discriminators of PCOS obese patients.

androgens [15]. Higher androgen levels and decreased levels of sex hormone-binding globulin. have been linked to polycystic ovarian syndrome (PCOS), which is characterized by long and irregular menstrual cycles. Through in-person interviews, data on PCOS, menstrual cycle duration, and irregularity were gathered [16].

IR is characterized by decreased insulin sensitivity in insulin-responsive tissues, with major repercussions including a diminished capacity of insulin to inhibit hepatic glucose synthesis and promote peripheral glucose excretion [17]. Insulin rules to adjust glucose balance by activating glucose pick via insulin- sensible of cells membrane in target organs such as adipose tissues, skeletal, and cardiac muscles, in addition to inhibiting liver glucose output [18], Therefore, IR is a feature of heightened insulin production in blood, mainly and in reply to an increased glucose level, whether pancreas duty is normal [19].

Insulin resistance (IR) is associated with a number of diseases including obesity, metabolic syndrome (Met), Type 2Diabetes Mellitus, PCOS and chronic infection, In muscle and fat cells, insulin resistance reduces glucose absorption, but in liver cells, it results in reduced glycogen synthesis and storage as well as an inability to prevent glucose production and release into the bloodstream [20].

Obesity besides insulin resistance (IR) are prevalent in women with PCOS, which is in line with the prevalence rate of IR in the current study [21]. Previously, it was believed that neck circumference (NC) and WHR were indicators of subcutaneous adipose tissue in the upper body. They may also have an impact on the cardiometabolic system and be linked to elevated systemic free fatty acids [22].

5. Conclusion

In the study illustrated that PCOS is an important metabolic- endocrine disease, and low grade inflammation has a significant impact on the life of reproductive-age women, and is currently a very common reproductive disease in obstetrics and gynecology. Since women with PCOS are more likely to gain weight, and excessive weight gain increases the prevalence of PCOS, lean women have milder reproductive phenotypes than overweight women. Insulin resistance (IR), a crucial etiological factor of PCOS, is traditionally attributed primarily to obesity. Adiposity and insulin resistance are described in more severe reproductive phenotypes (characterized by hyperandrogenism associated with chronic

anovulation). Moreover, they show the presence of intrinsic insulin resistance in PCOS, independent of obesity. The hormones, including insulin, GH, GnRH, LH/FSH ratio, androgens, and estrogens, are abnormally altered with a close correlation in the diagnosis and clinical manifestations of PCOS, which provides directions for the treatment of PCOS.

Acknowledgments

The authors express their gratitude to the patients and the entire medical staff at AL-Zahra'a Teaching Hospital for Gynecology and Obstetrics in Al-Najaf, Iraq, and the Center of Fertility at AL Sader Medical City for their assistance.

Declaration of interest

There is no conflict of interest, according to the authors.

Funding

None.

Ethical Approval

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