RESEARCH ARTICLE

Insulin Resistance, Adiponectin, and Dyslipidemia as Key Determinants of Metabolic and Reproductive Dysregulation in Polycystic Ovary Syndrome

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Abstract

BACKGROUND: Polycystic ovary syndrome (PCOS) is a common endocrine disorder associated with insulin resistance, dyslipidemia, and metabolic dysfunction. However, the predictive value of insulin resistance (HOMA-IR), dyslipidemia, and adiponectin in identifying PCOS and stratifying metabolic risk remains unclear, particularly in underrepresented populations, such as Iraqi women. This study evaluated these parameters to improve risk stratification and early intervention strategies in resource-limited settings.

METHODS: This case-control study included 100 women (50 with PCOS diagnosed using the Rotterdam criteria and 50 age-matched healthy controls). Anthropometric and clinical assessments, including BMI and hirsutism scores, were performed. Fasting blood samples were analyzed for glucose and lipid profile using colorimetric assays, insulin via electrochemiluminescence immunoassay (ECLIA), and adiponectin via enzyme-linked immunosorbent assay (ELISA), and HOMA-IR was calculated to quantify insulin resistance.

RESULTS: Women with PCOS exhibited significantly higher BMI, fasting glucose, insulin, and HOMA-IR values (p<0.001 for all) than controls. Dyslipidemia was evident, characterized by elevated total cholesterol, LDL-C, and triglyceride levels, as well as lower HDL-C levels (p<0.001). Adiponectin levels were markedly reduced in the PCOS group (p<0.001) and showed strong inverse correlations with HOMA-IR (r=–0.554, p<0.001) and fasting insulin (r=–0.453, p<0.001). Logistic regression indicated that HOMA-IR was the most significant predictor of PCOS (OR=28, 95% CI 4.86–161.44, p=0.0002), whereas higher adiponectin levels offered significant protective effects (OR=0.54, 95% CI 0.36–0.82, p=0.0039).

CONCLUSION: Insulin resistance, dyslipidemia, and low adiponectin levels are strongly associated with PCOS and metabolic dysfunction in Iraqi women. HOMA-IR is a key predictor, whereas adiponectin may have protective effects. These findings highlight the potential of these biomarkers in risk stratification and early intervention in resource-limited settings.

KEYWORDS: PCOS, adiponectin, HOMA-IR, dyslipidemia

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Introduction

Polycystic ovary syndrome (PCOS) is a complex endocrine disorder characterized by multifactorial etiology, affecting an estimated 4–20% of women within the reproductive age bracket globally.(1-3) Characterized by persistent anovulation, either clinical or biochemical hyperandrogenism, and the presence of polycystic ovarian morphology, PCOS is often diagnosed using the Rotterdam

European Society of Human Reproduction and Embryology/ American Society for Reproductive Medicine (ESHRE/ ASRM) criteria, which necessitate the identification of two of these three characteristics for a conclusive diagnosis. (4) Although these parameters primarily highlight reproductive dysfunction, the syndrome extends far beyond the ovaries and encompasses a range of metabolic abnormalities, most notably insulin resistance, which affects up to 70% of women with PCOS.(5,6)

Insulin resistance is a central feature in PCOS pathophysiology, contributing not only to hyperglycemia and dyslipidemia, but also to hyperinsulinemia, which further amplifies ovarian androgen secretion by enhancing the sensitivity of theca cells.(3) This hyperinsulinemic state perpetuates a vicious cycle wherein androgens promote abdominal adiposity and systemic inflammation, resulting in even greater insulin resistance and metabolic risk. Chronic low-grade inflammation, common in PCOS, is thought to exacerbate adipose tissue dysfunction, underlining the complexity of the disorder at the intersection of reproductive endocrinology, metabolism, and immunology. (7) Consequently, women with PCOS are more likely to develop type 2 diabetes mellitus (T2DM), cardiovascular complications, and other long-term metabolic sequelae.(8)

Contemporary research has increasingly focused on the function of adipokine hormones released by adipose tissue that influence insulin sensitivity and systemic inflammation. Adiponectin has attracted significant interest owing to its robust insulin-sensitizing, anti-inflammatory, and anti-atherogenic characteristics.(9) Under normal physiological conditions, adiponectin enhances glucose uptake and fatty acid oxidation, thereby helping maintain metabolic homeostasis.(10) However, in PCOS, circulating adiponectin concentrations are often significantly lower than those in healthy controls.(11) This deficiency may further compound the insulin resistance and dyslipidemia characteristics of the syndrome, reflecting a pathophysiological link between impaired adipose tissue function and ovarian dysfunction. (12) Despite these observations, the precise cut-off values for adiponectin and their clinical utility as diagnostic or prognostic biomarkers remain areas of active investigation.

Given the heterogeneity and complexity of PCOS, a comprehensive approach to assess its metabolic and reproductive dimensions is essential. Surrogate indices of insulin resistance, such as the homeostatic model assessment of insulin resistance (HOMA-IR), are routinely employed in clinical and research settings because of their practicality, although more precise methods (*e.g.*, the hyperinsulinemic-euglycemic clamp) exist.(13) Nonetheless, refining the HOMA-IR threshold to best predict PCOS risk or severity in different populations remains a topic of ongoing debate, as ethnic and lifestyle differences may influence baseline insulin sensitivity.(14) Beyond its diagnostic importance, identifying and validating robust predictors of metabolic risk (*e.g.*, HOMA-IR and adiponectin) may facilitate early intervention strategies ranging from lifestyle modifications to pharmacological treatments such as metformin or thiazolidinediones aimed at mitigating hyperandrogenemia, improving fertility outcomes, and reducing cardiovascular risk.(15)

Against this backdrop, the current study was designed to systematically evaluate insulin resistance (HOMA-IR), dyslipidemia, and adiponectin levels in Iraqi women with PCOS relative to age-matched controls, addressing the paucity of data in this underrepresented population with unique genetic and environmental risk factors. While the association between HOMA-IR and PCOS has been established, we explored the novel combined predictive value of HOMA-IR and adiponectin for identifying PCOS using logistic regression, along with their correlations with clinical features (*e.g.*, hirsutism and menstrual irregularities) and biochemical markers (*e.g.*, fasting insulin), offering new insights into the interplay between metabolic and reproductive dysfunction. By elucidating these interrelationships, our findings aim to address the unmet clinical needs for reliable biomarkers in resource-limited settings, paving the way for more precise risk stratification and targeted interventions to alleviate the syndrome's complex clinical burden.

Methods

Study Design and Participants

A comparative cross-sectional study was conducted between February 2023 and July 2024 at the Al-Sadr Teaching Hospital in Najaf, Iraq, following approval from the Institutional Review Board (Approval Number: 34328). Written informed consent was obtained from all participants prior to inclusion, in accordance with the principles of the Declaration of Helsinki.(16) The minimal sample size (n) was determined using the formula to compare two proportions.(17)

A total of 100 women aged 18–40 years were recruited and divided into two groups: 50 women diagnosed with PCOS according to the revised Rotterdam criteria (18) and 50 age-matched healthy controls without PCOS. The diagnostic criteria for PCOS include at least two of the

following: 1) oligo- or anovulation, 2) clinical and/or biochemical signs of hyperandrogenism, and 3) polycystic ovarian morphology on ultrasound, with exclusion of other endocrine disorders such as congenital adrenal hyperplasia, Cushing's syndrome, thyroid dysfunction, or androgen-secreting tumors. Control participants were recruited from the general population and had regular menstrual cycles (21–35 days), no clinical or biochemical signs of hyperandrogenism, and a normal ovarian morphology on transvaginal ultrasonography.

Exclusion criteria for all participants included current pregnancy, lactation, use of hormonal medications or insulin-sensitizing agents within the last three months, smoking, alcohol abuse, and chronic systemic diseases such as diabetes mellitus, hypertension, or cardiovascular disease.

Data Collection

Demographic and clinical data were collected through structured interviews and physical examinations conducted by trained clinician. The information gathered included age, body mass index (BMI), and physical activity levels assessed using the International Physical Activity Questionnaire (IPAQ) short form.(19)

Anthropometric measurements were taken with the participants wearing light clothing and no shoes. Weight was measured to the nearest 0.1 kg using a calibrated digital scale (Seca 803; Seca GmbH & Co. KG, Hamburg, Germany), and height was measured to the nearest 0.1 cm using a wall-mounted stadiometer (Seca 217). BMI was calculated as the weight in kilograms divided by the height in meters squared (kg/m²).

Clinical assessments included detailed menstrual history (age at menarche, cycle length, duration, and regularity), reproductive history (e.g., pregnancies, miscarriages), and evaluation of signs of hyperandrogenism, such as hirsutism. Hirsutism was evaluated using the modified Ferriman-Gallwey scoring system (20), with a score of ≥8 indicating hirsutism.

Sample Collection

Venous blood samples were collected from all participants between 8:00 AM and 9:00 AM after an overnight fast of at least 8 hours. For women with regular menstrual cycles, samples were collected during the early follicular phase of the menstrual cycle (days 2–5). For women with oligomenorrhea or amenorrhea, samples were collected on a random day and progesterone levels were measured to confirm the absence of ovulation. Blood samples were centrifuged at 3,000 rpm for 10 min at 4°C, and the serum was separated and stored at −80°C until analysis.

Enzymatic Colorimetric Assays

Fasting plasma glucose (FPG) levels were measured using an enzymatic colorimetric method (Catalog No. 10009582; Cayman Chemical, Ann Arbor, MI, USA) that employs glucose oxidase to catalyze the oxidation of glucose. The resulting colorimetric changes were quantified using an automated analyzer (Hitachi 912; Roche Diagnostics, Basel, Switzerland). Serum lipid profiles were evaluated using enzymatic colorimetric assays for total cholesterol and triglyceride (Catalog No. CH201, and TR201; Randox Laboratories, Crumlin, UK). High-density lipoprotein cholesterol (HDL-C) levels were measured using a direct enzymatic method (Catalog No. HD381; Randox), and low-density lipoprotein cholesterol (LDL-C) levels were calculated using the Friedewald formula for triglyceride levels <400 mg/dL. When triglyceride levels exceeded 400 mg/dL, a direct LDL-C assay (Catalog No. LD381; Randox) was used. All assays were conducted strictly according to the manufacturer's instructions, and quality controls were assessed in each run.

Electrochemiluminescence Immunoassay (ECLIA)

The serum insulin concentrations were determined by ECLIA (Catalog No. 12017547122; Roche Diagnostics, Mannheim, Germany). Briefly, ECLIA employs a ruthenium-labeled detection antibody that binds to the target analyte, and upon electrochemical stimulation, the oxidized ruthenium emits light in proportion to the concentration of insulin in the sample. Each sample was analyzed in duplicate, and all runs included calibrators and quality controls spanning the expected concentration range. The intra- and inter-assay coefficients of variation (CV) were maintained below 10%. Insulin resistance was estimated using the homeostatic model assessment of insulin resistance (HOMA-IR) and subsequently calculated as HOMA-IR = (Fasting Insulin (μU/mL) × Fasting Glucose (mg/dL)) / 405.(21)

Enzyme-linked Immunosorbent Assay (ELISA)

Serum adiponectin was quantified using a quantitative sandwich ELISA (Catalog No. DRP300; R&D Systems, Minneapolis, MN, USA). This assay has a reported sensitivity of 0.2 μg/mL and uses paired antibodies specific to adiponectin. The samples, standards, and controls were assayed in duplicate, and replicates with a CV above 10% were repeated.

Quality Assurance and Control

All biochemical analyses were performed according to the respective kit protocols, and assay performance was continuously monitored using standardized controls. Calibration curves were generated for each analyte, and only data from runs in which the control values fell within the predefined acceptance limits were used for subsequent calculations.

Statistical Analysis

GraphPad Prism 9 (GraphPad Software, San Diego, CA, USA) was used to detect the effect of different groups (PCOS subjects and controls) on the study parameters. A t-test was used to compare the means. Chi-square test was used to compare the percentages. Estimation of the correlation coefficient and multiple linear regression between variables. Sensitivity and specificity of parameters in the patient and control groups cut-off values for biomarkers were determined using Receiver Operating Characteristic (ROC) curve analysis to maximize sensitivity and specificity. The Youden Index was used to identify the optimal threshold for each parameter.(22)

Results

Demographic Characteristics of the Study Groups

Table 1 presented a comprehensive comparison of the demographic, anthropometric, reproductive, and clinical parameters between the control and PCOS groups. The results showed that women with PCOS had a higher BMI, prolonged menstrual cycle length, and more hirsutism. A higher proportion of participants had not experience pregnancy, indicating potential subfertility. Elevated blood pressure in the PCOS group indicated potential metabolic and cardiovascular risks.

Biochemical Parameters and Characteristics

Table 2 showed significant lipid profile changes in women with PCOS compared to controls. Total cholesterol, LDL-C, triglycerides, and very low-density lipoprotein (VLDL) levels were higher in the PCOS group, while HDL-C was lower. These findings suggested that PCOS's dyslipidemic pattern and potential metabolic risk factor role in cardiovascular risk. There were significantly elevated

Table 1. Comparison of demographic, clinical, and reproductive characteristics between control and PCOS groups.

Characteristic	Control (n=50)	PCOS (n= 50)	*p*- value
Age (years)			
Mean±SD	27.88±6.12	29.4±6.6	0.220[a]
Range	18–39	18–39	
BMI (kg/m²)			
Mean±SD	24.4±2.1	31.98±3.21	0.000[a,*]
Range	20.27–29.9	25.46–39.9	
Cycle Length (days)			
Mean±SD	30.86±2.06	43.4±4.02	0.000[a,*]
Range	28–34	35–50	
Pregnancies[1], n (%)			
Non-Pregnancies	0 (0)	17 (34)	0.000[b,*]
Pregnancies (1)	19 (38)	18 (36)	
Pregnancies (2)	14 (28)	15 (30)	
Pregnancies (3)	17 (34)	0 (0)	
Hirsutism (Ferriman-Gallwey score)			
Mean±SD	3.06±0.9	8.2±1.94	
Range (normal to mild)	1.31–5.03	4.13–14.2	0.000[a,*]
Range (moderate to severe)	65.4–86.1	74.5– 96.2	

[1]Pregnancies (Number of past pregnancies) are categorized as follows: Non-Pregnancies = no previous pregnancy; Pregnancies (1) = one previous pregnancy; Pregnancies (2) = two previous pregnancies; Pregnancies (3) = three or more previous pregnancies. [a]Tested with independent samples t-test; [b]Tested with Fisher's Exact Test. *Significantly different if $p<0.05$.

Table 2. Comparison of lipid profile and glucose homeostasis between control and PCOS groups.

Characteristic	Control (n= 50)	PCOS (n= 50)	*p*- value
Cholesterol (mg/dL)			
Mean±SD	191.3±16.9	226.8±22.3	0.000[a,*]
Range	151–226	178–270	
HDL-C (mg/dL)			
Mean±SD	61.2±11.2	44.4±10.9	0.000[a,*]
Range	39–83	22.2–70.7	
LDL-C (mg/dL)			
Mean±SD	98.8±21.6	138.7±25.6	0.000[a,*]
Range	42.5–137	76.53–195	
Triglycerides (mg/dL)			
Mean±SD	138±18.3	183±39.6	0.000[a,*]
Range	104.7–193.3	102.8–275	
VLDL (mg/dL)			
Mean±SD	27.7±3.66	36.6±7.9	0.000[a,*]
Range	20.9–38.6	20.56–55.05	
Fasting blood sugar (mg/dL)			
Mean±SD	90.3±8.94	110.7±16.1	0.000[a,*]
Range	73.9–111.6	81.8–158.8	
Insulin (µIU/mL)			
Mean±SD	7.64±2.01	14.45±4.19	0.000[a,*]
Range	2.22–12.93	4.74–22.25	
HOMA-IR			
Mean±SD	1.92±0.49	3.84±0.98	0.000[a,*]
Range	0.84–3.03	0.52–5.9	

[a]Tested with independent samples t-test. *Significant difference if $p<0.05$.

fasting blood glucose, serum insulin, and homeostatic model assessment of insulin resistance (HOMA-IR) in women with PCOS compared to controls ($p<0.001$).

Decline in Adiponectin Levels in PCOS

The mean adiponectin level in the control group was significantly higher (14.87± 3.32 µg/mL) than that in the PCOS group (9.87±1.89 µg/mL), with a statistically significant difference ($p<0.001$) (Figure 1). Circulating adiponectin levels were significantly lower among women with PCOS than among controls. This finding aligns with the known role of adiponectin as an insulin-sensitizing and anti-inflammatory adipokine, suggesting that its decreased secretion may contribute to heightened insulin resistance and metabolic disturbances observed in PCOS.

Correlation analysis showed strong associations between HOMA-IR and metabolic parameters, with a positive correlation of 0.594 for fasting insulin, 0.477 for fasting glucose; moderate to strong positive associations of 0.539 for total cholesterol, 0.486 for LDL-C, and 0.524 for triglycerides; and inverse correlations (r=-0.484) for HDL-C (with $p<0.001$ for all parameters). Additional associations were observed by inter-variable analyses included the correlation of fasting insulin and fasting glucose (r=0.485), total cholesterol and LDL-C (r=0.397),

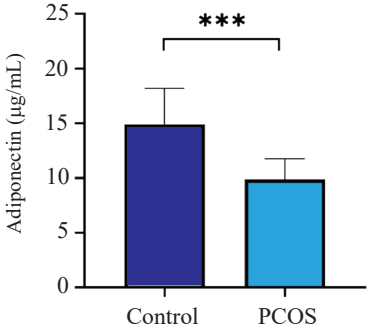

Figure 1. Comparison of adiponectin among control and POCS groups.

total cholesterol and triglycerides (r=0.407), LDL-C and triglycerides (r=0.444), LDL-C and fasting glucose (r=0.485), triglycerides and HDL (r=0.381), adiponectin and triglycerides (r=-0.506), adiponectin and LDL (r=-0.423), as well as adiponectin and HDL (r=0.366) (with $p<0.001$ for all parameters). Adiponectin showed a strong negative correlation with HOMA-IR (r=-0.554) and fasting insulin (r=-0.453) (with $p<0.001$ for both parameters) as shown in Figure 2, reflecting its insulin-sensitizing properties and inverse association with endocrine and metabolic dysfunction in PCOS.

Diagnostic Efficacy of Biomarkers in PCOS

The ROC curves illustrated the diagnostic performance of fasting insulin, HOMA-IR and adiponectin levels in identifying women with PCOS (Figure 3). Notably, a HOMA-IR cut-off >2.64 provided high sensitivity (94%) and specificity (94%), yielding an area under curve (AUC) of 0.97 (p=0.001) and underscoring its robustness in detecting insulin resistance. Adiponectin levels ≤12.27 µg/mL also demonstrated strong discriminatory power with 96% sensitivity and 86% specificity (AUC=0.90, p=0.001).

Statistical Analysis of Adiponectin and Insulin Resistance in PCOS

Table 3 showed the results of multiple logistic regression analysis examining the predictive value of adiponectin and HOMA-IR in PCOS. A one-unit increase in HOMA-IR markedly increased the odds of PCOS by nearly 28-fold (OR=28, 95% CI: 4.86–161.44, p=0.0002), reinforcing the critical role of insulin resistance in PCOS pathophysiology. Logistic regression analysis indicated that HOMA-IR was the most robust predictor of PCOS (odds ratio [OR]=28, 95% CI: 4.86–161.44, p=0.0002). Lower adiponectin levels were associated with increased odds of PCOS (OR=1.85, 95% CI: 1.22–2.78, p=0.0039), reflecting its role in metabolic dysregulation.

Discussion

In the present study, we provide evidence that reinforces the centrality of insulin resistance in driving both metabolic and reproductive disturbances that are characteristic of PCOS. The current findings indicate that women with PCOS exhibit significantly elevated homeostatic model assessment of insulin resistance (HOMA-IR) values, higher fasting insulin and glucose levels, and a more adverse lipid profile than age-matched controls. These observations mirror earlier reports suggesting that up to52% of women with PCOS have some degree of insulin resistance, irrespective of their BMI.(23) Hyperinsulinemia, a hallmark of insulin resistance, amplifies ovarian androgen secretion via increased stimulation of theca cells, thereby perpetuating the hyperandrogenic state central to PCOS pathophysiology.(24)

An important contribution of this study is the exploration of adiponectin, an insulin-sensitizing anti-inflammatory adipokine. Our data showed that adiponectin levels were markedly lower in women with PCOS, corroborating findings from previous studies that identified adiponectin deficiency as a contributor to the metabolic and inflammatory milieu of PCOS.(25) The inverse correlation between adiponectin and HOMA-IR implies that decreased adiponectin levels could aggravate insulin resistance by impeding normal glucose and lipid metabolism in peripheral tissues.(26) Additionally, low adiponectin levels have been linked to chronic low-grade inflammation and endothelial dysfunction, which further predispose women with PCOS to cardiovascular risk.(27)

The logistic regression findings substantiate the robust predictive value of insulin resistance in PCOS, with elevated HOMA-IR significantly increasing the odds of developing the disorder. Notably, a HOMA-IR cutoff above 2.64 (as revealed by the ROC analysis) displayed high sensitivity and specificity in diagnosing PCOS, aligning with certain

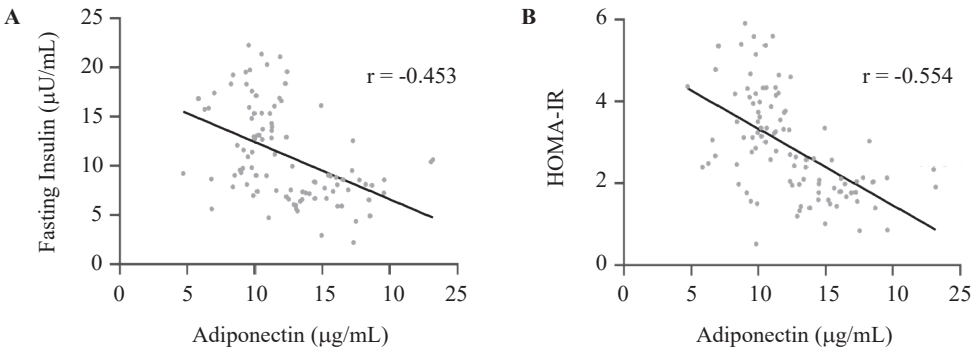

Figure 2. Correlation of adiponectin with HOMA-IR and fasting insulin.

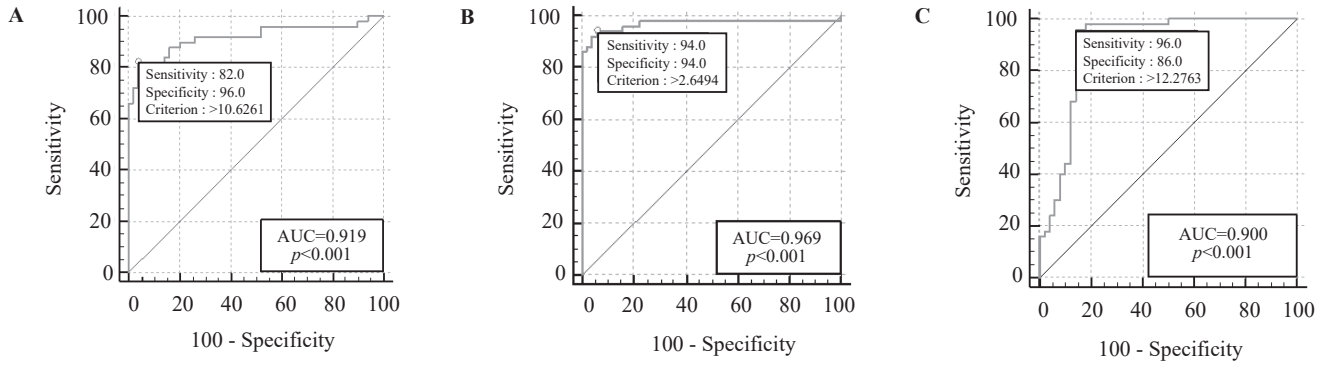

Figure 3. ROC curve for glucose homeostasis parameters. A: ROC curve for fasting insulin; B: ROC curve for HOMA-IR; C: ROC curve for adiponectin.

population-based studies but also underscoring the need for population-specific thresholds due to variations in ethnicity and lifestyle factors.(28, 29) Meanwhile, higher adiponectin levels appear to be protective, lowering the likelihood of PCOS, which aligns with the recognized role of adiponectin in improving insulin sensitivity and mitigating androgen excess.(30) This has important clinical implications, suggesting that strategies aimed at increasing adiponectin through weight reduction, dietary modifications, or novel pharmacotherapeutic agents could potentially improve insulin sensitivity and reproductive outcomes in PCOS.(31) The dyslipidemia patterns observed in the PCOS group (elevated LDL-C, triglycerides, total cholesterol, and reduced HDL-C) are consistent with earlier evidence that PCOS is a high-risk state for cardiovascular comorbidities. (32,33) Insulin resistance likely underpins these lipid abnormalities by promoting hepatic VLDL production and inhibiting lipolysis, thereby contributing to atherogenic dyslipidemia.(34) This highlights the importance of routine lipid screening and early intervention in managing long-term cardiovascular risk in this population.

Beyond the core insulin resistance–hyperandrogenism axis, it is also essential to recognize the multifactorial nature of PCOS pathogenesis, which encompasses genetic predisposition, environmental influences, and epigenetic mechanisms.(35) The interplay among these factors contributes to the heterogeneity in PCOS presentations, meaning that a subset of lean women with PCOS may still show pronounced insulin resistance, whereas others may predominantly exhibit normoinsulinemic or metabolically healthy phenotypes.(36) Accordingly, personalized management strategies that integrate insulin-sensitizing treatments, dietary and exercise interventions, and potentially anti-inflammatory or adipokine-targeted therapies could yield meaningful improvements in both metabolic and reproductive outcomes.(37,38)

The results underscore the need for prospective research to elucidate the causality and potential reversibility of these endocrine–metabolic abnormalities. Further interventional trials examining the effects of lifestyle modifications, metformin, and adiponectin-enhancing agents on HOMA-IR, adiponectin levels, and reproductive outcomes (*e.g.*, ovulation and pregnancy rates) could provide deeper insights into effective management pathways.(39,40) Additionally, longer-term follow-up focusing on cardiovascular endpoints would shed light on the clinical significance of dyslipidemia and suboptimal adiponectin levels in this population.

Taken together, our data emphasize that insulin resistance is not merely a secondary feature but rather a driving force in the pathophysiology of PCOS, fueling both hyperandrogenism and metabolic dysfunction. Low adiponectin levels have emerged as critical mediators of insulin resistance, offering a potential therapeutic target. Establishing clear diagnostic cut-offs for HOMA-IR and

Table 4. Multiple logistic regression analysis of adiponectin and HOMA-IR in predicting PCOS.

Variables	Odds Ratio	95% CI for Odds Ratio	*p*-value
Adiponectin	0.54	0.36 to 0.82	0.0039*
HOMA-IR	28	4.86 to 161.44	0.0002*

Model 1 (R^2 = 0.87). *Significant if $p<0.05$.

adiponectin in diverse populations could further refine risk stratification and guide individualized treatment strategies. Ultimately, a multifaceted approach addressing hormonal, metabolic, and lifestyle factors is key to reducing the long-term reproductive and cardiometabolic burden faced by women with PCOS.

The strength of this study lies in its comprehensive evaluation of clinical, anthropometric, and metabolic parameters, particularly insulin resistance indices (HOMA-IR) and adiponectin levels, to elucidate the associations between these metabolic markers and PCOS. Rigorous inclusion criteria and standardized assays enhance internal validity, ensuring reliable comparisons between women with PCOS and age-matched controls. The inclusion of a composite risk score further strengthened the study's contribution, offering a novel tool for risk stratification in this population. Several limitations of this study should be considered when interpreting our findings. The cross-sectional nature of this study, which measures exposures (HOMA-IR and adiponectin) and outcomes (PCOS) simultaneously, precludes inferences about temporality, causality, or pathophysiology. Retrospective case-control studies with temporal data or longitudinal designs are required to explore these relationships. While the sample size was adequate for detecting group differences (n=100), larger multicenter studies would improve generalizability, particularly given the focus on Iraqi women, which may limit the applicability to other populations with different genetic and environmental risk factors. The reliance on logistic regression coefficients for the composite risk score requires external validation to confirm its applicability across diverse cohorts. Future research should address these gaps to enhance the understanding of PCOS mechanisms and refine the risk stratification tools.

Conclusion

Our findings support the association between insulin resistance and low adiponectin levels with PCOS and metabolic dysfunction. Women with PCOS exhibited higher HOMA-IR, dyslipidemia, and lower adiponectin levels than controls, with HOMA-IR being a strong predictor of PCOS. A composite risk score integrating these markers enhances risk stratification, highlighting its potential as a biomarker for identifying PCOS and assessing metabolic risks. These results emphasize the importance of metabolic screening in the diagnosis and management of PCOS, particularly for insulin resistance and adiponectin levels.

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Authors Contribution

KHH, BRY, RDAA, and KOH contributed equally in conceptualizing the research, collecting data, analysing the data, as well as drafting, editing and reviewing the manuscript.

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