



Original Paper

Association between IL-6 Gene Expression, Adipokines, and Reproductive Hormones in Iraqi Women with Polycystic Ovary Syndrome

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ABSTRACT

Polycystic ovary syndrome (PCOS) is a complex endocrine–metabolic disorder defined by clinical and/or biochemical hyperandrogenism and ovulatory dysfunction and accompanied by chronic low-grade inflammation and altered adipokine and cytokine profiles. This study assessed interleukin-6 (IL-6) gene expression and its relationship with adipokines (adiponectin, leptin, ghrelin and resistin) and reproductive hormones (FSH, LH and prolactin) in women with PCOS compared with healthy controls. A case–control study was conducted from September 2025 to May 2026 at Al-Zahraa Teaching Hospital, Wasit, Iraq, and included 247 women (127 with PCOS and 120 controls). Venous blood (5 mL) was collected from each participant for biochemical, hormonal and molecular analyses; hormones were measured on Cobas analysers, adipokines by ELISA and IL-6 expression by RT-qPCR. Most patients were aged 26–35 years (53.5%) and had a BMI of 25–30 kg/m² (56.7%). FSH was significantly lower in PCOS patients than in controls (5.04 ± 0.49 vs 7.52 ± 0.61 IU/L, $p < 0.001$), whereas LH was higher (8.72 ± 0.91 vs 5.95 ± 0.37 IU/L, $p < 0.001$), giving an increased LH/FSH ratio (1.73 vs 0.79); prolactin did not differ (7.85 ± 1.15 vs 7.29 ± 1.63 ng/mL, $p = 0.12$). Adiponectin (4.73 ± 1.25 vs 9.17 ± 1.16 ng/mL) and ghrelin (217.41 ± 28.35 vs 649.82 ± 42.05 pg/mL) were significantly decreased, while leptin (531.28 ± 39.51 vs 107.6 ± 13.82 pg/mL) and resistin (2.16 ± 0.34 vs 0.17 ± 0.08 ng/mL) were markedly increased in PCOS (all $p < 0.001$). IL-6 gene expression was significantly upregulated in PCOS (3.38-fold vs 1.70-fold in controls, $p = 0.001$). In ROC analysis leptin had the highest diagnostic accuracy (AUC = 0.94), followed by resistin (0.93), adiponectin (0.92), the LH/FSH ratio (0.91) and IL-6 (0.89), whereas prolactin performed poorly (AUC = 0.56). These findings illustrate the central role of inflammatory, metabolic and endocrine biomarkers in the pathophysiology and diagnosis of PCOS, with leptin, resistin and IL-6 showing the best diagnostic capacity.

KEYWORDS: PCOS, IL-6 gene expression, Adipokines, Reproductive hormones, RT-qPCR.

1-INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders of women of reproductive age and is characterised by hyperandrogenism, ovulatory dysfunction and polycystic ovarian morphology [1,2]. It is frequently associated with obesity, insulin resistance and infertility, and with an increased risk of metabolic and cardiovascular complications. Because PCOS is multifactorial, involving genetic, endocrine, metabolic and environmental influences [3], the causative and pathophysiological mechanisms of the syndrome remain incompletely understood despite extensive research.

Chronic low-grade inflammation has recently been identified as an important contributor to the pathophysiology of PCOS. Increased levels of inflammatory mediators such as C-reactive protein, tumour necrosis factor- α (TNF- α) and interleukin-6 (IL-6) have been reported in women with PCOS and may participate in the development of insulin resistance, ovarian dysfunction and metabolic abnormalities. A systematic review and

meta-analysis concluded that inflammation plays a key role in the pathophysiology of PCOS and may affect reproductive and metabolic outcomes [3,4], and a recent meta-analysis found higher circulating IL-6 levels in women with PCOS than in healthy subjects [5], further suggesting that IL-6 is a salient inflammatory biomarker of this condition.

IL-6 is a pleiotropic cytokine involved in immune modulation, inflammation, cellular signalling and the maintenance of metabolic homeostasis. Alterations in IL-6-related signalling pathways may influence follicular growth and turnover, steroidogenesis and ovulation. Polymorphisms in inflammatory cytokine genes, including IL-6, are also significantly associated with susceptibility to PCOS in genetic studies, indicating that dysregulation of inflammatory pathways contributes to disease aetiology [6,7]. In addition, a recent study in Iraqi women showed that IL-6 gene expression was significantly higher in PCOS patients and correlated positively with several biochemical abnormalities, reinforcing the clinical relevance of this cytokine in specific populations [7]. Besides inflammation, adipose tissue dysfunction has emerged as a key player in the pathophysiology of PCOS. Adipose tissue, once regarded as a passive energy reservoir, is now recognised as an active endocrine organ that secretes numerous bioactive molecules, termed adipokines, which regulate energy metabolism, insulin sensitivity, the inflammatory response and reproductive function [8]. Growing evidence indicates that adipose tissue dysfunction plays a major role in the metabolic derangements seen in women with PCOS [9]. Among the adipokines, adiponectin, leptin, ghrelin and resistin have attracted particular interest because of their roles in metabolic and reproductive control. Adiponectin is an anti-inflammatory, insulin-sensitising adipokine that is usually decreased in women with PCOS, whereas leptin and resistin are often increased and closely linked to obesity, insulin resistance and reproductive dysfunction [10,11]. Because of their close correlation with disease severity and metabolic status, adipokines have been proposed as potential biomarkers for the diagnosis and monitoring of PCOS [11]. Recent studies have also shed light on the intricate dialogue between adipokines and ovarian function: altered ovarian expression of adipokines has been associated with characteristic features of PCOS, including follicular growth arrest, ovulatory dysfunction and abnormal steroid hormone production [12]. Moreover, dysregulation of intracellular signalling pathways, such as the PI3K–AKT pathway, in response to inflammatory and metabolic factors may mediate reproductive dysfunction and affect ovarian function and reproductive outcomes [13].

Given the rising need for well-defined and reproducible biomarkers for the diagnosis and management of PCOS, several recent systematic reviews have emphasised the value of a holistic approach that combines inflammatory, metabolic and endocrine biomarkers for accurate disease characterisation and clinical management [14].

Nevertheless, few studies have examined the relationship between IL-6 gene expression, circulating adipokines and reproductive hormones in women with PCOS. The present study was therefore designed to analyse the associations among IL-6 gene expression, adiponectin, leptin, ghrelin, resistin, FSH, LH and prolactin in Iraqi women with PCOS, in order to improve understanding of the inflammatory–metabolic–endocrine interactions underlying the pathogenesis of the syndrome.

2-MATERIALS AND METHODS

2.1. Study design and sample collection

This case–control study was conducted between September 2025 and May 2026. A total of 247 women were enrolled: 127 women diagnosed with PCOS and 120 apparently healthy women who served as the control group. Participants were recruited from Al-Zahraa Teaching Hospital in Wasit, Iraq. A venous blood sample (about 5 mL) was collected aseptically from each subject. A portion of the sample was reserved for molecular analysis: for gene expression by RT-qPCR, 250 µL of whole blood was mixed with 750 µL of TRIzol reagent and stored at –20 °C until RNA extraction and determination of IL-6 gene expression. The remainder of the blood was placed in gel tubes and left to clot for 10–30 min at room temperature, and serum was then separated by centrifugation at

3000 rpm for 5 min. The serum was used to measure adiponectin, leptin, ghrelin, resistin, follicle-stimulating hormone (FSH), luteinising hormone (LH), prolactin and other required biochemical parameters.

2.1.1. Inclusion criteria

Women aged 18–45 years diagnosed with PCOS according to the Rotterdam criteria (2003) were included. The diagnosis was confirmed by the presence of at least two of the following: oligo- or anovulation, clinical and/or biochemical hyperandrogenism, and polycystic ovarian morphology on ultrasonography, after exclusion of other related endocrine disorders.

2.2. Biochemical and hormonal measurements

Anthropometric measurements (including body mass index, BMI) and clinical parameters were recorded for the PCOS patients and the healthy control women. Serum FSH, LH and prolactin were measured on Cobas e411 and Cobas Integra 400 Plus automated analysers in the hospital laboratory. Serum adipokines (adiponectin, leptin, ghrelin and resistin) were quantified using commercial ELISA kits (SunLong Biotech Co., Ltd, China) according to the manufacturer's instructions.

2.3. Quantitative real-time PCR (RT-qPCR)

Total RNA was extracted from peripheral blood according to the manufacturer's protocol (GENzol™ TriRNA Pure Kit, Promega, USA). The concentration and purity of the extracted RNA were measured with a NanoDrop spectrophotometer, and A260/A280 ratios ranged from 1.9 to 2.1. RNA integrity was further verified by 1% agarose gel electrophoresis, as indicated by clear and distinct 28S and 18S rRNA bands. Complementary DNA (cDNA) was synthesised from 1 µg of total RNA using the AccuPower® RocketScript™ PreMix Kit (Bioneer, Korea) according to the manufacturer's instructions. qRT-PCR was performed in 20 µL reactions of Luna Universal qPCR Master Mix (NEB) containing 10 µL of master mix, 0.5 µL of each primer (100 pmol/µL; Table 1), 3 µL of cDNA and 6 µL of RNase-free water. Amplification followed a standard cycling protocol: initial denaturation at 95 °C for 10 min, followed by 40 cycles of denaturation at 95 °C for 15 s, annealing at 60 °C for 60 s and extension at 72 °C for 15 s. A five-point serial-dilution standard curve was generated for each gene (IL-6 and β -actin); amplification efficiencies were within 90–110% and correlation coefficients (RZ) were greater than 0.99. Relative IL-6 expression was calculated by the $2^{-\Delta\Delta C_t}$ method with β -actin as the housekeeping gene. All samples were run in triplicate. To exclude contamination and genomic DNA amplification, no-template controls (NTC) and no-reverse-transcription controls (no-RT) were included in every run, and no amplification was detected in these controls.

Table (1) Primer sequences used for RT-qPCR analysis

Gene	Primer	Sequence (5' → 3')	Amplicon size (bp)	Ref.
IL-6	Forward	AATTCGGTACATCCTCGACGG	192	(7)
IL-6	Reverse	TTGGAAGGTTTCAGGTTGTTTCT	192	(7)
β -actin	Forward	GGGCGGCACCACCATGTACC	90	(7)
β -actin	Reverse	GACGATGGAGGGGCCCGACT	90	(7)

IL-6: interleukin-6; β -actin was used as the housekeeping (reference) gene.

2.4. Statistical analysis

All statistical analyses were carried out in R software (R Foundation for Statistical Computing, Vienna, Austria), and graphs were drawn in GraphPad Prism. The normality of continuous variables was tested with the Shapiro–Wilk test. Data are expressed as mean $\pm$ standard deviation (SD) for normally distributed variables and as median (interquartile range) for non-normally distributed variables, and comparisons between the PCOS and control groups were performed with the appropriate parametric or non-parametric tests. Receiver operating characteristic (ROC) curve analysis was performed in R to assess the diagnostic performance of IL-6 gene expression and the

other studied biomarkers in discriminating PCOS patients from healthy controls; the area under the curve (AUC), sensitivity, specificity and optimal cut-off values were determined. A p-value < 0.05 was considered statistically significant [15,16].

3-RESULTS

3.1. Age and BMI distribution of PCOS patients

The age and BMI distributions of the 127 women with PCOS are presented in Table 2. The majority of patients were aged 26–35 years (68 patients, 53.5%), followed by 15–25 years (31 patients, 24.4%), while the lowest proportion was in the 36–45 years group (28 patients, 22.1%). Regarding BMI, most patients were in the 25–30 kg/m² group (72 patients, 56.7%), followed by 31–35 kg/m² (41 patients, 32.3%), whereas the smallest proportion had a normal BMI of 18.5–24 kg/m² (14 patients, 11.0%).

Table (2) Age and BMI distribution of PCOS patients (n = 127)

Variable	Group	No. of patients (n)	Percentage (%)
Age (years)	15–25	31	24.4
	26–35	68	53.5
	36–45	28	22.1
BMI (kg/m ²)	18.5–24	14	11.0
	25–30	72	56.7
	31–35	41	32.3
Total		127	100

BMI: body mass index.

3.2. Reproductive hormones

Serum FSH was significantly lower in women with PCOS (5.04 ± 0.49 IU/L) than in the control group (7.52 ± 0.61 IU/L; $p < 0.001$). In contrast, LH was significantly higher in the PCOS group (8.72 ± 0.91 IU/L) than in healthy controls (5.95 ± 0.37 IU/L; $p < 0.001$), indicating a clear endocrine imbalance. Consequently, the LH/FSH ratio was markedly increased in PCOS patients (1.73) compared with controls (0.79). Prolactin did not differ significantly between the two groups (7.85 ± 1.15 ng/mL in PCOS patients vs 7.29 ± 1.63 ng/mL in controls; $p = 0.12$) (Table 3).

Table (3) Serum reproductive hormone levels and LH/FSH ratio in the PCOS and control groups

Parameter	Control (n = 120)	PCOS (n = 127)	p-value
FSH (IU/L)	7.52 ± 0.61	5.04 ± 0.49	< 0.001
LH (IU/L)	5.95 ± 0.37	8.72 ± 0.91	< 0.001
Prolactin (ng/mL)	7.29 ± 1.63	7.85 ± 1.15	0.12
LH/FSH ratio	0.79	1.73	—

Data are presented as mean $\pm$ SD. FSH: follicle-stimulating hormone; LH: luteinising hormone.

3.3. Serum adipokines

Serum adipokine levels differed significantly ($p < 0.001$) between women with PCOS and healthy controls (Table 4). Fasting adiponectin was significantly lower in women with PCOS (4.73 ± 1.25 ng/mL) than in controls (9.17 ± 1.16 ng/mL), and ghrelin was likewise significantly decreased in the PCOS group (217.41 ± 28.35 pg/mL) compared with healthy women (649.82 ± 42.05 pg/mL). Conversely, serum leptin was significantly higher in PCOS patients (531.28 ± 39.51 pg/mL) than in controls (107.6 ± 13.82 pg/mL), and resistin was significantly elevated in PCOS patients (2.16 ± 0.34 ng/mL) relative to controls (0.17 ± 0.08 ng/mL).

Table (4) Serum adipokine levels in the PCOS and control groups

Parameter	Control (n = 120)	PCOS (n = 127)	p-value
Adiponectin (ng/mL)	9.17 ± 1.16	4.73 ± 1.25	< 0.001
Leptin (pg/mL)	107.6 ± 13.82	531.28 ± 39.51	< 0.001
Ghrelin (pg/mL)	649.82 ± 42.05	217.41 ± 28.35	< 0.001
Resistin (ng/mL)	0.17 ± 0.08	2.16 ± 0.34	< 0.001

Data are presented as mean ± SD.

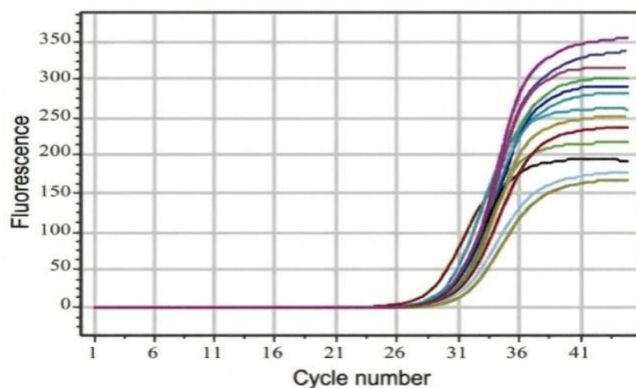
3.4. IL-6 gene expression

Expression analysis of the IL-6 gene revealed significant upregulation in women with PCOS compared with healthy controls. The mean fold change of IL-6 expression was 1.70 in the control group, whereas a marked increase was observed in the PCOS group, with a mean fold change of 3.38 ($p = 0.001$). Representative qRT-PCR data are shown in Table 5, and representative amplification curves are shown in Figure 1.

Table (5) Representative IL-6 qRT-PCR data (Δ Ct, $\Delta\Delta$ Ct and fold change) in control and PCOS samples

Group	IL-6 Ct	β -actin Ct	Δ Ct	$\Delta\Delta$ Ct	Fold change ($2^{-\Delta\Delta$ Ct)	Mean fold change	p-value
Control	31.7	26.2	5.5	-0.2	1.15	1.70	0.001
Control	30.1	25.5	4.6	-1.1	2.14		
Control	30.2	26.1	4.1	-1.6	3.03		
Control	31.8	25.1	6.7	1.0	0.50		
PCOS	29.1	24.2	4.9	-0.8	1.74	3.38	
PCOS	29.1	26.5	2.6	-3.1	8.57		
PCOS	30.3	25.2	5.1	-0.6	1.52		
PCOS	30.4	24.4	6.0	0.3	0.81		
PCOS	29.4	26.6	2.8	-2.9	7.46		
PCOS	31.2	24.9	6.3	0.6	0.66		
PCOS	28.7	25.5	3.2	-2.5	5.66		
PCOS	30.1	25.2	4.9	-0.8	1.74		
PCOS	29.4	24.9	4.5	-1.2	2.30		

Ct: threshold cycle; Δ Ct = Ct(IL-6) – Ct(β -actin); $\Delta\Delta$ Ct = Δ Ct(sample) – mean Δ Ct(control); fold change = $2^{-\Delta\Delta$ Ct. The p-value refers to the comparison of IL-6 expression between the PCOS and control groups.

**Figure (1): Representative real-time PCR amplification curves (fluorescence versus cycle number) of IL-6 in control and PCOS samples.**

3.5. ROC curve analysis

ROC curve analysis was performed to assess the diagnostic performance of each studied biomarker in differentiating women with PCOS from healthy controls (Table 6, Figure 2). Leptin showed the best

discrimination (AUC 0.94, 95% CI 0.90–0.98), and resistin (AUC 0.93, 95% CI 0.88–0.97) and adiponectin (AUC 0.92, 95% CI 0.87–0.96) were also highly accurate. The LH/FSH ratio likewise discriminated well (AUC 0.91, 95% CI 0.86–0.96). Among the inflammatory markers, IL-6 gene expression achieved an AUC of 0.89 (95% CI 0.83–0.94); at a cut-off of 2.45-fold expression it yielded 82.5% sensitivity and 84.3% specificity. The gonadotropins also showed moderate-to-strong performance, with AUCs of 0.87 (95% CI 0.81–0.93) for LH and 0.85 (95% CI 0.78–0.91) for FSH. By contrast, prolactin had an AUC of 0.56 (95% CI 0.48–0.64) with 55.0% sensitivity and 54.0% specificity.

Table (6) ROC curve analysis of the studied biomarkers for discrimination of PCOS

Marker	AUC (95% CI)	Cut-off value	Sensitivity (%)	Specificity (%)	Youden index	p-value
IL-6 gene expression	0.89 (0.83–0.94)	2.45-fold	82.5	84.3	0.67	0.001
FSH	0.85 (0.78–0.91)	6.20 IU/L	79.2	80.5	0.60	0.001
LH	0.87 (0.81–0.93)	7.10 IU/L	81.0	82.0	0.63	0.001
LH/FSH ratio	0.91 (0.86–0.96)	1.25	85.6	86.4	0.72	0.001
Adiponectin	0.92 (0.87–0.96)	6.10 ng/mL	86.8	88.0	0.75	0.001
Leptin	0.94 (0.90–0.98)	280 pg/mL	89.5	90.2	0.80	0.001
Ghrelin	0.90 (0.85–0.95)	420 pg/mL	84.0	85.7	0.70	0.001
Resistin	0.93 (0.88–0.97)	0.95 ng/mL	88.2	89.6	0.78	0.001
Prolactin	0.56 (0.48–0.64)	7.6 ng/mL	55.0	54.0	0.09	0.12

AUC: area under the curve; CI: confidence interval; FSH: follicle-stimulating hormone; LH: luteinising hormone; ROC: receiver operating characteristic.

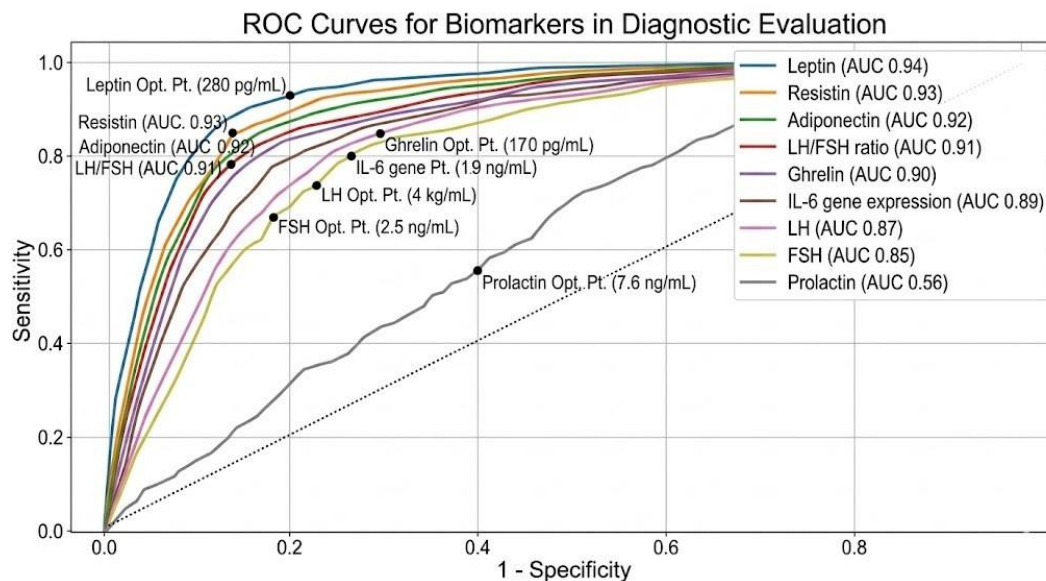


Figure (2): ROC curves of the studied biomarkers for discrimination of PCOS patients from healthy controls.

4-DISCUSSION

In the present study the largest proportion of women with PCOS was in the 26–35 years age group (53.5%), with lower frequencies in the 15–25 years (24.4%) and 36–45 years (22.1%) groups. This distribution accords with the long-established epidemiology of PCOS, in which the diagnosis is most commonly made during the reproductive years. It complements the findings of Alsaadi and Mohamad [17], who reported that hyperandrogenism, a clinical manifestation of PCOS, is most prevalent among women in their peak reproductive years. The pattern may also reflect better clinical recognition of the syndrome during evaluation for infertility or hormonal disturbances in this period.

Regarding BMI, most patients were overweight (25–30 kg/m², 56.7%) or obese (31–35 kg/m², 32.3%), and only 11.0% had a normal BMI. These findings reinforce the strong association between overweight/obesity and PCOS that is well established in the literature. Yildiz et al. [18] showed that a higher BMI strongly increases the risk of developing PCOS by increasing the degree of insulin resistance and hyperandrogenism, and Akshaya and Bhattacharya [19] demonstrated that obese PCOS patients have more severe metabolic and endocrine derangements than their lean counterparts, consistent with the high proportion of overweight patients in the present series. Adiposity therefore appears to be central to the pathophysiology and clinical phenotype of PCOS. With respect to reproductive hormones, FSH was significantly lower in PCOS patients than in controls (5.04 ± 0.49 vs 7.52 ± 0.61 IU/L, $p < 0.001$), whereas LH was significantly higher (8.72 ± 0.91 vs 5.95 ± 0.37 IU/L, $p < 0.001$), and the LH/FSH ratio was correspondingly increased (1.73 vs 0.79), consistent with the classical endocrine dysfunction of PCOS. These results agree with those of Le et al. [20], who reported that a high LH/FSH ratio is a cardinal diagnostic characteristic of PCOS and reflects dysregulation of the hypothalamic–pituitary–ovarian axis. Similarly, Naeem et al. [21] found marked hormonal dysregulation, with altered gonadotropin levels, in Iraqi women with PCOS and infertility, in parallel with the present findings. This hormonal profile is probably secondary to an increased GnRH pulse frequency, which enhances LH secretion and impairs follicular maturation. In contrast, prolactin did not differ between PCOS patients and controls (7.85 ± 1.15 vs 7.29 ± 1.63 ng/mL, $p = 0.12$), indicating that hyperprolactinaemia is not a feature of PCOS in this sample. This corroborates Baban et al. [22], who concluded that variations in prolactin concentration are not necessarily associated with PCOS and that any elevation may result from individual variability or coexisting conditions.

The adipokine profile was severely disturbed in women with PCOS, with a marked decrease in adiponectin and ghrelin and a pronounced increase in leptin and resistin compared with controls (all $p < 0.001$). The reduction in adiponectin observed here (4.73 ± 1.25 vs 9.17 ± 1.16 ng/mL) agrees well with the study of Fathi [23], who found that low adiponectin levels in PCOS are significantly related to insulin resistance and reduced antioxidant capacity. Similarly, Abdullah et al. [24] reported significantly lower adiponectin in PCOS patients, with the degree of reduction related to metabolic comorbidities and reproductive dysfunction. This decrease may underlie the adipose tissue dysfunction and chronic low-grade inflammation that are key mechanisms in the pathophysiology of PCOS [3].

Leptin was markedly increased in the present PCOS group (531.28 ± 39.51 vs 107.6 ± 13.82 pg/mL), which is consistent with Kargule and Dawood [25], who recently reported a strong positive correlation between leptin levels and BMI in Iraqi women with PCOS compared with healthy controls. Likewise, Shalal et al. [26] found that leptin concentrations are increased in these patients, supporting the hypothesis that leptin resistance contributes to metabolic dysregulation. Leptin was also identified by Rashed and Hadi [27] as a key pro-inflammatory adipokine related to PCOS severity, confirming its character as a metabolic–endocrine factor. In the current study, the higher leptin levels can be attributed to the increased adiposity and leptin resistance that are frequently present in PCOS.

A clear and significant decrease in ghrelin was also found in PCOS patients (217.41 ± 28.35 vs 649.82 ± 42.05 pg/mL), in keeping with the inverse relationship between this hormone and indices of insulin resistance described in several metabolic disorders. Because relatively few studies have addressed ghrelin in PCOS, the diminished level seen here may point to a mechanism leading to an imbalance in appetite regulation and energy homeostasis. As for resistin, PCOS patients showed a significant increase compared with controls (2.16 ± 0.34 vs 0.17 ± 0.08 ng/mL), consistent with Shamam et al. [28] and Al-Mayoofee et al. [29], who reported elevated resistin levels in PCOS and related them to insulin resistance and inflammatory status. Overall, these data confirm the role of resistin as a pro-inflammatory adipokine implicated in the metabolic and endocrine dysregulation associated with PCOS.

In addition to the adipokine alterations, IL-6 gene expression was significantly increased in PCOS patients compared with controls (3.38-fold vs 1.70-fold; $p = 0.001$). This result is in line with the meta-analysis of Peng et al. [30], which confirmed the association between higher circulating IL-6 and PCOS and thus reinforced elevated

IL-6 as a major inflammatory biomarker of the syndrome. Similarly, Zeb et al. [31] demonstrated higher systemic IL-6 levels in women with PCOS, especially those with insulin resistance, underlining the metabolic contribution of this cytokine. Furthermore, Raheem et al. [32] reported that IL-6 gene polymorphisms are associated with susceptibility to PCOS, providing genetic evidence for the inflammatory hypothesis, and experimental work by Zhuang et al. [33] showed that IL-6 is linked to adipogenesis and activation of the STAT3/AKT signalling pathway, supporting a biological mechanism by which IL-6 may contribute to the metabolic dysfunction of PCOS.

Taken together, the present findings indicate that inflammatory (IL-6), metabolic (adipokine) and endocrine (gonadotropin) disturbances coexist in Iraqi women with PCOS, and that leptin, resistin, adiponectin, the LH/FSH ratio and IL-6 expression all discriminate PCOS patients from healthy women with high accuracy, whereas prolactin does not. A limitation of the study is its single-centre, case-control design, which does not allow causal inferences to be drawn; in addition, correlations between IL-6 expression and the individual adipokines and hormones were not analysed, and the interplay among these markers should be explored in larger, prospective studies.

CONCLUSION

The present study shows that PCOS is associated with hormonal dysfunction, metabolic derangement and increased inflammatory activity. Leptin, resistin and IL-6 gene expression showed the highest diagnostic performance, suggesting that these biomolecules may be valuable in the assessment of PCOS. These results support the combined use of endocrine, adipokine and inflammatory markers to enhance the diagnosis of PCOS and provide insight into its pathophysiology.

DECLARATIONS

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REFERENCES

1. Teede HJ, Tay CT, Laven JSE, Dokras A, Moran LJ, Piltonen TT, et al. Recommendations from the 2023 International Evidence-based Guideline for the Assessment and Management of Polycystic Ovary Syndrome. *J Clin Endocrinol Metab.* 2023;108(10):2447-2469. doi:10.1210/clinem/dgad463
2. Taieb A, Feryel A. Deciphering the role of androgen in the dermatologic manifestations of polycystic ovary syndrome patients: a state-of-the-art review. *Diagnostics (Basel).* 2024;14(22):2578. doi:10.3390/diagnostics14222578
3. Mohammad Sadeghi H, Adeli I, Calina D, Docea AO, Mousavi T, Daniali M, et al. Polycystic ovary syndrome: a comprehensive review of pathogenesis, management, and drug repurposing. *Int J Mol Sci.* 2022;23(2):583. doi:10.3390/ijms23020583
4. Aboeldalyl S, James C, Seyam E, Ibrahim EM, Shawki HE, Amer S. The role of chronic inflammation in polycystic ovarian syndrome—a systematic review and meta-analysis. *Int J Mol Sci.* 2021;22(5):2734. doi:10.3390/ijms22052734
5. Bansal B, Kishore AT, Kathiresan S, Ghachi AF, Pradhan S, Paul S, et al. A systematic review of inflammatory markers in polycystic ovary syndrome (PCOS) and meta-analysis of interleukin-6 (IL-6) in case-control studies. *Cureus.* 2025;17(4):e82350. doi:10.7759/cureus.82350
6. Guo R, Zheng Y, Yang J, Zheng N. Association of TNF-alpha, IL-6 and IL-1beta gene polymorphisms with polycystic ovary syndrome: a meta-analysis. *BMC Genet.* 2015;16:5. doi:10.1186/s12863-015-0161-0
7. Adeeb Ahmed A, Zaid Ali R, Alazzawi MHA. Association of IL-1 beta and IL-6 gene expression and some

- biochemical indicators with polycystic ovary syndrome in Iraqi women. J Contemp Med Sci. 2026;12(1):68-75. doi:10.22317/jcms.v12i1.2114
8. Sartori C, Lazzeroni P, Merli S, Patianna VD, Viaroli F, Cirillo F, et al. From placenta to polycystic ovarian syndrome: the role of adipokines. Mediators Inflamm. 2016;2016:4981916. doi:10.1155/2016/4981916
 9. Bril F, Ezech U, Amiri M, Hatoum S, Pace L, Chen YH, et al. Adipose tissue dysfunction in polycystic ovary syndrome. J Clin Endocrinol Metab. 2024;109(1):10-24. doi:10.1210/clinem/dgad356
 10. Schüler-Toprak S, Ortmann O, Buechler C, Treeck O. The complex roles of adipokines in polycystic ovary syndrome and endometriosis. Biomedicines. 2022;10(10):2503. doi:10.3390/biomedicines10102503
 11. Orszulak D, Niziński K, Matonóg A, Zięba-Domalik M, Stojko R, Drosdzol-Cop A. Adipokines as biochemical marker of polycystic ovary syndrome in adolescents – review. Front Endocrinol (Lausanne). 2025;16:1475465. doi:10.3389/fendo.2025.1475465
 12. Bongrani A, Mellouk N, Rame C, Cornuau M, Guérif F, Froment P, et al. Ovarian expression of adipokines in polycystic ovary syndrome: a role for chemerin, omentin, and apelin in follicular growth arrest and ovulatory dysfunction? Int J Mol Sci. 2019;20(15):3778. doi:10.3390/ijms20153778
 13. Lin W, Wang Y, Zheng L. Polycystic ovarian syndrome (PCOS) and recurrent spontaneous abortion (RSA) are associated with the PI3K-AKT pathway activation. PeerJ. 2024;12:e17950. doi:10.7717/peerj.17950
 14. Walford H, Tyler B, Abbara A, Clarke S, Talaulikar V, Al Wattar B. Biomarkers to inform the management of polycystic ovary syndrome: a review of systematic reviews. Clin Endocrinol (Oxf). 2024;101(5):535-548. doi:10.1111/cen.15101
 15. Mohammed SH, Saleh AH, Abu-Elteen KH, Dheeb BI, Abdulateef SM. Role of fluconazole nanoemulsion in inhibiting liver candidiasis in female mice and their embryos. Jordan J Biol Sci. 2025;18(1):173-180.
 16. Saleh AH, Mohammed RH. Evaluating of the activity of *Equisetum arvense* extract as antioxidant against to goitrogen 6-n-propyl-2-thiouracil in albino rats. AIP Conf Proc. 2026;3396(1):030025. doi:10.1063/5.0215736
 17. Alsaadi YL, Mohamad BJ. Prevalence of hyperandrogenism in Iraqi women with polycystic ovary syndrome. Iraqi J Sci. 2019;60(12):2600-2608. doi:10.24996/ijsc.2019.60.12.8
 18. Yildiz BO, Knochenhauer ES, Azziz R. Impact of obesity on the risk for polycystic ovary syndrome. J Clin Endocrinol Metab. 2008;93(1):162-168. doi:10.1210/jc.2007-1834
 19. Akshaya S, Bhattacharya R. Comparative study of clinical profile of lean and obese polycystic ovary syndrome women. Int J Reprod Contracept Obstet Gynecol. 2016;5(8):2530-2533. doi:10.18203/2320-1770.ijrcog20162173
 20. Le MT, Le VNS, Le DD, Nguyen VQH, Chen C, Cao NT. Exploration of the role of anti-Mullerian hormone and LH/FSH ratio in diagnosis of polycystic ovary syndrome. Clin Endocrinol (Oxf). 2019;90(4):579-585. doi:10.1111/cen.13934
 21. Naeem RS, Jewad AM, Mahmoud RA. A biochemical study of infertile women with and without polycystic ovarian syndrome in Basra City, Iraq. Univ Thi-Qar J Sci. 2023;10(1 Spec No):62-67. doi:10.32792/utq/utjsci/v10i1(SI).968
 22. Baban ASS, Mahmood HM, Al-Bustany HA. The FSHR polymorphisms association with polycystic ovary syndrome in women of Erbil, Kurdistan in north of Iraq. Ibn Al-Haitham J Pure Appl Sci. 2018;IHSCICONF:257-272. doi:10.30526/2017.IHSCICONF.1799
 23. Fathi FH. Adiponectin and total antioxidant capacity and their association with insulin resistance among women with polycystic ovarian syndrome. Iraqi J Pharm. 2024;21(3):102-106. doi:10.33899/iraqij.p.2024.148669.1093
 24. Abdullah HM, Shaker SH, Salman HA. Study the concentrations of leptin, adiponectin and some parameters in women with polycystic ovaries syndrome. GSC Biol Pharm Sci. 2024;28(2):116-121.

doi:10.30574/gscbps.2024.28.2.0293

25. Kargule BB, Dawood FA. Monitoring of leptin hormone levels in child bearing-age women in Baghdad/Iraq with polycystic ovary syndrome, and the impact of BMI on leptin levels. *Al-Nisour J Med Sci.* 2023;5(2):Art 4. doi:10.70492/2664-0554.1108
26. Shalal MM, Miran NM, Mahddi ZI. Serum leptin levels in ovarian polycystic disease and its correlation to body weight. *J Fac Med Baghdad.* 2014;56(2):141-146. Available from: <https://www.ijjmc.uobaghdad.edu.iq/index.php/19JFacMedBaghdad36/article/view/454>
27. Rashed SH, Hadi EA. The role of visfatin, leptin, and IL-18 in polycystic ovarian syndrome patients. *Med J Babylon.* 2024;21(4):821-826. doi:10.4103/MJBL.MJBL_1258_23
28. Shamam KH, El-Yassin HD, Al-Shammaa H. Serum resistin levels, and other hormonal and biochemical parameters in patients with polycystic ovary syndrome (PCOS). *J Fac Med Baghdad.* 2009;51(2):200-203.
29. Al-Mayoofee SHB, Al-Snafi AE, Missaoui N, Hmissa S. Serum resistin and adiponectin levels in relation with metabolic changes in PCO patients. *Thi-Qar Med J.* 2024;27(1):91-98.
30. Peng Z, Sun Y, Lv X, Zhang H. Interleukin-6 levels in women with polycystic ovary syndrome: a systematic review and meta-analysis. *PLoS One.* 2016;11(2):e0148531. doi:10.1371/journal.pone.0148531
31. Zeb S, Gul R, Ashraf M, Rumman M. Comparative analysis of interleukin-6 levels in polycystic ovary syndrome (PCOS) patients with and without insulin resistance. *Cureus.* 2025;17(4):e81878. doi:10.7759/cureus.81878
32. Raheem BM, Mohammed R, Ali B, Al-Fahham A. The role of TNF- α and IL-6 SNP in polycystic ovary syndrome susceptibility. *Pol Merkur Lekarski.* 2024;52(3):286-291. doi:10.36740/Merkur202403104
33. Zhuang Z, Pan X, Zhao K, Gao W, Liu J, Deng T, et al. The effect of interleukin-6 (IL-6), interleukin-11 (IL-11), signal transducer and activator of transcription 3 (STAT3), and AKT signaling on adipocyte proliferation in a rat model of polycystic ovary syndrome. *Med Sci Monit.* 2019;25:7218-7227. doi:10.12659/MSM.916385