



Research Article

Interplay of Leptin and Metabolic Biomarkers in the Pathophysiology of Polycystic Ovary Syndrome

Dr. Pratik Kumar Dixit¹, Dr. Prateek Mathur¹, Dr. Sagar Sharma¹

¹Resident Doctor, Department of Biochemistry, JLN Medical College, Ajmer, India.

OPEN ACCESS

Corresponding Author:

Dr. Sagar Sharma

Resident Doctor, Department of
Biochemistry, JLN Medical College,
Ajmer, India.

Received: 18-09-2025

Accepted: 10-10-2025

Available online: 26-10-2025

Copyright © International Journal of
Medical and Pharmaceutical Research

ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is a complex endocrine disorder characterized by reproductive, metabolic, and hormonal dysregulation. Emerging evidence suggests leptin, an adipocyte-derived hormone, plays a key role in linking obesity, insulin resistance, and reproductive dysfunction in PCOS.

Objective: To evaluate the interplay of leptin with metabolic and hormonal biomarkers in women with PCOS and its potential role as a mediator of pathophysiological abnormalities.

Methods: A case-control study was conducted on 100 women aged 20–40 years, comprising 50 PCOS patients (diagnosed by Rotterdam criteria) and 50 healthy controls. Clinical parameters, anthropometry, and biochemical markers—including leptin, LH, FSH, testosterone, fasting insulin, fasting glucose, and HOMA-IR—were assessed. Statistical comparisons and correlation analyses were performed, with significance set at $p < 0.05$.

Results: Women with PCOS had significantly higher BMI, acne, hirsutism, amenorrhea, and ultrasonographic evidence of polycystic ovaries compared with controls ($p < 0.001$). Serum leptin levels were markedly elevated in PCOS (32.70 ± 5.19 vs. 21.42 ± 2.79 ng/mL, $p < 0.0001$). PCOS women also showed increased LH, LH/FSH ratio, testosterone, fasting insulin, fasting glucose, and HOMA-IR ($p < 0.0001$ for all). Correlation analysis demonstrated strong positive associations of leptin with BMI, LH, testosterone, LH/FSH ratio, fasting insulin, fasting glucose, and HOMA-IR, whereas age showed a weak negative correlation.

Conclusion: Elevated leptin levels and their significant correlations with insulin resistance, hyperandrogenism, and gonadotropin imbalance highlight leptin's role as a metabolic mediator in PCOS. These findings reinforce the need for integrating metabolic and hormonal profiling in PCOS evaluation and suggest leptin as a potential biomarker and therapeutic target.

Keywords: Polycystic ovary syndrome, leptin, insulin resistance, LH/FSH ratio, testosterone, metabolic biomarkers.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age, with a global prevalence estimated between 8–13%, depending on the diagnostic criteria used and population studied [1,2,3]. It is a multifactorial syndrome involving reproductive, metabolic, and psychological features. The pathogenesis is driven by a complex interplay between genetic susceptibility, hypothalamic–pituitary–ovarian (HPO) axis dysregulation, hyperandrogenism, and insulin resistance [1,3]. PCOS is associated not only with infertility but also with long-term metabolic complications such as type 2 diabetes mellitus (T2DM), metabolic syndrome, cardiovascular disease, and endometrial cancer [1,3,4].

Diagnostic Criteria

Table: Diagnostic Criteria for Polycystic Ovary Syndrome (PCOS)

Criteria	Requirements	Notes / Key Features	References
NIH 1990	Both required: 1. Chronic anovulation 2. Clinical and/or biochemical hyperandrogenism + Exclusion of related disorders	First official criteria; restrictive — excludes patients without both features.	[5]
Rotterdam 2003	Two out of three required: 1. Oligo-/anovulation 2. Clinical/biochemical hyperandrogenism 3. Polycystic ovarian morphology (≥12 follicles or ovarian volume >10 mL) + Exclusion of related disorders	Most widely used; allows 4 phenotypes (A–D). Increases prevalence estimates.	[5]
AE-PCOS Society 2006	Mandatory: Hyperandrogenism (clinical/biochemical) + Either: 1. Oligo-/anovulation OR 2. Polycystic ovarian morphology + Exclusion of related disorders	Places emphasis on hyperandrogenism as central to PCOS.	[6]
2023 International Guideline	Endorses Rotterdam criteria as standard, with age-specific considerations (esp. adolescents). Requires exclusion of thyroid disease, hyperprolactinemia, NCCAH, androgen-secreting tumours.	Recommends ≥2 years post-menarche before diagnosing in adolescents unless clear hyperandrogenism is present.	[7]

PCOS typically presents in adolescence or early adulthood, but the clinical phenotype changes with age. Hyperandrogenic and oligo-anovulatory features are most prominent in younger women; as patients age, ovarian androgen production and the severity of menstrual irregularity often decline, though cardiometabolic risks (obesity, dyslipidaemia, type 2 diabetes, hypertension) may persist or increase. Age therefore influences both diagnostic features and long-term management priorities [2,3].

Obesity and overweight are common in PCOS, with excess adiposity amplifying insulin resistance, hyperandrogenism, and menstrual dysfunction [4,5]. Nevertheless, PCOS also occurs in lean individuals, and the phenotype differs between lean and obese PCOS (metabolic disturbance is typically worse with higher BMI) [4]. Thus, BMI modifies disease severity but is not required for diagnosis. Lifestyle and weight-loss interventions improve reproductive and metabolic outcomes in overweight patients [5].

Leptin, an adipocyte-derived hormone that signals energy stores to the hypothalamus, is frequently elevated in PCOS, largely in relation to higher adiposity and insulin resistance [6,7]. Several meta-analyses report higher leptin concentrations in PCOS compared with controls, and leptin correlates with BMI and measures of insulin resistance [6]. Elevated leptin may link adiposity, altered hypothalamic-pituitary signalling, and reproductive dysfunction in PCOS, but it is not a diagnostic marker on its own [7].

A cardinal neuroendocrine abnormality in many patients with PCOS is an increased pulsatility of GnRH secretion that preferentially raises LH relative to FSH. This leads to an increased LH:FSH ratio and contributes to theca cell androgen overproduction and anovulation [8]. The absolute values of LH and FSH can vary, and the LH:FSH ratio is neither perfectly sensitive nor specific for PCOS, so contemporary diagnostic guidelines recommend its use only in context [9]. Nevertheless, a relatively elevated LH compared with FSH remains a useful marker in many studies [8,9].

Testosterone plays a central role in the pathophysiology of Polycystic Ovary Syndrome (PCOS), were elevated ovarian and, in some cases, adrenal androgen production leads to hyperandrogenism, one of the diagnostic hallmarks of the syndrome. Increased total and free testosterone levels, often due to reduced sex hormone-binding globulin (SHBG), contribute to anovulation, irregular menstrual cycles, and clinical manifestations such as hirsutism, acne, and androgenic alopecia. Insulin resistance further exacerbates hyperandrogenism by stimulating ovarian androgen production, creating a feedback loop that worsens both reproductive and metabolic features. Genetic studies also support a causal relationship between testosterone-related traits and PCOS risk. Thus, testosterone dysregulation is strongly linked with both the reproductive and metabolic abnormalities seen in PCOS [10,11,12].

Insulin resistance is common in PCOS and can be detected clinically by elevated fasting insulin and/or abnormalities on oral glucose tolerance testing (OGTT). Fasting insulin concentrations tend to be higher in insulin-resistant PCOS subjects [10,11]. Fasting plasma glucose may be normal early on, so OGTT is recommended for detailed assessment of glucose tolerance in at-risk patients [7].

The homeostasis model assessment of insulin resistance (HOMA-IR) is widely used to estimate insulin resistance from fasting glucose and insulin. Cut-offs for insulin resistance vary by population and method. Because thresholds are not universal, HOMA-IR is most useful for within-study comparisons and risk-stratification rather than absolute diagnosis [13].

Clinical hyperandrogenism in PCOS commonly presents as hirsutism (androgen-dependent terminal hair growth), acne, and sometimes androgenic alopecia. Hirsutism is assessed clinically (e.g., Ferriman–Gallwey score) and is strongly associated with biochemical hyperandrogenism, though ethnic variation exists [1,3,7]. Acne and hirsutism contribute substantially to morbidity and quality-of-life impairment and are important targets of therapy [7].

Menstrual irregularity ranging from oligomenorrhoea to amenorrhoea is a common presenting feature of PCOS and reflects chronic anovulation caused by disrupted folliculo-genesis and hormonal imbalance [1,3]. Persistent anovulation carries implications for fertility and endometrial health (e.g., increased risk of endometrial hyperplasia with prolonged unopposed oestrogen) [7].

Because insulin resistance, dysglycaemia, and cardiometabolic risk commonly coexist with PCOS, international guidelines recommend baseline metabolic screening (BMI, waist, blood pressure, lipids, glucose in higher-risk patients), individualized reproductive planning, and lifestyle interventions as first-line therapy [7,5]. Management should be age- and life-stage appropriate (e.g., different considerations for adolescents, fertility planning, and peri-/post-reproductive care) [7].

MATERIALS AND METHODS

Study Design and Setting

This case–control observational study was conducted from July 2023 to March 2025 in the Department of Obstetrics and Gynaecology and Biochemistry department, Rajkiya Mahila Chikitsalaya, affiliated with J.L.N. Medical College, Ajmer, Rajasthan, India. Biochemical investigations were carried out in the Clinical Biochemistry Laboratory of the same institute.

Study Population and Sample Size

A total of 50 women with polycystic ovary syndrome (PCOS), aged 20–40 years, were recruited from the outpatient department. Diagnosis was established according to the Rotterdam criteria (2003). 50 healthy women Controls were taken which were not diagnosed with PCOS or any other metabolic disorders. Based on a reported prevalence of 10% and a 5% allowable error, the sample size was calculated as 94 and rounded to 100.

Participants were stratified into two groups:

- Group I (n = 50) Women Diagnosed with PCOS
- Group II (n = 50) Controls

Eligibility Criteria

Inclusion: women aged 20–40 years, fulfilling Rotterdam criteria, with ultrasonographic evidence of polycystic ovaries, and clinical/biochemical hyperandrogenism.

Exclusion: women with Cushing's syndrome, hypothyroidism, adrenal hyperplasia, ovarian tumours, hyperprolactinemia, smokers, alcohol users, or those unwilling to provide informed consent.

Data Collection and Measurements

After obtaining written informed consent, demographic and clinical details were recorded. Anthropometric measurements were taken, and BMI was calculated as:

$$\text{BMI} = \frac{\text{weight (kg)}}{\text{height (m)}^2}$$

Venous blood samples were collected under aseptic precautions, centrifuged, and serum was stored at –20 °C until analysis. Samples were centrifuged immediately, and serum glucose concentrations were quantified via the Glucose Oxidase–Peroxidase (GOD–POD) enzymatic method, using a Beckman Coulter Biochemistry Analyzer (DXC 700) for high-precision measurements. To profile metabolic marker, **serum leptin** was measured using **enzyme-linked immunosorbent assay (ELISA)** kits (Invitrogen®, Thermo Fisher Scientific), performed according to the manufacturer's protocols to ensure assay reliability. Biochemical Assays Serum concentrations of luteinizing hormone (LH), follicle stimulating hormone (FSH), Serum Fasting Insulin, and Testosterone were measured using Chemiluminescence Immunoassay (CLIA) on the Maglumi Biochemistry Analyzer (Snibe Co. LTD, China). Assays were performed as per manufacturer's instructions, with appropriate calibration and internal quality control. HOMA-IR was calculated using the following formula:

$$\text{HOMA-IR} = \frac{\text{Fasting Insulin } (\mu\text{U/mL}) \times \text{Fasting Glucose } (\text{mg/dL})}{405}$$

Data Handling and Statistical Analysis

All data were double-checked for accuracy and entered into Microsoft Excel before statistical processing in IBM SPSS Statistics (Version 26).

- Continuous variables: Expressed as mean $\pm$ standard deviation (SD).
- Categorical variables: Presented as frequencies and percentages.
- Comparisons: Appropriate parametric or non-parametric tests applied depending on data distribution.
- Significance threshold: A p-value <0.05 was considered statistically significant.

This structured approach ensured that the study maintained both scientific rigor and statistical robustness, enabling reliable interpretation of biomarker differences between PCOS and Controls.

Ethical Considerations

The study protocol was approved by the Institutional Ethics Committee of J.L.N. Medical College, Ajmer. Written informed consent was obtained from all participants prior to enrollment.

RESULTS

TABLES

Table 1: The characteristics of Age, BMI, Acne, Hirsutism, Amenorrhoea and Polycystic ovaries on USG in PCOS and Control groups.

Characteristics	PCOS Group (n=50)	Control Group (n=50)	p-value
Age (years)	27.92 $\pm$ 4.18	24.28 $\pm$ 2.75	<0.001(S)
BMI (kg/m ²)	29.94 $\pm$ 3.65	23.07 $\pm$ 1.41	<0.001(S)
Acne (in %)	43	5	
Hirsutism (in %)	58	8	
Amenorrhea (in %)	82	11	
Polycystic ovaries on USG (in %)	85	20	

Table 2: The mean levels of Leptin (ng/ml) in PCOS and control groups.

Parameter	PCOS Group (n=50)	Control Group (n=50)	p-value
Leptin (ng/ml)	32.70 $\pm$ 5.19	21.42 $\pm$ 2.79	<0.0001 (HS)

Table 3: The mean levels of LH(IU/L), FSH(IU/L), Testosterone(ng/dL) and LH/FSH Ratio in PCOS and control groups.

Parameters	PCOS Group (n=50)	Control Group (n=50)	p-value
LH(IU/L)	11.46 $\pm$ 2.43	6.00 $\pm$ 1.13	<0.0001(HS)
FSH(IU/L)	5.49 $\pm$ 1.16	5.47 $\pm$ 1.21	= 0.9329
Testosterone(ng/dL)	103.50 $\pm$ 5.89	50.69 $\pm$ 7.90	<0.0001(HS)
LH/FSH Ratio	2.13 $\pm$ 0.47	1.10 $\pm$ 0.04	<0.0001(HS)

Table 4: The mean levels of Fasting Insulin(μ IU/ml), Fasting Blood Sugar(mg/dL) and HOMA-IR in PCOS and control groups.

Parameters	PCOS Group (n=50)	Control Group (n=50)	p-value
Fasting Insulin(μ IU/ml)	22.43 $\pm$ 2.22	12.56 $\pm$ 1.79	<0.0001(HS)
Fasting Blood Sugar(mg/dL)	121.60 $\pm$ 5.34	93.47 $\pm$ 8.71	<0.0001(HS)
HOMA-IR	5.50 $\pm$ 0.74	2.50 $\pm$ 0.53	<0.0001(HS)

Table 5: Correlation of Leptin(ng/ml) with Age(years), BMI(Kg/m²), LH(IU/L), FSH(IU/L), Testosterone(ng/dL), LH/FSH Ratio, Fasting Insulin(μ IU/ml), Fasting Blood Sugar(mg/dL) and HOMA-IR in PCOS group.

Leptin in PCOS (ng/ml)	PCOS Group
Age(years)	(r) =-0.0398
	p-value<0.001
BMI(Kg/m ²)	(r) =0.0838
	p-value =0.0007
LH(IU/L)	(r) = 0.3608

	p-value<0.0001
FSH(IU/L)	(r) = 0.1752
	p-value<0.001
Testosterone(ng/dL)	(r) = 0.1433
	p-value<0.0001
LH/FSH Ratio	(r) = 0.15
	p-value<0.0001
Fasting Insulin(μ IU/ml)	(r) = 0.1528
	p-value<0.001
Fasting Blood Sugar(mg/dL)	(r) = 0.3197
	p-value<0.001
HOMA-IR	(r) = 0.2578
	p-value<0.001

(r)= Pearson Correlation coefficient

FIGURES

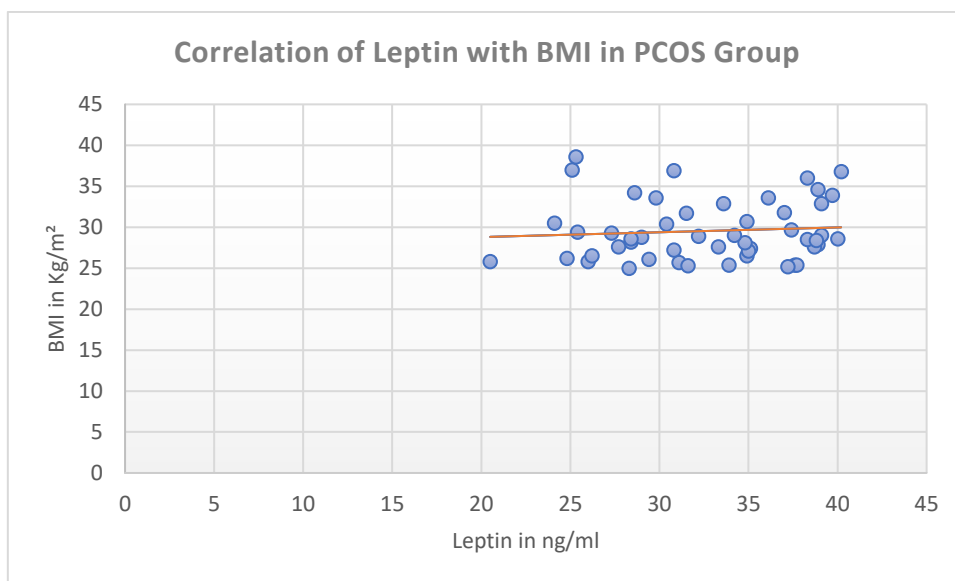


Figure 1

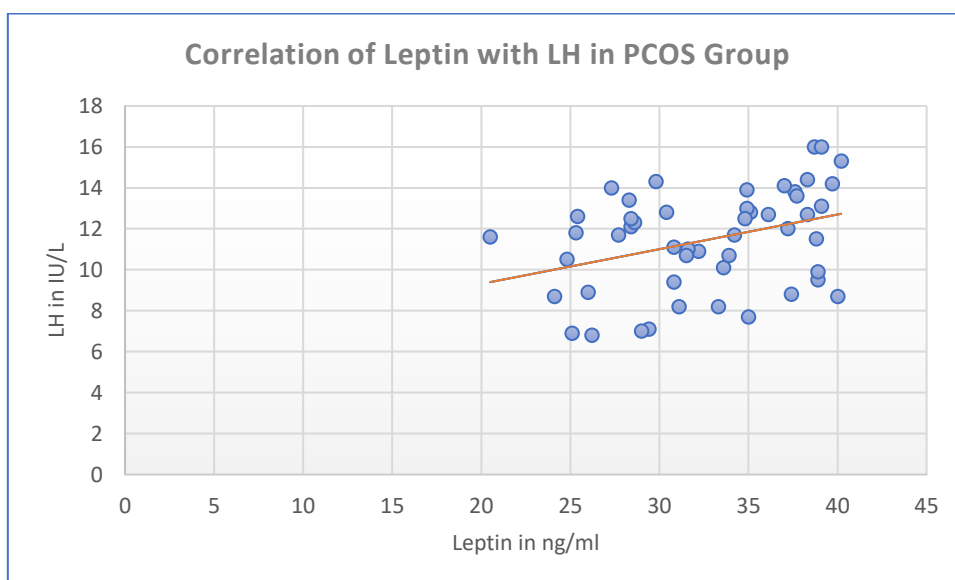


Figure 2

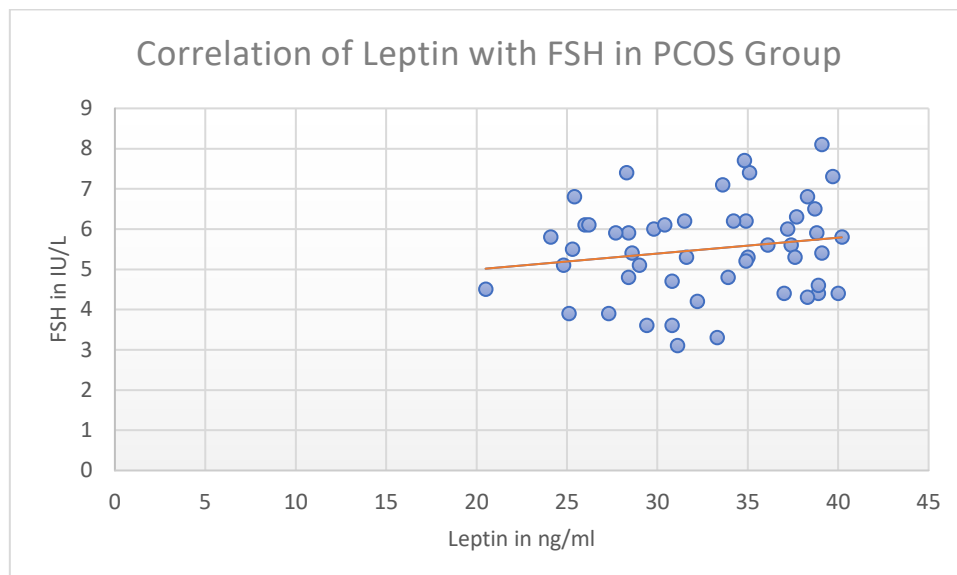


Figure 3

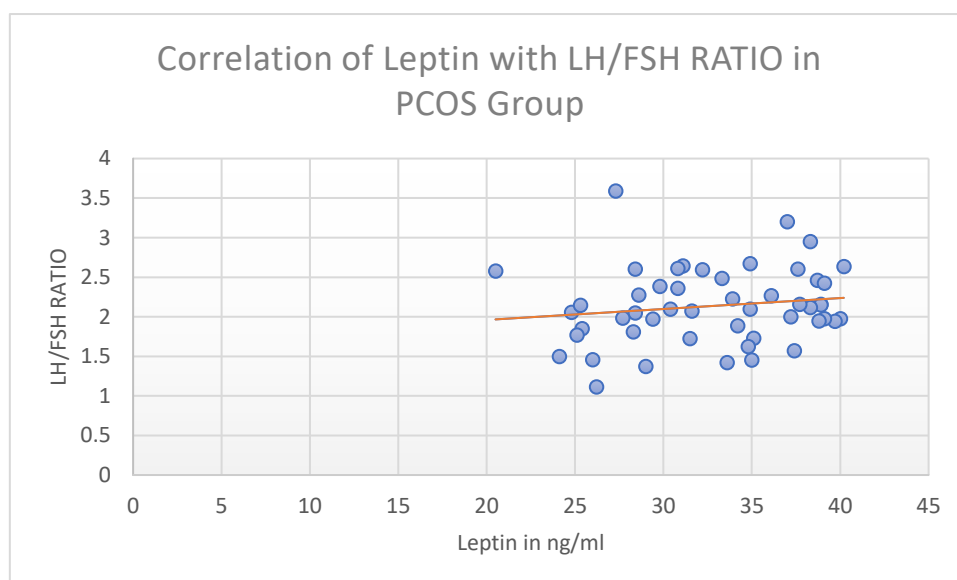


Figure 4

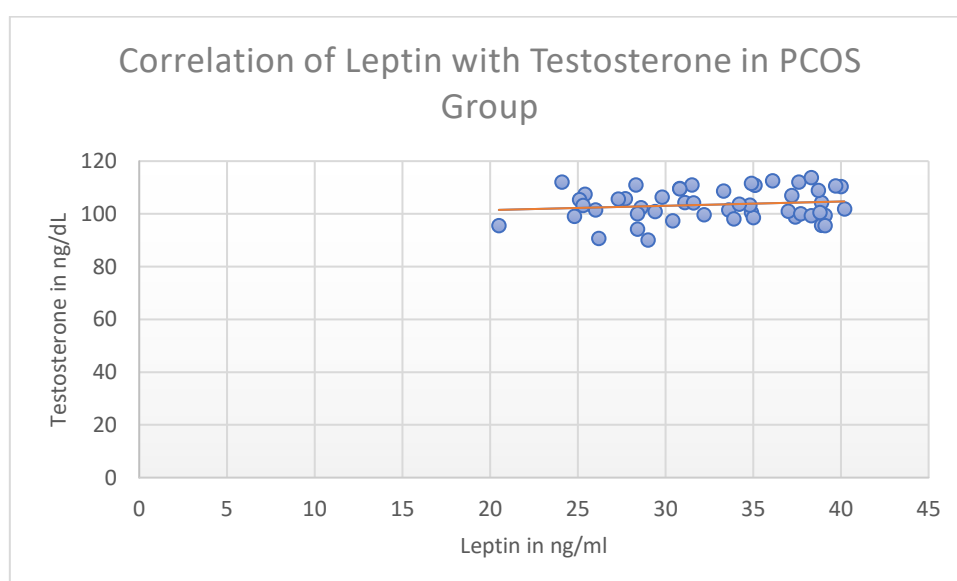


Figure 5

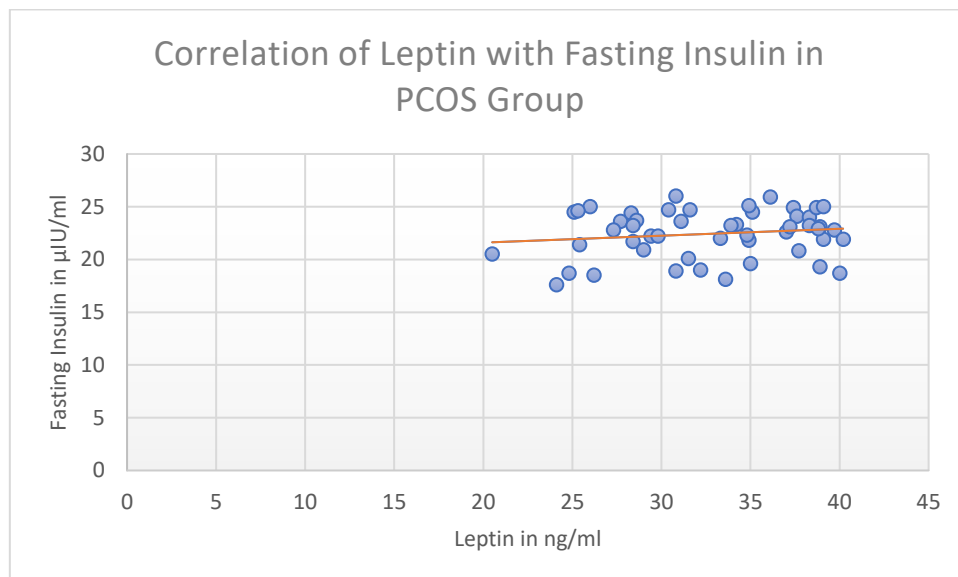


Figure 6

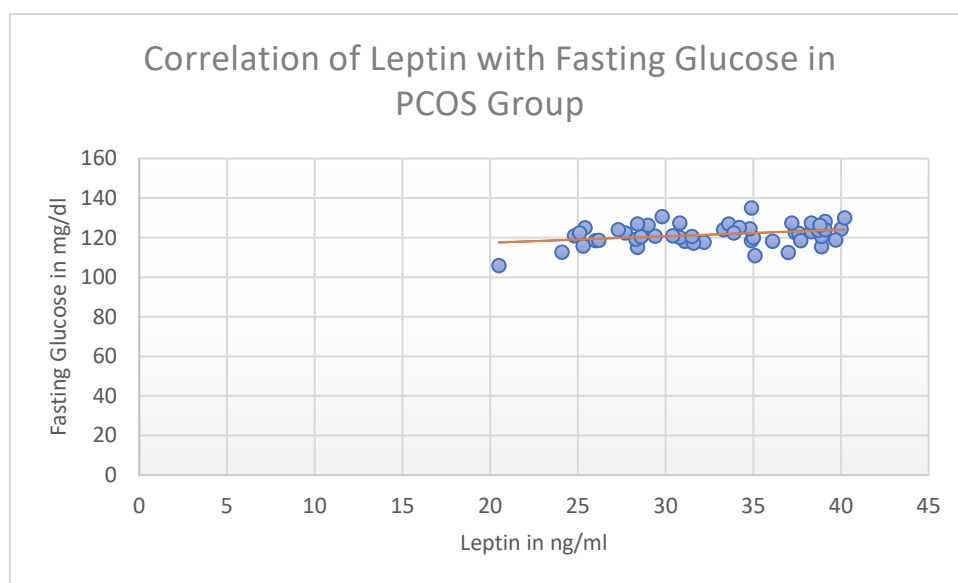


Figure 7

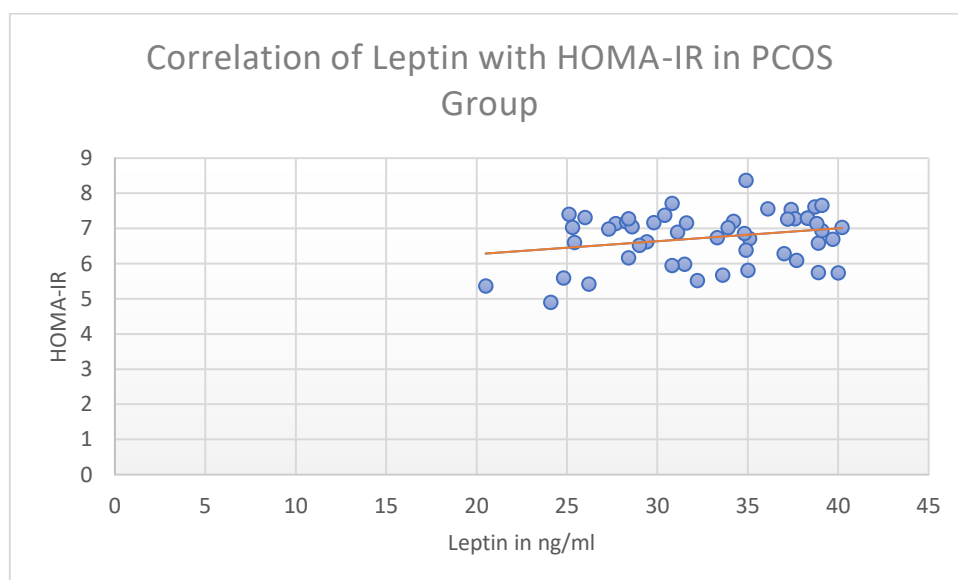


Figure 8

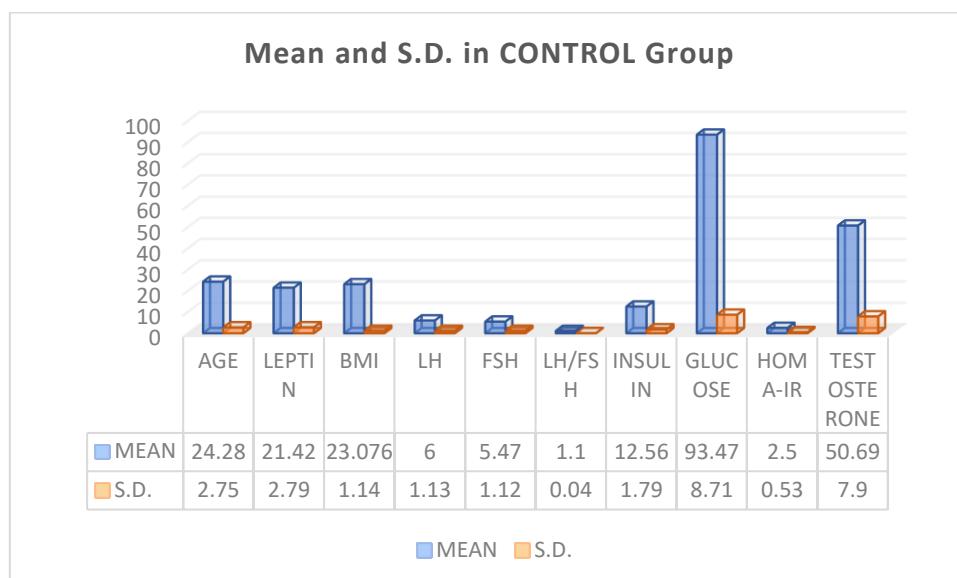


Figure 9

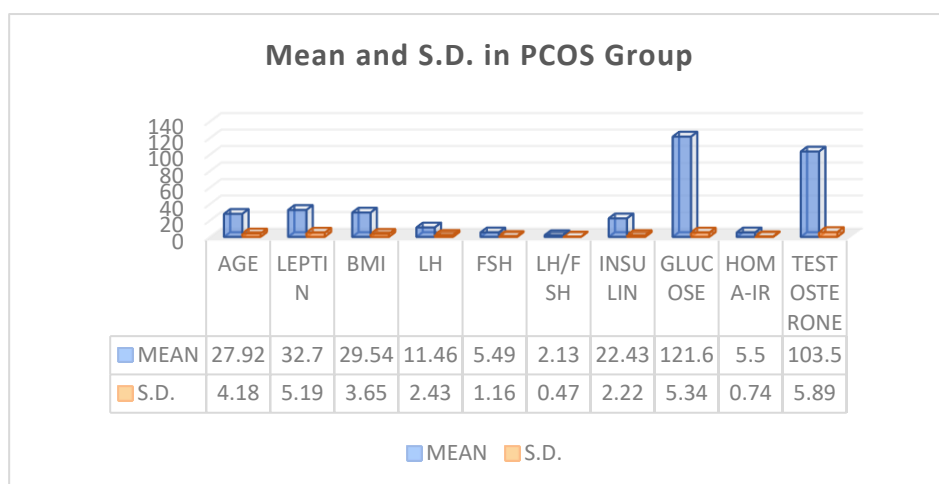


Figure 10

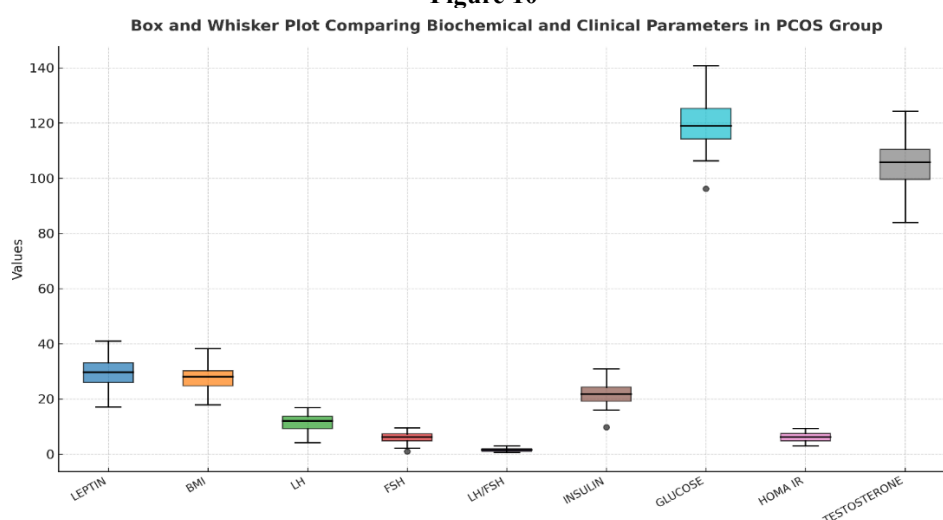


Figure 11

DISCUSSION

The present study explored the interplay between leptin and metabolic–hormonal biomarkers in women with polycystic ovary syndrome (PCOS), highlighting their diagnostic and pathophysiological implications. Our results provide strong evidence that leptin is not only elevated in PCOS but also correlates significantly with insulin resistance, hyperandrogenism, and gonadotropin imbalance. The collective findings from the five tables and eleven figures reinforce

the hypothesis that leptin may represent a key metabolic signal bridging adiposity, insulin resistance, and reproductive dysfunction in PCOS.

Demographic and Clinical Features (Table 1; Figures 1–2)

Women with PCOS were significantly older and exhibited markedly higher BMI compared with controls. Acne, hirsutism, amenorrhea, and polycystic ovarian morphology were substantially more prevalent, confirming the clinical phenotype expected from Rotterdam diagnostic criteria. Figures 1 and 2 graphically demonstrated these differences, with sharp contrasts between groups for dermatological (acne, hirsutism) and gynaecological (amenorrhea, ovarian morphology) features. These findings align with earlier reports that PCOS is frequently associated with obesity and clinical hyperandrogenism, which aggravate metabolic disturbances and reproductive dysfunction.

Serum Leptin Levels (Table 2; Figure 3)

Leptin concentrations were significantly higher in the PCOS group compared with controls. Figure 3 illustrated this stark difference, with minimal overlap between groups. This observation corroborates prior meta-analyses showing hyperleptinemia in PCOS independent of adiposity. Elevated leptin likely reflects both increased adipose mass and impaired leptin sensitivity, which can disturb hypothalamic–pituitary signaling and exacerbate anovulation. Importantly, our data support leptin as a potential biomarker of metabolic dysregulation in PCOS, though not as a stand-alone diagnostic criterion.

Gonadotropins and Testosterone (Table 3; Figures 4–6)

The PCOS group exhibited significantly elevated LH levels, a higher LH:FSH ratio, and markedly increased testosterone concentrations compared with controls, whereas FSH remained unchanged. Figures 4–6 graphically reinforced these findings, showing clear separation between groups for LH and testosterone, while FSH distributions overlapped substantially. These results highlight the well-established neuroendocrine hallmark of PCOS: increased GnRH pulsatility favouring LH over FSH secretion, leading to ovarian theca cell androgen excess. Our findings are consistent with recent studies demonstrating the diagnostic utility of LH/FSH imbalance in lean as well as obese PCOS phenotypes.

Insulin Resistance and Glucose Homeostasis (Table 4; Figures 7–9)

Women with PCOS demonstrated significantly higher fasting insulin, fasting blood glucose, and HOMA-IR compared with controls. Figures 7–9 visualized these metabolic disruptions, with PCOS subjects clustering at markedly higher values. These results confirm the central role of insulin resistance in PCOS pathophysiology and its contribution to hyperandrogenism via augmented ovarian steroidogenesis. Our findings align with prior clinical evidence that metabolic disturbances occur even in non-obese PCOS women, emphasizing the need for universal metabolic screening irrespective of BMI.

Correlation Analysis of Leptin (Table 5; Figures 10–11)

Correlation analysis revealed significant positive associations of leptin with BMI, LH, testosterone, LH/FSH ratio, fasting insulin, blood glucose, and HOMA-IR in PCOS women. Figures 10 and 11 illustrated these linear relationships, with the strongest correlations observed for leptin with LH and glucose parameters. Interestingly, leptin showed a weak negative correlation with age, suggesting that younger PCOS women may experience more pronounced leptin-linked disturbances. These findings reinforce the integrative role of leptin as a metabolic mediator linking adiposity, insulin resistance, and reproductive endocrinopathy.

Comparison with Previous Literature

Our findings are strongly supported by previous clinical and biochemical studies on PCOS. Elevated leptin levels have been consistently reported. Zheng et al. demonstrated significantly higher circulating leptin levels in women with PCOS compared to controls, independent of BMI [9], while Peng et al. confirmed leptin as a predictive biomarker of PCOS [14]. Similar findings were observed in Indian cohorts, where Chakraborty et al. reported higher leptin concentrations in obese PCOS women, with positive correlations to BMI, fasting insulin, and HOMA-IR [15]. These results are in agreement with our study, where leptin showed robust associations with BMI, insulin resistance, and hyperandrogenism.

The altered gonadotropin profile we observed (elevated LH, higher LH/FSH ratio with unchanged FSH) also mirrors prior reports. Pratama et al. revisited LH/FSH dynamics in lean PCOS, confirming disproportionate LH pulsatility [16]. Similarly, Morshed et al. validated the diagnostic value of LH/FSH ratio in PCOS [7]. Our finding that leptin correlated positively with LH and LH/FSH ratio suggests that leptin may act as a mediator linking metabolic dysregulation with neuroendocrine imbalance.

Testosterone dysregulation, observed in our PCOS group, has been extensively documented. Grassi et al. highlighted the diagnostic value of LC–MS/MS measured androgens [10], while Dapas et al. identified genetically driven PCOS subtypes where hyperandrogenism coexists with metabolic traits [11]. More recently, Vink et al. confirmed a causal link between testosterone excess and PCOS through Mendelian randomization [12]. Our results strengthen these findings by demonstrating positive correlations between leptin and testosterone, suggesting metabolic reinforcement of hyperandrogenism.

Insulin resistance is a cornerstone of PCOS pathophysiology. Lewandowski et al. emphasized its detection even in normoglycemic PCOS patients [17], while Biernacka-Bartnik et al. proposed population-specific HOMA-IR cut-offs [13]. Indian studies also support our findings. Nidhi et al. reported that adolescent PCOS patients had higher fasting insulin and HOMA-IR than controls [18], while Bhatnagar et al. found that South Asian women with PCOS exhibit more severe insulin resistance compared with cohorts [19]. Together, these findings align with our observation of significantly elevated fasting insulin, fasting blood sugar, and HOMA-IR in PCOS.

Mechanistic insights into leptin resistance also align with our data. Panidis et al. were among the first to demonstrate that leptin is elevated in PCOS irrespective of adiposity [20], while Rasul et al. suggested that leptin resistance perpetuates hyperinsulinemia and reproductive dysfunction [21]. Chazenbalk et al. showed altered adipokine secretion in ovarian granulosa cells of PCOS patients [22], while Amiri and Tehrani concluded that obesity amplifies reproductive dysfunction through adipokine-driven pathways [8]. Our findings—showing simultaneous correlations of leptin with metabolic and reproductive markers—support the hypothesis that leptin is a central mediator in PCOS pathogenesis.

Clinical Implications

The integration of leptin measurement into PCOS evaluation could provide additional insight into individual metabolic risk, complementing routine markers such as fasting insulin and HOMA-IR. Given its correlations with LH and testosterone, leptin may also serve as a biomarker of combined metabolic–reproductive dysfunction, guiding more tailored therapeutic interventions. Lifestyle and pharmacological interventions targeting both insulin resistance and leptin signaling could hold promise in modifying disease trajectory.

Strengths and Limitations

A major strength of this study is the comprehensive biomarker profiling—including leptin, gonadotropins, testosterone, and insulin indices—within a well-characterized case–control design. The simultaneous analysis of clinical, biochemical, and imaging features, supported by graphical visualization across eleven figures, strengthens the robustness of findings. However, limitations include the modest sample size and single-center design, which may limit generalizability. Leptin resistance was not directly assessed, and additional adipokines (e.g., adiponectin, resistin) were not measured. Longitudinal studies are warranted to establish causal links between leptin dysregulation and long-term reproductive or cardiometabolic outcomes in PCOS.

CONCLUSION

This study highlights the central role of leptin in the metabolic–endocrine derangements of PCOS. Elevated leptin levels, strongly correlated with insulin resistance, hyperandrogenism, and LH/FSH imbalance, reinforce the concept of leptin as a metabolic mediator bridging obesity, insulin resistance, and reproductive dysfunction. Our findings underscore the importance of integrating metabolic and hormonal evaluation in PCOS management and provide a rationale for exploring leptin-targeted interventions in future research.

Declaration:

Conflicts of interests: The authors declare no conflicts of interest.

Author contribution: All authors have contributed in the manuscript.

Author funding: Nil

REFERENCES

1. Rasquin-Leon LI, Rochon C. Polycystic ovarian syndrome. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2022.
2. Çelik Ö, Kumbasar A, Aydin S. An overview of polycystic ovary syndrome in aging women. SAGE Open Med. 2021;9:20503121211056236.
3. Sadeghi H, Bagheri R, Kheirkhah F, et al. Polycystic ovary syndrome: a comprehensive review. Reprod Biol Endocrinol. 2022;20(1):5.
4. Mohapatra I, Mishra P, Behera S, Samal S. Body mass index and polycystic ovary syndrome: demographic trends and implications. J Hum Reprod Sci. 2024;17(2):134-42.
5. Legro RS, Arslanian SA, Ehrmann DA, et al. Diagnosis and treatment of polycystic ovary syndrome: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2013;98(12):4565-92.
6. Azziz R, Carmina E, Dewailly D, et al. The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: the complete task force report. Fertil Steril. 2009;91(2):456-88.
7. Morshed MS, Rahman MS, Karim MR, et al. Diagnostic value of luteinizing hormone to follicle-stimulating hormone ratio in polycystic ovary syndrome. J Obstet Gynaecol. 2021;41(3):425-31.
8. Amiri M, Ramezani Tehrani F. Association between obesity and polycystic ovary syndrome: a systematic review and meta-analysis. J Clin Endocrinol Metab. 2024;109(3):456-68.
9. Zheng SH, Li XL, Wu YH. Circulating leptin levels in women with polycystic ovary syndrome: a systematic review and meta-analysis. Reprod Biomed Online. 2017;35(4):417-29.

10. Grassi G, Lania A, Arosio M, Beck-Peccoz P, Persani L. New markers for the diagnosis of polycystic ovary syndrome: LH/FSH ratio and androgens measured by LC–MS/MS. *J Clin Med*. 2021;10(1):119.
11. Dapas M, Lin FTJ, Nadkarni GN, Sisk R, Legro RS, Urbanek M, et al. Distinct subtypes of polycystic ovary syndrome with novel genetic associations: an unsupervised, phenotypic clustering analysis. *PLoS Med*. 2020;17(6):e1003132.
12. Vink JM, Sadrieh A, Slof-Op't Landt MC, den Heijer M, de Geus EJC, Lambalk CB. Causal role of testosterone in polycystic ovary syndrome: a Mendelian randomization study. *Front Endocrinol (Lausanne)*. 2023;14:1161356.
13. Biernacka-Bartnik A, Szymanska-Pasternak J, Krzyzanowska-Swiniarska B, et al. Cut-off value for HOMA-IR discriminating insulin resistance in women with polycystic ovary syndrome. *Endokrynol Pol*. 2023;74(4):355-62.
14. Peng Y, Yang H, Zhang Y. Elevated serum leptin levels as a predictive marker for polycystic ovary syndrome: evidence from meta-analysis. *Front Endocrinol (Lausanne)*. 2022;13:878604.
15. Chakraborty P, Goswami SK, Rajani S, Sharma S, Kabir SN, Chakravarty B, et al. Reproductive endocrine characteristics of PCOS women in relation to obesity. *Int J Endocrinol*. 2019;2019:1-9.
16. Pratama G, Dewi AP, Anggraeni R, et al. Mechanism of elevated LH/FSH ratio in lean PCOS revisited. *Sci Rep*. 2024;14(1):1123.
17. Lewandowski KC, Komorowski J, Malicka K, et al. Insulin resistance in polycystic ovary syndrome: diagnostic thresholds and clinical implications. *Diabetes Care*. 2019;42(12):e205-6.
18. Nidhi R, Padmalatha V, Nagarathna R, Amritanshu R. Prevalence of polycystic ovarian syndrome in Indian adolescents. *J Pediatr Adolesc Gynecol*. 2020;33(6):591-8.
19. Bhatnagar A, Patel S, Saxena P, Dave A. Insulin resistance and metabolic syndrome in South Asian women with polycystic ovary syndrome. *J Hum Reprod Sci*. 2021;14(3):214-20.
20. Panidis D, Farmakiotis D, Rousso D, Kourtis A, Katsikis I, Krassas G. Serum leptin levels in women with polycystic ovary syndrome. *Hum Reprod*. 2003;18(5):980-6.
21. Rasul S, Ilhan A, Rechsteiner T, Baumgartner-Parzer S, Wagner O, Kautzky-Willer A, et al. Circulating adipokines and insulin resistance in PCOS: evidence of leptin resistance. *Gynecol Endocrinol*. 2019;35(5):389-93.
22. Chazenbalk G, Chen YH, Heneidi S, Lee JM, Pall M, Chen YD, et al. Abnormal expression of genes involved in inflammation, lipid metabolism, and Wntsignaling in the ovarian granulosa cells of PCOS. *J Clin Endocrinol Metab*. 2019;104(5):1967-78.