JHWCR JOURNAL OF HEALTH, WELLNESS AND COMMUNITY RESEARCH 3007-0570

https://doi.org/10.61919/048mec09

Review Article

Insulin Resistance, Thyroid Dysregulation, and Androgen Excess in Polycystic Ovary Syndrome: A Narrative Review of a Triangular Hormonal–Metabolic Model

Javeria Shabbir[1], Maryam Manzoor[1], Amber Tehseen[1], Rameen Shahzad[1], Zaira Arif[1], Arooj Saleem[1], Adan Amjad[2]

[1] Department of Nutrition and Dietetics, The University of Faisalabad, Pakistan
[2] University of Biological and Applied Sciences, Lahore, Pakistan

***Corresponding author: Adan Amjad, amjadadan80@gmail.com; jschoohan@gmail.com**

"Cite this Article" Received: 04 January 2026; **Accepted**: 26 April 2026; **Published**: 07 May 2026

Author Contributions: Concept: JS, MM, AA; Design: AT, RS, ZA; Literature Search: JS, MM, AS; Drafting: JS, MM, AT, RS, ZA, AS; Critical Revision: AA; Final Approval: JS, MM, AT, RS, ZA, AS, AA. **Ethical Approval**: University of Biological and Applied Sciences, Lahore, Pakistan. **Informed Consent**: Written informed consent was obtained from all participants; **Conflict of Interest**: The authors declare no conflict of interest. **Funding**: No external funding; **Data Availability**: Available from the corresponding author on reasonable request; **Acknowledgments**: N/A.

ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is a heterogeneous endocrine–metabolic disorder characterized by reproductive dysfunction, androgen excess, and variable metabolic risk. Although insulin resistance, thyroid dysfunction, and hyperandrogenism are frequently discussed as separate abnormalities, their interaction may better explain the diversity of PCOS phenotypes and long-term cardiometabolic consequences. Objective: This narrative review aims to synthesize current evidence on the interrelationship among insulin resistance, thyroid dysregulation, and androgen excess in PCOS and to present these mechanisms as an integrated triangular hormonal–metabolic model. Methods: A targeted narrative literature search was conducted using PubMed, Google Scholar, and Scopus. Search terms included combinations of "polycystic ovary syndrome," "PCOS," "insulin resistance," "hyperinsulinemia," "hyperandrogenism," "thyroid dysfunction," "subclinical hypothyroidism," "autoimmune thyroiditis," and "cardiometabolic risk." Priority was given to international guidelines, systematic reviews, meta-analyses, mechanistic studies, observational studies, and clinically relevant interventional evidence. The synthesis was organized thematically around epidemiology, pathophysiology, clinical manifestations, and phenotype-directed management. Results: The reviewed evidence supports insulin resistance as a central metabolic driver of PCOS through compensatory hyperinsulinemia, increased ovarian androgen synthesis, reduced sex hormone-binding globulin, and impaired ovulatory function. Hyperandrogenism may further aggravate insulin resistance through visceral adiposity and adipose dysfunction. Thyroid dysfunction, particularly subclinical hypothyroidism and thyroid autoimmunity, appears to modify metabolic and reproductive severity in selected patients by influencing insulin sensitivity, lipid metabolism, inflammation, and follicular function. Conclusion: PCOS should be approached as an integrated endocrine–metabolic syndrome in which insulin resistance, androgen excess, and thyroid dysfunction may interact bidirectionally. Integrated assessment and phenotype-directed management may improve clinical care, although further longitudinal and interventional studies are needed. Keywords: Polycystic Ovary Syndrome; Insulin Resistance; Hyperandrogenism; Thyroid Dysfunction; Subclinical Hypothyroidism; Autoimmune Thyroiditis; Metabolic Syndrome; Reproductive Health.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is among the most common endocrine and metabolic disorders affecting reproductive-aged women, with reported prevalence ranging from 6% to 20% depending on the diagnostic criteria, ethnicity, and population studied (1). Although classically defined by ovulatory

dysfunction, clinical or biochemical hyperandrogenism, and polycystic ovarian morphology, PCOS is now increasingly understood as a systemic disorder involving reproductive, metabolic, inflammatory, and neuroendocrine pathways rather than an isolated ovarian condition. Its clinical expression is highly heterogeneous, ranging from menstrual irregularity, infertility, acne, and hirsutism to insulin resistance, dyslipidemia, obesity, impaired glucose tolerance, psychological morbidity, and increased long-term cardiometabolic risk (1–3).

Among the multiple biological disturbances implicated in PCOS, insulin resistance, androgen excess, and thyroid dysfunction appear to occupy particularly important and interrelated positions. Insulin resistance is one of the most consistent metabolic abnormalities in PCOS and may occur in both obese and lean phenotypes. Compensatory hyperinsulinemia promotes ovarian theca-cell androgen synthesis, suppresses hepatic sex hormone-binding globulin production, increases free testosterone levels, and contributes to chronic anovulation (1,4,5). At the same time, hyperandrogenism may worsen adipose tissue dysfunction, visceral fat accumulation, and systemic insulin resistance, creating a self-reinforcing metabolic–reproductive cycle. This bidirectional relationship helps explain why many patients present with overlapping reproductive and metabolic manifestations rather than isolated clinical features.

Thyroid dysfunction has also gained increasing attention as a clinically relevant comorbidity in PCOS. Subclinical hypothyroidism and autoimmune thyroiditis have been reported more frequently among women with PCOS than in matched controls, and these abnormalities may aggravate menstrual dysfunction, infertility, dyslipidemia, weight gain, insulin resistance, and inflammatory burden (6–8). Thyroid hormones influence glucose metabolism, lipid turnover, ovarian steroidogenesis, gonadotropin dynamics, and follicular maturation; therefore, even mild thyroid dysregulation may modify the severity and phenotype of PCOS. However, thyroid dysfunction is often discussed separately from insulin resistance and androgen excess, which limits understanding of their combined contribution to PCOS heterogeneity.

Existing reviews and guidelines have addressed the diagnosis, metabolic risk, and management of PCOS, but the interaction among insulin resistance, thyroid dysregulation, and androgen excess remains insufficiently integrated into a single conceptual framework. Much of the available literature evaluates these mechanisms independently, whereas clinical practice often encounters them together in the same patient. A narrative synthesis is therefore useful to connect mechanistic, epidemiologic, and therapeutic evidence and to clarify how these endocrine axes may interact in shaping reproductive dysfunction, metabolic risk, and individualized treatment response.

This narrative review aims to synthesize current evidence on the bidirectional relationships among insulin resistance, thyroid dysfunction, and androgen excess in PCOS and to present these interactions as a triangular hormonal–metabolic model. By integrating epidemiologic findings, mechanistic pathways, and clinical implications, this review seeks to support more comprehensive assessment and phenotype-directed management of women with PCOS.

MATERIALS AND METHODS

This article was designed as a narrative review because the objective was to provide an integrated conceptual synthesis of endocrine and metabolic mechanisms in PCOS rather than to answer a narrowly defined PICO question or generate pooled quantitative estimates. The review focused on three interrelated domains: insulin resistance, thyroid dysfunction, and androgen excess. These domains were selected because they represent frequently overlapping biological disturbances in PCOS and because their interaction may explain important variation in reproductive, metabolic, and cardiometabolic phenotypes.

Relevant literature was identified through targeted searches of PubMed, Google Scholar, and Scopus. Search terms included combinations of “polycystic ovary syndrome,” “PCOS,” “insulin resistance,”

"hyperinsulinemia," "hyperandrogenism," "androgen excess," "thyroid dysfunction," "subclinical hypothyroidism," "autoimmune thyroiditis," "metabolic syndrome," "ovulatory dysfunction," and "cardiometabolic risk." Priority was given to international guidelines, systematic reviews, meta-analyses, mechanistic studies, observational studies, and clinically relevant interventional studies. Recent publications from 2018 onward were emphasized to reflect the contemporary evidence landscape, while older seminal literature was retained where it provided foundational mechanistic or diagnostic context.

Articles were selected according to their relevance to the review objective, methodological credibility, clinical importance, and contribution to understanding the interaction between metabolic, thyroid, and androgenic pathways in PCOS. Studies were considered particularly relevant if they addressed insulin resistance in PCOS phenotypes, thyroid hormone or thyroid autoimmunity abnormalities in PCOS populations, androgen-mediated reproductive or metabolic dysfunction, or treatment approaches targeting one or more components of the proposed triangular model. Publications not directly related to PCOS pathophysiology, endocrine interaction, or clinical management were not prioritized.

The synthesis was organized conceptually and thematically. First, epidemiologic evidence was summarized to establish the burden and coexistence of insulin resistance, hyperandrogenism, and thyroid dysfunction in PCOS. Second, mechanistic evidence was integrated to explain bidirectional pathways linking hyperinsulinemia, ovarian androgen production, thyroid hormone abnormalities, inflammation, and metabolic risk. Third, clinical and therapeutic implications were reviewed, including lifestyle modification, insulin-sensitizing therapy, thyroid optimization, and anti-androgen treatment. Because this was a narrative review, no formal risk-of-bias assessment, meta-analysis, or certainty-of-evidence grading was performed. This approach allows flexible integration of mechanistic and clinical evidence but introduces potential selection bias; therefore, conclusions were interpreted cautiously and framed as a conceptual synthesis rather than definitive causal evidence.

RESULTS

The reviewed evidence supports the interpretation of PCOS as a heterogeneous endocrine–metabolic syndrome rather than a disorder restricted to ovarian morphology or menstrual irregularity alone. Current diagnostic and guideline literature emphasizes that PCOS includes overlapping reproductive, metabolic, dermatologic, and psychological features, with prevalence varying according to the diagnostic criteria and population studied (1,3,5). This heterogeneity is important because it explains why some patients present predominantly with infertility or ovulatory dysfunction, whereas others show marked insulin resistance, obesity, dyslipidemia, thyroid abnormalities, or cardiometabolic risk. Within this broader framework, insulin resistance, thyroid dysregulation, and androgen excess emerge as interconnected mechanisms that may jointly influence the severity and clinical phenotype of PCOS.

Table 1. Summary Evidence Matrix for the Triangular Hormonal–Metabolic Model in PCOS

Evidence Domain	Main Evidence Source	Study / Evidence Type	Population or Focus	Key Findings
PCOS burden and diagnostic heterogeneity	Azziz; Teede et al.; Chang and Dunaif	Review / guideline evidence	Women of reproductive age with PCOS	PCOS prevalence varies widely depending on diagnostic criteria and population characteristics; clinical expression includes reproductive, metabolic, and psychological manifestations (1,3,5).
Insulin resistance in PCOS	Azziz; Wijeyaratne et al.; Diamanti-Kandarakis and Christakou	Review / observational and mechanistic evidence	Women with PCOS, including South Asian phenotypes	Insulin resistance occurs in both obese and lean PCOS phenotypes and contributes to compensatory hyperinsulinemia, impaired ovulation, and metabolic risk (1,4,10).
Hyperinsulinemia and androgen excess	Rosenfield and Dumesic; Chang and Dunaif	Mechanistic / endocrine review evidence	Ovarian steroidogenesis and adiposity-related PCOS mechanisms	Hyperinsulinemia stimulates ovarian theca-cell androgen production and reduces SHBG, increasing free androgen activity (5,9).

Evidence Domain	Main Evidence Source	Study / Evidence Type	Population or Focus	Key Findings
Thyroid dysfunction in PCOS	Xing et al.; Shekarian et al.; Kwiatkowski et al.	Meta-analysis / systematic review evidence	Women with PCOS and thyroid abnormalities	Subclinical hypothyroidism and thyroid autoimmunity appear more common in PCOS populations and may worsen insulin resistance, menstrual dysfunction, and metabolic abnormalities (6–8).
Inflammation and immune-metabolic interaction	Rudnicka et al.; González et al.	Review / clinical mechanistic evidence	Inflammation in PCOS	Chronic low-grade inflammation, oxidative stress, and cytokine activation are implicated in PCOS pathogenesis and may interact with insulin resistance and androgen excess (2,12).
Genetic and developmental contributors	Tay et al.; Dumesic et al.; Sánchez-Garrido et al.	Review / mechanistic evidence	Genetic susceptibility and reproductive programming	Genetic predisposition, prenatal androgen exposure, neuroendocrine programming, and metabolic environment may contribute to later PCOS expression (13,14,17).
Dietary and lifestyle interventions	Che et al.; Rodriguez Paris et al.	Review / experimental and translational evidence	Dietary patterns and metabolic regulation in PCOS	Low-glycemic and Mediterranean-style dietary approaches may improve insulin sensitivity, inflammatory profile, and reproductive outcomes (19,20).
Insulin-sensitizing therapy	Brand et al.; Facchinetti et al.	Review / expert consensus evidence	Metformin and inositols in PCOS	Metformin and inositol-based therapies may improve insulin signaling, menstrual cyclicity, ovulatory function, and androgen-related outcomes (15,21).
GLP-1 receptor agonists	Jensterle et al.	Review evidence	Weight, insulin resistance, and metabolic dysfunction in PCOS	GLP-1 receptor agonists show therapeutic potential for weight reduction, insulin resistance, and metabolic improvement in PCOS (22).
Thyroid optimization	Xing et al.; Shekarian et al.; Biondi and Cappola	Meta-analysis / endocrine review evidence	Subclinical hypothyroidism and thyroid-related metabolic dysfunction	Thyroid dysfunction may worsen lipid abnormalities, insulin resistance, and reproductive dysfunction; correction may benefit selected patients with confirmed thyroid disease (6,7,11).

Insulin resistance appears to be one of the most consistently reported metabolic abnormalities in PCOS. Evidence from reviews and observational studies indicates that insulin resistance may occur in both obese and lean phenotypes, although the metabolic burden is often greater in populations with higher adiposity or increased cardiometabolic vulnerability (1,4,10). The mechanistic relevance of insulin resistance lies in compensatory hyperinsulinemia, which can stimulate ovarian theca-cell androgen production and reduce hepatic sex hormone-binding globulin synthesis, thereby increasing biologically active free androgens (5,9). This mechanism provides a plausible explanation for the frequent coexistence of metabolic dysfunction and hyperandrogenic manifestations such as hirsutism, acne, anovulation, and impaired follicular maturation.

Hyperandrogenism is not only a reproductive or cosmetic feature of PCOS but also a contributor to metabolic dysfunction. Excess androgen activity may promote visceral adiposity, impair adipocyte differentiation, worsen insulin sensitivity, and intensify inflammatory signaling (9,16). This creates a self-reinforcing cycle in which insulin resistance increases androgen production, while androgen excess further aggravates insulin resistance and metabolic dysfunction. The strength of evidence is greatest for the association between insulin resistance and androgen excess, supported by mechanistic studies, endocrine reviews, and clinical observations; however, the magnitude of this interaction varies across PCOS phenotypes and should not be generalized uniformly to all patients.

Thyroid dysfunction represents the third node of the proposed triangular model. Meta-analytic and review evidence suggests that subclinical hypothyroidism and autoimmune thyroiditis are more frequently reported among women with PCOS than in non-PCOS comparison groups (6–8). Thyroid hormones influence basal metabolic rate, lipid metabolism, glucose handling, gonadotropin regulation,

ovarian steroidogenesis, and follicular development. Therefore, thyroid dysregulation may worsen insulin resistance, menstrual disturbance, weight gain, dyslipidemia, and reproductive dysfunction in selected PCOS phenotypes (6,7,11). However, the available evidence does not establish that thyroid dysfunction is a universal causal driver of PCOS. Rather, it should be interpreted as a clinically relevant comorbidity and potential disease modifier, particularly in patients with metabolic abnormalities, menstrual irregularity, infertility, or autoimmune features.

Inflammation appears to provide an additional pathway linking metabolic and endocrine dysfunction in PCOS. Chronic low-grade inflammation, oxidative stress, and altered cytokine activity have been implicated in PCOS pathogenesis and may interact with insulin resistance, adipose dysfunction, androgen excess, and thyroid autoimmunity (2,12). This immune-metabolic component strengthens the rationale for viewing PCOS as a systemic condition. It also helps explain why lifestyle interventions, dietary quality, weight management, insulin-sensitizing therapy, and metabolic optimization may influence reproductive outcomes even when they do not directly target the ovary.

The therapeutic literature supports phenotype-directed management rather than a single uniform treatment strategy. Dietary interventions, particularly low-glycemic and Mediterranean-style dietary patterns, may improve insulin sensitivity, inflammatory burden, and metabolic risk markers in PCOS (19,20). Metformin remains one of the most widely discussed insulin-sensitizing therapies and may improve menstrual cyclicity, insulin indices, and androgen-related outcomes in selected patients (15). Inositol-based therapies, especially myo-inositol and D-chiro-inositol combinations, have also been proposed to improve ovarian insulin signaling and ovulatory function (21). GLP-1 receptor agonists have emerging relevance in PCOS phenotypes characterized by obesity, insulin resistance, and cardiometabolic risk, although their role should be interpreted within the limits of available clinical evidence (22).

For patients with confirmed thyroid dysfunction, thyroid assessment and appropriate correction may be clinically important, particularly where menstrual disturbance, infertility, weight gain, dyslipidemia, or insulin resistance coexist. Nevertheless, thyroid-directed therapy should not be presented as a universal PCOS treatment. Its potential benefit is most defensible in patients with biochemical thyroid abnormalities rather than euthyroid individuals. Similarly, anti-androgen therapy may improve hirsutism and acne but does not address the full metabolic basis of PCOS and should be integrated with contraception counseling and metabolic assessment where clinically indicated.

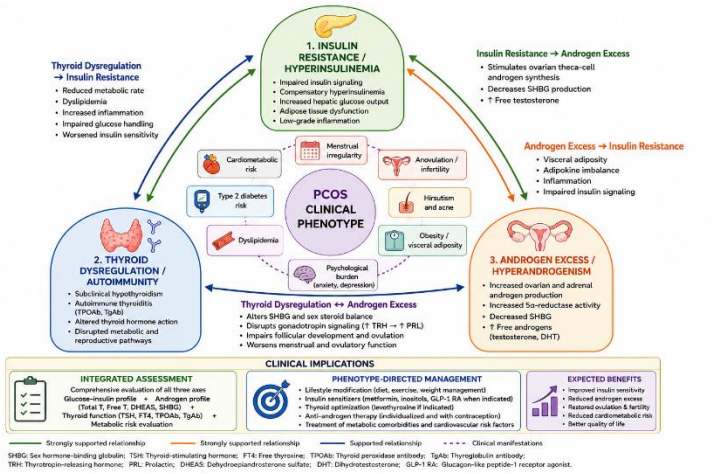

Figure 1 Integrated triangular hormonal–metabolic model of PCOS.

The figure illustrates the bidirectional interactions among insulin resistance/hyperinsulinemia, thyroid dysregulation/autoimmunity, and androgen excess/hyperandrogenism in polycystic ovary syndrome. Insulin resistance promotes hyperinsulinemia, increased ovarian androgen synthesis, reduced SHBG production, and elevated free testosterone, while androgen excess may worsen visceral adiposity,

inflammation, and impaired insulin signaling. Thyroid dysfunction may further aggravate insulin resistance, dyslipidemia, inflammatory burden, altered SHBG balance, gonadotropin disruption, and impaired follicular development. These interconnected pathways contribute to the heterogeneous PCOS clinical phenotype, including menstrual irregularity, anovulation, infertility, hirsutism, acne, obesity, dyslipidemia, type 2 diabetes risk, cardiometabolic risk, and psychological burden. The model supports integrated endocrine–metabolic assessment and phenotype-directed management.

DISCUSSION

This narrative review synthesized current evidence on the interaction among insulin resistance, thyroid dysregulation, and androgen excess in polycystic ovary syndrome (PCOS), framing these mechanisms as an interconnected hormonal–metabolic triangle rather than isolated abnormalities. The reviewed literature indicates that insulin resistance is one of the most consistent metabolic disturbances in PCOS and contributes directly to compensatory hyperinsulinemia, increased ovarian androgen synthesis, reduced sex hormone-binding globulin, and impaired ovulatory function (1,4,5,10). Hyperandrogenism, in turn, may worsen visceral adiposity, adipose tissue dysfunction, and systemic insulin resistance, forming a bidirectional cycle that helps explain the coexistence of reproductive and metabolic manifestations in many PCOS phenotypes (9,16). Thyroid dysfunction, particularly subclinical hypothyroidism and autoimmune thyroiditis, appears to act as an important modifying factor in a subset of women with PCOS by influencing metabolic rate, lipid metabolism, insulin sensitivity, inflammatory burden, and reproductive function (6–8,11).

The strongest and most biologically coherent evidence supports the relationship between insulin resistance and androgen excess. This interaction is supported by endocrine mechanisms, clinical observations, and therapeutic evidence showing that insulin-sensitizing interventions may improve menstrual cyclicity, ovulatory function, and androgen-related outcomes in selected patients (15,21). However, PCOS remains heterogeneous, and not all patients demonstrate the same degree of insulin resistance, obesity, or hyperandrogenism. Therefore, the triangular model should be interpreted as a conceptual framework that helps explain common overlapping pathways rather than as a universal mechanism applicable to every patient with PCOS.

The role of thyroid dysfunction in PCOS is clinically important but requires more cautious interpretation. Meta-analytic evidence suggests higher rates of subclinical hypothyroidism and thyroid autoimmunity among women with PCOS, yet the directionality and causality of this association remain uncertain (6–8). Thyroid abnormalities may aggravate metabolic and reproductive dysfunction, but current evidence does not justify treating thyroid dysfunction as a primary cause of PCOS in all patients. Instead, thyroid screening appears most relevant in patients with menstrual irregularity, infertility, weight gain, dyslipidemia, insulin resistance, symptoms suggestive of hypothyroidism, or autoimmune risk. This interpretation avoids overgeneralization while supporting integrated endocrine assessment in clinically appropriate cases.

The therapeutic implications of this model favor phenotype-directed management. Lifestyle modification, dietary quality, physical activity, and weight management remain foundational because they target insulin resistance, inflammatory burden, and cardiometabolic risk (19,20). Metformin and inositol-based therapies may be useful in patients with insulin resistance, menstrual irregularity, or metabolic dysfunction, whereas GLP-1 receptor agonists may have a role in selected patients with obesity and marked metabolic risk (15,21,22). Thyroid hormone correction should be reserved for patients with confirmed thyroid dysfunction, and anti-androgen therapy should be individualized for clinical hyperandrogenism with appropriate contraceptive counseling. This integrated approach is more clinically defensible than treating PCOS solely as either a reproductive disorder or a metabolic disorder.

This review has several limitations. Because it was conducted as a narrative review, the literature search was not exhaustive, no formal risk-of-bias assessment was performed, and no certainty-of-evidence

grading was applied. Selection bias is possible, particularly because mechanistic and clinically relevant studies were prioritized over a fully systematic evidence map. In addition, PCOS definitions vary across studies, and differences in diagnostic criteria, ethnicity, age, body mass index, thyroid status, and metabolic phenotype limit direct comparison across the evidence base. Future research should prioritize longitudinal studies that evaluate insulin resistance, androgen profiles, thyroid function, thyroid autoimmunity, inflammatory markers, and reproductive outcomes simultaneously. Randomized trials are also needed to determine whether combined metabolic and thyroid-directed management improves outcomes beyond standard phenotype-based treatment.

CONCLUSION

PCOS is best understood as a heterogeneous endocrine–metabolic syndrome in which insulin resistance, androgen excess, and thyroid dysregulation may interact through bidirectional hormonal, metabolic, and inflammatory pathways. The strongest evidence supports the insulin resistance–hyperandrogenism axis, while thyroid dysfunction appears to modify metabolic and reproductive severity in selected patients. A triangular hormonal–metabolic framework supports integrated assessment of glucose–insulin status, androgen profile, thyroid function, and cardiometabolic risk rather than isolated symptom-based management. This approach may improve phenotype-directed care, but further longitudinal and interventional studies are required to clarify causality, treatment sequencing, and long-term clinical benefit.

REFERENCES

1. Azziz R. Polycystic ovary syndrome. Obstet Gynecol. 2018;132(2):321-336.
2. González F, Considine RV, Abdelhadi OA, Xue J, Acton AJ. Saturated fat ingestion stimulates proatherogenic inflammation in polycystic ovary syndrome. Am J Physiol Endocrinol Metab. 2021;321(5):E689-E701.
3. Teede HJ, Tay CT, Laven JJ, 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. Eur J Endocrinol. 2023;189(2):G43-G64.
4. Wijeyaratne CN, Seneviratne RD, Dahanayake S, Kumarapeli V, Palipane E, Kuruppu N, et al. Phenotype and metabolic profile of South Asian women with polycystic ovary syndrome: results of a large database from a specialist endocrine clinic. Hum Reprod. 2011;26(1):202-213.
5. Chang S, Dunaif A. Diagnosis of polycystic ovary syndrome: which criteria to use and when? Endocrinol Metab Clin North Am. 2021;50(1):11-23.
6. Xing Y, Chen J, Liu J, Ma H. The impact of subclinical hypothyroidism on patients with polycystic ovary syndrome: a meta-analysis. Horm Metab Res. 2021;53(6):382-390.
7. Shekarian A, Mazaheri-Tehrani S, Shekarian S, Pourbazargan M, Setudeh M, Abhari AP, et al. Prevalence of subclinical hypothyroidism in polycystic ovary syndrome and its impact on insulin resistance: a systematic review and meta-analysis. BMC Endocr Disord. 2025;25(1):75.
8. Kwiatkowski J, Akpang N, Zaborowska L, Ludwin A. Prevalence and levels of thyroid autoantibodies in polycystic ovary syndrome—impact of TSH- and BMI-matched comparisons: a systematic review and meta-analysis. Int J Mol Sci. 2025;26(15):7525.
9. Rosenfield RL, Dumesic DA. On the intimate relationship of adiposity to polycystic ovary syndrome. J Clin Endocrinol Metab. 2025;dgaf527.
10. Diamanti-Kandarakis E, Christakou CD. Insulin resistance in PCOS. In: Diagnosis and management of polycystic ovary syndrome. Boston: Springer; 2009. p. 35-61.

11. Biondi B, Cappola AR. Subclinical hypothyroidism in older individuals. Lancet Diabetes Endocrinol. 2022;10(2):129-141.

12. Rudnicka E, Suchta K, Grymowicz M, Calik-Ksepka A, Smolarczyk K, Duszewska AM, et al. Chronic low-grade inflammation in pathogenesis of PCOS. Int J Mol Sci. 2021;22(7):3789.

13. Tay CT, Garrad R, Mousa A, Bahri M, Joham A, Teede H. Polycystic ovary syndrome: international collaboration to translate evidence and guide future research. J Endocrinol. 2023;257(3).

14. Dumesic DA, Crespi BJ, Padmanabhan V, Abbott DH. The endocrinological basis for polycystic ovary syndrome: an evolutionary perspective. Endocrinology. 2025;bqaf160.

15. Brand KM, Gottwald-Hostalek U, Andag-Silva A. Update on the therapeutic role of metformin in the management of polycystic ovary syndrome: effects on pathophysiologic process and fertility outcomes. Womens Health (Lond). 2025;21:17455057241311759.

16. Carmina E, Dreno B, Lucky WA, Agak WG, Dokras A, Kim JJ, et al. Female adult acne and androgen excess: a report from the multidisciplinary androgen excess and PCOS committee. J Endocr Soc. 2022;6(3):bvac003.

17. Sánchez-Garrido MA, García-Galiano D, Tena-Sempere M. Early programming of reproductive health and fertility: novel neuroendocrine mechanisms and implications in reproductive medicine. Hum Reprod Update. 2022;28(3):346-375.

18. Zahra M, Shah M, Iqbal F, Zubair T, Habib R, Zulfiqar F. Efficacy of combined nutritional and pharmacological interventions in PCOS: a six-month randomized controlled trial. Naunyn Schmiedebergs Arch Pharmacol. 2025.

19. Che X, Chen Z, Liu M, Mo Z. Dietary interventions: a promising treatment for polycystic ovary syndrome. Ann Nutr Metab. 2021;77(6):313-323.

20. Rodriguez Paris V, Wong XY, Solon-Biet SM, Edwards MC, Aflatounian A, Gilchrist RB, et al. The interplay between PCOS pathology and diet on gut microbiota in a mouse model. Gut Microbes. 2022;14(1):2085961.

21. Facchinetti F, Appetecchia M, Aragona C, Bevilacqua A, Bezerra Espinola MS, Bizzarri M, et al. Experts' opinion on inositols in treating polycystic ovary syndrome and non-insulin-dependent diabetes mellitus: a further help for human reproduction and beyond. Expert Opin Drug Metab Toxicol. 2020;16(3):255-274.

22. Jensterle M, Herman R, Janež A. Therapeutic potential of glucagon-like peptide-1 agonists in polycystic ovary syndrome: from current clinical evidence to future perspectives. Biomedicines. 2022;10(8):1989.

23. Escobar-Morreale HF. Defining PCOS: a syndrome with an intrinsic heterogeneous nature. In: Polycystic Ovary Syndrome. Amsterdam: Elsevier; 2022. p. 3-13.

24. Pasquali R. Contemporary approaches to the management of polycystic ovary syndrome. Ther Adv Endocrinol Metab. 2018;9(4):123-134.

25. Zore T, Lizneva D, Brakta S, Walker W, Suturina L, Azziz R. Minimal difference in phenotype between adolescents and young adults with polycystic ovary syndrome. Fertil Steril. 2019;111(2):389-396.