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# Polycystic Ovary Syndrome in Reproductive-Age Women: Diagnostic Challenges, Metabolic-Reproductive Consequences and Individualized Management

**Dr. Sucheta Talele**

*Associate Professor, Obstetrics and Gynecology, GMERS Medical College, Himmatnagar, Gujarat, India*

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## Abstract

Polycystic ovary syndrome (PCOS) is a heterogeneous endocrine-reproductive disorder characterized by variable combinations of ovulatory dysfunction, hyperandrogenism, and polycystic ovarian morphology. Its clinical importance extends beyond irregular menses and infertility because affected women have higher burdens of obesity, insulin resistance, dysglycemia, adverse pregnancy outcomes, and psychological distress. This narrative review summarizes evidence available through 30 June 2021 on diagnosis, pathophysiology, cardiometabolic risk, reproductive consequences, and treatment. The Rotterdam framework remains widely used, but diagnosis requires exclusion of alternative causes of androgen excess or menstrual dysfunction and careful interpretation in adolescents. Insulin resistance and compensatory hyperinsulinemia amplify ovarian androgen production and reduce hepatic sex-hormone-binding globulin, while obesity can worsen both metabolic and reproductive phenotypes. Management should be goal directed rather than syndrome directed: lifestyle intervention is foundational; combined oral contraceptive pills are commonly used for cycle regulation and hyperandrogenic symptoms when pregnancy is not desired; metformin is most useful for metabolic indications and selected reproductive contexts; and letrozole has superior live-birth evidence compared with clomiphene for anovulatory infertility. Women with PCOS should also be assessed for dysglycemia, cardiovascular risk factors, and psychological comorbidity. Pregnancy requires heightened awareness of gestational diabetes, hypertensive disorders, and preterm birth. A long-term, individualized model of care is therefore more appropriate than episodic treatment focused only on fertility.

**Keywords:** polycystic ovary syndrome; hyperandrogenism; anovulation; infertility; insulin resistance; letrozole; metformin; lifestyle

## 1. Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders of reproductive-age women and is also a leading cause of anovulatory infertility [4,6]. The syndrome is clinically heterogeneous: one woman may present with hirsutism and irregular menses, another with infertility, and another with obesity, dysglycemia, or a combination of reproductive and metabolic features. This heterogeneity has contributed to continuing debate over diagnostic criteria and makes a single treatment algorithm inappropriate.

Population prevalence depends heavily on the diagnostic framework and population studied. Community studies have reported prevalence estimates ranging from approximately 6-18%, with broader Rotterdam criteria identifying more women than stricter National Institutes of Health criteria [7-9]. Beyond reproductive symptoms, PCOS is associated with excess adiposity, insulin resistance, type 2 diabetes risk, psychological morbidity, and adverse pregnancy outcomes [10-14,19].

The aim of this review is to provide a clinically focused synthesis of diagnostic principles, pathophysiology, long-term health consequences, and evidence-based management using literature available by 30 June 2021.

## 2. Methods

A focused narrative review was performed using PubMed/MEDLINE-indexed literature and major professional guidance available on or before 30 June 2021. Search concepts included polycystic ovary syndrome, Rotterdam criteria, hyperandrogenism, insulin resistance, obesity, metabolic risk, lifestyle intervention, metformin, letrozole, clomiphene, infertility, pregnancy complications, depression, and quality of life. Priority was given to international or specialty guidelines, randomized trials, systematic reviews/meta-analyses, landmark epidemiologic studies, and widely cited mechanistic reviews. Evidence published after the cutoff was excluded from the synthesis.

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## 3. Diagnostic Framework and Epidemiology

The 2003 Rotterdam consensus, published in 2004, broadened the diagnosis of PCOS to require any two of three features after exclusion of relevant alternative disorders: oligo/anovulation, clinical or biochemical hyperandrogenism, and polycystic ovarian morphology [1]. This creates multiple phenotypes and explains why prevalence increases when Rotterdam criteria are applied compared with narrower definitions [7].

Diagnosis remains one of exclusion. Depending on presentation, evaluation may include pregnancy testing, thyroid function, prolactin, and assessment for nonclassic congenital adrenal hyperplasia; more extensive testing is indicated when androgen excess is severe, rapidly progressive, or accompanied by virilization. The Endocrine Society and international evidence-based guideline emphasize appropriate exclusion of mimicking conditions and attention to life stage [2,3].

Epidemiologic studies reinforce the substantial hidden burden. In a community cohort, March and colleagues estimated PCOS prevalence at 8.7% using NIH criteria and higher estimates under Rotterdam and Androgen Excess Society definitions, while most affected women had no previous diagnosis [7]. Azziz and colleagues reported a prevalence of 6.6% in an unselected population using a hyperandrogenism-and-ovulatory-dysfunction framework [9]. Ethnicity, obesity prevalence, referral patterns, and ultrasound technology further influence estimates [8].

**Table 1. Rotterdam-based diagnostic framework for PCOS [1-3].**

| Domain | Typical finding | Interpretive point |
|---|---|---|
| Ovulatory dysfunction | Oligomenorrhea, amenorrhea, or objective evidence of anovulation | Exclude pregnancy, thyroid/prolactin disorders and other causes as clinically indicated |
| Hyperandrogenism | Clinical hirsutism/acne or biochemical androgen excess | Consider assay quality; rapid virilization requires evaluation for alternative causes |
| Polycystic ovarian morphology | Ultrasound morphology consistent with accepted criteria | Interpret in context; morphology alone does not establish the syndrome |
| Diagnosis | Any two of the three Rotterdam features after exclusion of mimics | Phenotype should guide counseling and treatment priorities |

## 4. Pathophysiology: Interaction of Androgen Excess and Metabolic Dysfunction

PCOS does not arise from a single defect. Genetic susceptibility, hypothalamic-pituitary signaling, ovarian theca-cell steroidogenesis, insulin resistance, adipose dysfunction, and environmental influences interact to produce the phenotype [4-6]. Hyperandrogenism is central to many clinical manifestations, but insulin resistance can be present independently of obesity and can intensify ovarian androgen production [10].

Compensatory hyperinsulinemia acts synergistically with luteinizing hormone at the ovary and suppresses hepatic sex-hormone-binding globulin, increasing bioavailable androgens. These mechanisms help explain why weight gain and insulin resistance can worsen hirsutism, cycle irregularity, and anovulation. Conversely, not all women with PCOS are obese, and lean phenotypes can still display substantial reproductive and metabolic abnormalities.

Obesity is a clinically important modifier. A large meta-analysis found higher prevalence of overweight, general obesity, and central obesity among women with PCOS than among controls [11]. This matters because adiposity increases the likelihood of dysglycemia, obstructive sleep apnea, fatty liver disease, and adverse pregnancy outcomes, while also complicating ovulation induction and fertility treatment.

## 5. Reproductive, Metabolic and Psychological Consequences

### 5.1 Menstrual dysfunction and infertility

Chronic oligo/anovulation produces irregular cycles and is a major mechanism of infertility. Prolonged unopposed estrogen exposure also raises concern for endometrial hyperplasia in women with infrequent withdrawal bleeding, making cycle regulation or endometrial protection an important management goal when pregnancy is not desired [2,3,5].

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### 5.2 Metabolic risk

Insulin resistance and dysglycemia are core long-term concerns. Longitudinal evidence synthesized in 2020 showed substantially higher risks of type 2 diabetes and hypertension in women with PCOS compared with women without the syndrome [12]. Risk is amplified by obesity, family history, age, and previous gestational diabetes. Periodic assessment of glycemia, blood pressure, weight/waist measures, and lipid risk is therefore part of comprehensive care rather than an optional add-on.

Cardiovascular-event data are less definitive than data for risk factors, partly because most PCOS cohorts are still relatively young and phenotypes vary. Nevertheless, the clustering of obesity, dyslipidemia, hypertension, insulin resistance, and diabetes justifies active prevention of conventional cardiovascular risk factors [3,12,20].

### 5.3 Psychological health and quality of life

PCOS can have a marked psychosocial burden related to hirsutism, acne, weight concerns, infertility, and unpredictable cycles. Large observational data demonstrate impaired quality of life and substantial depressive symptoms [13]. A systematic review and meta-analysis also found increased prevalence of moderate and severe depression and anxiety symptoms among women with PCOS [14]. Routine clinical encounters should therefore include attention to mood, anxiety, body image, eating behavior, and the impact of fertility-related stress.

## 6. Individualized Management

### 6.1 Lifestyle intervention

Lifestyle management is foundational for all women with PCOS, particularly when excess weight or metabolic risk is present. The goal is not a specific branded diet but a sustainable pattern of nutrition, physical activity, sleep, and behavioral support that improves weight trajectory and cardiometabolic health. Cochrane evidence available by 2019 suggested that lifestyle interventions can improve weight-related and metabolic outcomes, although studies were heterogeneous and long-term data were limited [15].

Even modest weight reduction may improve ovulatory function and metabolic parameters in some women with overweight or obesity. Equally important, clinicians should avoid implying that weight loss is the sole treatment or that lean women do not require metabolic assessment.

### 6.2 Menstrual regulation and hyperandrogenic symptoms

When pregnancy is not desired, combined oral contraceptive pills are commonly used to regulate bleeding and improve androgen-related symptoms. Choice should consider contraindications and cardiovascular risk. Cosmetic measures and pharmacologic anti-androgens may be added for hirsutism in selected patients, but reliable contraception is essential when using potentially teratogenic anti-androgen therapy. Metformin should not be viewed as a universal substitute for hormonal therapy; its strongest rationale is metabolic dysfunction and selected patients with impaired glucose tolerance, diabetes risk, or menstrual irregularity when other strategies are unsuitable [2,3,20].

### 6.3 Anovulatory infertility

The therapeutic objective in infertility is live birth rather than ovulation alone. A pivotal multicenter randomized trial showed higher cumulative live-birth and ovulation rates with letrozole than with clomiphene in infertile women with PCOS [16]. This evidence contributed to the 2018 international guideline recommending letrozole as the preferred first-line pharmacologic ovulation-induction agent where its use is permitted [3].

Earlier randomized evidence established that clomiphene was superior to metformin alone for live birth, while combination therapy did not clearly outperform clomiphene enough to justify metformin as a primary fertility drug [17]. A Cochrane review similarly concluded that metformin has a limited role as a stand-alone strategy for improving live birth in anovulatory PCOS infertility [18]. Gonadotropins and assisted reproductive technologies are appropriate for resistant cases but require specialist oversight because of multiple-gestation and ovarian-hyperstimulation risks.

**Table 2. Goal-directed management of PCOS using evidence available by June 2021.**

| Clinical goal | Management emphasis | Key sources |
|---|---|---|

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| Clinical goal | Management emphasis | Key sources |
|---|---|---|
| Cycle irregularity / endometrial protection | Combined hormonal contraception or periodic progestin, individualized to risk and goals | [2,3] |
| Hirsutism / acne | Hormonal therapy plus cosmetic measures; consider anti-androgen therapy with effective contraception | [2,3,20] |
| Metabolic risk / dysglycemia | Lifestyle intervention; metformin for appropriate metabolic indications; monitor BP, glucose and lipids | [2,3,12,15] |
| Anovulatory infertility | Letrozole preferred first-line pharmacologic ovulation induction where appropriate | [3,16] |
| Pregnancy | Early assessment of gestational diabetes and hypertensive risk; standard obstetric surveillance tailored to comorbidity | [19] |

## 7. PCOS and Pregnancy

Pregnancy does not eliminate the systemic implications of PCOS. Reviews and meta-analyses have consistently found higher rates of gestational diabetes, pregnancy-induced hypertension or pre-eclampsia, preterm birth, and other obstetric complications among women with PCOS compared with controls [19]. Some of the excess risk is mediated by obesity, infertility treatment, and metabolic dysfunction, but PCOS itself appears to identify a higher-risk obstetric population.

Preconception care should therefore address weight and metabolic health, optimize chronic disease, review medications for pregnancy safety, and encourage early antenatal care. During pregnancy, clinicians should maintain a low threshold for appropriate glucose and blood-pressure surveillance. Routine continuation of metformin throughout pregnancy solely to prevent PCOS-associated complications was not supported by sufficiently consistent evidence to be considered universal practice by mid-2021.

## 8. Discussion

By 2021, the evidence base had moved PCOS care away from a fertility-only model toward lifelong reproductive, metabolic, and psychological management. The syndrome should not be treated as a single disease with one medication. Instead, phenotype, age, pregnancy intention, cardiometabolic risk, symptom burden, and patient priorities should guide treatment.

Several evidence-practice gaps remained. Diagnostic criteria were still debated, especially in adolescents. Long-term randomized data for prevention of diabetes and cardiovascular events were sparse. Many treatment trials were short and focused on surrogate outcomes rather than live birth, quality of life, or hard metabolic endpoints. Access to multidisciplinary care was also uneven, despite the need for coordination among gynecology, endocrinology, primary care, fertility services, nutrition, and mental-health care.

A practical approach is to confirm the diagnosis carefully, screen for metabolic and psychological comorbidity, protect the endometrium when cycles are infrequent, use evidence-based ovulation induction when fertility is desired, and revisit goals over time as reproductive plans and metabolic risk change.

## 9. Conclusion

PCOS is a heterogeneous, lifelong endocrine-reproductive condition with consequences that extend well beyond menstrual irregularity. Evidence available through June 2021 supports careful Rotterdam-based diagnosis with exclusion of mimicking disorders, lifestyle intervention as a foundation of care, combined hormonal contraception for many non-fertility presentations, targeted use of metformin for metabolic indications, and letrozole as the preferred first-line pharmacologic treatment for anovulatory infertility where appropriate. Regular assessment of glycemic, cardiovascular, psychological, and pregnancy-related risks is essential to comprehensive care.

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## Declarations

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## References

1. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertil Steril. 2004;81(1):19-25. doi:10.1016/j.fertnstert.2003.10.004.
2. Legro RS, Arslanian SA, Ehrmann DA, et al.; Endocrine Society. Diagnosis and treatment of polycystic ovary syndrome: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2013;98(12):4565-4592. doi:10.1210/jc.2013-2350.
3. Teede HJ, Misso ML, Costello MF, et al.; International PCOS Network. Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. Fertil Steril. 2018;110(3):364-379. doi:10.1016/j.fertnstert.2018.05.004.
4. Azziz R, Carmina E, Chen Z, et al. Polycystic ovary syndrome. Nat Rev Dis Primers. 2016;2:16057. doi:10.1038/nrdp.2016.57.
5. Escobar-Morreale HF. Polycystic ovary syndrome: definition, aetiology, diagnosis and treatment. Nat Rev Endocrinol. 2018;14(5):270-284. doi:10.1038/nrendo.2018.24.
6. Norman RJ, Dewailly D, Legro RS, Hickey TE. Polycystic ovary syndrome. Lancet. 2007;370(9588):685-697. doi:10.1016/S0140-6736(07)61345-2.
7. March WA, Moore VM, Willson KJ, Phillips DIW, Norman RJ, Davies MJ. The prevalence of polycystic ovary syndrome in a community sample assessed under contrasting diagnostic criteria. Hum Reprod. 2010;25(2):544-551. doi:10.1093/humrep/dep399.
8. Ding T, Hardiman PJ, Petersen I, Wang FF, Qu F, Baio G. The prevalence of polycystic ovary syndrome in reproductive-aged women of different ethnicity: a systematic review and meta-analysis. Oncotarget. 2017;8(56):96351-96358. doi:10.18632/oncotarget.19180.
9. Azziz R, Woods KS, Reyna R, Key TJ, Knochenhauer ES, Yildiz BO. The prevalence and features of the polycystic ovary syndrome in an unselected population. J Clin Endocrinol Metab. 2004;89(6):2745-2749. doi:10.1210/jc.2003-032046.
10. Dunaif A. Insulin resistance and the polycystic ovary syndrome: mechanism and implications for pathogenesis. Endocr Rev. 1997;18(6):774-800. doi:10.1210/edrv.18.6.0318.
11. Lim SS, Davies MJ, Norman RJ, Moran LJ. Overweight, obesity and central obesity in women with polycystic ovary syndrome: a systematic review and meta-analysis. Hum Reprod Update. 2012;18(6):618-637. doi:10.1093/humupd/dms030.
12. Wekker V, van Dammen L, Koning A, et al. Long-term cardiometabolic disease risk in women with PCOS: a systematic review and meta-analysis. Hum Reprod Update. 2020;26(6):942-960. doi:10.1093/humupd/dmaa029.
13. Barnard L, Ferriday D, Guenther N, Strauss B, Balen AH, Dye L. Quality of life and psychological well being in polycystic ovary syndrome. Hum Reprod. 2007;22(8):2279-2286. doi:10.1093/humrep/dem108.
14. Cooney LG, Lee I, Sammel MD, Dokras A. High prevalence of moderate and severe depressive and anxiety symptoms in polycystic ovary syndrome: a systematic review and meta-analysis. Hum Reprod. 2017;32(5):1075-1091. doi:10.1093/humrep/dex044.
15. Lim SS, Hutchison SK, Van Ryswyk E, Norman RJ, Teede HJ, Moran LJ. Lifestyle changes in women with polycystic ovary syndrome. Cochrane Database Syst Rev. 2019;3:CD007506. doi:10.1002/14651858.CD007506.pub4.
16. Legro RS, Brzyski RG, Diamond MP, et al.; NICHD Reproductive Medicine Network. Letrozole versus clomiphene for infertility in the polycystic ovary syndrome. N Engl J Med. 2014;371(2):119-129. doi:10.1056/NEJMoa1313517.
17. Legro RS, Barnhart HX, Schlaff WD, et al.; Cooperative Multicenter Reproductive Medicine Network. Clomiphene, metformin, or both for infertility in the polycystic ovary syndrome. N Engl J Med. 2007;356(6):551-566. doi:10.1056/NEJMoa063971.
18. Tang T, Lord JM, Norman RJ, Yasmin E, Balen AH. Insulin-sensitising drugs (metformin, rosiglitazone, pioglitazone, D-chiro-inositol) for women with polycystic ovary syndrome, oligo amenorrhoea and subfertility. Cochrane Database Syst Rev. 2012;(5):CD003053. doi:10.1002/14651858.CD003053.pub5.
19. Palomba S, de Wilde MA, Falbo A, Koster MPH, La Sala GB, Fauser BCJM. Pregnancy complications in women with polycystic ovary syndrome. Hum Reprod Update. 2015;21(5):575-592. doi:10.1093/humupd/dmv029.
20. Conway G, Dewailly D, Diamanti-Kandarakis E, et al.; ESE PCOS Special Interest Group. The polycystic ovary syndrome: a position statement from the European Society of Endocrinology. Eur J Endocrinol. 2014;171(4):P1-P29. doi:10.1530/EJE-14-0253.