



Review Article

Anti-Mullerian Hormone as a Surrogate Diagnostic Marker for Polycystic Ovary Syndrome

Nishtha Jaiswal¹, Manju Puri²

¹Department of Obstetrics and Gynaecology, Lady Hardinge Medical College and Smt Sucheta Kriplani Hospital, New Delhi, ²Department of Obstetrics and Gynaecology, Shree Guru Gobind Singh Tricentenary Medical College, Gurugram, India.



***Corresponding author:**

Nishtha Jaiswal,
Department of Obstetrics and
Gynaecology, Lady Hardinge
Medical College and Smt
Sucheta Kriplani Hospital,
New Delhi, India.

nishtha.amu@gmail.com

Received: 11 April 2025

Accepted: 08 June 2025

Published: 19 July 2025

DOI
10.25259/FSR_24_2025

Quick Response Code:



ABSTRACT

Worldwide, polycystic ovary syndrome (PCOS) has emerged as one of the commonest endocrinological disorders amongst women in the reproductive age group. The ovarian follicle number, mostly the preantral and small antral follicles in the ovaries, increases in PCOS along with raised serum Anti-Mullerian Hormone (AMH) levels. As per recent ESHRE guidelines on PCOS, AMH is suggested as an alternative marker of polycystic ovarian morphology in the diagnosis of PCOS. AMH promotes androgen excess and ovulatory dysfunction in females with PCOS, and its increased levels suggest poor response to treatment for infertility. However, due to heterogeneity in the existing literature and varying thresholds of AMH values in different phenotypes of PCOS, it's challenging to identify a standard threshold of AMH for diagnosing PCOS.

Keywords: AMH, Diagnostic threshold, PCOM, PCOS, Surrogate marker

INTRODUCTION

Polycystic ovary syndrome (PCOS) is the commonest gynae-endocrine disorder affecting approximately 6%–13% of women in the reproductive age group globally.^[1] Ganie MA, *et al.*^[2] did a study amongst women in India to observe the prevalence and comorbidities of PCOS. They found the PCOS prevalence as 7.2% (95% CI, 4.8%–10.8%) according to NIH 1990 criteria, 19.6% (95% CI, 12.7%–29.2%) as per Rotterdam 2003 criteria, and 13.6% (95% CI, 8.4%–21.6%) by Androgen Excess and PCOS Society (AE-PCOS) criteria.^[2]

PCOS is a heterogeneous disorder comprising anovulation, androgen excess and ultrasound findings suggestive of polycystic ovaries. It is a common cause of normogonadotropic anovulation. It is associated with menstrual irregularities, infertility, acne, hirsutism and obesity, which can impact women's physical as well as emotional health. It is associated with long-term complications like metabolic syndrome, cancer of the uterus and coronary artery disease. As many as 70% of women with PCOS remain undiagnosed.^[1] The diagnosis of PCOS has been evolving over the years, and various criteria have emerged. The Rotterdam's criteria have been modified to an evidence-based criterion, including the original clinical criteria but a more defined and specific ultrasound criterion for polycystic ovarian morphology (PCOM). In PCOS, there is increased ovarian follicle count, mainly the preantral and small antral follicles in the ovaries, as

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, transform, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

©2025 Published by Scientific Scholar on behalf of Fertility Science and Research

well as raised serum Anti-Mullerian Hormone (AMH) levels. There exists a positive correlation between serum AMH levels and antral follicle count seen on ultrasound; hence, AMH may be considered as an alternative marker for PCOM in diagnosing PCOS.

DIAGNOSTIC CRITERIA FOR PCOS

Various criteria for diagnosing PCOS have evolved over the years [Table 1]. The first classification emerged from a conference held in April 1990, at a National Institute of Child Health and Human Development of the US,^[3] where hyperandrogenism (HA), either clinical or biochemical, and chronic oligo-anovulation (OA) were described as prime criteria for diagnosing PCOS after excluding other related hyperandrogenic disorders. The next definition of PCOS was formulated after the consensus opinion of experts for PCOS, held in May 2003 at Rotterdam. As per the Rotterdam European society of human reproduction and embryology (ESHRE), American society of reproductive medicine (ASRM) 2003 criteria, the diagnosis of PCOS requires the presence of two of the following three findings to be present as follows: signs of clinical or biochemical HA, chronic ovulatory dysfunction (OD) and PCOM, after ruling out other secondary causes.^[4]

Later in 2006, the AE-PCOS conducted a systematic review to study different phenotypes of PCOS. They concluded that HA is the main underlying disorder in PCOS, and this syndrome should be diagnosed based upon the presence of clinical or biochemical HA along with ovarian dysfunction (i.e., OD or PCOM), but only after ruling out other causes of androgen excess.^[5,6]

NIH conducted an Evidence-Based PCOS Workshop in the year 2012, which focused on the pros and cons of existing diagnostic criteria. They suggested the use of the initial ESHRE/ASRM 2003 criteria, but incorporated these PCOS sub-phenotypes classified as follows^[7]:

Phenotype A: HA (clinical or biochemical) + OD + PCOM

Phenotype B: HA + OD

Phenotype C: HA + PCOM; and

Phenotype D: OD + PCOM.

Current ESHRE 2023 Guidelines Summary: Diagnosis of PCOS should be done as per the revised Rotterdam criteria, which have now been modified to an evidence-based criterion. For diagnosing PCOS in adult women, any two of the following characteristics must be included: (i) clinical/biochemical features of androgen excess, (ii) OD and (iii) presence of polycystic ovaries on ultrasound or raised serum AMH levels, after excluding other important causes of HA. In those women where menstrual cycle irregularities and HA co-exist, characteristic ultrasound features of the ovaries

Table 1: Varying diagnostic criteria for PCOS.

Clinical features	NIH consensus, 1990	Rotterdam consensus, 2003 ESHRE/ASRM 2023	AE-PCOS definition, 2006
Clinical/biochemical HA	+	+/-	+
Oligo/amenorrhea, anovulation	+	+/-	+/-
Polycystic ovaries on USG	+	+/-	+/-
	All required	2 out of 3 required	Androgen excess + one other criterion

NIH: National institute of health; AE-PCOS: Androgen excess and PCOS society; ESHRE: European society of human reproduction and embryology; ASRM: American society of reproductive medicine; HA: Hyperandrogenism; USG: Ultrasonography.
+ stands for: present; - stands for: absent.

or doing a serum test for AMH levels are not necessary for further diagnosis. In adolescents, both HA and OD must be present for the diagnosis of PCOS. However, features of PCOM on ultrasound or serum AMH levels are not recommended in adolescents due to their poor specificity.^[8]

As per the original Rotterdam consensus criteria of 2003, the definition of polycystic ovaries included ≥ 12 follicles in ovaries with a size of 2–9 mm and/or an ovarian volume (OV) > 10 cc in at least one ovary. This ultrasound criterion to diagnose PCOM in adults has been revised in the ESHRE guideline 2023 and includes the following: the follicle number per ovary (FNPO), the follicle number per cross-section (FNPS), and OV. According to ESHRE guideline 2023, the most reliable ultrasound marker for identifying PCOM in adults is FNPO. A threshold of FNPO ≥ 20 in at least one ovary is now recognised for diagnosing PCOM in adults.^[8] Wherever feasible, the transvaginal approach (with 8 MHz probe frequency) is most accurate for making a diagnosis of PCOM. If older imaging technology is utilised or if the image quality does not allow for precise evaluation of follicular counts, a volume of ovary more than or equal to 10 ml or FNPS ≥ 10 in at least one ovary can still be utilised to define PCOM. Transabdominal ultrasonography (USG) should also report OV or FNPS.

They have also recommended that raised serum AMH levels can be used to define PCOM in reproductive-age women. Serum AMH can be used in patients having either irregular menstrual cycles or HA for diagnosing PCOS. But the use of serum AMH as the only diagnostic test for PCOS cannot be recommended.

AMH AND ITS ROLE IN DIAGNOSING PCOS

AMH is a dimeric glycoprotein and is a part of the transforming growth factor beta family of growth and differentiation factors.^[9] AMH is produced by granulosa cells of the ovary, located in preantral to small antral follicles ($\leq 4-6$ mm), and this synthesis is critical for follicle-stimulating hormone (FSH)-dependent folliculogenesis. The primordial follicles, dominant follicles, and atretic follicles show reduced expression of AMH. In females, AMH levels are not detectable at birth; they increase gradually until puberty, after which they remain almost static during the early reproductive years. AMH levels start declining after the age of 30 years and become very low just before menopause.^[10,11]

AMH serves to inhibit the recruitment and development of follicles, thereby resulting in the arrest of follicular growth. Through its paracrine effect, it inhibits the selection of the dominant follicle from a group of small antral follicles during the course of the gonadotropin-stimulated cycle.^[10,12]

The aromatase enzyme, essential for the production of oestrogens from androgens within granulosa cells, is downregulated by AMH until follicular selection. Expression of AMH remains elevated until a follicle becomes approximately 8 mm in size. As the size of the antral follicle increases, AMH concentration within the antral follicle progressively decreases, followed by a sharp decline once the follicle size exceeds 8 mm.^[11]

This sharp reduction in AMH coincides with the selection of the dominant follicle. Once the dominant follicle is selected, due to a decrease in AMH activity, there is increased expression of the aromatase enzyme in granulosa cells, resulting in higher oestrogen production. Thus, AMH functions as a controller of follicular selection and oestrogen production.

The serum AMH concentration can be regarded as an effective biochemical indicator of the antral follicle pool during the early follicular phase of the menstrual cycle.^[13-15] Consequently, a low count of antral follicles may lead to reduced serum AMH levels.

Proposed Pathophysiology in PCOS

FSH has a prime role in the development of follicles. The typical HPO axis becomes disrupted in women with PCOS, which leads to increased luteinising hormone (LH) levels and decreased levels of FSH, resulting in the reversal of the LH/FSH ratio.^[16] Since FSH is vital for the development of a follicle, which in itself is required for ovulation, the OA seen in PCOS may arise from either a quantitative or qualitative dysfunction of FSH or possibly both. As compared to a normal ovary, the polycystic ovaries have been found to have approximately six times

more pre-antral and small antral follicular count^[17] and therefore result in higher serum AMH levels in those with PCOS. For women with PCOM as observed on ultrasound, significantly elevated serum AMH levels are seen in comparison to women with normal ovaries, but their levels are still notably lower than those found in women with PCOS. So, as per AMH serum concentrations, the category of women with only PCOM lies somewhat in between those with normal ovaries and those diagnosed with PCOS.^[18]

In research conducted by Bhide P *et al.*,^[19] the ratio of serum AMH level to antral follicle count (AFC) (which serves as an indicator of AMH production per antral follicle) was compared amongst women diagnosed with PCOS, PCOM and those with normal-looking ovaries. There was a significantly higher AMH/AFC ratio in women with PCOS than in those without PCOS, thereby suggesting increased AMH production per follicle in women with PCOS, besides a greater number of antral follicle counts per se. On the contrary, women with only PCOM and no OD were found to have a ratio of AMH/AFC comparable to those of women having normal-looking ovaries on ultrasound.^[19]

The production of AMH per follicle has also been assessed among different phenotypes of PCOS. In a study by Alebic MS *et al.*, the AMH/AFC ratio was notably raised in women with anovulatory PCOS compared to those with ovulatory PCOS or PCOM ($p < 0.001$), irrespective of their androgen status.^[20]

Threshold of AMH Level: Is There Any Cut-Off?

Dewailly *et al.* (2011) did a cross-sectional study and suggested that serum AMH > 4.9 ng/ml (or > 35 pmol/l) is found to be more sensitive and specific than an AFC > 19 and should thus be part of one of the criteria in diagnosing PCOS.^[21]

An Indian study done by Vijayan A *et al.* in 2022 suggested that serum AMH concentration > 3.52 ng/ml (25.1 pmol/l) may be considered as a cutoff value in evaluating its potential role as a diagnostic marker for PCOS across all age groups.^[22]

Butt MS *et al.*^[23] did a cross-sectional study to compare normal and PCOS women and found that PCOS women with elevated AMH levels (≥ 3.9 ng/ml) revealed a significant variation in ovarian morphology ($p < 0.05$) in contrast to the normal AMH group. They also observed a significant mean difference in AMH levels ($p = 0.03$) in women with oligomenorrhea or amenorrhoea in comparison to women with regular menses. They concluded that serum AMH level could serve as a predictive tool for diagnosing PCOS, especially in women fulfilling other features of OD.^[23]

The research conducted by Malhotra N *et al.*^[24] analysed serum AMH levels among various phenotypes of PCOS and related their AMH levels to clinical, hormonal, and metabolic

parameters in women diagnosed with PCOS in India. In the PCOS group, the mean serum AMH was recorded to be 12.39 ± 5.3 ng/ml, and it was 3.83 ± 1.5 ng/ml in the non-PCOS group ($p < 0.01$). Among 608 PCOS women, phenotype A was found in 273 (44.9%) women and phenotype D was seen in 230 (37.8%) women. Phenotypes C and B were observed in 12.17% and 5.10% of women, respectively. The majority of women exhibiting a high AMH value (AMH > 20 ng/ml; 8.05%) were of phenotype A. A positive correlation was noted ($p < 0.05$) between serum AMH levels and length of menstrual cycle, serum testosterone, fasting total cholesterol levels, and number of follicles per ovary. The ROC analysis determined that the cut-off value of AMH for diagnosing PCOS was identified to be ≥ 6.06 ng/ml with 91.45% sensitivity and 90.71% specificity. This study also showed that elevated levels of serum AMH in women with PCOS are linked with poorer clinical, endocrinological, and metabolic parameters.^[24]

In 2024, Noguchi H *et al.* did a study in the Japanese population and stated that the serum AMH level serves as a reliable biochemical marker of ovarian features in PCOS.^[25] Therefore, it may function as a substitute for AFC as an indicator of PCOM in the criteria used for diagnosing PCOS.^[25]

A systematic review and meta-analysis by Van der Ham K *et al.* was published in October 2024 to study the role of AMH levels for diagnosing PCOS.^[26] They investigated significant changes in 2023 international evidence-based guidelines for PCOS, which support the use of AMH levels for defining PCOM in adults in concordance with other diagnostic features. Whereas in adolescents, it's a non-specific marker, and isolated raised AMH levels are not sufficient in diagnosing PCOS in them. Numerous factors affect serum AMH levels, therefore making it impossible to propose a universal cut-off value.^[26]

It is evident from the literature cited above that elevated AMH levels in women with PCOS play a pivotal role in the pathogenesis of this syndrome. The increased intrafollicular concentration of AMH in women with PCOS is postulated to increase its inhibitory action on follicular selection and growth. Though AMH indicates the ovarian reserve, no standard cut-off value has been identified for the diagnosis of PCOS.

CONCLUSION

Serum AMH level is notably raised in women with PCOS as compared to healthy subjects and is no doubt a valuable diagnostic indicator for PCOS and correlates well with the diagnosis of PCOM on ultrasound. AMH level can help diagnose PCOS, especially if transvaginal ultrasound is not feasible and there is difficulty in assessing the ovaries during transabdominal scans. The establishment of a specific cut-off for serum AMH levels is challenging, as it is multifactorial, and, as per current evidence, the serum AMH levels cannot

be relied upon as the only diagnostic criterion for PCOS. Instead, it can be used as an alternative marker of PCOM along with other Rotterdam criteria in diagnosing PCOS. In the future, with the improvement of standards and betterment of assays, the role of AMH as a surrogate marker for diagnosing PCOS will become more evident.

Author contributions

NJ, MP: Acquisition of clinical data, preparation of the manuscript and critical review of the manuscript. All authors approve the final version of the manuscript.

Ethical approval: Institutional Review Board approval is not required.

Declaration of patients consent: Patient's consent is not required as there are no patients in this study.

Financial support and sponsorship: Nil.

Conflicts of interest: There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation: The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

REFERENCES

1. World Health Organization. Factsheet: Polycystic Ovary Syndrome. Geneva: World Health Organization; 2025. Available from: <https://www.who.int/news-room/fact-sheets/detail/polycystic-ovary-syndrome> [Last accessed 05 April 2025].
2. Ganje MA, Chowdhury S, Malhotra N, Sahay R, Bhattacharya PK, Agrawal S, *et al.* Prevalence, Phenotypes, and Comorbidities of Polycystic Ovary Syndrome Among Indian Women. *JAMA Netw Open* 2024;7:e2440583.
3. Lujan ME, Chizen DR, Pierson RA. Diagnostic Criteria for Polycystic Ovary Syndrome: Pitfalls and Controversies. *J Obstet Gynaecol Can* 2008;30:671–9.
4. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 Consensus on Diagnostic Criteria and Long-Term Health Risks Related to Polycystic Ovary Syndrome (PCOS). *Hum Reprod Oxf Engl* 2004;19:41–7.
5. Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, *et al.* Positions Statement: Criteria for Defining Polycystic Ovary Syndrome as a Predominantly Hyperandrogenic Syndrome: An Androgen Excess Society Guideline. *J Clin Endocrinol Metab* 2006;91:4237–45.
6. Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, *et al.* The Androgen Excess and PCOS Society Criteria for the Polycystic Ovary Syndrome: The Complete Task Force Report. *Fertil Steril* 2009;91:456–88.
7. Johnson T, Kaplan L, Ouyang P, Rizza P. National Institutes of Health Evidence-Based Methodology Workshop on Polycystic Ovary Syndrome. NIH EbMW Reports. Vol. 1. Bethesda, MD: National Institutes of Health; 2012. p. 1–14.
8. Teede HJ, Tay CT, Laven JJE, 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;108:2447–69.
9. Pepinsky RB, Sinclair LK, Chow EP, Mattaliano RJ, Manganaro TF, Donahoe PK, *et al.* Proteolytic Processing of Mullerian Inhibiting Substance Produces a Transforming Growth Factor-Beta-Like Fragment. *J Biol Chem* 1988;263:18961–64.
 10. Lv PP, Jin M, Rao JP, Chen J, Wang LQ, Huang CC. Role of Anti-Mullerian Hormone and Testosterone in Follicular Growth: A Cross-Sectional Study. *BMC Endocr Disord* 2020;20:101.
 11. Andersen CY, Schmidt KT, Kristensen SG, Rosendahl M, Byskov AG, Ernst E. Concentrations of AMH and Inhibin-B in Relation to Follicular Diameter in Normal Human Small Antral Follicles. *Hum Reprod* 2010;25:1282–7.
 12. Silva MSB, Giacobini P. New Insights into Anti-Mullerian Hormone Role in the Hypothalamic-Pituitary-Gonadal Axis and Neuroendocrine Development. *Cell Mol Life Sci* 2021;78:1–16.
 13. Moolhuijsen LME, Visser JA. AMH in PCOS: Controlling the Ovary, Placenta, or Brain? *Curr Opin Endocr Metab Res* 2020;12:91–7.
 14. Kostrzewa M, Głowacka E, Stetkiewicz T, Grzesiak M, Szytło K, Stachowiak G, *et al.* Is Serum Anti-Mullerian Hormone (AMH) Assay a Satisfactory Measure for Ovarian Reserve Estimation? A Comparison of Serum and Peritoneal Fluid AMH Levels. *Adv. Clin Exp Med Wroc Med Univ* 2020;29:853–6.
 15. Dumont A, Robin G, Dewailly D. Anti-Mullerian Hormone in the Pathophysiology and Diagnosis of Polycystic Ovarian Syndrome. *Curr Opin Endocrinol Diabetes Obes* 2018;25:377–84.
 16. Balen AH, Laven JSE, Tan S-L, Dewailly D. Ultrasound Assessment of the Polycystic Ovary: International Consensus Definitions. *Hum Reprod Update* 2003;9:505–14.
 17. Webber L, Stubbs S, Stark J, Trew G, Margara R, Hardy K, *et al.* Formation and Early Development of Follicles in the Polycystic Ovary. *Lancet* 2003;362(9389):1017–21.
 18. Homburg R, Ray A, Bhide P, Gudi A, Shah A, Timms P, *et al.* The Relationship of Serum Anti-Mullerian Hormone with Polycystic Ovarian Morphology and Polycystic Ovary Syndrome: A Prospective Cohort Study. *Hum Reprod* 2013;28:1077–83.
 19. Bhide P, Dilgil M, Gudi A, Shah A, Akwaa C, Homburg R. Each Small Antral Follicle in Ovaries of Women with Polycystic Ovary Syndrome Produces More Antimullerian Hormone than Its Counterpart in a Normal Ovary: An Observational Cross-Sectional Study. *Fertil Steril* 2015;103:537–41.
 20. Alebic MS, Stojanovic A, Duhamel A, Dewailly D. The Phenotypic Diversity in Per-Follicle Anti-Müllerian Hormone Production in Polycystic Ovary Syndrome. *Hum Reprod* 2015;30:1927–33.
 21. Dewailly D, Gronier H, Poncelet E, Robin G, Leroy M, Pigny P, *et al.* Diagnosis of Polycystic Ovary Syndrome (PCOS): Revisiting the Threshold Values of Follicle Count on Ultrasound and of the Serum AMH Level for the Definition of Polycystic Ovaries. *Hum Reprod Oxf Engl* 2011;26:3123–9.
 22. Vijayan A, Shankar KMK, Geetha. Age Specific References for Anti-Mullerian Hormone and Use as a Potential Diagnostic Marker of PCOS in an Indian Population. *Indian J Obstet Gynecol Res* 2022;9:176–80.
 23. Butt MS, Saleem J, Aiman S, Zakar R, Sadique I, Fischer F. Serum Anti-Müllerian Hormone as a Predictor of Polycystic Ovarian Syndrome Among Women of Reproductive Age. *BMC Womens Health* 2022;22:199.
 24. Malhotra N, Mahey R, Cheluvvaraju R, Rajasekaran K, Patkar D, Prabhakar P, *et al.* Serum Anti-Mullerian Hormone (AMH) Levels Among Different PCOS Phenotypes and Its Correlation with Clinical, Endocrine, and Metabolic Markers of PCOS. *Reprod Sci* 2023;30:2554–62.
 25. Noguchi H, Iwasa T, Iwase A, Kanasaki H, Kimura F, Kugu K, *et al.* Cut-Off Value for Anti-Müllerian Hormone in the Diagnostic Criteria for Polycystic Ovary Syndrome in the Japanese Population. *J Obstet Gynaecol Res* 2024;50:1368–82.
 26. Van der Ham K, Laven JSE, Tay CT, Mousa A, Teede H, Louwers YV. Anti-Müllerian Hormone as a Diagnostic Biomarker for Polycystic Ovary Syndrome and Polycystic Ovarian Morphology: A Systematic Review and Meta-Analysis. *Fertil Steril* 2024;122:727–39.

How to cite this article: Jaiswal N, Puri M. Anti-Mullerian Hormone as a Surrogate Diagnostic Marker for Polycystic Ovary Syndrome. *Fertil Sci Res.* 2025;12:21. doi: 10.25259/FSR_24_2025