Endocrinology Committee of FOGSI

PCOS ASSESSMENT- Do we have the Consensus?

Dr Rakhi Singh
Chairperson Endocrinology Committee FOGSI

Dr Alpesh Gandhi
President FOGSI

DR Anita Singh
Vice President FOGSI

Editor :Dr Meenu Handa

Senior IVF specialist , Fortis Bloom IVF center Gurugram.

Author: Dr Shehla Jamal

Associate Professor RMRI, Barreily

Polycystic ovary syndrome (PCOS) is a public health issue with paramount reproductive, metabolic and psychological impacts. PCOS is one of the most common presentations in reproductive aged women and affects 8-13% of reproductive-aged women. The pertinent issue is that up to 70% of affected women remain ***undiagnosed*** [1]and 45% of the females taking treatment for PCOS are actually ***not PCOS***! Diagnosis and treatment of PCOS remain controversial till date due to the challenges in defining individual components within the diagnostic criteria, significant clinical heterogeneity and thus, a range of phenotypes.1

There is a great diversity in the clinical presentation of PCOS ranging from psychological features (anxiety, depression, body image) [2], reproductive (irregular menstrual cycles, hirsutism, infertility and pregnancy complications [3] and metabolic features (insulin resistance (IR), metabolic syndrome, prediabetes, type 2 diabetes (DM2) and cardiovascular risk factors). The difficulty in treatment of PCOS is faced due to the challenges in defining individual components within the diagnostic criteria, significant clinical heterogeneity generating a range of phenotypes with significant variation in clinical features across the life course. [4] These factors contribute to variation in diagnosis and care across geographical regions and health professional groups. This culminates in delayed diagnosis, poor diagnosis experience and dissatisfaction with care reported by women internationally.[5]

This governance included an international advisory board from six continents, a project board, five guideline development groups with 63 members, consumer and translation committees. The Australian Centre for Research Excellence in PCOS, funded by the National Health and Medical Research Council (NHMRC), partnered with European Society of Human Reproduction and Embryology (ESHRE) and the American Society for Reproductive Medicine (ASRM). Thirty seven organizations across 71 countries including India's FOGSI collaborated with 23 face to face international meetings over 15 months.

The International consensus for diagnosing PCOS still remains the Rotterdam's criteria. The different phenotypes of PCOS and the different components of the Rotterdam criteria can help to predict the reproductive outcomes to some extent, so it is necessary to understand those criteria.

Rotterdam's- two out of the three of

1. Oligo/ anovulation
2. Hyperandrogenism/hyperandrogenemia
3. PCO morphology on ultrasound

➢ *Rule out other etiologies like- thyroid disorders, hyperprolactinemia and adult onset CAH.*

1. Oligo/anovulation

- Cycle disturbance is the commonest complaint by gynecology endocrinology visitors.
- It can be primarily evaluated by meticulous history taking.
- According to ESHRE guidelines (2018), irregular cycles should be defined as-
  - > *1 to* < *3 years post menarche*: < 21 or > 45 days
  - > *3 years post menarche to perimenopause:* < 21 or > 35 days or < 8 cycles per year
  - > *1 year post menarche* > 90 days for any one cycle
- First 12 months from menarche should be disregarded from evaluation point of view.
- Always rule out drug history, contraception usage, especially DMPA in such presenters.
- Encourage menstrual calendar marking for better evaluation.

Ovulatory dysfunction can still occur with regular cycles and if anovulation needs to be confirmed serum progesterone levels can be measured.

Hyperandrogenism/hyperandrogenemia:

- History and physical examination should be elicited for symptoms and signs of clinical hyperandrogenism- acne, alopecia and hirsutism and, in adolescents, severe acne and hirsutism.
- Clinical tools like modified Ferriman Gallwey score should be used for assessing severity of hirsutism, (mFG) with a level ≥ 4 - 6 indicating hirsutism.
- The Ludwig visual score is preferred for assessing the degree and distribution of alopecia.
- Calculated free testosterone, free androgen index (FAI) or calculated bio-available testosterone should be used to assess biochemical evidence of hyperandrogenism in the diagnosis of PCOS.
- Liquid chromatography–mass spectrometry (LCMS)/mass spectrometry and extraction/chromatography immunoassays should preferably be used in assessing free testosterone or FAI.
- Androstenedione and dehydroepiandrosterone sulfate (DHEAS) could be considered if total or free testosterone are not elevated; *however, these provide limited additional information in the diagnosis of PCOS.*
- Rapid and severe progression of hirsutism should prompt to look out for androgen secreting tumor (ovarian or adrenal origin).

Ultrasound and polycystic ovarian morphology (PCOM)

- Age-specific cut off values for PCOM should be defined for every population.
- Transvaginal ultrasound approach is preferred

With transducer probe of 8 mHz/ TVS:

The threshold for PCOM should be on either ovary, a follicle number per ovary of > 20 and/ or an ovarian volume ≥ 10ml, and rule out corpus Luteum, cysts of other origins, or dominant follicles.

- In *transabdominal ultrasound* reporting is best focused on ovarian volume with a threshold of ≥ 10ml, and generally follicle count is suboptimal.
- In patients with irregular menstrual cycles and hyperandrogenism, an ovarian ultrasound is *not necessary* for PCOS *diagnosis*; however, ultrasound will determine the complete PCOS phenotype.

Recommended guidelines for PCO morphology diagnosis are:

- Last menstrual period
- Transducer bandwidth frequency
- Route of USG
- Total follicle number per ovary measuring 2-9mm
- Three dimensions and volume of each ovary
- Reporting of endometrial thickness and appearance is preferred – triple layer endometrial assessment may be useful to screen for endometrial pathology
- Other ovarian and uterine pathology, as well as ovarian cysts, corpus luteum, dominant follicles ≥ equal 10mm.
    - Remember, PCOM is a normal finding in adolescents, perimenopausal females, thyroid disorders and on COCs.

Other important points to keep in point while assessing for PCOS :

- Serum AMH levels should not yet be used as an alternative for the detection of PCOM or as a single test for the diagnosis of PCOS.
- 17- OHP to rule out CAH
- Thyroid dysfunction and prolactin levels to be estimated before making a diagnosis of PCOS
- OGTT with 75 gram glucose(specially in periconceptional period) and otherwise Fasting blood glucose and HbA1c, for insulin resistance.
- Lipid profile to calculate risk of CVD.

As far as serum AMH is concerned, it is not yet considered as an alternative for the detection of PCOM or as a single test for the diagnosis of PCOS. Once there is improved standardization of assays and established cut off levels or thresholds based on large scale validation in populations of different ages and ethnicities, AMH assays will be more accurate in the detection of PCOM.

Ethnic variation in the presentation and manifestations of PCOS should always be kept in mind by healthcare professionals while making a diagnosis for PCOS:

- A relatively mild phenotype in Caucasians
- Higher body mass index (BMI) in Caucasian women, especially in North America and Australia
- More severe hirsutism in Middle Eastern, Hispanic and Mediterranean women
- Increased central adiposity, insulin resistance, diabetes, metabolic risks and acanthosis nigricans in South East Asians and Indigenous Australians
- Lower BMI and milder hirsutism in East Asians
- Higher BMI and metabolic features in Africans

Conclusion

Strict adherence to these diagnostic protocols will help in making and refuting a diagnosis of PCOS. It was important to have a comprehensive, international dissemination and implementation program in order to amplify the impact of the international guideline for the assessment and treatment of PCOS. This will enable the health professionals to deliver high-quality, evidence-based assessment and management of PCOS.

Reference links:

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3. Boomsma, C., et al., A meta-analysis of pregnancy outcomes in women with polycystic ovary syndrome. Human Reproduction Update, 2006. 12(6): p. 673-83.
4. International evidence-based guideline for the assessment and management of polycystic ovary syndrome 2018. https://www.monash.edu/data/assets/pdf_file/0004/1412644/PCOS_Evidence-Based-Guidelines_20181009.pdf
5. Gibson-Helm, M., et al., Delayed diagnosis and a lack of information associated with dissatisfaction in women with polycystic ovary syndrome. Journal of Clinical Endocrinology and Metabolism, 2017. 102(2): p. 604-612.