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Diagnosis and Management of Polycystic Ovarian Syndrome: Primary Care Perspective

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Abstract **Review Article**

Polycystic ovarian syndrome (PCOS) is a prevalent endocrine disorder in young women, marked by irregular periods, hyperandrogenism, insulin resistance, and risks like infertility, metabolic syndrome, and cardiovascular issues. This article outlines a streamlined physician approach to suspected cases, using Rotterdam criteria for diagnosis via symptoms, labs (e.g., testosterone, LH:FSH), and ultrasound while ruling out differentials like thyroid dysfunction or tumors. For a 20s patient with irregular menses and acne not seeking pregnancy, it recommends lifestyle changes, cyclical progesterone or low-androgen OCPs for cycles, anti-androgens for acne/hirsutism, and metformin for insulin sensitivity—tailored to priorities, with specialist referral and preconception counseling for future fertility.

Keywords: PCOS, infertility, androgen excess, acne, oligomenorrhea, menstrual irregularity.

INTRODUCTION

Polycystic ovarian syndrome [PCOS] is one of the most common endocrine disorders and frequently becomes manifest in young women of reproductive age. It is the most common cause of infertility in women [1]. It is estimated to affect 5–15% of women [2]; in fact, it may affect up to 20% of women if the 2003 Rotterdam criteria are used [3,4]. PCOS can present with a wide spectrum of symptoms and signs, including acne, hirsutism, obesity, menstrual irregularities, and infertility. These are primarily characterized by ovulatory dysfunction, hyperandrogenism, insulin resistance, and the ensuing metabolic syndrome. Women with PCOS are also more likely than other women of the same age to have cardiovascular risk factors, such as central body fat distribution, obesity, hypertension, hypertriglyceridemia, and reduced HDL-cholesterol concentrations [5].

Aim of study

This study aims to simplify a physician's approach to a suspected case of polycystic ovarian syndrome [PCOS]. It will help in evaluating the patient's presenting complaint across the spectrum of symptoms with which PCOS can present, requesting appropriate investigations, and interpreting the results to reach a diagnosis. In doing so, it encourages physicians to remain mindful of certain differential diagnoses that may be more serious and require earlier, more thorough evaluation. Treatment is then tailored, keeping the patient's priorities at the time of presentation at the forefront. This includes educating patients about diet and lifestyle, explaining their metabolic, cardiovascular, and reproductive risks, and offering medical management strategies. It also involves discussing the need for referral to a specialist while enabling full patient participation in the process.

A female patient in her early twenties presents with a history of irregular, infrequent periods and poor acne control. She is married and not keen to start a family soon; she would like to regularize her periods first. She asks whether there is anything she could do to help regulate her periods and maintain overall health, and she would like to know what steps she should take now and when she plans to have her first child. How would you approach this case?

Aetiology

The primary defect in polycystic ovarian syndrome is insulin resistance in adipose tissue and skeletal muscle and insulin sensitivity in the ovary. Hyperinsulinemia occurs as a compensatory mechanism, which in turn results in increased androgen secretion by the ovaries and inhibition of sex hormone–binding globulin production in the liver. These changes can lead

to increased serum concentrations of free [active] testosterone.

Among women with the syndrome, raised testosterone levels are found in approximately 30%, and raised luteinising hormone [LH] levels are found in about 40% [6]. Some women may be genetically predisposed to the development of the syndrome [7].

Definition

Polycystic ovarian syndrome [PCOS] is generally defined as the presence of polycystic ovaries together with one or more characteristic features, including hirsutism, acne, male-pattern baldness, amenorrhoea or oligomenorrhoea, or raised serum concentrations of testosterone and/or luteinising hormone [8].

Table 1

Rotterdam [2003] Diagnostic criteria for PCOS - two out of three of:
Clinical Hyperandrogenism [Ferriman-Gallwey Score >8] or Biochemical Hyperandrogenism [Elevated Total/Free Testosterone] **OR**
Oligomenorrhea [Less Than 6-9 Menses per Year] or Oligo-Ovulation **OR**
Polycystic Ovaries on Ultrasound [>= 12 Antral Follicles in One Ovary or Ovarian Volume >= 10 cm3]

Source Table 1: https://gpnotebook.com/pages/gynaecology/polycystic-ovary-syndrome [9]

Based on these criteria, a diagnosis of PCOS requires two out of three of the following: hyperandrogenism, menstrual irregularities, and polycystic ovaries on ultrasonography.
[The Ferriman–Gallwey score helps assess the degree of hirsutism on physical examination.]

The diagnosis of PCOS has lifelong implications, with an increased risk of metabolic syndrome, type 2 diabetes mellitus, obstructive sleep apnoea, endometrial hyperplasia, and possibly cardiovascular disease and endometrial carcinoma [10-13]. PCOS should be considered in any adolescent female presenting with hirsutism, treatment-resistant acne, menstrual irregularity, or obesity.

Applying diagnostic criteria for PCOS to mid- to late-pubertal girls has been challenging for multiple reasons. Anovulatory cycles and menstrual irregularity are common in normal adolescents. In addition, the common signs of hyperandrogenism are less reliable in adolescents because hirsutism and acne vulgaris are frequent during development, and measurement of testosterone concentrations is problematic, as levels rise during anovulatory cycles. International expert conferences, representing all relevant subspecialties, have published recommendations for the diagnosis of adolescent PCOS [14-16]. They agree that adolescents with evidence of PCOS within one to two years after menarche should be assigned a provisional diagnosis of "at risk for PCOS" and treated symptomatically.

Clinical manifestations:

The syndrome is characterized clinically by oligomenorrhoea and hyperandrogenism, as well as by the frequent presence of associated risk factors for cardiovascular disease, including obesity, glucose intolerance, dyslipidaemia, fatty liver disease, and obstructive sleep apnoea. The clinical features of polycystic ovarian syndrome include [8]:

- Menstrual disturbances such as oligomenorrhoea, amenorrhoea, or dysfunctional uterine bleeding.
- Hirsutism is defined as excess terminal [thick, pigmented] body hair in a male distribution, over the upper lip, chin, peri-areolar area, midsternum, and back.
- Acne
- Male-pattern hair loss
- Anovulatory infertility
- Acanthosis nigricans may occur as a cutaneous marker of hyperinsulinemia.
- Central obesity
- Psychological well-being, affected by PCOS-related physical changes [e.g., weight gain, acne, and hirsutism], is also an important consideration. Mental health assessment should be performed to screen for symptoms and signs of depression, anxiety, and self-harm. Validated screening tools, such as the Patient Health Questionnaire [PHQ-9] for depression and the Generalized Anxiety Disorder 7 [GAD-7] scale for anxiety disorders, should be used.

Investigations:

Elevated androgens result in the main clinical and endocrine abnormalities. The biochemical markers taken into consideration include:
[Blood should be taken during the first week after menstruation.]

- Increased total testosterone level
- Decreased serum sex hormone-binding globulin [SHBG] level
- LH:FSH ratio – In the past, many clinicians measured LH and FSH and used an elevated LH:FSH ratio ≥2 as evidence for the diagnosis of PCOS. However, the LH:FSH ratio was never a formal diagnostic criterion, and its use can be misleading [e.g., if there has been recent ovulation, LH may be suppressed and the ratio ≤2:1].

- Anti-Müllerian hormone [AMH] – Serum AMH concentrations are generally in the upper range of normal or markedly elevated in women with PCOS [17]. Currently, AMH is not part of the routine laboratory evaluation, it can be considered an alternative investigation for patients who prefer not to undergo a transvaginal ultrasound.

Ovulatory dysfunction:

This can still occur in women with regular cycles. If anovulation needs to be confirmed, serum progesterone levels can be measured.

Insulin resistance with compensatory hyperinsulinemia:

As PCOS is associated with insulin resistance, all women with PCOS should be screened for diabetes mellitus [DM] or pre-DM, especially if they are planning to conceive, since poorly controlled DM is associated with adverse pregnancy outcomes [18].

Screening for coronary artery disease and obstructive sleep apnoea [OSA]:

This can be considered in women who are at high risk.

Characteristically, serum testosterone concentrations are above 2.5 nmol/L, and serum LH is above 10 IU/L. A serum testosterone level above 4.8 nmol/L requires exclusion of other causes of androgen hypersecretion, such as an androgen-secreting adrenal or ovarian tumour, Cushing's syndrome, or non-classical congenital adrenal hyperplasia [19].

The free androgen index [FAI] can be calculated as:

$$\text{FAI} = \frac{\text{Total testosterone [nmol/L]} \times 100}{\text{Sex hormone-binding globulin [SHBG] [nmol/L]}}$$

- Free testosterone and FAI appear to be sensitive markers for detecting hyperandrogenaemia [19].
- In women, approximately 80% of serum testosterone is bound to SHBG. Consequently, free serum testosterone levels are influenced by SHBG levels, and the FAI accounts for this dependency. FAI levels of 5 or above are indicative of polycystic ovary syndrome.

Hormonal testing should be performed only if the patient is not taking hormonal medications. Oestrogens increase SHBG levels, while testosterone levels may be only slightly affected. Therefore, the FAI can be significantly altered by hormonal contraception, and a minimum pause of 2 months is recommended before testing. Blood samples should be taken between 08:00 and 09:00 h, ideally between the second and fifth days of the menstrual cycle [20,21].

Ultrasonography:

The ovaries are usually enlarged, with a smooth outer covering that is thicker than normal. The surface is covered with many small cysts and shows increased stromal tissue. Up to one-third of women may have the appearance of polycystic ovaries, and of these, an estimated one-third have polycystic ovarian syndrome.

Note that according to the Rotterdam criteria, polycystic ovaries need not be present to make a diagnosis of PCOS, and conversely, their presence alone does not establish the diagnosis [22]

Differential diagnosis:

Thyroid dysfunction, congenital adrenal hyperplasia, hyperprolactinemia, androgen-secreting tumours, and Cushing's syndrome must be excluded before making a diagnosis of PCOS [8].

Women with evidence of virilization and/or rapidly progressive hirsutism of recent onset require immediate evaluation for the most serious causes of hyperandrogenism, such as ovarian and adrenal androgen-secreting tumours.

Suggested differential diagnoses and screening tests [8]:

- **Pregnancy:** Pregnancy test
- **Hypothyroidism:** TSH
- **Hyperprolactinemia:** Prolactin level
- **Cushing's syndrome:** 24-hour urine free cortisol
- **Late-onset congenital adrenal hyperplasia [CAH]:** Measure serum 17-hydroxyprogesterone to rule out non-classic congenital adrenal hyperplasia [NCCAH] due to 21-hydroxylase deficiency. The clinical presentation of NCCAH can be similar to PCOS [hyperandrogenism, oligomenorrhea, and polycystic ovaries]. NCCAH is less common than PCOS but should be ruled out because there is a risk that offspring could be affected with the more severe classic 21-hydroxylase deficiency.
- **Ovarian tumour:** Total testosterone
- **Adrenal tumour:** Dehydroepiandrosterone sulphate [DHEAS]

Complications

The complications of PCOS include:

- **Infertility** [2]
- **Type 2 diabetes:** Women with PCOS have a threefold increased risk of developing type 2 diabetes. About 20% to 40% of obese women with PCOS have glucose intolerance or type 2 diabetes by the end of their fourth decade [3]
- **TIA/stroke:** Threefold increased risk [1]
- **Endometrial cancer:** Threefold increased risk of development [4]

- **Obstructive sleep apnoea:** Approximately 20% to 45% of women with PCOS have sleep apnoea or sleep-disordered breathing and may complain of daytime somnolence, fatigue, and snoring [8]
- **Metabolic syndrome:** The prevalence of metabolic syndrome in women with PCOS is approximately 30% [9]

Management

PCOS management should be individualized and symptom-directed, considering the patient's most pressing concerns and reproductive goals. Pharmacological treatment is guided by presenting symptoms. If there are no immediate pregnancy plans, management focuses on symptom control. This is elaborated further below.

Lifestyle modification:

There are several steps a patient can take to improve overall health. If a patient with PCOS is overweight, dietary changes and regular exercise can be recommended. These interventions help improve insulin resistance, glucose intolerance, menstrual irregularity, and infertility. Reducing body weight by just 2%–5% has been shown to restore ovulation and increase insulin sensitivity in obese anovulatory women [23]. Weight reduction also has additional benefits, including reducing the risk of diabetes mellitus, hypertension, cardiovascular disease, obstructive sleep apnoea, and certain malignancies.

Treatment of menstrual irregularities:

Oligomenorrhea is a common presenting symptom, and patients with this condition are at risk of endometrial hyperplasia. It is important to induce a withdrawal bleed if periods are delayed by two months or more. Pharmacological therapy can be used to induce menstruation and help shed the endometrium.

For this purpose:

- **Cyclical progesterone:** Agents such as Duphaston [dydrogesterone 10 mg twice daily for one week] can be administered every two months to ensure regular shedding of the endometrium.
- **Oral contraceptive pills [OCPs]:** These are effective in normalizing periods, with the added benefits of providing contraception and improving androgenic symptoms. Before initiating hormonal therapy, it is important to note that women with PCOS are often obese, which, together with OCP use, may increase the risk of thrombosis. Therefore, careful patient selection is essential.
- **OCP selection:** Avoid OCPs with higher oestrogen doses or those containing 19-norprogesterone derivatives, as these androgenic progestins may adversely affect cardiovascular risk [24].
- **Individualized treatment:** Start with low-dose ethinylestradiol combined with a third-generation progestin [i.e., desogestrel, gestodene, or norgestimate] or a fourth-generation progestin [i.e., drospirenone], as these have the least intrinsic androgenic activity [25].

In summary, it is important to balance the potential benefits and risks of combined oral contraceptives individually before prescribing them to women with PCOS.

Treatment of symptoms of androgen excess [hirsutism, acne vulgaris]:

Androgen level increases in PCOS are driven by insulin resistance, hypersecretion of luteinising hormone [LH], and increased ovarian androgen production. Medications commonly used to treat androgen excess target these mechanisms.

First-line treatment for acne vulgaris includes topical creams, antibiotics, and retinoic acid derivatives. Anti-androgens, such as cyproterone acetate, competitively inhibit androgens at peripheral receptors and may also reduce androgen synthesis. Cyproterone acetate is often used in a combined preparation [2 mg cyproterone and 35 mcg ethinyl oestradiol], which is useful for women who also wish to receive oral contraception.

The Androgen Excess and PCOS Society has a protocol for the treatment of hirsutism in PCOS, recommending combined oral contraceptives [COCs] containing progestogens with greater antiandrogen potential, such as cyproterone, chlormadinone, and drospirenone [9]. However, clinicians should be aware of risk factors such as age, smoking, obesity, diabetes, systemic arterial hypertension, dyslipidaemia, and a personal or family history of venous thromboembolic events or thrombophilia.

COCs suppress LH secretion, thereby reducing ovarian androgen production, while metformin improves insulin resistance. Spironolactone is an anti-androgen that blocks the effect of testosterone at the androgen receptor. In cases of severe hirsutism, all three medications may be used. Patients should be counselled that symptoms of androgen excess, particularly hirsutism, usually take at least six months to improve [25].

Eflornithine can be offered as a topical treatment for facial hirsutism. It is a specific, irreversible inhibitor of the enzyme ornithine decarboxylase present in hair follicles. Since ornithine decarboxylase is continually regenerated, hair growth resumes when enzyme inhibition ceases. Permanent laser hair removal can also be an effective treatment and should be considered if symptoms are causing severe distress.

Treatment of infertility:

- For overweight and obese patients who are keen to conceive, the first-line treatment should be diet and exercise, as weight reduction can help

stimulate ovulation. This is particularly important for women preparing for pregnancy, as it reduces the risk of complications such as gestational diabetes mellitus [GDM], preeclampsia, preterm delivery, macrosomia, birth defects, and stillbirth. Anti-androgens, such as spironolactone, should be stopped at least three months before conception. Patients should also be counselled about the possible recurrence of androgen excess symptoms while preparing for fertility.

- Metformin may help, although it is unclear whether its effect is independent of the weight loss it facilitates. The latest European Society of Human Reproduction and Embryology [ESHRE] guidance on PCOS recommends a shared decision-making approach, considering the following [8]: Metformin generally has similar efficacy to active lifestyle interventions. Its use may be associated with low vitamin B12 levels. Side effects are usually self-limiting and may be minimized by starting at a low dose or using an extended-release preparation.
- For further management and interventions, patients are referred to the gynaecology department or managed under a shared care agreement with primary care. Ovulation induction with clomiphene citrate or letrozole is effective for fertility treatment. Monitoring the first cycle with ultrasonography allows for dose titration and detection of multiple follicle development [7], which helps minimize the risk of multiple pregnancies. For women taking clomiphene citrate, treatment should not continue for longer than six months. Second-line treatments, depending on clinical circumstances and patient preference, may include laparoscopic ovarian drilling or gonadotrophins.

It is important to note that weight loss can be difficult to achieve; therefore, do not delay referring a woman over 35 years of age who is overweight for specific treatment to induce ovulation if she has failed to lose weight.

METABOLIC COMPLICATIONS

Lifestyle modification remains the primary step in delaying the development of metabolic complications in PCOS. Metformin plays an important role in improving insulin sensitivity and may also aid in weight loss. If conception and pregnancy are not required, statins can be used to treat dyslipidaemia. Bariatric surgery may be effective for patients with severe obesity, as the marked weight loss after the procedure usually resolves not only the metabolic disorders associated with PCOS but also PCOS itself, thereby restoring ovulatory function and fertility [7].

CONCLUSION

Due to its varying effects at different stages of a woman's life, PCOS can have a significant impact on cardiovascular, reproductive, metabolic, and psychological well-being. This makes timely and appropriate diagnosis and treatment essential. Once a diagnosis of PCOS is made, a cardiometabolic risk assessment should be conducted. This review aims to summarize evidence-based steps for diagnosing and managing PCOS and to help physicians understand the importance of shared care management, offering both pharmacological and non-pharmacological strategies. Management should be individualized, guided by the patient's predominant symptoms, and include early recognition of metabolic involvement to prevent long-term complications.

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