

# Polycystic Ovary Syndrome: A Review on Etiology, Pathogenesis, and Management

DrS.rajini, A.venkataharshitha, N.thishitha,S.divya, DrM.prasadhrao  
*Department of pharmacy practice, MAM collage of pharmacy, Kesanupalli, narasaraopet*

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## ABSTRACT

PCOS, or poly-cystic ovarian syndrome, is an endocrine condition. Unlike other ovulation diseases, which occur when the ovaries are defective or non-functioning, this syndrome is characterized by prolonged anovulation and ovarian failure. The World Health Organization (WHO) estimates that approximately 116 million women (3.4%) globally suffer from PCOS. The primary pathophysiological factors of PCOS are hyperandrogenism, insulin resistance, and hormonal dysfunction, which decrease folliculogenesis and increase the risk of related comorbidities such type II diabetes and endometrial cancer. Reducing symptoms of hyperandrogenism, reestablishing monthly regularity, and achieving pregnancy are the main goals of treatment. This review addresses both therapeutic options and potential causes of this elevated risk.

**KEYWORD:** The complication, causes, and treatments of polycystic ovarian syndrome (PCOS) include oral contraceptive pill use, irregular menstruation, hyperandrogenism, and lifestyle modifications.

## I. INTRODUCTION

Polycystic ovary syndrome (PCOS) is a problem with hormones that happens during the reproductive years. If you have PCOS, you may not have periods very often. Or you may have periods that last many days. You may also have too much of a hormone called androgen in your body.

With PCOS, many small sacs of fluid develop along the outer edge of the ovary. These are called cysts. The small fluid-filled cysts contain immature eggs. These are called follicles. The follicles fail to regularly release egg.

Polycystic ovary syndrome (PCOS) is considered to be a multifaceted disease with a spectrum of manifestations affecting not only women of childbearing age, but also adolescents and postmenopausal women<sup>1</sup>. PCOS, by the nature of the disease, adversely influences the fertility and reproductive health of the affected women<sup>2</sup>;

moreover, with its association with other lifestyle diseases, it is also the cause of significant cardiovascular and metabolic morbidity<sup>3</sup>. The exact aetiology and pathogenesis of PCOS are still an area of active research, although multiple hypotheses have been postulated, ranging from genetic susceptibility to environmental exposure, both *in utero* and in the postnatal life<sup>4</sup>. Data on the genetics, metabolic parameters and clinical aspects of PCOS in Indian women are available. This article was aimed at reviewing the literature related to the pathogenesis, epidemiology and genetics of PCOS in India, and biochemical and hormonal abnormalities in this disorder besides providing a brief overview of the management options.

## ETIOLOGY

The exact cause of PCOS isn't known. Factors that might play a role include:

- **Insulin resistance.**
- **Low-grade inflammation.**
- **Heredity.**
- **Excess androgen.**

## SYMPTOMS

Symptoms of PCOS often start around the time of the first menstrual period. Sometimes symptoms develop later after you have had periods for a while. The symptoms of PCOS vary. A diagnosis of PCOS is made when you have at least two of these:

- **Irregular periods.** Having few menstrual periods or having periods that aren't regular are common signs of PCOS. So is having periods that last for many days or longer than is typical for a period. For example, you might have fewer than nine periods a year. And those periods may occur more than 35 days apart. You may have trouble getting pregnant.
- **Too much androgen.**

High levels of the hormone androgen may result in excess facial and body hair. This is called hirsutism. Sometimes, severe acne and male-pattern baldness can happen, too.

- **Polycystic ovaries.** Your ovaries might be bigger. Many follicles containing immature eggs may develop around the edge of the ovary. The ovaries might not work the way they should. PCOS signs and symptoms are typically more severe in people with obesity.

### PATHOPHYSIOLOGY

The exact cause of PCOS isn't known. Factors that might play a role include:

- **Insulin resistance.** Insulin is a hormone that the pancreas makes. It allows cells to use sugar, your body's primary energy supply. If cells become resistant to the action of insulin, then blood sugar levels can go up. This can cause your body to make more insulin to try to bring down the blood sugar level.

Too much insulin might cause your body to make too much of the male hormone androgen. You could have trouble with ovulation, the process where eggs are released from the ovary.

One sign of insulin resistance is dark, velvety patches of skin on the lower part of the neck, armpits, groin or under the breasts. A bigger appetite and weight gain may be other signs.

- **Low-grade inflammation.** White blood cells make substances in response to infection or injury. This response is called low-grade inflammation. Research shows that people with PCOS have a type of long-term, low-grade inflammation that leads to polycystic ovaries to produce androgens. This can lead to heart and blood vessel problems.

- **Heredity.** Research suggests that certain genes might be linked to PCOS. Having a family history of PCOS may play a role in developing the condition.

- **Excess androgen.** With PCOS, the ovaries may produce high levels of androgen. Having too much androgen interferes with ovulation. This means that eggs don't develop on a regular basis and aren't released from the follicles where they develop. Excess androgen also can result in hirsutism and can

### RISK FACTORS

- **Genetics:** family history plays a role
- **Obesity:** excess weight can increase insulin resistance
- **Insulin resistance:** linked to type 2 DM
- **Hormonal imbalance:** androgen excess, insulin issues
- **Lifestyle factors:** lack of exercise, unhealthy diet
- **Other medical conditions:** thyroid issues, Cushing's syndrome

### COMPLICATIONS

Complications of PCOS can include:

- Infertility
  - Gestational diabetes or pregnancy-induced high blood pressure
  - Miscarriage or premature birth
  - Nonalcoholic steatohepatitis — a severe liver inflammation caused by fat buildup in the liver
  - Metabolic syndrome — a cluster of conditions including high blood pressure, high blood sugar, and unhealthy cholesterol or triglyceride levels that significantly increase your risk of heart and blood vessel (cardiovascular) disease
  - Type 2 diabetes or prediabetes
  - Sleep apnea
  - Depression, anxiety and eating disorders
  - Cancer of the uterine lining (endometrial cancer)
- Obesity commonly occurs with PCOS and can worsen complications of the disorder.

### DIAGNOSIS

- **Pelvic exam.** During a pelvic exam, your provider can check your reproductive organs for masses, growths or other changes.
- **Blood tests.** Blood tests can measure hormone levels. This testing can exclude possible causes of menstrual problems or androgen excess that mimic PCOS. You might have other blood testing, such as fasting cholesterol and triglyceride levels. A glucose tolerance test can measure your body's response to sugar (glucose).
- **Ultrasound.** An ultrasound can check the appearance of your ovaries and the thickness of the lining of your uterus. A wandlike device (transducer) is placed in your vagina. The transducer emits sound waves that

are translated into images on a computer screen. If you have a diagnosis of PCOS, your provider might recommend more tests for complications. These tests can include:

- Regular check of blood pressure, glucose tolerance, and cholesterol and triglyceride levels
- Screening for depression and anxiety
- Screening for obstructive sleep apnea

## TREATMENT

### NONPHARMACOLOGICAL TREATMENT

#### Lifestyle changes

Your health care provider may recommend weight loss through a low-calorie diet combined with moderate exercise activities. Even a modest reduction in your weight — for example, losing 5% of your bodyweight — might improve your condition. Losing weight may increase the effectiveness of medications your provider recommends for PCOS, and it can help with infertility. Your health care provider and a registered dietitian can work with you to determine the best weight-loss plan.

### PHARMACOLOGICAL TREATMENT

#### Medications

To regulate your periods, your health care provider might recommend:

- **Combination birth control pills.** Pills that contain both estrogen and progestin decrease androgen production and regulate estrogen. Regulating your hormones can lower your risk of endometrial cancer and correct irregular bleeding, excess hair growth and acne.
- **Progestin therapy.** Taking progestin for 10 to 14 days every 1 to 2 months can regulate your periods and protect against endometrial cancer. This progestin therapy doesn't improve androgen levels and won't prevent pregnancy. The progestin-only minipill or progestin-containing intrauterine device is a better choice if you also wish to avoid pregnancy. To help you ovulate so that you can become pregnant, your health care provider might recommend:

- **Clomiphene.** This is an anti-

estrogen medication that is taken during the first part of your menstrual cycle.

- **Letrozole (Femara).** This breast cancer treatment can work to stimulate the ovaries.
- **Metformin.** This medicine for type 2 diabetes that you take by mouth improves insulin resistance and lowers insulin levels. If you don't become pregnant using clomiphene, your provider might recommend adding metformin to help you ovulate. If you have prediabetes, metformin can slow the progression to type 2 diabetes and help with weight loss.
- **Gonadotropins.** These hormone medications are given by injection.

- **Birth control pills.**

These pills decrease androgen production that can cause excessive hair growth and acne.

**Spirolactone (Aldactone).** This medication blocks the effects of androgen on the skin, including excessive hair growth and acne. Spirolactone can cause birth defects, so effective birth control is needed while taking this medication. This medication isn't recommended if you're pregnant or planning to become pregnant.

- **Eflornithine (Vaniqa).** This cream can slow facial hair growth.
- **Hair removal.** Electrolysis and laser hair removal are two options for removing hair. Electrolysis uses a tiny needle inserted into each hair follicle. The needle sends out a pulse of electric current. The current damages and then destroys the follicle. Laser hair removal is a medical procedure that uses a concentrated beam of light to remove unwanted hair. You might need multiple treatments of electrolysis or laser hair removal. Shaving, plucking or using creams that dissolve unwanted hair may be other options. But these are temporary, and hair may thicken when it grows back.
- **Acne treatments.** Medications, including pills and topical creams or gels, may help improve acne. Talk to your health care provider about options.

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